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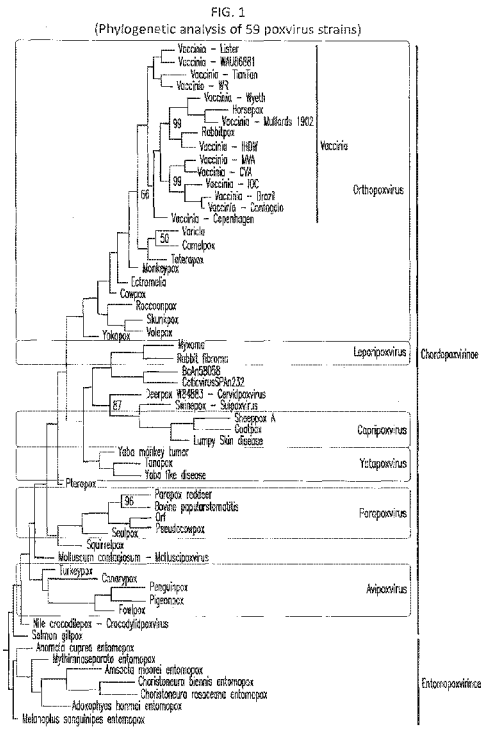

(57) Abstract: The disclosure relates to modified orthopoxvirus vectors, as well as methods of using the same for the treatment of various cancers. The disclosure provides modified orthopoxvirus vectors that exhibit various beneficial therapeutic activities, including enhanced oncolytic activity, spread of infection, immune evasion, tumor persistence, capacity for incorporation of exogenous DNA sequences, amenability for large scale manufacturing, and safety.

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MODIFIED ORTHOPOXVIRUS VECTORS

Cross-Reference to Related Applications

[0001] This application claims the benefit of priority to U.S. Provisional Patent Application No. 62/930,524, filed November 4, 2019, U.S. Provisional Patent Application No. 62/872,699, filed July 10, 2019, and U.S. Provisional Patent Application No. 62/784,372, filed December 21, 2018, the disclosure of each of which is incorporated by reference herein in its entirety.

Sequence Listing

[0002] This application incorporates by reference a Sequence Listing submitted with this application as an ASCII text file, entitled 14596-050-228_SL.txt, created on December 18, 2019, and having a size of 1,252,729 bytes.

1. Field

[0003] The invention relates to the field of immunotherapy, *e.g.*, for the treatment of cell proliferation disorders, such as cancers. Particularly, the invention relates to genetically modified orthopoxviruses, as well as methods of making and using the same.

2. Background

[0004] The immune system may be stimulated to identify tumor cells and target them for destruction. Immunotherapy employing oncolytic orthopoxviruses is a rapidly evolving area in cancer research. New approaches are needed to engineer and/or enhance tumor-selectivity for oncolytic viruses in order to maximize efficiency and safety. This selectivity is especially important when potentially toxic therapeutic agents or genes are added to the viruses.

[0005] Although the use of orthopoxviruses as clinical oncolytic vectors is a promising paradigm for cancer treatment, due to toxicity, such as pox lesions in patients, and immunosuppressive side effects, most current clinical candidates have shown only modest clinical success. There exists a need for methods to engineer orthopoxviruses that exhibit more robust virus replication, cancer cell killing, and spreading from the point of infection. The present invention addresses this need and provides a solution to selectivity and safety limitations by employing a modified orthopoxvirus.

3. Summary

[0006] The present disclosure describes the use of orthopoxviruses for the treatment of cancer. In particular, the disclosure is based in part on the enhanced oncolytic activity, spread of infection, and safety results engendered when an orthopoxvirus is genetically modified to contain deletions in one or more, or all, of the following genes: the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes. Genetically modified orthopoxviruses, such as vaccinia viruses (e.g., Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16mO, Tashkent, Tian Tan, and WAU86/88-1 viruses) that exhibit mutations in one or more, or all, of these genes may exhibit an array of beneficial features, such as improved oncolytic ability, replication in tumors, infectivity, immune evasion, tumor persistence, capacity for incorporation of exogenous DNA sequences, and/or amenability for large scale manufacturing. The present disclosure describes orthopox viruses further genetically modified to contain deletions in the B8R gene. In various embodiments, the modified orthopoxvirus expresses at least one of three transgenes: Interleukin 12 containing a transmembrane domain (IL-12-TM), FMS-like tyrosine kinase 3 ligand (FLT3-L) and anti-Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4) antibody.

[0007] In one aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ inverted terminal repeat (ITR): B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4); wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[0008] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter. In another specific

embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

[0009] In some embodiments, the first nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the first nucleotide sequence.

[0010] In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[0011] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and (d) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene.

[0012] In certain embodiments, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

[0013] In some embodiments, the first nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the first nucleotide sequence.

[0014] In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[0015] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′

ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and (c) a second transgene comprising a second nucleotide sequence encoding an Interleukin 12 (IL-12) polypeptide; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[0016] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[0017] In some embodiments, the second nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the second nucleotide sequence.

[0018] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70. In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[0019] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (d) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene.

[0020] In certain embodiments, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[0021] In some embodiments, the second nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the second nucleotide sequence.

[0022] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70. In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[0023] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and (c) a third transgene comprising a third nucleotide sequence encoding FMS-like tyrosine kinase 3 ligand (FLT3L); wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[0024] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID

NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[0025] In some embodiments, the third nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0026] In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[0027] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a third transgene comprising a third nucleotide sequence encoding FLT3L; and (d) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[0028] In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter

comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[0029] In some embodiments, the third nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0030] In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[0031] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[0032] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter. In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

[0033] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[0034] In some embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence.

[0035] In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[0036] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70. In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[0037] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; and/or (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene.

[0038] In certain embodiments, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

[0039] In certain embodiments, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[0040] In some embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence.

[0041] In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[0042] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70. In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[0043] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[0044] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter. In another specific

embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

[0045] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[0046] In some embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0047] In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[0048] In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[0049] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the

deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; and/or (ii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[0050] In certain embodiments, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

[0051] In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[0052] In some embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0053] In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[0054] In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[0055] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[0056] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[0057] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID

NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[0058] In some embodiments, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0059] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70. In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[0060] In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[0061] In another aspect, provided here is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter; and/or (ii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R

gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[0062] In certain embodiments, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[0063] In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[0064] In some embodiments, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0065] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70. In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[0066] In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[0067] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[0068] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter. In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

[0069] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[0070] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide

sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[0071] In some embodiments, the first nucleotide sequence, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0072] In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[0073] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70. In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[0074] In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[0075] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding

an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter; and/or (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[0076] In certain embodiments, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

[0077] In certain embodiments, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[0078] In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter

comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[0079] In some embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0080] In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[0081] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70. In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[0082] In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[0083] In a specific embodiment, the first transgene is inserted between the partial C2L and F3L vaccinia genes (that is, is present between the partial C2L and F3L genes), and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene (that is, are present in the locus of the deletion in the B8R gene). In a specific embodiment, the first transgene is inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains (that is, is present between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains), and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene (that is, are present in the locus of the deletion in the B8R gene). In a further specific embodiment, the third transgene is upstream of the second transgene.

[0084] In some embodiments of the various embodiments and aspects described herein, the deletion in the B8R gene is a deletion of at least 50% of the B8R gene sequence. In other

embodiments, the deletion in the B8R gene is a deletion of at least 60% of the B8R gene sequence. In other embodiments, the deletion in the B8R gene is a deletion of at least 70% of the B8R gene sequence. In other embodiments, the deletion in the B8R gene is a deletion of at least 80% of the B8R gene sequence. In a specific embodiment, the deletion in the B8R gene is a deletion of about 75% of the B8R gene sequence. In another specific embodiment, the deletion in the B8R gene is a deletion of about 80% of the B8R gene sequence.

[0085] In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome is derived from the genome of a Copenhagen strain vaccinia virus.

[0086] In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome comprises the nucleotide sequence of SEQ ID NO: 210.

[0087] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as

endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

[0088] In specific embodiments, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the first transgene is inserted between the partial B14R and B29R vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the first transgene is inserted between the portion of the B14R vaccinia gene that remains and the portion of the B29R vaccinia gene that remains, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the third transgene is upstream of the second transgene. In specific embodiments, the third transgene is downstream of the second transgene. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564.

[0089] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is inserted between the partial C2L and F3L vaccinia genes; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is inserted into the locus of the deletion in the B8R gene; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the

second transgene; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565

[0090] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is inserted between the partial C2L and F3L vaccinia genes; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is inserted into the locus of the deletion in the B8R gene; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; and wherein the nucleic acid further comprises: (i) a nucleotide sequence

comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[0091] In a specific embodiment, any one, two or three of the first transgene, the second transgene and the third transgene is/are inserted between the partial C2L and F3L vaccinia genes (that is, is/are present between the partial C2L and F3L genes). In a specific embodiment, any one, two or three of the the first transgene, the second transgene and the third transgene is/are inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains.

[0092] In a specific embodiment, any one, two or three of the first transgene, the second transgene and the third transgene is/are inserted in the locus of the deletion in the B8R gene (that is, is/are present in the locus of the B8R gene).

[0093] In a specific embodiment, any one, two or three of the first transgene, the second transgene and the third transgene is/are inserted between the partial B13R and B29R vaccinia genes (that is, is/are present between the partial B13R and B29R genes). In a specific embodiment, any one, two or three of the the first transgene, the second transgene and the third transgene is/are inserted between the portion of the B13R vaccinia gene that remains and the portion of the B29R vaccinia gene that remains.

[0094] In a specific embodiment, the first transgene is inserted between the partial C2L and F3L vaccinia genes (that is, is present between the partial C2L and F3L genes), the second transgene is inserted into the locus of the deletion in the B8R gene (that is, is present in the locus of the deletion in the B8R gene) and the third transgene is inserted between the partial B14R and B29R vaccinia genes (that is, is present between the partial B14R and B29R vaccinia genes). In a specific embodiment, the first transgene is inserted between the portion

of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains, the second transgene is inserted into the locus of the deletion in the B8R gene and the third transgene is inserted between the portion of the B14R vaccinia gene that remains and portion of the B29R vaccinia gene that remains.

[0095] In a specific embodiment, the second transgene is inserted between the partial C2L and F3L vaccinia genes (that is, is present between the partial C2L and F3L genes), the third transgene is inserted into the locus of the deletion in the B8R gene (that is, is present in the locus of the deletion in the B8R gene) and the first transgene is inserted between the partial B14R and B29R vaccinia genes (that is, is present between the partial B14R and B29R vaccinia genes). In a specific embodiment, the second transgene is inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains, the second transgene is inserted into the locus of the deletion in the B8R gene and the first transgene is inserted between the portion of the B14R vaccinia gene that remains and portion of the B29R vaccinia gene that remains.

[0096] In a specific embodiment, the third transgene is inserted between the partial C2L and F3L vaccinia genes (that is, is present between the partial C2L and F3L genes), the second transgene is inserted into the locus of the deletion in the B8R gene (that is, is present in the locus of the deletion in the B8R gene) and the first transgene is inserted between the partial B14R and B29R vaccinia genes (that is, is present between the partial B14R and B29R vaccinia genes). In a specific embodiment, the third transgene is inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains, the second transgene is inserted into the locus of the deletion in the B8R gene and the first transgene is inserted between the portion of the B14R vaccinia gene that remains and portion of the B29R vaccinia gene that remains.

[0097] In a specific embodiment, the first transgene and the second transgene are inserted between the partial C2L and F3L vaccinia genes (that is, are present between the partial C2L and F3L genes), and the third transgene is inserted into the locus of the deletion in the B8R gene (that is, is present in the locus of the deletion in the B8R gene). In a specific embodiment, the first transgene and the second transgene are inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains, and the third transgene is inserted into the locus of the deletion in the B8R gene

[0098] In a specific embodiment, the first transgene and the second transgene are inserted between the partial C2L and F3L vaccinia genes (that is, are present between the partial C2L

and F3L genes), and the third transgene is inserted between the partial B14R and B29R vaccinia genes (that is, is present between the partial B14R and B29R vaccinia genes). In a specific embodiment, the first transgene and the second transgene are inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains, and the third transgene is inserted between the portion of the B14R vaccinia gene that remains and portion of the B29R vaccinia gene that remains.

[0099] In a specific embodiment, the third transgene is inserted between the partial C2L and F3L vaccinia genes (that is, is present between the partial C2L and F3L genes), and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene (that is, is are present in the locus of the deletion in the B8R gene). In a specific embodiment, the third transgene is inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains, and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene

[00100] In a specific embodiment, the third transgene is inserted between the partial C2L and F3L vaccinia genes (that is, is present between the partial C2L and F3L genes), and the first transgene and the second transgene are inserted between the partial B14R and B29R vaccinia genes (that is, are present between the partial B14R and B29R vaccinia genes). In a specific embodiment, the third transgene is inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains, and the first transgene and the second transgene are inserted between the portion of the B14R vaccinia gene that remains and portion of the B29R vaccinia gene that remains.

[00101] In a specific embodiment, the third transgene is inserted into the locus of the deletion in the B8R gene (that is, is present in the locus of the deletion in the B8R gene) and the first transgene and the second transgene are inserted between the partial B13R and B29R vaccinia genes (that is, are present between the partial B13R and B29R genes). In a specific embodiment, the third transgene is inserted into the locus of the deletion in the B8R gene and the first transgene and the second transgene are inserted between the portion of the B13R vaccinia gene that remains and the portion of the B29R vaccinia gene that remains.

[00102] In a specific embodiment, the third transgene is inserted between the partial B13R and B29R vaccinia genes (that is, is present between the partial B13R and B29R genes) and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene (that is, are present in the locus of the deletion in the B8R gene). In a specific embodiment, the third transgene is inserted between the portion of the B13R vaccinia gene

that remains and portion of the B29R vaccinia gene that remains and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene.

[00103] In a specific embodiment, the first transgene, the second transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes (that is, are present between the partial C2L and F3L genes). In a specific embodiment, the first transgene, the second transgene and the third transgene are inserted between the portion of the C2L vaccinia gene that remains and the portion of the F3L vaccinia gene that remains.

[00104] In a specific embodiment, the first transgene, the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene (that is, are present in the locus of the B8R gene).

[00105] In a specific embodiment, the first transgene, the second transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes (that is, are present between the partial B14R and B29R genes). In a specific embodiment, the first transgene, the second transgene and the third transgene are inserted between the portion of the B14R vaccinia gene that remains and the portion of the B29R vaccinia gene that remains.

[00106] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is inserted between the partial B14R and B29R vaccinia genes; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is inserted into the locus of the deletion in the B8R gene; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the

second transgene; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564.

[00107] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is inserted between the partial B14R and B29R vaccinia genes; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is inserted into the locus of the deletion in the B8R gene; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii)

a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564.

[00108] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214; (c) a second transgene comprising a second nucleotide sequence encoding an Interleukin 12 (IL-12) polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215; and (d) a third transgene comprising a third nucleotide sequence encoding FMS-like tyrosine kinase 3 ligand (FLT3L), wherein the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00109] In some embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

[00110] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an H5R promoter, a pS promoter, or a LEO promoter. In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an H5R promoter.

[00111] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00112] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence encoding FLT3L. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00113] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide

sequence is set forth in SEQ ID NO: 215; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence. In specific embodiments, the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the third transgene is upstream of the second transgene. In specific embodiments, the third transgene is downstream of the second transgene.

[00114] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth

in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

[00115] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first

nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

[00116] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide

sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

[00117] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late

promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

[00118] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments,

the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

[00119] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments,

the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

[00120] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments,

the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

[00121] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments,

the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

[00122] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at

least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

[00123] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO:

564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

[00124] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence

is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

[00125] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one

promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

[00126] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the

first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00127] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the

first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00128] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the

first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00129] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the

first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00130] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the

first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557. In specific embodiments, the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563. In specific embodiments, the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00131] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one

promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557. In specific embodiments, the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563. In specific embodiments, the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00132] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence

is a E3L promoter. In specific embodiments, the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557. In specific embodiments, the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563. In specific embodiments, the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00133] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557. In specific embodiments, the nucleotide sequence of the F17R promoter comprises the

nucleotide sequence of SEQ ID NO: 563. In specific embodiments, the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00134] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the first transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the first transgene is inserted between the partial B14R and B29R vaccinia genes.

[00135] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene, the second transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene, the second transgene is inserted between the partial B14R and B29R vaccinia genes.

[00136] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the third transgene, the third transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the third transgene, the third transgene is inserted between the partial B14R and B29R vaccinia genes.

[00137] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene and the second transgene are inserted between the partial C2L and F3L vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein

wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene and the second transgene are inserted between the partial B14R and B29R vaccinia genes.

[00138] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes.

[00139] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes.

[00140] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic

acid comprises the first transgene and the second transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes.

[00141] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes.

[00142] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the third transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes.

[00143] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene, the second transgene, and the third transgene are inserted between the partial C2L and F3L vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene, the second transgene, and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene, the second transgene, and the third transgene are inserted between the partial B14R and B29R vaccinia genes.

[00144] In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the second transgene are inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted within between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various

embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene and the second transgene are inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the second transgene are inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the second transgene are inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various

embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes.

[00145] In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, the second transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, the third transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, the first transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first

transgene, the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes.

[00146] In various embodiments and aspects described herein wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 210, the partial C2L and F3L vaccinia genes are partial C2L and F3L vaccinia genes in SEQ ID NO: 210. In various embodiments and aspects described herein wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 210, the partial B14R and B29R vaccinia genes are partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

[00147] In one aspect, provided herein is a virus comprising the nucleic acid described herein.

[00148] In one aspect, provided are packaging cell lines comprising nucleic acids or viruses disclosed herein.

[00149] In one aspect, provided herein are pharmaceutical compositions comprising a virus disclosed herein and a physiologically acceptable carrier.

[00150] In one aspect, provided are methods of treating cancer in a mammalian patient, said method comprising administering a therapeutically effective amount of a virus as disclosed herein to said patient. In another aspect, provided are methods of treating cancer in a mammalian patient, said method comprising administering a therapeutically effective amount of a pharmaceutical composition as disclosed herein to said patient. In some embodiments, the mammalian patient is a human patient.

[00151] In some embodiments, the virus is used as a prime in a prime:boost treatment. In some embodiments, the virus is used as a boost in a prime:boost treatment.

[00152] In some embodiments, the mammalian patient has cancer. For example, in some embodiments, the cancer is selected from the group consisting of leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, and throat cancer.

[00153] In some embodiments, the cancer is selected from the group consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), adrenocortical carcinoma, AIDS-

related lymphoma, primary CNS lymphoma, anal cancer, appendix cancer, astrocytoma, atypical teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, extrahepatic cancer, Ewing sarcoma family, osteosarcoma and malignant fibrous histiocytoma, central nervous system embryonal tumors, central nervous system germ cell tumors, craniopharyngioma, ependymoma, bronchial tumors, Burkitt lymphoma, carcinoid tumor, primary lymphoma, chordoma, chronic myeloproliferative neoplasms, colon cancer, extrahepatic bile duct cancer, ductal carcinoma in situ (DCIS), endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, extracranial germ cell tumor, extragonadal germ cell tumor, fallopian tube cancer, fibrous histiocytoma of bone, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), testicular germ cell tumor, gestational trophoblastic disease, glioma, childhood brain stem glioma, hairy cell leukemia, hepatocellular cancer, Langerhans cell histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, islet cell tumors, pancreatic neuroendocrine tumors, Wilms tumor and other childhood kidney tumors, Langerhans cell histiocytosis, small cell lung cancer, cutaneous T cell lymphoma, intraocular melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer, midline tract carcinoma, multiple endocrine neoplasia syndromes, multiple myeloma/plasma cell neoplasm, myelodysplastic syndromes, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin's lymphoma (NHL), non-small cell lung cancer (NSCLC), epithelial ovarian cancer, germ cell ovarian cancer, low malignant potential ovarian cancer, pancreatic neuroendocrine tumors, papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pituitary tumor, pleuropulmonary blastoma, primary peritoneal cancer, rectal cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, Kaposi's sarcoma, rhabdomyosarcoma, Sézary syndrome, small intestine cancer, soft tissue sarcoma, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, urethral cancer, endometrial uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, and Waldenström macroglobulinemia.

[00154] In some embodiments, provided methods further comprise administering to said patient an immune checkpoint inhibitor. In some embodiments, the immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding

fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof. In some embodiments, the immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof. In some embodiments, the immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof. In some embodiments, the immune checkpoint inhibitor is an anti-PD-L1 antibody or antigen-binding fragment thereof. In some embodiments, the immune checkpoint inhibitor is an anti-PD1 or anti-PD-L1 antibody or antigen-binding fragment thereof. In some embodiments, the immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

[00155] In some embodiments, provided methods further comprise administering to said patient an interleukin.

[00156] In some embodiments, said interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23. In some embodiments, the interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70. In some embodiments, the interleukin is membrane-bound.

[00157] In some embodiments, the method further comprises administering to said patient an interferon. In some embodiments, the interferon is selected from the group consisting of IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

[00158] In some embodiments, provided methods further comprises administering to said patient a cytokine. In some embodiments, the cytokine is a TNF superfamily member protein. In some embodiments, the TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand. In some embodiments, the cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, TGF-beta, VEGF-R2, and cKit. In some embodiments, the cytokine is Flt3 ligand.

[00159] In one aspect, provided are kits comprising a nucleic acid or virus as disclosed herein and a package insert instructing a user of said kit to express said nucleic acid or said virus in a host cell.

[00160] In one aspect, provided are kits comprising a virus as disclosed herein and a package insert instructing a user to administer a therapeutically effective amount of said virus

to a mammalian patient having cancer, thereby treating said cancer. In some embodiments, the mammalian patient is a human patient.

3.1. Definitions

[00161] As used herein, the term "about" refers to a value that is no more than 10% above or below the value being described. For example, the term "about 5 nM" indicates a range of from 4.5 nM to 5.5 nM.

[00162] As used herein, the term "antibody" (Ab) refers to an immunoglobulin molecule that specifically binds to, or is immunologically reactive with, a particular antigen, and includes polyclonal, monoclonal, genetically engineered and otherwise modified forms of antibodies, including but not limited to chimeric antibodies, humanized antibodies, heteroconjugate antibodies (e.g., bi- tri- and quad-specific antibodies, diabodies, triabodies, and tetrabodies), and antigen-binding fragments of antibodies, including e.g., Fab', F(ab')2, Fab, Fv, rIgG, and scFv fragments. Moreover, unless otherwise indicated, the term "monoclonal antibody" (mAb) is meant to include both intact molecules, as well as, antibody fragments (such as, for example, Fab and F(ab')2 fragments) that are capable of specifically binding to a target protein. Fab and F(ab')2 fragments lack the Fc fragment of an intact antibody, clear more rapidly from the circulation of the animal, and may have less non-specific tissue binding than an intact antibody (*see* Wahl *et al.*, J. Nucl. Med. 24:31 6, 1 983; incorporated herein by reference).

[00163] The term "antigen-binding fragment," as used herein, refers to one or more fragments of an antibody that retain the ability to specifically bind to a target antigen. The antigen-binding function of an antibody can be performed by fragments of a full-length antibody. The antibody fragments can be a Fab, F(ab')2, scFv, SMIP, diabody, a triabody, an affibody, a nanobody, an aptamer, or a domain antibody. Examples of binding fragments encompassed of the term "antigen-binding fragment" of an antibody include, but are not limited to: (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL, and CH1 domains; (ii) a F(ab')2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a dAb including VH and VL domains; (vi) a dAb fragment (Ward *et al.*, Nature 341 :544-546, 1 989), which consists of a VH domain; (vii) a dAb which consists of a VH or a VL domain; (viii) an isolated complementarity determining region (CDR); and (ix) a

combination of two or more isolated CDRs which may optionally be joined by a synthetic linker. Furthermore, although the two domains of the Fv fragment, VL and VH, are coded for by separate genes, they can be joined, using recombinant methods, by a linker that enables them to be made as a single protein chain in which the VL and VH regions pair to form monovalent molecules (known as single-chain Fv (scFv); *see, e.g.*, Bird *et al.*, Science 242:423-426, 1988, and Huston *et al.*, Proc. Natl. Acad. Sci. USA 85:5879-5883, 1988). These antibody fragments can be obtained using conventional techniques known to those of skill in the art, and the fragments can be screened for utility in the same manner as intact antibodies. Antigen-binding fragments can be produced by recombinant DNA techniques, enzymatic or chemical cleavage of intact immunoglobulins, or, in some embodiments, by chemical peptide synthesis procedures known in the art.

[00164] As used herein, the term "bispecific antibodies" refers to monoclonal, often human or humanized antibodies that have binding specificities for at least two different antigens.

[00165] As used herein, the terms “cell,” “cell line,” and “cell culture” may be used interchangeably. All of these terms also include their progeny, which is any and all subsequent generations. It is understood that all progeny may not be identical due to deliberate or inadvertent mutations.

[00166] As used herein, the term "chimeric" antibody refers to an antibody having variable sequences derived from an immunoglobulin of one source organism, such as rat or mouse, and constant regions derived from an immunoglobulin of a different organism (*e.g.*, a human). Methods for producing chimeric antibodies are known in the art. *See, e.g.*, Morrison, 1985, Science 229(4719): 1202-7; Oi *et al.*, 1986, BioTechniques 4:214-221; Gillies *et al.*, 1985, J. Immunol. Methods 125:191 -202; U.S. Pat. Nos. 5,807,715; 4,816,567; and 4,816,397; incorporated herein by reference.

[00167] As used herein, the term "complementarity determining region" (CDR) refers to a hypervariable region found both in the light chain and the heavy chain variable domains. The more highly conserved portions of variable domains are called the framework regions (FRs). As is appreciated in the art, the amino acid positions that delineate a hypervariable region of an antibody can vary, depending on the context and the various definitions known in the art. Some positions within a variable domain may be viewed as hybrid hypervariable positions in that these positions can be deemed to be within a hypervariable region under one set of criteria while being deemed to be outside a hypervariable region under a different set of criteria. One or more of these positions can also be found in extended hypervariable regions.

The variable domains of native heavy and light chains each comprise four framework regions that primarily adopt a β-sheet configuration, connected by three CDRs, which form loops that connect, and in some cases form part of, the β-sheet structure. The CDRs in each chain are held together in close proximity by the FR regions in the order FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4 and, with the CDRs from the other antibody chains, contribute to the formation of the target binding site of antibodies (*see* Kabat *et al.*, Sequences of Proteins of Immunological Interest (National Institute of Health, Bethesda, Md. 1987; incorporated herein by reference).

[00168] As used herein, numbering of immunoglobulin amino acid residues is done according to the immunoglobulin amino acid residue numbering system of Kabat *et al.*, unless otherwise indicated.

[00169] As used herein, the terms "conservative mutation," "conservative substitution," or "conservative amino acid substitution" refer to a substitution of one or more amino acids for one or more different amino acids that exhibit similar physicochemical properties, such as polarity, electrostatic charge, and steric volume. These properties are summarized for each of the twenty naturally-occurring amino acids in Table 1 below. From this table it is appreciated that the conservative amino acid families include (i) G, A, V, L and I; (ii) D and E; (iii) C, Sand T; (iv) H, K and R; (v) N and Q; and (vi) F, Y and W. A conservative mutation or substitution is therefore one that substitutes one amino acid for a member of the same amino acid family (*e.g.*, a substitution of Ser for Thr or Lys for Arg).

Table 1. Representative physicochemical properties of naturally occurring amino acids

Amino Acid	**3 Letter Code**	**1 Letter Code**	**Side-chain Polarity**	**Electrostatic character at physiological pH (7.4)**	**Steric Volume†**
Alanine	Ala	A	nonpolar	neutral	small
Arginine	Arg	R	polar	cationic	large
Asparagine	Asn	N	polar	neutral	intermediate
Aspartic acid	Asp	D	polar	anionic	intermediate
Cysteine	Cys	C	nonpolar	neutral	intermediate
Glutamic acid	Glu	E	polar	anionic	intermediate

Amino Acid	3 Letter Code	1 Letter Code	Side-chain Polarity	Electrostatic character at physiological pH (7.4)	Steric Volume†
Glutamine	Gln	Q	polar	neutral	intermediate
Glycine	Gly	G	nonpolar	neutral	small
Histidine	His	H	polar	Both neutral and cationic forms in equilibrium at pH 7.4	large
Isoleucine	Ile	I	nonpolar	neutral	large
Leucine	Leu	L	nonpolar	neutral	large
Lysine	Lys	K	polar	cationic	large
Methionine	Met	M	nonpolar	neutral	large
Phenylalanine	Phe	F	nonpolar	neutral	large
Proline	Pro	P	non-polar	neutral	intermediate
Serine	Ser	S	polar	neutral	small
Threonine	Thr	T	polar	neutral	intermediate
Tryptophan	Trp	W	nonpolar	neutral	bulky
Tyrosine	Tyr	Y	polar	neutral	large
Valine	Val	V	nonpolar	neutral	intermediate

†based on volume in A^3: 50-100 is small, 100-150 is intermediate, 150-200 is large, and >200 is bulky

[00170] As used herein, the terms "delete," "deletion," and the like refer to modifications to a gene or a regulatory element associated therewith or operatively linked thereto (*e.g.*, a transcription factor-binding site, such as a promoter or enhancer element) that remove the gene or otherwise render the gene nonfunctional. Exemplary deletions, as described herein, include the removal of the entirety of a nucleic acid encoding a gene of interest, from the start codon to the stop codon of the target gene. Other examples of deletions as described herein include the removal of a portion of the nucleic acid encoding the target gene (*e.g.*, one or more codons, or a portion thereof, such as a single nucleotide deletion) such that, upon

expression of the partially-deleted target gene, the product (*e.g.*, RNA transcript, protein product, or regulatory RNA) is nonfunctional or less functional then a wild-type form of the target gene. Exemplary deletions as described herein include the removal of all or a portion of the regulatory element(s) associated with a gene of interest, such as all or a portion of the promoter and/or enhancer nucleic acids that regulate expression of the target gene.

[00171] In specific embodiments, the recombinant vaccinia virus genome described in this disclosure comprises deletions in one or more of the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, B20R, B21R (in 3' ITR), B22R (in 3' ITR), B23R (in 3' ITR), B24R (in 3' ITR), B25R (in 3' ITR), B26R (in 3' ITR), B27R (in 3' ITR), B28R (in 3' ITR), and B29R (in 3' ITR). In a specific embodiment, the recombinant vaccinia virus genome described in this disclosure comprises deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; and deletions in the following genes in the 3' ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R. In specific embodiments, the recombinant vaccinia virus genome described in this disclosure comprises deletions in one or more of the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, B20R, B20R, B21R (in 3' ITR), B22R (in 3' ITR), B23R (in 3' ITR), B24R (in 3' ITR), B25R (in 3' ITR), B26R (in 3' ITR), B27R (in 3' ITR), B28R (in 3' ITR), and B29R (in 3' ITR), and also comprises a deletion in the B8R gene.

[00172] In some embodiments, a gene deletion removes the entire sequence of the gene. In other embodiments, a gene deletion is a partial deletion, that is, one that removes part of the sequence of the gene. In one embodiment, a gene deletion is a partial deletion that removes at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90% or at least 95% of the sequence of the gene. In one embodiment, a gene deletion is a partial deletion that removes at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% of the protein coding sequence of the gene. In other embodiments, a gene deletion removes 100% of the sequence of the gene. In yet other embodiments, a gene deletion removes 100% of the protein coding sequence of the gene. In one embodiment, a gene deletion removes at least 50, at least 100, at least 200, at least 300, at least 400, at least 500, at least 600, at least 700, at least 800, at least 900, or at least 1000 nucleotides of the sequence of the gene. In another embodiment, a gene deletion is a partial deletion that

removes at least 50, at least 100, at least 200, at least 300, at least 400, at least 500, at least 600, at least 700, at least 800, at least 900, or at least 1000 nucleotides of the sequence of the gene. In a specific embodiment, a partial deletion in a gene results in a partial gene.

[00173] As used herein, the term "derivatized antibodies" refers to antibodies that are modified by a chemical reaction so as to cleave residues or add chemical moieties not native to an isolated antibody. Derivatized antibodies can be obtained by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by addition of known chemical protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein. Any of a variety of chemical modifications can be carried out by known techniques, including, without limitation, specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. using established procedures. Additionally, the derivative can contain one or more non-natural amino acids, e.g., using amber suppression technology (*see, e.g.*, US Patent No. 6,964,859; incorporated herein by reference).

[00174] As used herein, the term "diabodies" refers to bivalent antibodies comprising two polypeptide chains, in which each polypeptide chain includes VH and VL domains joined by a linker that is too short (*e.g.*, a linker composed of five amino acids) to allow for intramolecular association of VH and VL domains on the same peptide chain. This configuration forces each domain to pair with a complementary domain on another polypeptide chain so as to form a homodimeric structure. Accordingly, the term "triabodies" refers to trivalent antibodies comprising three peptide chains, each of which contains one VH domain and one VL domain joined by a linker that is exceedingly short (*e.g.*, a linker composed of 1 -2 amino acids) to permit intramolecular association of VH and VL domains within the same peptide chain. In order to fold into their native structure, peptides configured in this way typically trimerize so as to position the VH and VL domains of neighboring peptide chains spatially proximal to one another to permit proper folding (*see* Holliger *et al.*, Proc. Natl. Acad. Sci. USA 90:6444-48, 1993; incorporated herein by reference).

[00175] As used herein, a "dual variable domain immunoglobulin" ("DVD-Ig") refers to an antibody that combines the target-binding variable domains of two monoclonal antibodies via linkers to create a tetravalent, dual-targeting single agent. (Gu *et al.*, Meth. Enzymol., 502:25-41, 2012; incorporated by reference herein).

[00176] As used herein, the term "endogenous" describes a molecule (*e.g.*, a polypeptide, nucleic acid, or cofactor) that is found naturally in a particular organism (*e.g.*, a human) or in

a particular location within an organism (*e.g.*, an organ, a tissue, or a cell, such as a human cell).

[00177] As used herein, the term "exogenous" describes a molecule (*e.g.*, a polypeptide, nucleic acid, or cofactor) that is not found naturally in a particular organism (*e.g.*, a human) or in a particular location within an organism (*e.g.*, an organ, a tissue, or a cell, such as a human cell). Exogenous materials include those that are provided from an external source to an organism or to cultured matter extracted there from.

[00178] As used herein, the term "framework region" or "FW region" includes amino acid residues that are adjacent to the CDRs. FW region residues may be present in, for example, human antibodies, rodent-derived antibodies (*e.g.*, murine antibodies), humanized antibodies, primatized antibodies, chimeric antibodies, antibody fragments (*e.g.*, Fab fragments), single-chain antibody fragments (*e.g.*, scFv fragments), antibody domains, and bispecific antibodies, among others.

[00179] As used herein, the term "heterospecific antibodies" refers to monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. Traditionally, the recombinant production of heterospecific antibodies is based on the co-expression of two immunoglobulin heavy chain-light chain pairs, where the two heavy chains have different specificities (Milstein *et al.*, Nature 305:537, 1 983). Similar procedures are disclosed, *e.g.*, in WO 93/08829, U.S. Pat. Nos. 6,210,668; 6,193,967; 6,132,992; 6,106,833; 6,060,285; 6,037,453; 6,010,902; 5,989,530; 5,959,084; 5,959,083; 5,932,448; 5,833,985; 5,821,333; 5,807,706; 5,643,759, 5,601 ,819; 5,582,996, 5,496,549, 4,676,980, WO 91 /00360, WO 92/00373, EP 03089, Traunecker *et al.*, EMBO J. 10:3655 (1991), Suresh *et al.*, Methods in Enzymology 121 :210 (1986); incorporated herein by reference. Heterospecific antibodies can include Fc mutations that enforce correct chain association in multi-specific antibodies, as described by Klein *et al.*, mAbs 4(6):653-663, 2012; incorporated herein by reference.

[00180] As used herein, the term “human antibody” refers to an antibody in which substantially every part of the protein (*e.g.*, CDR, framework, C_L, C_H domains (*e.g.*, C_H1, C_H2, C_H3), hinge, (V_L, V_H)) is substantially non-immunogenic in humans, with only minor sequence changes or variations. A human antibody can be produced in a human cell (*e.g.*, by recombinant expression), or by a non-human animal or a prokaryotic or eukaryotic cell that is capable of expressing functionally rearranged human immunoglobulin (*e.g.*, heavy chain and/or light chain) genes. Further, when a human antibody is a single-chain antibody, it can

include a linker peptide that is not found in native human antibodies. For example, an Fv can comprise a linker peptide, such as two to about eight glycine or other amino acid residues, which connects the variable region of the heavy chain and the variable region of the light chain. Such linker peptides are considered to be of human origin. Human antibodies can be made by a variety of methods known in the art including phage display methods using antibody libraries derived from human immunoglobulin sequences. *See* U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 1998/46645; WO 1998/50433; WO 1998/24893; WO 1998/16654; WO 1996/34096; WO 1996/33735; and WO 1991/10741; incorporated herein by reference. Human antibodies can also be produced using transgenic mice that are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. *See, e.g.*, PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; U.S. Patent Nos. 5,413,923; 5,625, 126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598; incorporated by reference herein.

[00181] As used herein, the term "humanized" antibodies refers to forms of non-human (e.g., murine) antibodies that are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', $F(ab')_2$ or other target-binding subdomains of antibodies) which contain minimal sequences derived from non-human immunoglobulin. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin. All or substantially all of the FR regions may also be those of a human immunoglobulin sequence. The humanized antibody can also comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin consensus sequence. Methods of antibody humanization are known in the art. *See, e.g.*, Riechmann *et al.*, Nature 332:323-7, 1988; U.S. Patent Nos: 5,530,101; 5,585,089; 5,693,761; 5,693,762; and 6,180,370 to Queen et al; EP239400; PCT publication WO 91/09967; U.S. Patent No. 5,225,539; EP592106; and EP519596; incorporated herein by reference.

[00182] As used herein, the term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

[00183] As used herein, the term "multi-specific antibodies" refers to antibodies that exhibit affinity for more than one target antigen. Multi-specific antibodies can have structures similar

to full immunoglobulin molecules and include Fc regions, for example IgG Fc regions. Such structures can include, but not limited to, IgG-Fv, IgG-(scFv)2, DVD-Ig, (scFv)2-(scFv)2-Fc and (scFv)2-Fc-(scFv)2. In case of IgG-(scFv)2, the scFv can be attached to either the N-terminal or the C- terminal end of either the heavy chain or the light chain. Exemplary multi-specific molecules have been reviewed by Kontermann, 2012, mAbs 4(2):182-197, Yazaki *et al.*, 2013, Protein Engineering, Design & Selection 26(3):1 87-1 93, and Grote *et al.*, 2012, in Proetzel & Ebersbach (eds.), Antibody Methods and Protocols, Methods in Molecular Biology vol. 901, chapter 16:247-263; incorporated herein by reference. Exemplary multi-specific molecules that lack Fc regions and into which antibodies or antibody fragments can be incorporated include scFv dimers (diabodies), trimers (triabodies) and tetramers (tetrabodies), Fab dimers (conjugates by adhesive polypeptide or protein domains) and Fab trimers (chemically conjugated), are described by Hudson and Souriau, 2003, Nature Medicine 9:129-134; incorporated herein by reference.

[00184] As used herein, the term "percent(%) sequence identity" refers to the percentage of amino acid (or nucleic acid) residues of a candidate sequence that are identical to the amino acid (or nucleic acid) residues of a reference sequence after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity (*e.g.*, gaps can be introduced in one or both of the candidate and reference sequences for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). Alignment for purposes of determining percent sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software, such as BLAST, ALIGN, or Megalign (ONASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For example, a reference sequence aligned for comparison with a candidate sequence may show that the candidate sequence exhibits from 50% to 100% sequence identity across the full length of the candidate sequence or a selected portion of contiguous amino acid (or nucleic acid) residues of the candidate sequence. The length of the candidate sequence aligned for comparison purposes may be, for example, at least 30%, (e.g., 30%, 40, 50%, 60%, 70%, 80%, 90%, or 100%) of the length of the reference sequence. When a position in the candidate sequence is occupied by the same amino acid residue as the corresponding position in the reference sequence, then the molecules are identical at that position.

[00185] As used herein, the term "primatized antibody" refers to an antibody comprising framework regions from primate-derived antibodies and other regions, such as CDRs and constant regions, from antibodies of a non-primate source. Methods for producing primatized antibodies are known in the art. *See e.g.*, U.S. Patent Nos. 5,658,570; 5,681,722; and 5,693,780; incorporated herein by reference.

[00186] As used herein, the term "operatively linked" in the context of a polynucleotide fragment is intended to mean that the two polynucleotide fragments are joined such that the amino acid sequences encoded by the two polynucleotide fragments remain in-frame.

[00187] As used herein, the terms "regulatory element" and the like refer to promoters, enhancers, and other expression control elements (*e.g.*, polyadenylation signals) that control the transcription or translation of the antibody chain genes. Such regulatory sequences are described, for example, in Goeddel, Gene Expression Technology: Methods in Enzymology 185 (Academic Press, San Diego, CA, 1990); incorporated herein by reference.

[00188] As used herein, the terms "subject" and "patient" refer to an organism that receives treatment for a particular disease or condition as described herein (such as cancer or an infectious disease). Examples of subjects and patients include mammals, such as humans, receiving treatment for diseases or conditions, for example, cell proliferation disorders, such as cancer.

[00189] As used herein, the term “scFv” refers to a single-chain Fv antibody in which the variable domains of the heavy chain and the light chain from an antibody have been joined to form one chain. scFv fragments contain a single polypeptide chain that includes the variable region of an antibody light chain (VL) (*e.g.*, CDR-L1, CDR-L2, and/or CDR-L3) and the variable region of an antibody heavy chain (VH) (*e.g.*, CDR-H1, CDR-H2, and/or CDR-H3) separated by a linker. The linker that joins the VL and VH regions of a scFv fragment can be a peptide linker composed of proteinogenic amino acids. Alternative linkers can be used to so as to increase the resistance of the scFv fragment to proteolytic degradation (*e.g.*, linkers containing D-amino acids), in order to enhance the solubility of the scFv fragment (*e.g.*, hydrophilic linkers such as polyethylene glycol-containing linkers or polypeptides containing repeating glycine and serine residues), to improve the biophysical stability of the molecule (*e.g.*, a linker containing cysteine residues that form intramolecular or intermolecular disulfide bonds), or to attenuate the immunogenicity of the scFv fragment (*e.g.*, linkers containing glycosylation sites). scFv molecules are known in the art and are described, *e.g.*, in US patent 5,892,019, Flo *et al.*, (Gene 77:51, 1989); Bird *et al.*, (Science 242:423, 1988);

Pantoliano *et al.*, (Biochemistry 30:10117, 1991); Milenic *et al.*, (Cancer Research 51:6363, 1991); and Takkinen *et al.*, (Protein Engineering 4:837, 1991). The VL and VH domains of a scFv molecule can be derived from one or more antibody molecules. It will also be understood by one of ordinary skill in the art that the variable regions of the scFv molecules of the invention can be modified such that they vary in amino acid sequence from the antibody molecule from which they were derived. For example, in some embodiments, nucleotide or amino acid substitutions leading to conservative substitutions or changes at amino acid residues can be made (*e.g.*, in CDR and/or framework residues). Alternatively or in addition, mutations are made to CDR amino acid residues to optimize antigen binding using art recognized techniques. scFv fragments are described, for example, in WO 2011/084714; incorporated herein by reference.

[00190] As used herein, the phrase "specifically binds" refers to a binding reaction which is determinative of the presence of an antigen in a heterogeneous population of proteins and other biological molecules that is recognized, *e.g.*, by an antibody or antigen-binding fragment thereof, with particularity. An antibody or antigen-binding fragment thereof that specifically binds to an antigen may bind to the antigen with a K_D of less than 100 nM. For example, an antibody or antigen-binding fragment thereof that specifically binds to an antigen may bind to the antigen with a K_D of up to 100 nM (*e.g.*, between 1 pM and 100 nM). An antibody or antigen-binding fragment thereof that does not exhibit specific binding to a particular antigen or epitope thereof may exhibit a K_D of greater than 100 nM (*e.g.*, greater than 500 nm, 1 μM, 100 μM, 500 μM, or 1 mM) for that particular antigen or epitope thereof. A variety of immunoassay formats may be used to select antibodies specifically immunoreactive with a particular protein or carbohydrate. For example, solid-phase ELISA immunoassays are routinely used to select antibodies specifically immunoreactive with a protein or carbohydrate. *See* Harlow & Lane, Antibodies, A Laboratory Manual, Cold Spring Harbor Press, New York (1988) and Harlow & Lane, Using Antibodies, A Laboratory Manual, Cold Spring Harbor Press, New York (1999), for a description of immunoassay formats and conditions that can be used to determine specific immunoreactivity.

[00191] As used herein, the term "transfection" refers to any of a wide variety of techniques commonly used for the introduction of exogenous DNA into a prokaryotic or eukaryotic host cell, *e.g.*, electroporation, lipofection, calcium- phosphate precipitation, DEAE- dextran transfection and the like.

[00192] As used herein, the terms "treat" or "treatment" refer to therapeutic treatment, in which the object is to prevent or slow down (lessen) an undesired physiological change or disorder, such as the progression of a cell proliferation disorder, such as cancer. Beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilized (*i.e.*, not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether detectable or undetectable. Those in need of treatment include those already with the condition or disorder, as well as those prone to have the condition or disorder or those in which the condition or disorder is to be prevented.

[00193] As used herein, the term "vector" refers to a nucleic acid vector, *e.g.*, a DNA vector, such as a plasmid, a RNA vector, virus or other suitable replicon (e.g., viral vector). A variety of vectors have been developed for the delivery of polynucleotides encoding exogenous proteins into a prokaryotic or eukaryotic cell. Examples of such expression vectors are disclosed in, *e.g.*, WO 1994/1 1026; incorporated herein by reference. Expression vectors of the invention may contain one or more additional sequence elements used for the expression of proteins and/or the integration of these polynucleotide sequences into the genome of a host cell, such as a mammalian cell (*e.g.*, a human cell). Exemplary vectors that can be used for the expression of antibodies and antibody fragments described herein include plasmids that contain regulatory sequences, such as promoter and enhancer regions, which direct gene transcription. Vectors may contain nucleic acids that modulate the rate of translation of a target gene or that improve the stability or nuclear export of the mRNA that results from gene transcription. These sequence elements may include, *e.g.*, 5' and 3' untranslated regions, an internal ribosomal entry site (IRES), and polyadenylation signal site in order to direct efficient transcription of the gene carried on the expression vector. The vectors described herein may also contain a polynucleotide encoding a marker for selection of cells that contain such a vector. Examples of a suitable marker include genes that encode resistance to antibiotics, such as ampicillin, chloramphenicol, kanamycin, or nourseothricin.

[00194] As used herein, the term "VH" refers to the variable region of an immunoglobulin heavy chain of an antibody, including the heavy chain of an Fv, scFv, or Fab. References to "VL" refer to the variable region of an immunoglobulin light chain, including the light chain of an Fv, scFv, dsFv or Fab. Antibodies (Abs) and immunoglobulins (Igs) are glycoproteins having the same structural characteristics. While antibodies exhibit binding specificity to a specific target, immunoglobulins include both antibodies and other antibody-like molecules

which lack target specificity. Native antibodies and immunoglobulins are usually heterotetrameric glycoproteins of about 150,000 Daltons, composed of two identical light (L) chains and two identical heavy (H) chains. Each heavy chain of a native antibody has at the amino terminus a variable domain (VH) followed by a number of constant domains. Each light chain of a native antibody has a variable domain at the amino terminus (VL) and a constant domain at the carboxy terminus.

3.2. Gene Definitions

[00195] As used herein, "**B8R**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a secreted protein with homology to the gamma interferon (IFN-γ) receptor. A nonlimiting example of a protein sequence encoded by an exemplary B8R gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21004 and is reproduced below:
MRYIIILAVLFINSIHAKITSYKFESVNFDSKIEWTGDGLYNISLKNYGIKTWQTMYTN
VPEGTYDISAFPKNDFVSFWVKFEQGDYKVEEYCTGLCVEVKIGPPTVTLTEYDDHI
NLYIEHPYATRGSKKIPIYKRGDMCDIYLLYTANFTFGDSEEPVTYDIDDYDCTSTGC
SIDFATTEKVCVTAQGATEGFLEKITPWSSEVCLTPKKNVYTCAIRSKEDVPNFKDK
MARVIKRKFNKQSQSYLTKFLGSTSNDVTTFLSMLNLTKYS (SEQ ID NO: 1).

[00196] The term "B8R" may also include fragments or variants of the protein listed above, or of homologous genes from another vaccinia virus strain. Variants include, without limitation, those sequences having 85 percent or greater identity to the sequences disclosed herein.

[00197] As used herein, "**B14R**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene. An example of a protein sequence encoded by an exemplary B14R gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P20842 and is reproduced below:
MNHCLLAISAVYFKAKWLTPFEKEFTSDYPFYVSPTEMVDVSMMSMYGELFNHASV
KESFGNFSIIELPYVGDTSMMVILPDKIDGLESIEQNLTDTNFKKWCNSLDAMFIDVHI
PKFKVTGSYNLVDTLVKSGLTEVFGSTGDYSNMCNLDVSVDAMIHKTYIDVNEEYT
EAAAATCALVSDCASTITNEFCVDHPFIYVIRHVDGKILFVGRYCSPTTNC (SEQ ID NO: 2).

[00198] As used herein, "**B15R**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene. An example of a protein sequence encoded by an exemplary B15R gene

in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21089 and is reproduced below:

MTANFSTHVFSPQHCGCDRLTSIDDVKQCLTEYIYWSSYAYRNRQCAGQLYSTLLSF RDDAELVFIDIRELVKNMPWDDVKDCTEIIRCYIPDEQKTIREISAIIGLCAYAATYWG GEDHPTSNSLNALFVMLEMLNYVDYNIIFRRMN (SEQ ID NO: 3).

[00199] As used herein, "**B16R**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a IL-1-beta inhibitor. An example of a protein sequence encoded by an exemplary B16R gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21116 and is reproduced below:

MSILPVIFLP IFFYSSFVQT FNASECIDKG (SEQ ID NO: 4).

[00200] As used herein, "**B17L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene. An example of a protein sequence encoded by an exemplary B17L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21075 and is reproduced below:

MSRKFMQVYEYDREQYLDEFIEDRYNDSFITSPEYYSAEKYMCRYTTLNHNCVNVR RCALDSKLLHDIITNCKIYNNIELVRATKFVYYLDLIKCNWVSKVGDSVLYPVIFITHT STRNLDKVSVKTYKGVKVKKLNRCADHAIVINPFVKFKLTLPNKTSHAKVLVTFCKL RTDITPVEAPLPGNVLVYTFPDINKRIPGYIHVNIEGCIDGMIYINSSKFACVLKLHRSM YRIPPFPIDICSCCSQYTNDDIEIPIHDLIKDVAIFKNKETVYYLKLNNKTIARFTYFNNI DTAITQEHEYVKIALGIVCKLMINNMHSIVGVNHSNTFVNCLLEDNV (SEQ ID NO: 5).

[00201] As used herein, "**B18R**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes an Ankyrin repeat protein. An example of a protein sequence encoded by an exemplary B18R gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21076 and is reproduced below:

MSRRLIYVLNINRKSTHKIQENEIYTYFSHCNIDHTSTELDFVVKNYDLNRRQHVTGY TALHCYLYNNYFTNDVLKILLNHDVNVTMKTSSGRMPVYILLTRCCNISHDVVIDMI DKDKNHLSHRDYSNLLLEYIKSRYMLLKEEDIDENIVSTLLDKGIDPNFKQDGYTAL HYYYLCLAHVYKPGECRKPITIKKAKRIISLFIQHGANLNALDNCGNTPFHLYLSIEM CNNIHMTKMLLTFNPNFKICNNHGLTPILCYITSDYIQHDILVMLIHHYETNVGEMPID ERRMIVFEFIKTYSTRPADSITYLMNRFKNINIYTRYEGKTLLHVACEYNNTQVIDYLI RINGDINALTDNNKHATQLIIDNKENSPYTINCLLYILRYIVDKNVIRSLVDQLPSLPIF DIKSFEKFISYCILLDDTFYDRHVKNRDSKTYRYAFSKYMSFDKYDGIITKCHDETML

LKLSTVLDTTLYAVLRCHNSRKLRRYLTELKKYNNDKSFKIYSNIMNERYLNVYYK DMYVSKVYDKLFPVFTDKNCLLTLLPSEIIYEILYMLTINDLYNISYPPTKV (SEQ ID NO: 6).

[00202] As used herein, "**B19R**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a IFN-alpha-beta-receptor-like secreted glycoprotein. An example of a protein sequence encoded by an exemplary B19R gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21077 and is reproduced below:

MTMKMMVHIYFVSLSLLLLLFHSYAIDIENEITEFFNKMRDTLPAKDSKWLNPACMF GGTMNDMATLGEPFSAKCPPIEDSLLSHRYKDYVVKWERLEKNRRRQVSNKRVKH GDLWIANYTSKFSNRRYLCTVTTKNGDCVQGIVRSHIKKPPSCIPKTYELGTHDKYGI DLYCGILYAKHYNNITWYKDNKEINIDDIKYSQTGKELIIHNPELEDSGRYDCYVHYD DVRIKNDIVVSRCKILTVIPSQDHRFKLILDPKINVTIGEPANITCTAVSTSLLIDDVLIE WENPSGWLIGFDFDVYSVLTSRGGITEATLYFENVTEEYIGNTYKCRGHNYYFEKTL TTTVVLE (SEQ ID NO: 7).

[00203] As used herein, "**B20R**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes an Ankyrin repeat protein. An example of a protein sequence encoded by an exemplary B20R gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21078 and is reproduced below:

MDEDTRLSRYLYLTDREHINVDSIKQLCKISDPNACYRCGCTALHEYFYNYRSVNGK YKYRYNGYYQYYSSSDYENYNEYYYDDYDRTGMNSESDSESDNISIKTEYENEYEF YDETQDQSTQHNDL (SEQ ID NO: 8).

[00204] As used herein, "**C1L**" refers to an orthopoxvirus (*e.g.*, vaccinia, e.g., Copenhagen) gene. An example of a protein sequence encoded by an exemplary C1L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21036 and is reproduced below:

MVKNNKISNSCRMIMSTNPNNILMRHLKNLTDDEFKCIIHRSSDFLYLSDSDYTSITKE T

LVSEIVEEYPDDCNKILAIIFLVLDKDIDVDIETKLKPKPAVRFAILDKMTEDIKLTDLV RHYFRYIEQDIPLGPLFKKIDSYRTRAINKYSKELGLATEYFNKYGHLMFYTLPIPYNR F

FCRNSIGFLAVLSPTIGHVKAFYKFIEYVSIDDRRKFKKELMSK (SEQ ID NO: 9).

[00205] As used herein, "**C2L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a kelch-like protein that affects calcium-independent adhesion to the extracellular matrix. An example of a protein sequence encoded by an exemplary C2L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21037 and is reproduced below: MESVIFSINGEIIQVNKEIITASPYNFFKRIQDHHLKDEAIILNGINYHAFESLLDYMRW KKINITINNVEMILVAAVIIDVPPVVDLCVKTMIHNINSTNCIRMFNFSKRYGIKKLYN ASMSEIINNITAVTSDPEFGKLSKDELTTILSHEDVNVNHEDVTAMILLKWIHKNPND VDIINILHPKFMTNTMRNAISLLGLTISKSTKPVTRNGIKHNIVVIKNSDYISTITHYSPR TEYWTIVGNTDRQFYNANVLHNCLYIIGGMINNRHVYSVSRVDLETKKWKTVTNMS SLKSEVSTCVNDGKLYVIGGLEFSISTGVAEYLKHGTSKWIRLPNLITPRYSGASVFV NDDIYVMGGVYTTYEKYVVLNDVECFTKNRWIKKSPMPRHHSIVYAVEYDGDIYVI TGITHETRNYLYKYIVKEDKWIELYMYFNHVGKMFVCSCGDYILIIADAKYEYYPKS NTWNLFDMSTRNIEYYDMFTKDETPKCNVTHKSLPSFLSNCEKQFLQ (SEQ ID NO: 10).

[00206] As used herein, "**F1L**" refers to a orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a caspase-9 inhibitor. An example of a protein sequence encoded by an exemplary F1L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P68450 and is reproduced below: MLSMFMCNNIVDYVDDIDNGIVQDIEDEASNNVDHDYVYPLPENMVYRFDKSTNIL DYLSTERDHVMMAVRYYMSKQRLDDLYRQLPTKTRSYIDIINIYCDKVSNDYNRDM NIMYDMASTKSFTVYDINNEVNTILMDNKGLGVRLATISFITELGRRCMNPVKTIKM FTLLSHTICDDCFVDYITDISPPDNTIPNTSTREYLKLIGITAIMFATYKTLKYMIG (SEQ ID NO: 11).

[00207] As used herein, "**F2L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a deoxyuridine triphosphatase (dUTPase). An example of a protein sequence encoded by an exemplary F2L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P68634 and is reproduced below: MFNMNINSPVRFVKETNRAKSPTRQSPGAAGYDLYSAYDYTIPPGERQLIKTDISMS MPKICYGRIAPRSGLSLKGIDIGGGVIDEDYRGNIGVILINNGKCTFNVNTGDRIAQLI YQRIYYPELEEVQSLDSTNRGDQGFGSTGLR (SEQ ID NO: 12).

[00208] As used herein, "**F3L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a kelch-like protein that is an innate immune response

modifier and a virulence factor. An example of a protein sequence encoded by an exemplary F3L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21013 and is reproduced below:

MPIFVNTVYCKNILALSMTKKFKTIIDAIGGNIIVNSTILKKLSPYFRTHLRQKYTKNK
DPVTRVCLDLDIHSLTSIVIYSYTGKVYIDSHNVVNLLRASILTSVEFIIYTCINFILRDF
RKEYCVECYMMGIEYGLSNLLCHTKNFIAKHFLELEDDIIDNFDYLSMKLILESDELN
VPDEDYVVDFVIKWYIKRRNKLGNLLLLIKNVIRSNYLSPRGINNVKWILDCTKIFHC
DKQPRKSYKYPFIEYPMNMDQIIDIFHMCTSTHVGEVVYLIGGWMNNEIHNNAIAVN
YISNNWIPIPPMNSPRLYATGIPANNKLYVVGGLPNPTSVERWFHGDAAWVNMPSLL
KPRCNPAVASINNVIYVMGGHSETDTTTEYLLPNHDQWQFGPSTYYPHYKSCALVF
GRRLFLVGRNAEFYCESSNTWTLIDDPIYPRDNPELIIVDNKLLLIGGFYRGSYIDTIEV
YNHHTYSWNIWDGK (SEQ ID NO: 13).

[00209] As used herein, "**K1L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes an NF-κB inhibitor. An example of a protein sequence encoded by an exemplary K1L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P20632 and is reproduced below:

MDLSRINTWKSKQLKSFLSSKDTFKADVHGHSALYYAIADNNVRLVCTLLNAGALK
NLLENEFPLHQAATLEDTKIVKILLFSGMDDSQFDDKGNTALYYAVDSGNMQTVKL
FVKKNWRLMFYGKTGWKTSFYHAVMLNDVSIVSYFLSEIPSTFDLAILLSCIHTTIKN
GHVDMMILLLDYMTSTNTNNSLLFIPDIKLAIDNKDIEMLQALFKYDINIYSVNLENV
LLDDAEITKMIIEKHVEYKSDSYTKDLDIVKNNKLDEIISKNKELRLMYVNCVKKN
(SEQ ID NO: 14).

[00210] As used herein, "**K2L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a serine protease inhibitor that prevents cell fusion. An example of a protein sequence encoded by an exemplary K2L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P20532 and is reproduced below:

MIALLILSLTCSVSTYRLQGFTNAGIVAYKNIQDDNIVFSPFGYSFSMFMSLLPASGNT
RIELLKTMDLRKRDLGPAFTELISGLAKLKTSKYTYTDLTYQSFVDNTVCIKPLYYQQ
YHRFGLYRLNFRRDAVNKINSIVERRSGMSNVVDSNMLDNNTLWAIINTIYFKGTWQ
YPFDITKTRNASFTNKYGTKTVPMMNVVTKLQGNTITIDDEEYDMVRLPYKDANIS
MYLAIGDNMTHFTDSITAAKLDYWSFQLGNKVYNLKLPKFSIENKRDIKSIAEMMAP

SMFNPDNASFKHMTRDPLYIYKMFQNAKIDVDEQGTVAEASTIMVATARSSPEKLEF NTPFVFIIRHDITGFILFMGKVESP (SEQ ID NO: 15).

[00211] As used herein, "**K3L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a PKR inhibitor. An example of a protein sequence encoded by an exemplary K3L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P20639 and is reproduced below: MLAFCYSLPNAGDVIKGRVYEKDYALYIYLFDYPHSEAILAESVKMHMDRYVEYRD KLVGKTVKVKVIRVDYTKGYIDVNYKRMCRHQ (SEQ ID NO: 16).

[00212] As used herein, "**K4L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a DNA modifying nuclease (e.g., DNA nicking enzyme). An example of a protein sequence encoded by an exemplary K4L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P20537 and is reproduced below: MNPDNTIAVITETIPIGMQFDKVYLSTFNMWREILSNTTKTLDISSFYWSLSDEVGTNF GTIILNEIVQLPKRGVRVRVAVNKSNKPLKDVERLQMAGVEVRYIDITNILGGVLHTK FWISDNTHIYLGSANMDWRSLTQVKELGIAIFNNRNLAADLTQIFEVYWYLGVNNLP YNWKNFYPSYYNTDHPLSINVSGVPHSVFIASAPQQLCTMERTNDLTALLSCIRNASK FVYVSVMNFIPIIYSKAGKILFWPYIEDELRRSAIDRQVSVKLLISCWQRSSFIMRNFLR SIAMLKSKNIDIEVKLFIVPDADPPIPYSRVNHAKYMVTDKTAYIGTSNWTGNYFTDT CGASINITPDDGLGLRQQLEDIFMRDWNSKYSYELYDTSPTKRCKLLKNMKQCTNDI YCDEIQPEKEIPEYSLE (SEQ ID NO: 17).

[00213] As used herein, "**K5L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a putative monoglyceride lipase. An example of a protein sequence encoded by an exemplary K5L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21084 and is reproduced below: MGATISILASYDNPNLFTAMILMSPLVNADAVSRLNLLAAKLMGTITPNAPVGKLCP ESVSRDMDKVYKYQYDPLINHEKIKAGFASQVLKATNKVRKIISKINTPRLSYSREQT MRLVMFQVHIISCNMQIVIEK (SEQ ID NO: 18).

[00214] As used herein, "**K6L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes a putative monoglyceride lipase. An example of a protein sequence encoded by an exemplary K6L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P68465 and is reproduced below:

MSANCMFNLDNDYIYWKPITYPKALVFISHGAGKHSGRYDELAENISSLGILVFSHD HIGHGRSNGEKMMIDDFGTARGNY (SEQ ID NO: 19).

[00215] As used herein, "**K7R**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes an inhibitor of NF-κB and IRF3. An example of a protein sequence encoded by an exemplary K7R gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P68467 and is reproduced below: MATKLDYEDAVFYFVDDDKICSRDSIIDLIDEYITWRNHVIVFNKDITSCGRLYKELM KFDDVAIRYYGIDKINEIVEAMSEGDHYINFTKVHDQESLFATIGICAKITEHWGYKKI SESRFQSLGNITDLMTDDNINILILFLEKKLN (SEQ ID NO: 20).

[00216] As used herein, "**M1L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes an Ankyrin repeat protein. An example of a protein sequence encoded by an exemplary M1L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P20640 and is reproduced below: MIFVIESKLLQIYRNRNRNINFYTTMDNIMSAEYYLSLYAKYNSKNLDVFRNMLQAIE PSGNNYHILHAYCGIKGLDERFVEELLHRGYSPNETDDDGNYPLHIASKINNNRIVAM LLTHGADPNACDKHNKTPLYYLSGTDDEVIERINLLVQYGAKINNSVDEEGCGPLLA CTDPSERVFKKIMSIGFEARIVDKFGKNHIHRHLMSDNPKASTISWMMKLGISPSKPD HDGNTPLHIVCSKTVKNVDIIDLLLPSTDVNKQNKFGDSPLTLLIKTLSPAHLINKLLS TSNVITDQTVNICIFYDRDDVLEIINDKGKQYDSTDFKMAVEVGSIRCVKYLLDNDIIC EDAMYYAVLSEYETMVDYLLFNHFSVDSVVNGHTCMSECVRLNNPVILSKLMLHNP TSETMYLTMKAIEKDKLDKSIIIPFIAYFVLMHPDFCKNRRYFTSYKRFVTDYVHEGV SYEVFDDYF (SEQ ID NO: 21).

[00217] As used herein, "**M2L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes an inhibitor of NF-κB and apoptosis. An example of a protein sequence encoded by an exemplary M2L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry Q1PJ18 and is reproduced below: MVYKLVLLFCIASLGYSVEYKNTICPPRQDYRYWYFAAELTIGVNYDINSTIIGECHM SESYIDRNANIVLTGYGLEINMTIMDTDQRFVAAAEGVGKDNKLSVLLFTTQRLDKV HHNISVTITCMEMNCGTTKYDSDLPESIHKSSSCDITINGSCVTCVNLETDPTKINPHY LHPKDKYLYHNSEYGMRGSYGVTFIDELNQCLLDIKELSYDICYRE (SEQ ID NO: 22).

[00218] As used herein, "**N1L**" refers to an orthopoxvirus (*e.g.*, vaccinia, e.g., Copenhagen) gene, such as a gene that encodes a BCL-2-like protein that inhibits NF-κB and apoptosis. An example of a protein sequence encoded by an exemplary N1L gene in a

Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P21054 and is reproduced below:
MRTLLIRYILWRNDNDQTYYNDDFKKLMLLDELVDDGDVCTLIKNMRMTLSDGPLL DRLNQPVNNIEDAKRMIAISAKVARDIGERSEIRWEESFTILFRMIETYFDDLMIDLYG EK (SEQ ID NO: 23).

[00219] As used herein, "**N2L**" refers to an orthopoxvirus (*e.g.*, vaccinia, *e.g.*, Copenhagen) gene, such as a gene that encodes an inhibitor of IRF3. An example of a protein sequence encoded by an exemplary N2L gene in a Copenhagen strain of the vaccinia virus is given in UniProtKB database entry P20641 and is reproduced below:
MTSSAMDNNEPKVLEMVYDATILPEGSSMDPNIMDCINRHINMCIQRTYSSSIIAILNR FLTMNKDELNNTQCHIIKEFMTYEQMAIDHYGEYVNAILYQIRKRPNQHHTIDLFKKI KRTPYDTFKVDPVEFVKKVIGFVSILNKYKPVYSYVLYENVLYDEFKCFINYVETKY F (SEQ ID NO: 26).

[00220] Exemplary Copenhagen strain nucleotide sequences of the coding sequences (CDSs) of the genes described herein are provided in Table 42 below. The nucleotide sequence of an exemplary wild-type Copenhagen strain vaccinia virus genome is also provided in Table 42 below. Another exemplary wild-type Copenhagen strain vaccinia virus genome is SEQ ID NO: 590 (as provided in Table 42) but with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or all of the nucleotide polymorphisms identified in Table 46. In certain embodiments, the CDS of the genes described herein have nucleotide sequences that are identical to the nucleotide sequences provided in Table 42 except for 1, 2, 3, or more of the nucleotide polymorphisms identified in Table 46.

4. Brief Description of the Figures

[00221] **FIG. 1** shows a phylogenetic analysis of 59 poxvirus strains, including the Orthopoxvirus virus strains.

[00222] **FIG. 2** shows the abundances of different viral strains after passaging 5 Vaccinia viruses in different tumor types.

[00223] **FIG. 3** shows the abilities of Vaccinia wild-type strains to replicate in various different patient tumor cores.

[00224] **FIG. 4** shows plaque size measurements of different Vaccinia wild-type strains.

[00225] **FIG. 5** shows the genomic structure of a 5p deletion (CopMD5p) and a 3p deletion (CopMD3p). Both CopMD5p and CopMD3p were crossed to generate CopMD5p3p.

[00226] **FIG. 6** shows a heatmap showing cancer cell death following infection with either Copenhagen or CopMD5p3p at various doses.

[00227] **FIG. 7** shows the growth curves of Copenhagen and CopMD5p3p replication in 4 different cancer cell lines.

[00228] **FIG. 8** shows the ability of Copenhagen and CopMD5p3p to replicate in patient ex vivo samples as shown by titering.

[00229] **FIG. 9** shows that the modified CopMD5p3p virus forms different plaques than the parental virus. CopMD5p3p plaques are much clearer in the middle, with visible syncytia (cell fusion).

[00230] **FIG. 10** shows CopMD5p3p induces syncytia (cell fusion) in 786-O cells.

[00231] **FIG. 11** shows that CopMD5p3p is able to control tumor growth similarly to Copenhagen wild-type but does not cause weight loss.

[00232] **FIG. 12** shows that CopMD5p3p does not cause pox lesion formation when compared to two other Vaccinia strains (Copenhagen and Wyeth) harboring the oncolytic knockout of thymidine kinase.

[00233] **FIG. 13** shows the IVIS bio-distribution of Vaccinia after systemic administration in nude CD-1 mice. Luciferase encoding CopMD5p3p (TK KO) is tumor specific and does not replicate in off target tissues.

[00234] **FIG. 14** shows the bio-distribution of Vaccinia after systemic administration. CopMD5p3p replicates similarly to other oncolytic Vaccinia in the tumour but replicates less in off target tissues/organs.

[00235] **FIG. 15** shows the immunogenicity of Vaccinia in Human PBMCs. The ability of CopMD5p3p to induce human innate immune cell activation is stronger than that of wild-type Copenhagen.

[00236] **FIG. 16** shows the immunogenicity of Vaccinia in Mouse Splenocytes. The ability of CopMD5p3p to induce mouse innate immune cell activation is stronger than that of Copenhagen.

[00237] **FIG. 17** shows the immunogenicity of Vaccinia in Human cells. The ability of CopMD5p3p to activate NF-kB immune transcription factor is stronger than that of Copenhagen or VVdd but similar to that of MG-1.

[00238] **FIG. 18** shows the synergy with immune checkpoint inhibitor Anti-CTLA-4 antibody in an aggressive melanoma model (B16-F10 syngeneic melanoma model in

C57BL6 mice). In vivo efficacy measured by survival in an immune competent murine model treated with Vaccinia and Immune Checkpoint Inhibitors Anti-CTLA-4 antibody.

[00239] **FIG. 19** shows the synergy with immune checkpoint inhibitor Anti-CTLA-4 antibody. In vivo efficacy measured by tumor growth (top row) and survival (bottom row) in an immune competent murine model treated with Vaccinia and Immune Checkpoint Inhibitor Anti-CTLA-4 antibody. CopMD5p3p (left column) is compared to oncolytic Copenhagen TK KO (right column).

[00240] **FIG. 20** shows the synergy with immune checkpoint inhibitor Anti-PD1 antibody. In vivo efficacy measured by tumor growth (top row) and survival (bottom row) in an immune competent murine model treated with Vaccinia and Immune Checkpoint Inhibitor Anti-PD1 antibody. CopMD5p3p (left column) is compared to oncolytic Copenhagen TK KO (right column).

[00241] **FIG. 21** shows the synergy with immune checkpoint inhibitor Anti-PD1 antibody and Anti-CTLA-4 antibody. In vivo efficacy measured by tumor growth (top row) and survival (bottom row) in an immune competent murine model treated with Vaccinia and Immune Checkpoint Inhibitors Anti-PD1 antibody and Anti-CTLA-4 antibody. CopMD5p3p (left column) is compared to oncolytic Copenhagen TK KO (right column).

[00242] **FIG. 22** shows a scheme for the production of modified poxvirus vectors (e.g., modified vaccinia virus vectors, such as modified Copenhagen vaccinia virus vectors) harboring a 5' ("5p") major deletion locus (left) and a 3' ("3p") major deletion locus (right). 5p targeting construct is composed of 1 kb homologous region to C2L, followed by an eGFP expressing transgene, and 1 kb homologous region to F3L. 3p targeting construct is composed of 729bp homologous region to B14R, followed by the mCherry expressing transgene, and a 415bp homologous region to B29R.

[00243] **FIG. 23** shows the ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to proliferate in various cell lines.

[00244] **FIG. 24** shows the cytotoxic effects of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions on various cell lines, as assessed by crystal violet (upper panels) and an Alamar Blue assay (lower panel). The order of strains listed for each cell line along the x-axis of the chart shown in the lower panel is as follows: from left to right, CopMD5p, CopMD5p3p, CopMD3p, and CopWT (wildtype Copenhagen vaccinia strain).

[00245] **FIG. 25** shows the distribution of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions upon administration to mice.

[00246] **FIG. 26** shows the ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to activate Natural Killer (NK) cells and promote anti-tumor immunity.

[00247] **FIG. 27** shows the ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to enhance NK cell-mediated degranulation against HT29 cells, a measure of NK cell activity and anti-tumor immunity.

[00248] **FIG. 28** shows the ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to prime T-cells to initiate an anti-tumor immune response.

[00249] **FIG. 29** shows the ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to spread to distant locations from the initial point of infection.

[00250] **FIG. 30** shows the ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to form plaques, a measure of viral proliferation.

[00251] **FIG. 31** shows the ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to form plaques in U2OS cells.

[00252] **FIG. 32** shows the ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to form plaques in 786-O cells.

[00253] **FIG. 33** shows the percentage of genes deleted in CopMD5p3p in various poxvirus genomes.

[00254] **FIG. 34** shows infection of normal versus cancer cell lines of SKV-B8R+ virus.

[00255] **FIG. 35** shows SKV-B8R+ does not impair interferon signaling.

[00256] **FIG. 36** shows B8R recombination targeting strategy for FLt3-LG and IL-12-TM transgenes.

[00257] **FIG. 37** shows SKV (CopMD5p3p-B8R-) has similar efficacy in tumour control compared to SKV-B8R+.

[00258] **FIG. 38** shows a linear cartoon schematic depicting the genomic organization of the SKV-123v2 oncolytic platform compared to the base wildtype Copenhagen vaccinia virus genome. FRT is a recognition site for the Flippase enzyme.

[00259] **FIG. 39** shows SKV engineered to express 2 immunotherapeutic transgenes and an antibody.

[00260] **FIG. 40** shows SKV engineered to express 2 immunotherapeutic transgenes and an antibody.

[00261] **FIG. 41** shows hIL-12 production quantified for various SKV viruses expressing transgenes.

[00262] **FIG. 42** shows IL-12p35 (IL-12) cell surface immunostaining on live Vero cells infected with SKV-123, SKV-3 and control SKV-eGFP viruses (MOI 0.1, 24 hrs post infection).

[00263] **FIG. 43** shows SKV expressing murine IL-12 p35 membrane bound has greater efficacy in controlling murine tumors.

[00264] **FIG. 44** shows major double deletions engineered in various vaccinia strains enhance cancer cell killing in vitro.

[00265] **FIG. 45** shows the phenotypic characterization of HeLa cells infected with various vaccinia strains.

[00266] **FIG. 46** shows 5p3p vaccinia strains do not induce weight loss compared to wildtype strains. Mouse body mass measurements are shown. CD-1 nude mice were treated with 1 x 10^7 pfu (particle forming units) via intravenously tail vein injection and measured at the indicated time points.

[00267] **FIG. 47** shows 5p3p vaccinia strains do not induce pox lesions compared to wildtype strains. Assessment of the presence of pox lesions is shown. CD-1 nude mice were treated with 1 x 10^7 pfu with indicated vaccinia virus strains via intravenously tail vein injection. Mice were examined for pox lesions 6 days post-injection.

[00268] **FIGs. 48A-48H** show tumor volume over time and survival curves in eight xenograft mouse models treated with 0.05 ml of SKV (vaccinia virus) (dose: 1e7 pfu). FIG. 48A shows results from the MiaPaca-2 xenograft mouse model. FIG. 48B shows results from the PC-3 xenograft mouse model. FIG. 48C shows results from the U87MG xenograft model. FIG. 49D shows results from the UACC-62 xenograft model. FIG. 48E shows results from the UM-UC-3 xenograft mouse model. FIG. 48F shows results from the COLO-205 xenograft mouse model. FIG. 48G shows results from the NCI-H460 xenograft mouse model. FIG. 48H shows results from the HT29 xenograft model.

[00269] **FIG. 49** shows average tumor volumes over time and survival curves in a transgenic C57/BL6 mouse model expressing human CTLA-4, with MC-38 tumors treated with SKV encoding active transgenes. Animals were then randomized into 5 treatment groups and then treated with PBS, PBS plus Ipilimumab, SKV, anti-PD-1 antibody, SKV-

12m3v2-eGFP or SKV-12m3v2-eGFP plus anti-PD-1 antibody. SKV-12m3v2-eGFP is SKV expressing the human anti-CTLA-4 antibody, human Flt3 ligand and mouse IL-12 TM p35.

[00270] **FIG. 50** shows individual tumor volumes of the experiment shown in FIG. 49.

[00271] **FIG. 51** shows average tumor volumes over time in MC-38 mouse models treated with either membrane-bound mouse IL-12 p35 or membrane-bound mouse IL-12 p70.

[00272] **FIG. 52** shows results from a heterologous prime:boost oncolytic vaccine regimen using a virus ($SKVB^{8R+TK-}$ encoding OVA antigen)..

[00273] **FIGs. 53A-53F** show the biodistribution of FLT3-L and Anti-CTLA-4 Antibody in serum and tissue of BALB/c mice engrafted with CT26 tumor cells and administered SKV-123v2 either IT or IV.

[00274] **FIGs. 54A-54D** show the biodistribution of IL-12-TM in serum and tissue of BALB/c mice engrafted with CT26 tumor cells and administered SKV-123v2 either IT or IV.

[00275] **FIG. 55** shows tumor volume in NGS mice either untreated or treated with SKV-123v2.

[00276] **FIG. 56** shows Alamar Blue viability kinetics of SKV-123v2 virus-infected cancer cells (top panels) and normal cells (bottom panels).

[00277] **FIG. 57** shows virus replication growth curves in SKV-123v2 virus-infected cancer cells (786-O, HeLa) and normal cells (PBMC, PrEC).

[00278] **FIG. 58** shows anti-CTLA-4 antibody expression levels in SKV-123v2 virus-infected cancer cells (786-O, HeLa) and normal cells (PBMC, PrEC).

[00279] **FIG. 59** shows FLT3L expression levels in SKV-123v2 virus-infected cancer cells (786-O, HeLa) and normal cells (PBMC, PrEC).

[00280] **FIG. 60** shows the design of a targeting construct for insertion of a transgene in vaccinia virus genome. Construct can either be a PCR product of amplification or part of a bacterial plasmid. Number of transgenes as well as their orientation are flexible. Order of transgenes and Fluorescent marker are flexible.

5. Detailed Description

[00281] The present invention features genetically modified orthopoxviruses, such as vaccinia viruses (*e.g.*, Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16m8, LC16mO, Tashkent, Tian Tan, and WAU86/88-1 viruses), as well as the use of the same for the treatment of various cancers. The invention is based in part on the discovery

that orthopoxviruses, such as Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16m8, LC16mO, Tashkent, Tian Tan, and WAU86/88-1 viruses, exhibit markedly improved oncolytic activity, replication in tumors, infectivity, immune evasion, tumor persistence, capacity for incorporation of exogenous DNA sequences, and amenability for large scale manufacturing when the viruses are engineered to contain deletions in one or more, or all, of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, B20R, K ORF A, K ORF B, B ORF E, B ORF F, and B ORF G genes and copies of the B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R ITRs. In various embodiments of the invention, the modified orthopoxviruses contain a deletion of the B8R gene. While inactive in mice, the B8R gene neutralizes antiviral activity of human IFN-γ. In various embodiments, at least one transgene is subsequently inserted into locus of the B8R gene (now deleted) through a homologous recombination targeting strategy. In various embodiments, the modified orthopoxvirus expresses at least one of three transgenes: IL-12-TM, FLT3-L and anti-CLTA4 antibody. As used herein, FLT3L, Flt-3 ligand, FLT3LG, FLT3-LG, FLT3-L are synonyms and all refer to FMS-like tyrosine kinase 3 ligand.

[00282] The orthopoxviruses described herein can be administered to a patient, such as a mammalian patient (*e.g.*, a human patient) to treat a variety of cell proliferation disorders, including a wide range of cancers. The sections that follow describe orthopoxviruses and genetic modifications thereto, as well as methods of producing and propagating genetically modified orthopoxviruses and techniques for administering the same to a patient.

5.1. Poxvirus

[00283] Generally, a poxvirus viral particle is oval or brick-shaped, measuring some 200-400 nm long. The external surface is ridged in parallel rows, sometimes arranged helically. Such particles are extremely complex, containing over 100 distinct proteins. The extracellular forms contain two membranes (EEV: extracellular enveloped virions), whereas intracellular particles only have an inner membrane (IMV: intracellular mature virions). The outer surface is composed of lipid and protein that surrounds the core, which is composed of a tightly compressed nucleoprotein. Antigenically, poxviruses are also very complex, inducing both specific and cross-reacting antibodies. There are at least ten enzymes present in the particle, mostly concerned with nucleic acid metabolism/genome replication.

[00284] The genome of the wild-type poxvirus is linear double-stranded DNA of 130-300 Kbp. The ends of the genome have a terminal hairpin loop with several tandem repeat sequences. Several poxvirus genomes have been sequenced, with most of the essential genes being located in the central part of the genome, while non-essential genes are located at the ends. There are about 250 genes in the poxvirus genome. Replication takes place in the cytoplasm, as the virus is sufficiently complex to have acquired all the functions necessary for genome replication. There is some contribution by the cell, but the nature of this contribution is not clear. However, even though poxvirus gene expression and genome replication occur in enucleated cells, maturation is blocked, indicating some role by the cell.

[00285] Once into the cell cytoplasm, gene expression is carried out by viral enzymes associated with the core. Expression is divided into 2 phases: early genes, which represent about of 50% genome, and are expressed before genome replication, and late genes, which are expressed after genome replication. The temporal control of expression is provided by the late promoters, which are dependent on DNA replication for activity. Genome replication is believed to involve self-priming, leading to the formation of high molecular weight concatemers, which are subsequently cleaved and repaired to make virus genomes. Viral assembly occurs in the cytoskeleton and probably involves interactions with the cytoskeletal proteins (*e.g.*, actin-binding proteins). Inclusions form in the cytoplasm that mature into virus particles. Cell to cell spread may provide an alternative mechanism for spread of infection. Overall, replication of this large, complex virus is rather quick, taking just 12 hours on average. At least nine different poxviruses cause disease in humans, but variola virus and vaccinia are the best known. Variola strains are divided into variola major (25-30% fatalities) and variola minor (same symptoms but less than 1% death rate). Infection with both viruses occurs naturally by the respiratory route and is systemic, producing a variety of symptoms, but most notably with variola characteristic pustules and scarring of the skin.

5.2. Orthopoxvirus

5.2.1. Vaccinia Virus

[00286] Vaccinia virus is a member of the poxvirus or Poxviridae family, the Chordopoxyirinae subfamily, and the Orthopoxvirus genus. Orthopoxvirus is relatively more homogeneous than other members of the Chordopoxyirinae subfamily and includes 11 distinct but closely related species, which includes vaccinia virus, variola virus (causative

agent of smallpox), cowpox virus, buffalopox virus, monkeypox virus, mousepox virus and horsepox virus species as well as others (*see* Moss, 1996).

[00287] Vaccinia virus is a large, complex enveloped virus having a linear double-stranded DNA genome of about 190 kb and encoding approximately 250 genes. Vaccinia is well-known for its role as a vaccine that eradicated smallpox. Post-eradication of smallpox, scientists have been exploring the use of vaccinia as a tool for delivering genes into biological tissues (gene therapy and genetic engineering). Vaccinia virus is unique among DNA viruses as it replicates only in the cytoplasm of the host cell. Therefore, a large genome is required to encode various enzymes and proteins needed for viral DNA replication. During replication, vaccinia produces several infectious forms, which differ in their outer membranes: the intracellular mature virion (IMV), the intracellular enveloped virion (IEV), the cell-associated enveloped virion (CEV), and the extracellular enveloped virion (EEV). IMV is the most abundant infectious form and is thought to be responsible for spread between hosts. On the other hand, the CEV is believed to play a role in cell-to-cell spread, and the EEV is thought to be important for long range dissemination within the host organism.

[00288] Vaccinia virus is closely related to the virus that causes cowpox. The precise origin of vaccinia is unknown, but the most common view is that vaccinia virus, cowpox virus, and variola virus (the causative agent for smallpox) were all derived from a common ancestral virus. There is also speculation that vaccinia virus was originally isolated from horses. A vaccinia virus infection is mild and typically asymptomatic in healthy individuals, but it may cause a mild rash and fever, with an extremely low rate of fatality. An immune response generated against a vaccinia virus infection protects that person against a lethal smallpox infection. For this reason, vaccinia virus was used as a live-virus vaccine against smallpox. The vaccinia virus vaccine is safe because it does not contain the smallpox virus, but occasionally certain complications and/or vaccine adverse effects may arise, especially if the vaccine is immunocompromised.

[00289] Exemplary strains of the vaccinia virus include, but are not limited to, Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16m8, LC16mO, Tashkent, Tian Tan, and WAU86/88-1.

5.2.2. Thymidine Kinase Mutants and Hemagglutinin Mutants

[00290] Several current clinical studies testing vaccinia virus as an oncolytic virus harbor deletions in the viral Thymidine Kinase (TK) gene. This deletion attenuates the virus, rendering the virus dependent upon the activity of cellular thymidine kinase for DNA replication and, thus, viral propagation. Cellular thymidine kinase is expressed at a low level in most normal tissues and at elevated levels in many cancer cells. Through metabolic targeting, TK- viruses can grow in cells that have a high metabolic rate (e.g., healthy cells or tumor cells) and will not grow well in cells that have low levels of thymidine kinase. Since there exist quiescent tumor cells (*e.g.*, cancer stem cells), TK- viruses are likely compromised in their ability to kill this population of cancer cells just as chemotherapy is largely ineffective. In some embodiments, the modified viral vectors described in this disclosure retains virus synthetic machinery (including TK) and may propagate in quiescent cancer cells. In such embodiments, the viral modifications of this disclosure may allow the virus to be highly selective without deleting TK or other DNA metabolizing enzymes (e.g., ribonucleotide reductase) and could be more effective in tumors with a low metabolic rate. In some embodiments, the modified viral vectors described in this disclosure comprise a functional TK gene (for example, a wild-type TK gene). In other embodiments, the modified viral vectors described in this disclosure comprise a deletion(s) or loss-of-function mutation(s) in the TK gene.

[00291] Similarly, inactivation of the hemagglutinin (HA) gene of the vaccinia virus can result in attenuation of the virus. In some embodiments, the modified viral vectors described in this disclosure comprise a functional HA gene (for example, a wild-type HA gene). In other embodiments, the modified viral vectors described in this disclosure comprise a deletion(s) or loss-of-function mutation(s) in the HA gene.

[00292] In a specific embodiment, the modified viral vectors described in this disclosure comprise a functional TK gene (for example, a wild-type TK gene) and a functional HA gene (for example, a wild-type HA gene). In another specific embodiment, the modified viral vectors described in this disclosure comprise a functional TK gene (for example, a wild-type TK gene) and a deletion(s) or loss-of-function mutation(s) in the HA gene. In another specific embodiment, the modified viral vectors described in this disclosure comprise a deletion(s) or loss-of-function mutation(s) in the TK gene and a functional HA gene (for example, a wild-type HA gene). In another specific embodiment, the modified viral vectors described in this disclosure comprise a deletion(s) or loss-of-function mutation(s) in the TK gene and a deletion(s) or loss-of-function mutation(s) in the HA gene.

5.2.3. Recombinant Orthopoxvirus Genome

[00293] In one aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ inverted terminal repeat (ITR): B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4); wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[00294] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter. In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00295] In some embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B14R and B29R genes. In another specific embodiment, the flanking endogenous

vaccinia virus genes are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene.

[00296] In preferred embodiments, endogenous genes that flank a nucleotide sequence (*i.e.*, the flanking endogenous genes of a nucleotide sequence) in this disclosure are the two endogenous genes closest to the nucleotide sequence (with one upstream and the other downstream of the nucleotide sequence). The endogenous genes can be partial genes or full-length genes.

[00297] In specific embodiments, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence comprises the 6 complementarity-determining regions (CDRs) of ipilimumab. In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[00298] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4); and (d) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions. In specific embodiments, the nucleic acid further comprises a deletion in the B8R gene.

[00299] In certain embodiments, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00300] In some embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the first nucleotide sequence is in the same orientation as the flanking

endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene.

[00301] In specific embodiments, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence comprises the 6 complementarity-determining regions (CDRs) of ipilimumab. In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[00302] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and (c) a second transgene comprising a second nucleotide sequence encoding an Interleukin 12 (IL-12) polypeptide; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[00303] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00304] In some embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene.

[00305] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), IL-12 p40 (*e.g.*, human IL-12 p40) or IL-12 p70 (*e.g.*, human IL-12 p70). In specific embodiments, the IL-12 polypeptide is membrane-bound and comprises IL-12 p35 (*e.g.*, human IL-12 p35), or IL-12 p70 (*e.g.*, human IL-12 p70), and a transmembrane domain and a cytoplasmic domain

(*e.g.*, the transmembrane and cytoplasmic domains of B7-1, TNFα, or FLT3L). In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[00306] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (d) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions. In specific embodiments, the nucleic acid further comprises a deletion in the B8R gene.

[00307] In certain embodiments, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00308] In some embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes are the

C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene.

[00309] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), IL-12 p40 (*e.g.*, human IL-12 p40) or IL-12 p70 (*e.g.*, human IL-12 p70). In specific embodiments, the IL-12 polypeptide is membrane-bound and comprises IL-12 p35 (*e.g.*, human IL-12 p35), or IL-12 p70 (*e.g.*, human IL-12 p70), and a transmembrane domain and a cytoplasmic domain (*e.g.*, the transmembrane and cytoplasmic domains of B7-1, TNFα, or FLT3L). In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[00310] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and (c) a third transgene comprising a third nucleotide sequence encoding FMS-like tyrosine kinase 3 ligand (FLT3L); wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[00311] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide

sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00312] In some embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene.

[00313] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1).

In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00314] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00315] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L

extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00316] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00317] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain,

and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00318] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00319] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at

least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00320] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00321] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the

transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00322] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00323] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a third transgene comprising a third nucleotide sequence encoding FLT3L; and (d) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions. In specific embodiments, the nucleic acid further comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00324] In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00325] In some embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene.

[00326] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire

FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00327] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00328] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In

certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00329] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00330] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00331] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of

the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00332] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00333] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the

N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00334] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00335] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments,

the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00336] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4); and (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[00337] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter. In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00338] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00339] In some embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking

endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B14R and B29R genes. In another specific

embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene.

[00340] In specific embodiments, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence comprises the 6 complementarity-determining regions (CDRs) of ipilimumab. In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[00341] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), IL-12 p40 (*e.g.*, human IL-12 p40) or IL-12 p70 (*e.g.*, human IL-12 p70). In specific embodiments, the IL-12 polypeptide is membrane-bound and comprises IL-12 p35 (*e.g.*, human IL-12 p35), or IL-12 p70 (*e.g.*, human IL-12 p70), and a transmembrane domain and a cytoplasmic domain (*e.g.*, the transmembrane and cytoplasmic domains of B7-1, TNFα, or FLT3L). In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[00342] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4); and (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter

operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; and/or (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In specific embodiments, the nucleic acid further comprises a deletion in the B8R gene.

[00343] In certain embodiments, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00344] In certain embodiments, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00345] In some embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the

first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene.

[00346] In specific embodiments, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence comprises the 6 complementarity-determining regions (CDRs) of ipilimumab. In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[00347] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), IL-12 p40

(*e.g.*, human IL-12 p40) or IL-12 p70 (*e.g.*, human IL-12 p70). In specific embodiments, the IL-12 polypeptide is membrane-bound and comprises IL-12 p35 (*e.g.*, human IL-12 p35), or IL-12 p70 (*e.g.*, human IL-12 p70), and a transmembrane domain and a cytoplasmic domain (*e.g.*, the transmembrane and cytoplasmic domains of B7-1, TNFα, or FLT3L). In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[00348] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4); and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[00349] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter. In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00350] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R

promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00351] In some embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other

embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene.

[00352] In specific embodiments, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence comprises the 6 complementarity-determining regions (CDRs) of ipilimumab. In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[00353] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1).

In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00354] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00355] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the

carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00356] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00357] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the

transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00358] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00359] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the

carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00360] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00361] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00362] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00363] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4); and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; and/or (ii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter. In specific embodiments, the nucleic acid further comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00364] In certain embodiments, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00365] In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In certain embodiments, the at least one promoter

operably linked to the third nucleotide sequence is a B19R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00366] In some embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide

sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene.

[00367] In specific embodiments, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence comprises the 6 complementarity-determining regions (CDRs) of ipilimumab. In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[00368] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire

FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00369] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00370] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L

encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00371] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00372] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00373] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00374] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and

aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00375] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00376] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00377] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00378] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[00379] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00380] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular

embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00381] In some embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous

vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene.

[00382] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), IL-12 p40 (*e.g.*, human IL-12 p40) or IL-12 p70 (*e.g.*, human IL-12 p70). In specific embodiments, the IL-12 polypeptide is membrane-bound and comprises IL-12 p35 (*e.g.*, human IL-12 p35), or IL-12 p70 (*e.g.*, human IL-12 p70), and a transmembrane domain and a cytoplasmic domain (*e.g.*, the transmembrane and cytoplasmic domains of B7-1, TNFα, or FLT3L). In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[00383] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1).

In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00384] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00385] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L

extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00386] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00387] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain,

and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00388] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00389] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at

least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00390] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00391] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the

transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00392] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00393] In another aspect, provided here is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter; and/or (ii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter. In specific embodiments, the nucleic acid further comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00394] In certain embodiments, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment,

the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00395] In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00396] In some embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the same

orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene. In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), IL-12 p40 (*e.g.*, human IL-12 p40) or IL-12 p70 (*e.g.*, human IL-12 p70). In specific embodiments, the IL-12 polypeptide is membrane-bound and comprises IL-12 p35 (*e.g.*, human IL-12 p35), or IL-12 p70 (*e.g.*, human IL-12 p70), and a transmembrane domain and a cytoplasmic domain (*e.g.*, the transmembrane and cytoplasmic domains of B7-1, TNFα, or FLT3L). In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[00397] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in

GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00398] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00399] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00400] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00401] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another

embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00402] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00403] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L

extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00404] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00405] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8,

9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00406] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00407] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4); (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

[00408] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter. In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00409] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence is a late promoter. In a further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In

another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00410] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00411] In some embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C2L and F3L genes. In another specific

embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third

nucleotide sequence have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene.

[00412] In specific embodiments, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence comprises the 6 complementarity-determining regions (CDRs) of ipilimumab. In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[00413] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), IL-12 p40 (*e.g.*, human IL-12 p40) or IL-12 p70 (*e.g.*, human IL-12 p70). In specific embodiments, the IL-12 polypeptide is membrane-bound and comprises IL-12 p35 (*e.g.*, human IL-12 p35), or IL-12 p70 (*e.g.*, human IL-12 p70), and a transmembrane domain and a cytoplasmic domain (*e.g.*, the transmembrane and cytoplasmic domains of B7-1, TNFα, or FLT3L). In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence

set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[00414] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00415] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of

the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00416] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00417] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00418] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire

cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00419] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00420] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3,

4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00421] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00422] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by

the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00423] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00424] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4); (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter; and/or (iii) a nucleotide sequence comprising at least

one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter. In specific embodiments, the nucleic acid further comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00425] In certain embodiments, the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00426] In certain embodiments, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00427] In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter. In certain embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565

[00428] In some embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia

virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence

is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene.

[00429] In specific embodiments, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence comprises the 6 complementarity-determining regions (CDRs) of ipilimumab. In specific embodiments, the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211. In specific embodiments, the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214. In specific embodiments, the first nucleotide sequence is set forth in SEQ ID NO: 214.

[00430] In specific embodiments, the IL-12 polypeptide is membrane-bound. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), IL-12 p40

(*e.g.*, human IL-12 p40) or IL-12 p70 (*e.g.*, human IL-12 p70). In specific embodiments, the IL-12 polypeptide is membrane-bound and comprises IL-12 p35 (*e.g.*, human IL-12 p35), or IL-12 p70 (*e.g.*, human IL-12 p70)0, and a transmembrane domain and a cytoplasmic domain (*e.g.*, the transmembrane and cytoplasmic domains of B7-1, TNFα, or FLT3L). In specific embodiments, the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212. In specific embodiments, the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215. In specific embodiments, the second nucleotide sequence is set forth in SEQ ID NO: 215.

[00431] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane

and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00432] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00433] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00434] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20,

15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00435] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00436] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the

carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00437] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00438] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the

embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00439] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00440] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00441] In a specific embodiment, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In a further specific embodiment, the third transgene is upstream of the second transgene.

[00442] In some embodiments of the various embodiments and aspects described herein, the deletion in the B8R gene is a deletion of at least 30% of the B8R gene sequence. In other embodiments, the deletion in the B8R gene is a deletion of at least 40% of the B8R gene sequence. In other embodiments, the deletion in the B8R gene is a deletion of at least 50% of the B8R gene sequence. In other embodiments, the deletion in the B8R gene is a deletion of

at least 60% of the B8R gene sequence. In other embodiments, the deletion in the B8R gene is a deletion of at least 70% of the B8R gene sequence. In other embodiments, the deletion in the B8R gene is a deletion of at least 80% of the B8R gene sequence. In other embodiments, the deletion in the B8R gene is a deletion of 30% -90%, 30%-85%, 40%-90%, 40%-85%, 50%-90%, 50%-85%, 60%-90%, 60%-85%, 70%-90%, 70%-85%, 75%-90%, 75%-85%, or 80%-85% of the B8R gene sequence. In a specific embodiment, the deletion in the B8R gene is a deletion of about 75% of the B8R gene sequence. In another specific embodiment, the deletion in the B8R gene is a deletion of about 80% of the B8R gene sequence. In another specific embodiment, the deletion in the B8R gene is a deletion of about 82% of the B8R gene sequence.

[00443] For example, in some embodiments, the deletion in the B8R gene is a deletion of at least 30% of the nucleotide sequence of SEQ ID NO: 591. In other embodiments, the deletion in the B8R gene is a deletion of at least 40% of the nucleotide sequence of SEQ ID NO: 591. In other embodiments, the deletion in the B8R gene is a deletion of at least 50% of the nucleotide sequence of SEQ ID NO: 591. In other embodiments, the deletion in the B8R gene is a deletion of at least 60% of the nucleotide sequence of SEQ ID NO: 591. In other embodiments, the deletion in the B8R gene is a deletion of at least 70% of the nucleotide sequence of SEQ ID NO: 591. In other embodiments, the deletion in the B8R gene is a deletion of at least 80% of the nucleotide sequence of SEQ ID NO: 591. In other embodiments, the deletion in the B8R gene is a deletion of 30% -90%, 30%-85%, 40%-90%, 40%-85%, 50%-90%, 50%-85%, 60%-90%, 60%-85%, 70%-90%, 70%-85%, 75%-90%, 75%-85%, or 80%-85% of the nucleotide sequence of SEQ ID NO: 591. In a specific embodiment, the deletion in the B8R gene is a deletion of about 75% of the nucleotide sequence of SEQ ID NO: 591. In another specific embodiment, the deletion in the B8R gene is a deletion of about 80% of the nucleotide sequence of SEQ ID NO: 591. In another specific embodiment, the deletion in the B8R gene is a deletion of about 82% of the nucleotide sequence of SEQ ID NO: 591.

[00444] In another example, in some embodiments, the deletion in the B8R gene is a deletion of at least 30% of the nucleotide sequence of ACAACACCATGAGATATATTATA ATTCTCGCAGTTTTGTTCATTAATAGTATACACGCTAAAATAACTAGTTATAAGTT TGAATCCGTCAATTTTGATTCCAAAATTGAATGGACTGGGGATGGTCTATACAAT ATATCCCTTAAAAATTATGGCATCAAGACGTGGCAAACAATGTATACAAATGTAC CAGAAGGAACATACGACATATCCGCATTTCCAAAGAATGATTTCGTATCTTTCTG

GGTTAAATTTGAACAAGGCGATTATAAAGTGGAAGAGTATTGTACGGGACTATG
CGTCGAAGTAAAAATTGGACCACCGACTGTAACATTGACTGAATACGACGACCA
TATCAATTTGTACATCGAGCATCCGTATGCTACTAGAGGTAGCAAAAAGATTCCT
ATTTACAAACGCGGTGACATGTGTGATATCTACTTGTTGTATACGGCTAACTTCA
CATTCGGAGATTCTGAAGAACCAGTAACATATGATATCGATGACTACGATTGCAC
GTCTACAGGTTGCAGCATAGACTTTGCCACAACAGAAAAAGTGTGCGTGACAGC
ACAGGGAGCCACAGAAGGGTTTCTCGAAAAAATTACTCCATGGAGTTCGGAAGT
ATGTCTGACACCTAAAAAGAATGTATATACATGTGCAATTAGATCCAAAGAAGA
TGTTCCCAATTTCAAGGACAAAATGGCCAGAGTTATCAAGAGAAAATTTAATAA
ACAGTCTCAATCTTATTTAACTAAATTTCTCGGTAGCACATCAAATGATGTTACC
ACTTTTCTTAGCATGCTTAACTTGACTAAATATTCATAA (SEQ ID NO: 550. In other embodiments, the deletion in the B8R gene is a deletion of at least 40% of the nucleotide sequence of SEQ ID NO: 550. In other embodiments, the deletion in the B8R gene is a deletion of at least 50% of the nucleotide sequence of SEQ ID NO: 550. In other embodiments, the deletion in the B8R gene is a deletion of at least 60% of the nucleotide sequence of SEQ ID NO: 550. In other embodiments, the deletion in the B8R gene is a deletion of at least 70% of the nucleotide sequence of SEQ ID NO: 550. In other embodiments, the deletion in the B8R gene is a deletion of at least 80% of the nucleotide sequence of SEQ ID NO: 550. In other embodiments, the deletion in the B8R gene is a deletion of 30% -90%, 30%-85%, 40%-90%, 40%-85%, 50%-90%, 50%-85%, 60%-90%, 60%-85%, 70%-90%, 70%-85%, 75%-90%, 75%-85%, or 80%-85% of the nucleotide sequence of SEQ ID NO: 550. In a specific embodiment, the deletion in the B8R gene is a deletion of about 75% of the nucleotide sequence of SEQ ID NO: 550. In another specific embodiment, the deletion in the B8R gene is a deletion of about 80% of the nucleotide sequence of SEQ ID NO: 550. In another specific embodiment, the deletion in the B8R gene is a deletion of about 82% of the nucleotide sequence of SEQ ID NO: 550.

[00445] In certain embodiments, the deletion in the B8R gene does not disturb the function of the B9R gene of the vaccinia genome. In certain embodiments, the deletion in the B8R gene does not disturb the expression of the B9R gene. In certain embodiments, the deletion in the B8R gene does not remove the promoter(s) of the B9R gene. In certain embodiments, the deletion in the B8R gene does not remove the transcriptional regulatory sequences of the B9R gene. In a specific embodiment, the only sequence of the B8R gene that remains after deletion is the sequence necessary for proper B9R function and/or expression. In a specific

embodiment, the deletion in the B8R gene does not remove a nucleotide sequence comprising AAAATTTAATAAACA (SEQ ID NO: 551). In another specific embodiment, the deletion in the B8R gene does not remove the nucleotide sequence AAAATTTAATAAACA (SEQ ID NO: 551). In a specific embodiment, the only sequence of the B8R gene that remains is the nucleotide sequence of GATGTTCCCAATTTCAAGGACAAAATGGCCAGAGTTATCAAGAGAAAATTTAAT AAACAGTCTCAATCTTATTTAACTAAATTTCTCGGTAGCACATCAAATGATGTTA CCACTTTTCTTAGCATGCTTAACTTGACTAAATATTCATAA (SEQ ID NO: 552).

[00446] In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome is derived from the genome of a Copenhagen strain vaccinia virus. In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome is derived from the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590). In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome comprises the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590).

[00447] In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 of the nucleotide polymorphisms identified in Table 46. In some embodiments of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 1-3, 1-5, 2-4, 2-5, 1-9, 2-8, 4-8, 6-8, 1-9, 2-9, 4-9, 6-9, 7-9, 1-10, 2-10, 5-10, or 8-10 of the nucleotide polymorphisms identified in Table 46. In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 of the nucleotide polymorphisms identified in Table 46. In some embodiments of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 11-20, 12-15, 15-20, or 18-20 of the nucleotide polymorphisms identified in Table 46. In certain embodiments of the embodiments and aspects provided herein, the recombinant vaccinia

virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 1-20, 1-15, 5-20, or 10-20 of the nucleotide polymorphisms identified in Table 46. In some of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises all of the nucleotide polymorphisms identified in Table 46. In certain of such embodiments, the recombinant vaccinia virus genome may be engineered to comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In some of such embodiments, the recombinant virus genome may be engineered to comprise 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In certain of such embodiments, the recombinant vaccinia virus genome may be engineered to comprise 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, or 32 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In some of such embodiments, the recombinant virus genome may be engineered to comprise deletions in C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, and the following genes in the 3′ inverted terminal repeat (ITR): B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R, and insertions of one, two, or three of the transgene(s) described herein.

[00448] In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 1, 2, 3, or 4 of the nucleotide polymorphisms identified in Table 46 that are

synonymous variants. In some embodiments of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 1, 2, 3, 4, 5, 6 or 7 of the nucleotide polymorphisms identified in Table 46 that are not in a protein coding region. In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 1, 2, 3, 4, 5, 6 or 7 of the nucleotide polymorphisms identified in Table 46 that result in change in the amino acid sequence. In some embodiments of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises 1 or 2 of the nucleotide polymorphisms identified in Table 46 that result in a frameshift. In certain of such embodiments, the recombinant vaccinia virus genome may be engineered to comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In some of such embodiments, the recombinant virus genome may be engineered to comprise 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In certain of such embodiments, the recombinant vaccinia virus genome may be engineered to comprise 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, or 32 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In some of such embodiments, the recombinant virus genome may be engineered to comprise deletions in C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, and the following genes in the 3′ inverted terminal repeat (ITR): B19R, and B20R,

B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R, and insertions of one, two, or three of the transgene(s) described herein.

[00449] In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises the nucleotide polymorphisms found in 1, 2, 3, 4, 5, 6 or 7 of the genes identified in Table 46. In some of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises of the nucleotide polymorphisms found in 8, 9, 10, 11, 12, 12 or 13 of the genes identified in Table 46. In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises the nucleotide polymorphisms nucleotide polymorphisms found in all of the genes identified in Table 46. In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises the nucleotide polymorphisms found in 1-5, 5-10, 1-13, 5-13, or 10-13 of the genes identified in Table 46. In certain of such embodiments, the recombinant vaccinia virus genome may be engineered to comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In some of such embodiments, the recombinant virus genome may be engineered to comprise 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In certain of such embodiments, the recombinant vaccinia virus genome may be engineered to comprise 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, or 32 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R,

B15R, B16R, B17L, B18R, B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In some of such embodiments, the recombinant virus genome may be engineered to comprise deletions in C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, and the following genes in the 3′ inverted terminal repeat (ITR): B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R, and insertions of one, two, or three of the transgene(s) described herein.

[00450] In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises the nucleotide polymorphism(s) identified in Table 46 for vaccinia gene C14L, C2L, C1L, N2L, F3L, F13L, F16L, G7L, L3L, J3R, D6R, A41L, or A46R. In some of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises of the nucleotide polymorphisms identified in Table 46 for vaccinia gene C14L, C2L, C1L, N2L, F3L, F13L, F16L, G7L, L3L, J3R, D6R, A41L, and A46R. In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590),except that the nucleotide sequence comprises the nucleotide polymorphisms identified in Table 46 for 1, 2, 3, 4, 5, 6, or 7 of the following vaccinia genes: C14L, C2L, C1L, N2L, F3L, F13L, F16L, G7L, L3L, J3R, D6R, A41L, and A46R. In certain of the embodiments and aspects provided herein, the recombinant vaccinia virus genome comprises a nucleotide sequence identical to the nucleotide sequence of GenBank Accession No. M35027.1 (SEQ ID NO: 590) except that the nucleotide sequence comprises the nucleotide polymorphisms identified in Table 46 for 8, 9, 10, 11, 12, or 13 of the following vaccinia genes: C14L, C2L, C1L, N2L, F3L, F13L, F16L, G7L, L3L, J3R, D6R, A41L, and A46R. In certain of such embodiments, the recombinant vaccinia virus genome may be engineered to comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the

transgene(s) described herein. In some of such embodiments, the recombinant virus genome may be engineered to comprise 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In certain of such embodiments, the recombinant vaccinia virus genome may be engineered to comprise 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, or 32 of the deletions in the vaccinia virus genes identified herein (e.g., C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R), and insertions of one, two, or three of the transgene(s) described herein. In some of such embodiments, the recombinant virus genome may be engineered to comprise deletions in C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, and the following genes in the 3′ inverted terminal repeat (ITR): B19R, and B20R, B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R, and insertions of one, two, or three of the transgene(s) described herein.

[00451] In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome comprises the nucleotide sequence of SEQ ID NO: 210. In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome comprises a nucleotide sequence that is identical to the nucleotide sequence of SEQ ID NO: 210 except for 1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the nucleotide polymorphisms identified in Table 46.

[00452] In certain embodiments, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210; and (b) one, two, or three of the following: (i) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4) (for example, wherein the first nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 214); (ii) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide (for example, wherein the second nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 215); and (iii) a third transgene comprising a third nucleotide sequence

encoding FLT3L (for example, wherein the third nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 216).

[00453] In certain embodiments, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210; and (b) two or three of the following: (i) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4) (for example, wherein the first nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 214); (ii) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide (for example, wherein the second nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 215); and (iii) a third transgene comprising a third nucleotide sequence encoding FLT3L (for example, wherein the third nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 216).

[00454] In certain embodiments, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210; and (b): (i) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4) (for example, wherein the first nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 214); (ii) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide (for example, wherein the second nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 215); and (iii) a third transgene comprising a third nucleotide sequence encoding FLT3L (for example, wherein the third nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 216)

[00455] In specific embodiments of the above wherein the nucleic acid comprises the first transgene, the nucleic acid further comprises a nucleotide sequence comprising an H5R promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody. In specific embodiments of the above wherein the nucleic acid comprises the second transgene, the nucleic acid further comprises a nucleotide sequence comprising a late promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In specific embodiments of the above wherein the nucleic acid comprises the third transgene, the nucleic acid further comprises a nucleotide sequence comprising a B8R promoter operably linked to

the third nucleotide sequence encoding FLT3L. In specific embodiments of the above wherein the nucleic acid comprises the third transgene, the nucleic acid further comprises a nucleotide sequence comprising a B19R promoter operably linked to the third nucleotide sequence encoding FLT3L. In specific embodiments of the above wherein the nucleic acid comprises the third transgene, the nucleic acid further comprises a nucleotide sequence comprising a B8R promoter and a B19R promoter operably linked to the third nucleotide sequence encoding FLT3L. In specific embodiments of the above, the endogenous vaccinia virus genes that flank the first nucleotide sequence have the same orientation, and the first nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the first nucleotide sequence. In specific embodiments of the above, the endogenous vaccinia virus genes that flank the second nucleotide sequence have the same orientation, and the second nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the second nucleotide sequence. In specific embodiments of the above, the endogenous vaccinia virus genes that flank the third nucleotide sequence have the same orientation, and the third nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the third nucleotide sequence. In a specific embodiment of the above, the nucleic acid comprises the first transgene, the second transgene, and the third transgene, and the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00456] In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome comprises the nucleotide sequence of SEQ ID NO: 624. In certain embodiments of the various embodiments and aspects described herein, the recombinant vaccinia virus genome comprises a nucleotide sequence that is identical to the nucleotide sequence of SEQ ID NO: 624 except for 1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the nucleotide polymorphisms identified in Table 46.

[00457] In certain embodiments, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 624; and (b) one, two, or three of the following: (i) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4) (for example, wherein the first

nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 214); (ii) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide (for example, wherein the second nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 215); and (iii) a third transgene comprising a third nucleotide sequence encoding FLT3L (for example, wherein the third nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 216). In specific embodiments, the nucleic acid further comprises a promoter, such as described herein, operably linked to the first nucleotide sequence, a promoter, such as described herein, operably linked to the second nucleotide sequence, or a promoter, such as described herein, operably linked to the third promoter. In specific embodiments, the nucleic acid further comprises a promoter, such as described herein, operably linked to the first nucleotide sequence, a promoter, such as described herein, operably linked to the second nucleotide sequence, and a promoter, such as described herein, operably linked to the third promoter. In specific embodiments, the first transgene, second transgene and/or third transgene are inserted into a locus or loci described herein.

[00458] In certain embodiments, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 624; and (b) two or three of the following: (i) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4) (for example, wherein the first nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 214); (ii) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide (for example, wherein the second nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 215); and (iii) a third transgene comprising a third nucleotide sequence encoding FLT3L (for example, wherein the third nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 216). In specific embodiments, the nucleic acid further comprises a promoter, such as described herein, operably linked to the first nucleotide sequence, a promoter, such as described herein, operably linked to the second nucleotide sequence, or a promoter, such as described herein, operably linked to the third promoter. In specific embodiments, the two or three transgenes are inserted into a locus or loci described herein.

[00459] In certain embodiments, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 624; and (b): (i) a first transgene comprising a first nucleotide sequence

encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4) (for example, wherein the first nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 214); (ii) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide (for example, wherein the second nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 215); and (iii) a third transgene comprising a third nucleotide sequence encoding FLT3L (for example, wherein the third nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO: 216). In specific embodiments, the nucleic acid further comprises a promoter, such as described herein, operably linked to the first nucleotide sequence, a promoter, such as described herein, operably linked to the second nucleotide sequence, or a promoter, such as described herein, operably linked to the third promoter. In specific embodiments, the nucleic acid further comprises a promoter, such as described herein, operably linked to the first nucleotide sequence, a promoter, such as described herein, operably linked to the second nucleotide sequence, and a promoter, such as described herein, operably linked to the third promoter. In specific embodiments, the first transgene, second transgene and third transgene are inserted into a locus or loci described herein.

[00460] In specific embodiments of the above wherein the nucleic acid comprises the first transgene, the nucleic acid further comprises a nucleotide sequence comprising an H5R promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody. In specific embodiments of the above wherein the nucleic acid comprises the second transgene, the nucleic acid further comprises a nucleotide sequence comprising a late promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In specific embodiments of the above wherein the nucleic acid comprises the third transgene, the nucleic acid further comprises a nucleotide sequence comprising a B8R promoter operably linked to the third nucleotide sequence encoding FLT3L. In specific embodiments of the above wherein the nucleic acid comprises the third transgene, the nucleic acid further comprises a nucleotide sequence comprising a B19R promoter operably linked to the third nucleotide sequence encoding FLT3L. In specific embodiments of the above wherein the nucleic acid comprises the third transgene, the nucleic acid further comprises a nucleotide sequence comprising a B8R promoter and a B19R promoter operably linked to the third nucleotide sequence encoding FLT3L. In specific embodiments of the above, the endogenous vaccinia virus genes that flank the first nucleotide sequence have the same orientation, and the first

nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the first nucleotide sequence. In specific embodiments of the above, the endogenous vaccinia virus genes that flank the second nucleotide sequence have the same orientation, and the second nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the second nucleotide sequence. In specific embodiments of the above, the endogenous vaccinia virus genes that flank the third nucleotide sequence have the same orientation, and the third nucleotide sequence is in the same orientation as the endogenous vaccinia virus genes that flank the third nucleotide sequence. In specific embodiments, the nucleic acid further comprises a deletion in the B8R gene. In a specific embodiment of the above, the nucleic acid comprises the first transgene, the second transgene, and the third transgene, and further comprises a deletion in the B8R gene, and the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00461] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4); (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to

the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence. In specific embodiments, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the first transgene is inserted between the partial B14R and B29R vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the third transgene is upstream of the second transgene. In specific embodiments, the third transgene is downstream of the second transgene. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00462] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is inserted between the partial C2L and F3L vaccinia genes; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is inserted into the locus of the deletion in the B8R gene; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third

transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. .

[00463] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is inserted between the partial C2L and F3L vaccinia genes; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is inserted into the locus of the deletion in the B8R gene; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third

transgene is downstream of the second transgene; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565

[00464] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is inserted between the partial B14R and B29R vaccinia genes; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is inserted into the locus of the deletion in the B8R gene; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably

linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00465] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene; (b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is inserted between the partial B14R and B29R vaccinia genes; (d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is inserted into the locus of the deletion in the B8R gene; and (e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; and wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to

the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In a particular embodiment, the nucleic acid comprises a recombinant vaccinia virus genome that comprises a deletion in the B8R gene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00466] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214; (c) a second transgene comprising a second nucleotide sequence encoding an Interleukin 12 (IL-12) polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215; and (d) a third transgene comprising a third nucleotide sequence encoding FMS-like tyrosine kinase 3 ligand (FLT3L), wherein the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00467] In some embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have the same orientation, the first nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the first nucleotide sequence have opposite orientations, the first nucleotide sequence is in the same orientation

as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the first nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the first nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the first nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the first nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have the same orientation, the second nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the second nucleotide sequence have opposite orientations, the second nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the second nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the second nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the second nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the second nucleotide sequence is the B13R gene. In some embodiments, when the flanking endogenous

vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have the same orientation, the third nucleotide sequence is in the reverse orientation relative to the flanking endogenous vaccinia virus genes. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 5' end of the recombinant vaccinia virus genome. In other embodiments, when the flanking endogenous vaccinia virus genes of the third nucleotide sequence have opposite orientations, the third nucleotide sequence is in the same orientation as the flanking endogenous vaccinia virus gene that is closer to the 3' end of the recombinant vaccinia virus genome. In a specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C2L and F3L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the C3L and F4L genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B14R and B29R genes. In another specific embodiment, the flanking endogenous vaccinia virus genes of the third nucleotide sequence are the B13R and B29R genes. In yet another embodiment, the third nucleotide sequence is in the same orientation as an endogenous vaccinia gene adjacent to the third nucleotide sequence. In a specific embodiment, the endogenous vaccinia gene adjacent to the third nucleotide sequence is the B13R gene. In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody. In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an H5R promoter, a pS promoter, or a LEO promoter. In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an H5R promoter (*e.g.*, an early H5R promoter, a late H5R promoter, or an early H5R promoter and a late H5R promoter).

[00468] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide. In a specific embodiment, the at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide is a late promoter. In a

further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter. In another further specific embodiment, the late promoter comprises the nucleotide sequence of SEQ ID NO: 561. In another embodiment, the F17R promoter comprises the nucleotide sequence of SEQ ID NO:563. In yet another embodiment, the D13L promoter comprises the nucleotide sequence of SEQ ID NO:562.

[00469] In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence encoding FLT3L. In a specific embodiment, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, and/or a B2R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B19R promoter. In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In a particular embodiment, the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567. In a particular embodiment, the F11L promoter comprises the nucleotide sequence of SEQ ID NO: 568. In a particular embodiment, the B2R promoter comprises the nucleotide sequence of SEQ ID NO: 569.

[00470] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the

at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence. In specific embodiments, the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In specific embodiments, the third transgene is upstream of the second transgene. In specific embodiments, the third transgene is downstream of the second transgene. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00471] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and

the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

[00472] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second

nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

[00473] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first

nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

[00474] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which

comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

[00475] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

[00476] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

[00477] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

[00478] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

[00479] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early

promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

[00480] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first

nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

[00481] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R

promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

[00482] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third

nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter. In specific embodiments, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

[00483] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at

least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00484] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at

least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00485] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at

least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00486] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter; (ii) a nucleotide sequence comprising at

least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter. In specific embodiments, the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter. In specific embodiments, the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554. In specific embodiments, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00487] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least

one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557. In specific embodiments, the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563. In specific embodiments, the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00488] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide

sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557. In specific embodiments, the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563. In specific embodiments, the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00489] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO:

557. In specific embodiments, the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563. In specific embodiments, the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00490] In another aspect, provided herein is a nucleic acid comprising a recombinant vaccinia virus genome, comprising: (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene; (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4 (*e.g.*, human CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is inserted between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210; (c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is inserted into the locus of the deletion in the B8R gene; and (d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is inserted into the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; wherein the nucleic acid further comprises: (i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter; (ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and (iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter. In specific embodiments, the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557. In specific embodiments, the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563. In specific embodiments, the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

[00491] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia F3L gene. In another embodiment, the first transgene is inserted between vaccinia genes C3L and F4L. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the first transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene is inserted adjacent to the B13R gene.

[00492] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia C2L gene. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia F3L gene. In another embodiment, the second transgene is inserted between vaccinia genes C3L and F4L. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene, the second transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene, the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the second transgene is inserted adjacent to the B13R gene.

[00493] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene. In another embodiment, the third

transgene is inserted adjacent to the partial vaccinia F3L gene. In another embodiment, the third transgene is inserted between vaccinia genes C3L and F4L. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the third transgene, the third transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the third transgene, the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the third transgene is inserted adjacent to the B13R gene.

[00494] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene and the second transgene are inserted between the partial C2L and F3L vaccinia genes. In another embodiment, the first transgene and the second transgene are inserted adjacent to the partial vaccinia C2L gene. In another embodiment, the first transgene and the second transgene are inserted adjacent to the partial vaccinia F3L gene. In another embodiment, the first transgene and the second transgene are inserted between vaccinia genes C3L and F4L. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene and the second transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene and the second transgene are inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene and the second transgene are inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene and the second transgene are inserted adjacent to the B13R gene.

[00495] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes. In another embodiment, the first transgene and the third transgene are inserted adjacent to the partial vaccinia C2L gene. In another embodiment, the first transgene and the

third transgene are inserted adjacent to the partial vaccinia F3L gene. In another embodiment, the first transgene and the third transgene are inserted between vaccinia genes C3L and F4L. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene and the third transgene are inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene and the third transgene are inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene and the third transgene are inserted adjacent to the B13R gene.

[00496] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes. In another embodiment, the second transgene and the third transgene are inserted adjacent to the partial vaccinia C2L gene. In another embodiment, the second transgene and the third transgene are inserted adjacent to the partial vaccinia F3L gene. In another embodiment, the second transgene and the third transgene are inserted between vaccinia genes C3L and F4L. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene and the third transgene are inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the second transgene and the third transgene are inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the second transgene and the third transgene are inserted adjacent to the B13R gene.

[00497] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first

transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia F3L gene, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted between vaccinia genes C3L and F4L, and the second transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia C2L gene, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia F3L gene, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted between vaccinia genes C3L and F4L, and the first transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, and the second transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, and the first transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are

deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the second transgene, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the B13R gene.

[00498] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia F3L gene, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted between vaccinia genes C3L and F4L, and the third transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the third transgene is inserted between the partial C2L and

F3L vaccinia genes, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia F3L gene, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted between vaccinia genes C3L and F4L, and the first transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, and the third transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, and the first transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the first transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the B13R gene.

In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene and the third transgene, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the B13R gene.

[00499] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia C2L gene, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia F3L gene, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted between vaccinia genes C3L and F4L, and the third transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia F3L gene, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted between vaccinia genes C3L and F4L, and the second transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the

second transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, and the third transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, and the second transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the second transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the second transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the second transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the second transgene and the third transgene, the third transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the third transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the third transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the B13R gene.

[00500] In some embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene, the second transgene, and the third transgene are inserted between the partial C2L and F3L vaccinia genes. In another embodiment, the first transgene, the second transgene, and the third transgene are inserted adjacent to the partial vaccinia C2L gene. In another embodiment, the first transgene, the second transgene, and the third transgene are inserted adjacent to the partial vaccinia F3L gene. In another embodiment, the first transgene, the second transgene, and the third transgene are inserted between vaccinia genes C3L and F4L. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene, the second transgene, and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene, the second transgene, and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene, the second transgene, and the third transgene are inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene, the second transgene, and the third transgene are inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene, the second transgene, and the third transgene are inserted adjacent to the B13R gene.

[00501] In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia F3L gene, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene is inserted between vaccinia genes C3L and F4L, and the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic

acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia C2L gene, and the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia F3L gene, and the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene is inserted between vaccinia genes C3L and F4L, and the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene, and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia F3L gene, and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene. In another embodiment, the third transgene is inserted between vaccinia genes C3L and F4L, and the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the second transgene are inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene and the second transgene are inserted adjacent to the partial vaccinia C2L gene, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene and the second transgene are inserted adjacent to the partial vaccinia F3L gene, and the third transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene and the second transgene are inserted between vaccinia genes C3L and F4L, and the third transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second

transgene and the third transgene, the first transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene and the third transgene are inserted adjacent to the partial vaccinia C2L gene, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene and the third transgene are inserted adjacent to the partial vaccinia F3L gene, and the second transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the first transgene and the third transgene are inserted between vaccinia genes C3L and F4L, and the second transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene and the third transgene are is inserted adjacent to the partial vaccinia C2L gene, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene and the third transgene are inserted adjacent to the partial vaccinia F3L gene, and the first transgene is inserted into the locus of the deletion in the B8R gene. In another embodiment, the second transgene and the third transgene are inserted between vaccinia genes C3L and F4L, and the first transgene is inserted into the locus of the deletion in the B8R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted within between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L; and the second transgene and the third transgene are inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In

another embodiment, the second transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L; and the first transgene and the third transgene are inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, and the first transgene and the second transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L; and the first transgene and the second transgene are inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the second transgene are inserted between the partial C2L and F3L vaccinia genes, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene and the second transgene are inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L; and the third transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene and the third transgene are inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L; and the second transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the

first transgene, the second transgene and the third transgene, the second transgene and the third transgene are inserted between the partial C2L and F3L vaccinia genes, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene and the third transgene are inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L; and the first transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene and the third transgene are inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene and the third transgene are inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene and the third transgene are inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the third transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the third transgene are inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the third transgene are inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the third transgene are inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted into the locus of the deletion in the B8R gene,

and the first transgene and the second transgene are inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the second transgene are inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the second transgene are inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene and the second transgene are inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene and the second transgene are inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the first transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the

second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the partial vaccinia B14R gene. In another embodiment, the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the partial vaccinia B29R gene. In particular embodiments wherein the B14R to B29R genes are deleted, the second transgene and the third transgene are inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the B13R gene.

[00502] In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, the second transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, the second transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the first transgene is inserted between the partial C2L and F3L vaccinia genes, the third transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the first transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, the third transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia

genes, the first transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, the first transgene is inserted into the locus of the deletion in the B8R gene, and the third transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the second transgene is inserted between the partial C2L and F3L vaccinia genes, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the second transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, the third transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene, inserted adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, the first transgene is inserted into the locus of the deletion in the B8R gene, and the second transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene. In other embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises the first transgene, the second transgene and the third transgene, the third transgene is inserted between the partial C2L and F3L vaccinia genes, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted between the partial B14R and B29R vaccinia genes. In another embodiment, the third transgene is inserted adjacent to the partial vaccinia C2L gene, inserted

adjacent to the partial vaccinia F3L gene, or inserted between vaccinia genes C3L and F4L, the second transgene is inserted into the locus of the deletion in the B8R gene, and the first transgene is inserted adjacent to the partial vaccinia B14R gene, inserted adjacent to the partial vaccinia B29R gene, or, when the B14R to B29R genes are deleted, inserted adjacent to the B13R gene.

[00503] In various embodiments and aspects described herein wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 210, the partial C2L and F3L vaccinia genes are partial C2L and F3L vaccinia genes in SEQ ID NO: 210. In various embodiments and aspects described herein wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 210, the partial B14R and B29R vaccinia genes are partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

[00504] In various embodiments and aspects described herein wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 624, the partial C2L and F3L vaccinia genes are partial C2L and F3L vaccinia genes in SEQ ID NO: 624. In various embodiments and aspects described herein wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 624, the partial B14R and B29R vaccinia genes are partial B14R and B29R vaccinia genes in SEQ ID NO: 624.

[00505] In a specific embodiment of the various embodiments and aspects described herein, insertion into the partial C2L and F3L vaccinia genes is insertion within the boundaries of a 5p deletion present in the recombinant vaccinia virus genome. In a specific embodiment of the various embodiments and aspects described herein, insertion between the partial B14R and B29R vaccinia genes is insertion within the boundaries of a 3p deletion present in the recombinant vaccinia virus genome.

[00506] In some embodiments of the various embodiments and aspects described herein, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence is a full-length antibody (for example, a full-length human antibody, a full-length humanized antibody, or a full-length mouse antibody). In a specific embodiment, the first nucleotide sequence encodes a polypeptide that comprises the heavy chain and light chains of ipilimumab linked by a cleavage peptide, for example, a self-cleavage peptide, such as a 2A self-cleaving peptide (*e.g.*, a T2A peptide). In another specific embodiment, the first nucleotide sequence encodes a polypeptide that comprises the heavy chain signal peptide and heavy chain, and light chain signal peptide and light chain of ipilimumab, linked by a cleavage peptide, for example, a self-cleavage peptide, such as a 2A self-cleaving peptide

(*e.g.*, a T2A peptide). In other embodiments of the various embodiments and aspects described herein, the anti-CTLA-4 antibody or antigen-binding fragment thereof encoded by the first nucleotide sequence is a single chain antibody (for example, a single chain human antibody, single chain humanized antibody, or a single chain mouse antibody, such as, for example, 9D9).

[00507] In a specific embodiment of the various embodiments and aspects described herein, the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody or antigen-binding fragment thereof is a B8R promoter. In another specific embodiment of the various embodiments and aspects described herein, the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody or antigen-binding fragment thereof is an H5R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564.

[00508] In some embodiments of the various embodiments and aspects described herein, the IL-12 peptide encoded by the second nucleotide sequence is a membrane-bound version of the cytokine. In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35) and a transmembrane domain. In a specific embodiment, the IL-12 polypeptide consists of IL-12 p35 (*e.g.*, human IL-12 p35) and a transmembrane domain (IL12-TMp35). In specific embodiments, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35), a transmembrane domain and a cytoplasmic domain. In a specific embodiment, the IL-12 polypeptide consists of IL-12 p35 (*e.g.*, human IL-12 p35), a transmembrane domain and a cytoplasmic domain. The transmembrane domain can be derived from any membrane-bound protein (*e.g.*, B7-1, membrane-bound TNFα, or membrane-bound FLT3L). The cytoplasmic domain can be derived from any protein that contains a cytoplasmic domain (*e.g.*, B7-1, TNFα, or FLT3L). In a specific embodiment, the IL-12 polypeptide comprises IL-12 p35 (*e.g.*, human IL-12 p35) and a B7 cytoplasmic and membrane domain from the B7-1 antigen, a commonly used element for mammalian surface display. In a specific embodiment, the IL-12 polypeptide consists of IL-12 p35 (*e.g.*, human IL-12 p35) and a B7 cytoplasmic and membrane domain from the B7-1 antigen. In specific embodiments, the IL-12 polypeptide comprises IL-12 p70 (*e.g.*, human IL-12 p70), which comprises a p40 subunit (*e.g.*, human IL-12 p40) and a p35 subunit (*e.g.*, human IL-12 p35), and a transmembrane domain. In a specific embodiment, the IL-12 polypeptide consists of IL-12 p70 (*e.g.*, human IL-12 p70), which comprises a p40 subunit (*e.g.*, human IL-12 p40) and a p35 subunit (*e.g.*, human IL-12 p35), and a transmembrane domain (IL12-TMp70, or

p40-p35-TM). In specific embodiments, the IL-12 polypeptide comprises IL-12 p70 (*e.g.*, human IL-12 p70), which comprises a p40 subunit (*e.g.*, human IL-12 p40) and a p35 subunit (*e.g.*, human IL-12 p35), and a transmembrane domain and a cytoplasmic domain. In a specific embodiment, the IL-12 polypeptide comprises IL-12 p70 (*e.g.*, human IL-12 p70), which comprises a p40 subunit (*e.g.*, human IL-12 p40) and a p35 subunit (*e.g.*, human IL-12 p35), and a transmembrane domain and a cytoplasmic domain. The transmembrane domain can be derived from any membrane-bound protein (*e.g.*, B7-1, membrane-bound TNFα, or membrane-bound FLT3L). The cytoplasmic domain can be derived from any protein that contains a cytoplasmic domain (*e.g.*, B7-1, TNFα, or FLT3L). In a specific embodiment, the IL-12 polypeptide comprises IL-12 p70 (*e.g.*, human IL-12 p70), which comprises a p40 subunit (*e.g.*, human IL-12 p40) and a p35 subunit (*e.g.*, human IL-12 p35), and a B7 cytoplasmic and membrane domain from the B7-1 antigen. In a specific embodiment, the IL-12 polypeptide consists of IL-12 p70 (*e.g.*, human IL-12 p70), which comprises a p40 subunit (*e.g.*, human IL-12 p40) and a p35 subunit (*e.g.*, human IL-12 p35), and a B7 cytoplasmic and membrane domain from the B7-1 antigen. In certain embodiments, the IL-12 polypeptide is a human IL-12 polypeptide (for example, human IL12-TMp35 or human IL12-TMp70). In certain embodiments, the IL-12 polypeptide is a mouse IL-12 polypeptide (for example, mouse IL12-TMp35 or mouse IL12-TMp70).

[00509] In a specific embodiment of the various embodiments and aspects described herein, the at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide is a late promoter having the nucleotide sequence of SEQ ID NO: 561. In a specific embodiment of the various embodiments and aspects described herein, the at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide is a B8R promoter. In a specific embodiment of the various embodiments and aspects described herein, the at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide is a late promoter having the nucleotide sequence of SEQ ID NO: 561 and a B8R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564.

[00510] In specific embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of FLT3L. In particular embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of human FLT3L. In certain embodiments, the FLT3L encoded by the third nucleotide sequence is a soluble form of the human FLT3L set forth in GenBank Accession No. U03858.1. For example, in specific embodiments, the FLT3L

encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In other examples, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain (e.g., the transmembrane domain of the human FLT3L set forth in GenBank Accession No. U03858.1). In one embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and the entire FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, or 4 of the N-terminal amino acid residues of the FLT3L cytoplasmic domain. In certain of the embodiments and aspects, the transmembrane and cytoplasmic domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00511] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00512] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00513] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00514] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another

embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, the entire cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00515] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00516] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L

extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, or at least 95% of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00517] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks the entire FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00518] In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In another embodiment, the FLT3L encoded by the third nucleotide sequence lacks at least 80%, at least 85%, at least 90%, or at least 95% of the FLT3L transmembrane domain, 1, 2, 3, 4, 5, 6, 7, 8,

9, 10, 12, 13, 14, or 15 of the N-terminal amino acid residues of the cytoplasmic domain, and 1-5, 1-10, 5-10, 10-20, 15-20, 1-20, 5-20, or 10-20 amino acids from the carboxy-terminus of the FLT3L extracellular domain. In certain of the embodiments and aspects, the transmembrane, cytoplasmic and extracellular domains are of the FLT3L sequence set forth in GenBank Accession No. U03858.1.

[00519] In a specific embodiment, the FLT3L encoded by the third nucleotide sequence is an X7 isoform and the third nucleotide sequence lacks a 179-nucleotide sequence as described in Lyman *et al.*, 1994, Blood 83:2795-2801. In specific embodiments, the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213. In specific embodiments, the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216. In specific embodiments, the third nucleotide sequence is set forth in SEQ ID NO: 216.

[00520] In a specific embodiment of the various embodiments and aspects described herein, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter. In a specific embodiment of the various embodiments and aspects described herein, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B19R promoter. In a specific embodiment of the various embodiments and aspects described herein, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter and a B19R promoter. In a particular embodiment, the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564. In a particular embodiment, the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

[00521] The invention also contemplates nucleic acids as described herein which further comprise a fourth transgene comprising a fourth nucleotide sequence encoding a detectable marker, *e.g.*, a fluorescent marker (for example, a green fluorescent protein (GFP) such as an enhanced GFP (eGFP)). In certain embodiments, the nucleic acid further comprises a nucleotide sequence comprising at least one promoter operably linked to the fourth nucleotide sequence encoding the fluorescent marker. In certain embodiments, the fourth nucleotide sequence encoding the fluorescent marker is linked and downstream of one of the first, second, and third nucleotide sequences.

[00522] In a specific embodiment, the at least one promoter operably linked to the fourth nucleotide sequence encoding the fluorescent marker is an E3L promoter. In another specific embodiment, the at least one promoter operably linked to the fourth nucleotide sequence encoding the fluorescent marker is a p7.5 promoter.

[00523] In specific embodiments, provided herein is a vector comprising a nucleotide sequence of SEQ ID NO: 210 or SEQ ID NO: 624 with transgene(s) identified in Table 45, inserted into the locus (loci) identified in Table 45, and operably linked to the promoter(s) identified in Table 45. In specific embodiments, provided herein is a vector as described in Table 45.

[00524] It is also contemplated that the first transgene, the second transgene, the third transgene, and/or the fourth transgene can be inserted into the TK gene locus. The other transgenes (if any) can be inserted at other loci, for example, between the partial C2L and F3L vaccinia genes, the locus of the deletion in the B8R gene, between the partial B14R and B29R vaccinia genes, and/or the HA gene locus. In some embodiments, the recombinant vaccinia virus genome comprises a deletion in the TK gene. In a specific embodiment, the first transgene, the second transgene, the third transgene, and/or the fourth transgene is inserted into the locus of the deletion in the TK gene. In other embodiments, the TK gene is not deleted but the first transgene, the second transgene, the third transgene, and/or the fourth transgene is inserted into the TK gene and disrupts the function of the TK gene.

[00525] In other embodiments, the recombinant vaccinia virus genome comprises a functional, *e.g.*, wild-type, TK gene and none of the transgene(s) is inserted into the TK gene locus. A wild-type TK gene includes a TK gene naturally found in a vaccinia virus genome.

[00526] It is also contemplated that the first transgene, the second transgene, the third transgene, and/or the fourth transgene can be inserted into the HA gene locus. The other transgenes (if any) can be inserted at other loci, for example, between the partial C2L and F3L vaccinia genes, the locus of the deletion in the B8R gene, between the partial B14R and B29R vaccinia genes, and/or the TK gene locus. In some embodiments, the recombinant vaccinia virus genome comprises a deletion in the HA gene. In a specific embodiment, the first transgene, the second transgene, the third transgene, and/or the fourth transgene is inserted into the locus of the deletion in the HA gene. In other embodiments, the HA gene is not deleted but the first transgene, the second transgene, the third transgene, and/or the fourth transgene is inserted into the HA gene and disrupts the function of the HA gene.

[00527] In other embodiments, the recombinant vaccinia virus genome comprises a functional, *e.g.*, wild-type, HA gene and none of the transgene(s) is inserted into the HA gene locus. A wild-type HA gene includes a HA gene naturally found in a vaccinia virus genome.

[00528] In certain embodiments of the various embodiments and aspects described herein, at least one promoter is operably linked to the first nucleotide sequence, the second

nucleotide sequence and/or the third nucleotide sequence, wherein the at least one promoter is an early promoter, a late promoter, or an early/late promoter. In particular embodiments, the at least one promoter is an early promoter and a late promoter. In specific embodiments, a late promoter may comprise a TAAAT nucleotide sequence (SEQ ID NO. 631).

[00529] In certain embodiments of the various embodiments and aspects described herein, the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an early promoter, a late promoter, or an early/late promoter. In particular embodiments, the at least one promoter is an early promoter and a late promoter. In specific embodiments, a late promoter may comprise a TAAAT nucleotide sequence (SEQ ID NO. 631). In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R early promoter (*e.g.*, comprising the nucleotide sequence of AAAAATGAAAATAAA (SEQ ID NO. 630) or TAAAAAATGAAAATAAATACAAAGGTTCTT (SEQ ID NO. 553), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R late promoter (*e.g.*, comprising the nucleotide sequence of TAAAT (SEQ ID NO. 631), TCTTGAGGGTTGTGTTAAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 632), or AAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 554), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). In a specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is an H5R early promoter (*e.g.*, comprising the nucleotide sequence of AAAAATGAAAATAAA (SEQ ID NO. 630) or TAAAAAATGAAAATAAATACAAAGGTTCTT (SEQ ID NO. 553), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence) and an H5R late promoter (*e.g.*, comprising the nucleotide sequence of TAAAT (SEQ ID NO. 631), TCTTGAGGGTTGTGTTAAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 632), or AAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 554), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). When the H5R late promoter comprises the nucleotide sequence of TAAAT (SEQ ID NO. 631), in one embodiment, the nucleic acid comprises an intervening sequence between TAAAT and the ATG translation initiation codon (for example, an intervening sequence that is about 10, 20, 30, or 40-nucleotide in length); in another embodiment, there is no intervening sequence between TAAAT and the ATG translation initiation codon (for

example, the last two nucleotides of TAAAT are the first two nucleotides of the ATG translation initiation codon). In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is a pS early promoter (*e.g.*, comprising the nucleotide sequence of AAAATTGAAATTTTA (SEQ ID NO. 555)). In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is a pS late promoter (*e.g.*, comprising the nucleotide sequence of TTTTATTTTTTTTTTTGGAATATAAATA (SEQ ID NO. 556)). In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is a pS early/late promoter (*e.g.*, comprising the nucleotide sequence of AAAATTGAAATTTTATTTTTTTTTTTTGGAATATAAATA (SEQ ID NO. 557)). In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is a LEO early promoter (*e.g.*, comprising the nucleotide sequence of TTTTATTTTTTTTTTTGGAATATAAATA (SEQ ID NO. 556)). In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is a LEO late promoter (*e.g.*, comprising the nucleotide sequence of AAAATTGAAAAAATA (SEQ ID NO. 558)). In another specific embodiment, the at least one promoter operably linked to the first nucleotide sequence is a LEO early/late promoter (*e.g.*, comprising the nucleotide sequence of TTTTATTTTTTTTTTTGGAATATAAATATCCGGTAAAATTGAAAAAATA (SEQ ID NO. 559)).

[00530] In certain embodiments of the various embodiments and aspects described herein, the at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide is a late promoter. In a specific embodiment, the late promoter comprises the nucleotide sequence of TTNTTTTTTNTTTTTTTNNNNTATAAAT (SEQ ID NO: 560, wherein N is any nucleotide). In another specific embodiment, the late promoter comprises the nucleotide sequence of TTGTATTTTCTTTTGTTGGCATATAAAT (SEQ ID NO: 561). In another specific embodiment, the late promoter is a D13L promoter (*e.g.*, comprising the nucleotide sequence of TTTATTGTAAGCTTTTTCCATTTTAAAT (SEQ ID NO. 562)). In another specific embodiment, the late promoter is a F17R promoter (*e.g.*, comprising the nucleotide sequence of TCATTTTGTTTTTTTCTATGCTATAAAT (SEQ ID NO. 563)).

[00531] In certain embodiments of the various embodiments and aspects described herein, the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is an early promoter, a late promoter, or an early/late promoter. In a specific embodiment, the

at least one promoter operably linked to the third nucleotide sequence is the B8R promoter (*e.g.*, comprising the nucleotide sequence of TAAAAATTTAAAATATATTATCACTTCAGT (SEQ ID NO. 564)). In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is the B19R promoter (*e.g.*, comprising the nucleotide sequence of AAAAAACTGATATTATATAAATATTTTAGT (SEQ ID NO. 565)). In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence comprises the nucleotide sequence of NNAAAANTGAAAANATANNNNNNNNNNNN (SEQ ID NO. 566, wherein N is any nucleotide). In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is the E3L promoter (*e.g.*, comprising the nucleotide sequence of AAAAAAATGATAAAGTAGGTTCAGTTTTAT (SEQ ID NO. 567)). In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is the F11L promoter (*e.g.*, comprising the nucleotide sequence of TAAAAAGTGAAAAACAATATTATTTTTATC (SEQ ID NO. 568)). In another specific embodiment, the at least one promoter operably linked to the third nucleotide sequence is the B2R promoter (*e.g.*, comprising the nucleotide sequence of AAAATTAAAAAATAACTTAATTTATTATTG (SEQ ID NO. 569)).

[00532] In certain embodiments of the various embodiments and aspects described herein, the promoter sequence overlaps with or is within about 100 nucleotide of the translation initiation codon of transgene to which the promoter is operatively linked. In a specific embodiment, the promoter sequence is within about 80 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In a specific embodiment, the promoter sequence is within about 70 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In a specific embodiment, the promoter sequence is within about 60 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In a specific embodiment, the promoter sequence is within about 50 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In another specific embodiment, the promoter sequence is within about 40 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In another specific embodiment, the promoter sequence is within about 30 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In another specific embodiment, the promoter sequence is within about 20 nucleotides of the translation

initiation codon of the transgene to which the promoter is operatively linked. In another specific embodiment, the promoter sequence is within about 10 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In another specific embodiment, the promoter sequence is within about 5 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In another specific embodiment, the promoter sequence is within 2 nucleotides of the translation initiation codon of the transgene to which the promoter is operatively linked. In another specific embodiment, the promoter sequence overlaps with the translation initiation codon of the transgene to which the promoter is operatively linked.

[00533] In certain embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises a transgene comprising a nucleotide sequence the nucleic acid may further comprises a nucleotide sequence comprising an untranslated region (UTR), for example, a H5R UTR or a portion thereof, *e.g.*, at least 80%, at least 85%, at least 90%, or at least 95% of the H5R UTR, operably linked to the nucleotide sequence. In a specific embodiment, the H5R UTR or a portion thereof comprises a H5R early promoter (*e.g.*, comprising the nucleotide sequence of AAAAATGAAAATAAA (SEQ ID NO. 630) or TAAAAAATGAAAATAAATACAAAGGTTCTT (SEQ ID NO. 553), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). In another specific embodiment, the H5R UTR or a portion thereof comprises a H5R late promoter (*e.g.*, comprising the nucleotide sequence of TAAAT (SEQ ID NO. 631), TCTTGAGGGTTGTGTTAAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 632), or AAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 554), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). In another specific embodiment, the H5R UTR or a portion thereof comprises the H5R early promoter (*e.g.*, comprising the nucleotide sequence of AAAAATGAAAATAAA (SEQ ID NO. 630) or TAAAAAATGAAAATAAATACAAAGGTTCTT (SEQ ID NO. 553), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence) and the H5R late promoter (*e.g.*, comprising the nucleotide sequence of TAAAT (SEQ ID NO. 631), TCTTGAGGGTTGTGTTAAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 632), or AAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 554), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). In another specific embodiment, the H5R UTR comprises the nucleotide sequence of

TTAAAGTTACAAACAACTAGGAAATTGGTTTATGATGTATAATTTTTTTAGTTTTT
ATAGATTCTTTATTCTATACTTAAAAAATGAAAATAAATACAAAGGTTCTTGAGG
GTTGTGTTAAATTGAAAGCGAGAAATAATCATAAATTATTTCATTATCGCGATAT
CCGTTAAGTTTGTATCGTA (SEQ ID NO. 626).

[00534] In specific embodiments of the various embodiments and aspects described herein wherein the nucleic acid comprises a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, the nucleic acid may further comprise a nucleotide sequence encoding an untranslated region (UTR). For example, the UTR can comprise an H5R UTR or a portion thereof (*e.g.*, at least 80%, at least 85%, at least 90%, or at least 95% of the H5R UTR) operably linked to the first nucleotide sequence. In a specific embodiment, the H5R UTR comprises a H5R early promoter (*e.g.*, comprising the nucleotide sequence of AAAAATGAAAATAAA (SEQ ID NO. 630) or TAAAAAATGAAAATAAATACAAAGGTTCTT (SEQ ID NO. 553), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). In another specific embodiment, the H5R UTR comprises a H5R late promoter (*e.g.*, comprising the nucleotide sequence of TAAAT (SEQ ID NO. 631), TCTTGAGGGTTGTGTTAAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 632), or AAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 554), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). In another specific embodiment, the H5R UTR comprises a H5R early promoter (*e.g.*, comprising the nucleotide sequence of AAAAATGAAAATAAA (SEQ ID NO. 630) or TAAAAAATGAAAATAAATACAAAGGTTCTT (SEQ ID NO. 553), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence) and a H5R late promoter (*e.g.*, comprising the nucleotide sequence of TAAAT (SEQ ID NO. 631), TCTTGAGGGTTGTGTTAAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 632), or AAATTGAAAGCGAGAAATAATCATAAAT (SEQ ID NO. 554), optionally with one, two, three, four, five, or more nucleotides upstream and/or downstream of the sequence). In another specific embodiment, the H5R UTR comprises the nucleotide sequence of

TTAAAGTTACAAACAACTAGGAAATTGGTTTATGATGTATAATTTTTTTAGTTTTT
ATAGATTCTTTATTCTATACTTAAAAAATGAAAATAAATACAAAGGTTCTTGAGG
GTTGTGTTAAATTGAAAGCGAGAAATAATCATAAATTATTTCATTATCGCGATAT
CCGTTAAGTTTGTATCGTA (SEQ ID NO. 626).

[00535] In certain embodiments of the various embodiments and aspects described herein, at least one, two, three, four, five, six, seven, eight, nine, ten, twenty, thirty, forty, fifty, sixty, seventy, eighty, ninety, or a hundred of, or all of the following genes are not deleted from the recombinant vaccinia virus genome: C3L, C4L, C5L, C6L, C7L, C8L, C9L, C10L, C11R, C12L, C13L, C14L, C15L (in the 5' ITR), C16L (in the 5' ITR), C17L (in the 5' ITR), C18L (in the 5' ITR), C19L (in the 5' ITR), C20L (in the 5' ITR), C21L (in the 5' ITR), C22L (in the 5' ITR), C23L (in the 5' ITR), F4L, F5L, F6L, F7L, F8L, F9L, F10L, F11L, F12L, F13L, F14L, F15L, F16L, F17R, E1L, E2L, E3L, E4L, E5R, E6R, E7R, E8R, E9L, E10R, E11L, O1L, O2L, I1L, I2L, I3L, I4L, I5L, I6L, I7L, I8R, G1L, G2R, G3L, G4L, G5R, G6R, G7L, G8R, G9R, L1R, L2R, L3L, L4R, L5R, J1R, J2R, J3R, J4R, J5L, J6R, H1L, H2R, H3L, H4L, H5R, H6R, H7R, D1R, D2L, D3R, D4R, D5R, D6R, D7R, D8L, D9R, D10R, D11L, D12L, D13L, A1L, A2L, A3L, A4L, A5R, A6L, A7L, A8R, A9L, A10L, A11R, A12L, A13L, A14L, A15L, A16L, A17L, A18R, A19L, A20R, A21L, A22R, A23R, A24R, A25L, A26L, A27L, A28L, A29L, A30L, A31R, A32L, A33R, A34R, A35R, A36R, A37R, A38L, A39R, A40R, A41L, A42R, A43R, A44L, A45R, A46R, A47L, A48R, A49R, A50R, A51R, A52R, A53R, A54L, A55R, A56R, A57R, B1R, B2R, B3R, B4R, B5R, B6R, B7R, B8R, B9R, B10R, B11R, B12R, and B13R (*see, e.g.*, Goebel *et al.*, 1990, Virology 179(1):247-266 for a description of the genes, which is incorporated herein by reference for such description).

[00536] In another aspect, provided herein is a nucleic acid comprising the nucleic acid sequence described in Table 43.

[00537] In another aspect, provided herein is a nucleic acid described in an example in Section 6.

[00538] In one aspect, provided are nucleic acids comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00539] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00540] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the C2L, C1L,

N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes..

[00541] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00542] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00543] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 7 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00544] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 8 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00545] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 9 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00546] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 10 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00547] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 11 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00548] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 12 genes, each gene selected from the group consisting of the C2L, C1L,

N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00549] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 13 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00550] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 14 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00551] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 15 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00552] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 16 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00553] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 17 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00554] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 18 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00555] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 19 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00556] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 20 genes, each gene selected from the group consisting of the C2L, C1L,

N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00557] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 21 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00558] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 22 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00559] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00560] In one aspect, provided are nucleic acids comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00561] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00562] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00563] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00564] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00565] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00566] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of each of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

[00567] In one aspect, provided are nucleic acids comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00568] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00569] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00570] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00571] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00572] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00573] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 7 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00574] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 8 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00575] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 9 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00576] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 10 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00577] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 11 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00578] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 12 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00579] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 13 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00580] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 14 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00581] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 15 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00582] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00583] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a protein involved in host interaction. For example, in some embodiments, said protein affects calcium-independent adhesion to the extracellular matrix. In some embodiments, said protein is an NF-κB inhibitor, e.g., an NF-κB inhibitor encoded by a gene selected from the group consisting of the C2L, N1L, M2L, K1L, and K7R genes. In some embodiments, said protein is an apoptosis inhibitor, e.g., a caspase-9 inhibitor (such as one encoded by the F1L gene), a BCL-2-like protein (such as one encoded by N1L). In some embodiments, said protein is an interferon regulatory factor 3 (IRF3) inhibitor (such as one encoded by N2L or K7R), a serine protease inhibitor, a protein that prevents cell fusion (such as one encoded by K2L), an RNA-activated protein kinase (PKR) inhibitor (such as one encoded by K1L or K3L), a virulence factor (such as one encoded by F3L), an IL-1-beta inhibitor (such as one encoded by B16R), or a secreted IFNα sequestor (such as one encoded by B19R).

[00584] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene encoding a protein involved in DNA replication. For example, in

some embodiments, said protein is a DNA modifying nuclease (e.g., a protein encoded by K4L) or a deoxyuridine triphosphatase (dUTPase) (e.g., a protein encoded by is F2L).

[00585] In some embodiments, at least one deleted gene's entire nucleotide sequence is deleted. In some embodiments, at least one deleted gene is only partially deleted, and the partial deletion is sufficient to render said partially deleted gene nonfunctional upon introduction into a host cell.

[00586] In some embodiments, said recombinant orthopoxvirus genome comprises at least two copies of inverted terminal repeats (ITRs).

[00587] In some embodiments, said recombinant orthopoxvirus genome lacks any copies of ITRs.

[00588] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion in at least one copy of an ITR selected from the group consisting of B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

[00589] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion in at least all of the following copies of ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

[00590] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion in the B8R gene.

[00591] In some embodiments, said recombinant orthopoxvirus genome comprises an intact B8R gene.

[00592] In one aspect, provided are nucleic acids comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises (i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, B20R, and B8R genes; and (ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

[00593] In one aspect, provided are nucleic acids comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises (i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes; and (ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR,

B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR, wherein said recombinant orthopoxvirus genome comprises an intact B8R gene.

[00594] In some embodiments, provided nucleic acids further comprise at least one transgene selected from the group consisting of a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine. In some embodiments, provided nucleic acids further comprise at least two transgenes selected from the group consisting of a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine. In some embodiments, provided nucleic acids further comprise a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine.

[00595] For example, in some embodiments, provided nucleic acids comprise a transgene encoding an immune checkpoint inhibitor. In some embodiments, said immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof. In some embodiments, said immune checkpoint inhibitor is an anti-PD-L1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof. In some embodiments, said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof. In some embodiments, said immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

[00596] For example, in some embodiments, provided nucleic acids comprise a transgene encoding an interleukin (IL). In some embodiments, said interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23. In some embodiments, said interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70. In some embodiments, said interleukin is membrane-bound. In some embodiments, said interleukin is membrane-bound IL-12 p70. In some embodiments, said interleukin is membrane-bound IL-12 p35.

[00597] For example, in some embodiments, provided nucleic acids comprise a transgene encoding a cytokine. In some embodiments, said cytokine is an interferon (IFN). In some

embodiments, the interferon is selected from the group consisting of IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

[00598] In some embodiments, the cytokine is a TNF superfamily member protein. In some embodiments, the TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

[00599] In some embodiments, the cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, TGF-beta, VEGF-R2, and c-kit. In some embodiments, the cytokine is Flt3 ligand.

[00600] In some embodiments, said recombinant orthopoxvirus genome comprises a deletion in the B8R gene and at least one transgene is inserted into the deletion in the B8R gene. In some embodiments, at least two transgenes are inserted into the deletion in the B8R gene. In some embodiments, at least three transgenes are inserted into the deletion in the B8R gene. In some embodiments, at least one transgene is inserted in a locus that is not at the deletion in the B8R gene, for example, a locus at the boundary of a deletion at the 5' end of the orthopoxvirus genome or at a locus at the boundary of a deletion at the 3' end of the orthopoxvirus genome.

[00601] In one aspect, provided are nucleic acids comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises (i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, B20R, and B8R genes; (ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR; (iii) an IL-12-TM transgene inserted into the deletion in the B8R gene; (iv) an Flt3 ligand transgene inserted into the deletion in the B8R gene; and (v) one of: (a) a transgene encoding a single chain anti-CTLA-4 antibody or antigen-binding fragment thereof, or (b) (i) a transgene encoding a heavy chain of an anti-CTLA-4 antibody or antigen-binding fragment thereof, and (ii) a transgene encoding a light chain of an anti-CTLA-4 antibody or antigen-binding fragment thereof, wherein the transgene(s) in part (v) is/are inserted within the boundaries of a 5p deletion present in the recombinant orthopoxvirus genome, an wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is capable of binding CTLA-4.

[00602] In some embodiments, the orthopoxvirus genome is derived from a sequence of SEQ ID NO: 210, wherein (a) said derived sequence comprises a deletion of the B8R gene, and the IL-12-TM transgene, the Flt3 ligand transgene, and the transgene(s) encoding the

single or double-chain anti-CTLA-4 antibody; (b) the IL-12-TM transgene encodes a protein comprising an amino acid sequence of is SEQ ID NO: 212; (c) the Flt3 ligand transgene encodes a protein comprising an amino acid sequence of SEQ ID NO: 213; and (d) the anti-CTLA-4 antibody comprises an amino acid sequence of SEQ ID NO: 211.

[00603] In some embodiments of provided nucleic acids, the nucleic acid further comprises a transgene encoding a tumor-associated antigen, for example, a tumor-associated antigen listed in any one of Tables 3-30. In some embodiments, the tumor-associated antigen is a tumor-associated antigen selected from the group consisting of CD19, CD33, EpCAM, CEA, PSMA, EGFRvIII, CD133, EGFR, CDH19, ENPP3, DLL3, MSLN, ROR1, HER2, HLAA2, EpHA2, EpHA3, MCSP, CSPG4, NG2, RON, FLT3, BCMA, CD20, FAPα, FRα, CA-9, PDGFRα, PDGFRβ, FSP1, S100A4, ADAM12m, RET, MET, FGFR, INSR, and NTRK.

[00604] In some embodiments, the tumor-associated antigen comprises MAGE-A3, or one or more fragments thereof.

[00605] In some embodiments, the tumor-associated antigen comprises NY-ESO-1, or one or more fragments thereof.

[00606] In some embodiments, the tumor-associated antigen comprises one or more human papillomavirus (HPV) proteins, or fragments thereof. In some embodiments, the HPV proteins or fragments thereof comprise one or more of (i) E6 and E7 proteins, or fragments thereof, of HPV16 and (ii) E6 and E7 proteins, or fragments thereof, of HPV18. In some embodiments, the sequences of said HPV proteins or fragments are disclosed in International Patent Publication WO/2014/127478, the contents of which are incorporated herein by reference.

[00607] In some embodiments, the tumor-associated antigen comprises brachyury or one or more fragments thereof.

[00608] In some embodiments, the tumor-associated antigen comprises prostatic acid phosphatase, or one or more fragments thereof.

[00609] When more than one transgene described herein is inserted into a recombinant orthopoxvirus genome (*e.g.*, a recombinant vaccinia virus genome), the transgenes can be inserted into one locus or multiple loci (*e.g.*, two loci or three loci). When two or more transgenes described above are inserted into the same loci, the transgenes can be inserted with the same orientation or different orientations relative to one of or both of the flanking endogenous orthopoxvirus genes (*e.g.*, vaccinia virus genes), and also relative to each other. It is also contemplated that, when two or more transgenes are inserted into the same locus, the

order of the transgenes inserted into the same locus of the recombinant orthopoxvirus genome (*e.g.*, a recombinant vaccinia virus genome) can be different.

[00610] In certain embodiments of the various embodiments and aspects described herein, the nucleotide sequence encoding the antibody or antigen-binding fragment thereof that specifically binds to CTLA-4 encodes the heavy and light chains of the anti-CTLA-4 antibody (*e.g.*, ipilimumab) separated by cleavage peptide, for example a self-cleavage peptide, *e.g.*, a 2A self-cleaving peptide. In a specific embodiment, the 2A self-cleavage peptide is a T2A peptide. In a particular embodiment, the T2A peptide comprises the amino acid sequence of GSGEGRGSLLTCGDVEENPGP (SEQ ID NO: 570). In a particular embodiment, the T2A peptide comprises the amino acid sequence of PRGSGEGRGSLLTCGDVEENPGP (SEQ ID NO: 571). In another particular embodiment, the T2A peptide comprises the amino acid sequence of EGRGSLLTCGDVEENPGP (SEQ ID NO: 572). In another specific embodiment, the 2A self-cleavage peptide is a P2A peptide. In a particular embodiment, the P2A peptide comprises the amino acid sequence of GSGATNFSLLKQAGDVEENPGP (SEQ ID NO: 573). In another particular embodiment, the P2A peptide comprises the amino acid sequence of ATNFSLLKQAGDVEENPGP (SEQ ID NO: 574). In another specific embodiment, the 2A self-cleavage peptide is a E2A peptide. In a particular embodiment, the E2A peptide comprises the amino acid sequence of GSGQCTNYALLKLAGDVESNPGP (SEQ ID NO: 575). In another particular embodiment, the E2A peptide comprises the amino acid sequence of QCTNYALLKLAGDVESNPGP (SEQ ID NO: 576). In another specific embodiment, the 2A self-cleavage peptide is a F2A peptide. In a particular embodiment, the F2A peptide comprises the amino acid sequence of GSGVKQTLNFDLLKLAGDVESNPGP (SEQ ID NO: 577). In another particular embodiment, the F2A peptide comprises the amino acid sequence of VKQTLNFDLLKLAGDVESNPGP (SEQ ID NO: 578). Linking of the heavy and light chains of the antibody by a 2A self-cleavage peptide enables the antibody transgene to be translated in one open reading frame and self-cleavage to occur co-translationally, resulting in equal amounts of the co-expressed heavy and light chains. In a specific embodiment, the anti-CTLA-4 antibody encoded by a nucleotide sequence described herein comprises the amino acid sequence of SEQ ID NO: 211.

[00611] In various embodiments, the nucleic acid provided herein is a recombinant nucleic acid.

5.2.4. Modified Orthopoxviruses

[00612] In one aspect, provided herein is a virus comprising the nucleic acid described in Section 5.2.3. In a specific embodiment, provided herein is a virus comprising the nucleic acid described in Section 5.2.3, wherein the nucleic acid comprises a recombinant vaccinia virus genome that comprises a second transgene comprising a second nucleotide sequence encoding a membrane-bound IL-12 polypeptide.

[00613] In another aspect, provided herein is a virus described in an example in Section 6.

[00614] In another aspect, provided are viruses comprising the nucleic acid comprising the recombinant orthopoxvirus genome described herein. In some embodiments, a) the recombinant orthopoxvirus genome comprises a deletion of at least 2 genes selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes; b) said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes; or c) said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

[00615] In some embodiments, said virus is derived from a vaccinia virus. In some embodiments, said vaccinia virus is derived from a strain selected from the group consisting of Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16mO, Tashkent, Tian Tan, and WAU86/88-1. In some embodiments, said vaccinia virus is derived from a strain selected from the group consisting of Copenhagen, Western Reserve, Tian Tan, Wyeth, and Lister. In some embodiments, said vaccinia virus is derived from a Copenhagen strain vaccinia virus.

[00616] In some embodiments, said recombinant orthopoxvirus genome further comprises a Thymidine Kinase (TK) gene. In some embodiments, said recombinant orthopoxvirus genome further comprises a ribonucleotide reductase gene.

[00617] In some embodiments of provided viruses, upon contacting a population of cells (*e.g.*, mammalian cells) with said virus, the population of cells (*e.g.*, mammalian cells) exhibit increased syncytia formation relative to a population of cells (*e.g.*, mammalian cells) of the same type contacted with a form of the virus that does not comprise said deletion.

[00618] In some embodiments of provided viruses, upon contacting a population of cells (*e.g.*, mammalian cells) with said virus, the population of cells (*e.g.*, mammalian cells) exhibit increased spreading of the virus relative to a population of cells (*e.g.*, mammalian cells) of the same type contacted with a form of the virus that does not comprise said deletion.

[00619] In some embodiments of provided viruses, said recombinant orthopoxvirus vector exerts an increased cytotoxic effect on a population of cells (*e.g.*, mammalian cells) relative to that of a form of the virus that does not comprise said deletion.

[00620] In some embodiments, said mammalian cells are human cells.

[00621] In some embodiments, said human cells are cancer cells.

[00622] In some embodiments, said mammalian cells are from a cell line selected from the group consisting of U2OS, 293, 293T, Vero, HeLa, A549, BHK, BSC40, CHO, OVCAR-8, 786-0, NCI-H23, U251, SF-295, T-47D, SKMEL2, BT-549, SK-MEL-28, MDA-MB-231, SK-OV-3, MCF7, M14, SF-268, CAKI-1, HPAV, OVCAR-4, HCT15, K-562, and HCT-116.

[00623] In some embodiments of provided viruses, the virus further comprises a transgene encoding a tumor-associated antigen, for example, a tumor-associated antigen listed in any one of Tables 3-30. In some embodiments, the tumor-associated antigen is a tumor-associated antigen selected from the group consisting of CD19, CD33, EpCAM, CEA, PSMA, EGFRvIII, CD133, EGFR, CDH19, ENPP3, DLL3, MSLN, ROR1, HER2, HLAA2, EpHA2, EpHA3, MCSP, CSPG4, NG2, RON, FLT3, BCMA, CD20, FAPα, FRα, CA-9, PDGFRα, PDGFRβ, FSP1, S100A4, ADAM12m, RET, MET, FGFR, INSR, and NTRK.

[00624] In some embodiments, the tumor-associated antigen comprises MAGE-A3, or one or more fragments thereof.

[00625] In some embodiments, the tumor-associated antigen comprises NY-ESO-1, or one or more fragments thereof.

[00626] In some embodiments, the tumor-associated antigen comprises one or more human papillomavirus (HPV) proteins, or fragments thereof. In some embodiments, the HPV proteins or fragments thereof comprise one or more of (i) E6 and E7 proteins, or fragments thereof, of HPV16 and (ii) E6 and E7 proteins, or fragments thereof, of HPV18. In some embodiments, the sequences of said HPV proteins or fragments are disclosed in International Patent Publication WO/2014/127478, the contents of which are incorporated herein by reference.

[00627] In some embodiments, the tumor-associated antigen comprises brachyury or one or more fragments thereof.

[00628] In some embodiments, the tumor-associated antigen comprises prostatic acid phosphatase, or one or more fragments thereof.

[00629] In certain embodiments, the virus provided herein is isolated. In certain embodiments, the virus provided herein is purified.

[00630] In various embodiments, the virus provided herein is a recombinant virus.

[00631] In certain embodiments, the virus provided herein does not cause pox lesion formation when administered to a patient (*e.g.*, a mammalian patient). In certain embodiments, the virus provided herein is able to replicate *in vitro* and/or when administered to a patient (*e.g.*, a mammalian patient). In certain embodiments, the virus provided herein is able to express the transgene(s) described herein *in vitro* and/or when administered to a patient (*e.g.*, a mammalian patient). In certain embodiments, the virus provided herein is able to kill target tumor cells (*e.g.*, exhibits cancer cytotoxicity) *in vitro* and/or when administered to a patient (*e.g.*, a mammalian patient). See the examples in Section 6 for exemplary assays that may be used to determine pox lesion formation, replication, transgene expression, or killing of target tumor cells (*e.g.*, cancer cytotoxicity).

5.2.5. Assays for Measuring Virus Characteristics

[00632] In certain embodiments, the viruses described herein have been tested for their ability to replicate/spread, viability, transgene expression, and/or ability to kill target tumor cells (*e.g.*, cancer cytotoxicity), using a method known in the art. See the examples in Section 6 for exemplary assays that may be used to determine replication/spreading, viability, transgene expression, or killing of target tumor cells (*e.g.*, cancer cytotoxicity).

[00633] Assays known in the art to measure the tumor spreading and virulence of a virus include but are not limited to measuring plaque size, syncytia formation, and/or comet assays (EEVs). Assays known in the art to measure the immunostimulatory activity of a virus include but are not limited to NK activation (measured in % CD69 expression), NK degranulation (measured in fold increase of CD107a), and/or T-cell priming assays. Assays known in the art to measure the selectivity of a virus include, but are not limited to, tail pox lesions, biodistribution, and/or body mass measurements.

5.2.6. Cells, Cell Lines and Packaging Cell Lines

[00634] In one aspect, provided herein is a cell comprising the nucleic acid described in Section 5.2.3. In another aspect, provided herein is a cell comprising the virus described in Section 5.2.4. In certain embodiments, the cell provided herein is a mammalian cell (*e.g.*, a human cell). In certain embodiments, the cell provided herein is a host cell (*e.g.*, a host cell described in Section 5.4).

[00635] In one aspect, provided herein is a cell line comprising the nucleic acid described in Section 5.2.3. In another aspect, provided herein is a cell line comprising the virus described in Section 5.2.4. In certain embodiments, the cell line provided herein is a mammalian cell line (*e.g.*, a human cell line).

[00636] In one aspect, provided herein is a packaging cell line comprising the nucleic acid described in Section 5.2.3. In another aspect, provided herein is a packaging cell line comprising the virus described in Section 5.2.4. The packaging cell line can be any cell line suitable for packaging orthopoxvirus viruses (*e.g.*, vaccinia viruses). In certain embodiments, the packaging cell line provided herein is a mammalian packaging cell line (*e.g.*, a human packaging cell line).

[00637] Exemplary cells that can be used to culture a virus described herein include, for example, the HeLa cells, U2OS cells, 293T cells, NIH3T3 cells, Jurkat cells, 293 cells, COS cells, CHO cells, Saos cells, PC12 cells, and chicken embryo fibroblasts (CEF). Exemplary packaging cell lines that can be used to package a virus described herein include, for example, the HeLa cell line, the U2-OS cell line, the HEK293T cell line, the 786-O cell line, the A549 cell line or an adherent human cancer cell line. In certain embodiments, the cells also express or are engineered to express one or more factors necessary for the replication and/or packaging of the vaccinia virus.

[00638] In certain embodiments, the cell, cell line, or the packaging cell line provided herein is a cell, cell line or packaging cell line described in an example in Section 6.

5.2.7. Examples of Proteins Encoded by Orthopoxvirus Genes

[00639] Exemplary proteins encoded by orthopoxvirus genes described in this disclosure are reproduced in Tables 31-40 below. As used below, the term "location" refers to the location of the gene with respect to the deleted nucleic acids in exemplary orthopoxvirus vectors described herein. For various genes, amino acid sequence information and protein accession ID numbers are provided.

5.3. Methods of Genetic Modification

[00640] Methods for the insertion or deletion of nucleic acids from a target genome include those described herein and known in the art. Methods for nucleic acid delivery to effect expression of compositions of the present invention are believed to include virtually any method by which a nucleic acid (e.g., DNA, including viral and non-viral vectors) can be introduced into an organelle, a cell, a tissue or an organism, as described herein or as would be known to one of ordinary skill in the art. Such methods include, but are not limited to, direct delivery of DNA such as by injection (U.S. Pat. Nos. 5,994,624, 5,981,274, 5,945,100, 5,780,448, 5,736,524, 5,702,932, 5,656,610, 5,589,466 and 5,580,859, each incorporated herein by reference), including microinjection (Harland and Weintraub, 1985; U.S. Pat. No. 5,789,215, incorporated herein by reference); by electroporation (U.S. Pat. No. 5,384,253, incorporated herein by reference); by calcium phosphate precipitation (Graham and Van Der Eb, 1973; Chen and Okayama, 1987; Rippe et al., 1990); by using DEAE-dextran followed by polyethylene glycol (Gopal, 1985); by direct sonic loading (Fechheimer et al., 1987); by liposome mediated transfection (Nicolau and Sene, 1982; Fraley et al., 1979; Nicolau et al., 1987; Wong et al., 1980; Kaneda et al., 1989; Kato et al., 1991); by microprojectile bombardment (PCT Application Nos. WO 94/09699 and 95/06128; U.S. Pat. Nos. 5,610,042; 5,322,783, 5,563,055, 5,550,318, 5,538,877 and 5,538,880, and each incorporated herein by reference); by agitation with silicon carbide fibers (Kaeppler et al., 1990; U.S. Pat. Nos. 5,302,523 and 5,464,765, each incorporated herein by reference); by Agrobacterium-mediated transformation (U.S. Pat. Nos. 5,591,616 and 5,563,055, each incorporated herein by reference); or by PEG-mediated transformation of protoplasts (Omirulleh et al., 1993; U.S. Pat. Nos. 4,684,611 and 4,952,500, each incorporated herein by reference); by desiccation/inhibition-mediated DNA uptake (Potrykus et al., 1985). Through the application of techniques such as these, organelle(s), cell(s), tissue(s) or organism(s) may be stably or transiently transformed.

[00641] Depicted below are clusters of deleted genes and their function in CopMD5p, CopMD3p, and CopMD5p3p virus. ITR genes (designated in Table 2 by "-ITR" and "*") are deleted in one copy, the right ITR of the genome. However, these genes have a second copy in the left ITR, which remains intact in these virus. Deletions were confirmed by whole genome sequencing. Most of the deleted genes are either involved in blocking host response to viral infection or have an unknown function.

Table 2: Deleted genes in Vaccinia viruses

Name	Category	Function	Virus Deletions	
C2L	Host interaction	Inhibits NFkB	CopMD5p	CopMD5p3p
C1L	Unknown	Unknown		
N1L	Host interaction	Inhibits NFkB and Apoptosis		
N2L	Host interaction	Inhibits IRF3		
M1L	Unknown	Unknown		
M2L	Host interaction	Inhibits NFkB and Apoptosis		
K1L	Host interaction	Inhibits PKR and NF-kB		
K2L	Host interaction	Prevents cell fusion		
K3L	Host interaction	Inhibits PKR		
K4L	DNA replication	DNA modifying nuclease		
K5L	Pseudogene	Pseudogene		
K6L	Pseudogene	Pseudogene		
K7R	Host interaction	Inhibits NFkB and IRF3		
F1L	Host interaction	Inhibits Apoptosis		
F2L	DNA replication	Deoxyuridine triphosphatase		
F3L	Host interaction	Virulence factor		
B14R	Pseudogene	Pseudogene	CopMD3p	
B15R	Unknown	Unknown		
B16R	Host interaction	IL-1-beta-inhibitor		
B17L	Unknown	Unknown		
B18R	Unknown	Ankyrin-like		
B19R	Host interaction	Secreted IFNα sequestor		
B20R	Unknown	Ankyrin-like		
B21R-ITR*	Unknown	Unknown		
B22R-ITR*	Unknown	Unknown		
B23R-ITR*	Unknown	Unknown		
B24R-ITR*	Unknown	Unknown		

Name	Category	Function	Virus Deletions	
B25R-ITR*	Unknown	Unknown		
B26R-ITR*	Unknown	Unknown		
B27R-ITR*	Unknown	Unknown		
B28R-ITR*	Pseudogene	TNF-a receptor		
B29R-ITR*	Host interaction	Secreted CC-chemokine sequestor		

[00642] In various embodiments, the orthopox viruses are further genetically modified to contain deletions in the B8R gene. The vaccinia virus B8R gene encodes a secreted protein with homology to gamma interferon receptor (IFN-γ). In vitro, the B8R protein binds to and neutralizes the antiviral activity of several species of gamma interferon including human and rat gamma interferon; it does not, however, bind significantly to murine IFN-γ. Deleting the B8R gene prevents the impairment of IFN-γ in humans. In various embodiments, one, two or three transgenes are inserted into the locus of the deleted B8R gene. In some strains, in addition to the transgene(s) present at the site of the B8R deletion, the strain also has, at least one transgene is inserted into an additional locus on the orthopox virus that is not the locus of the deleted B8R gene. In various embodiments, at least one transgene is inserted into boundaries of the 5p deletions, at least one transgene is inserted into the boundaries of the 3p deletions or both. In various, embodiments at least three, four, five or more transgenes are inserted into the modified orthopox virus genome.

[00643] In various embodiments, the sequence of the modified orthopoxvirus vector is the sequence depicted below in Table 43 as SEQ ID NO: 210. In some embodiments, the sequence of the modified orthopoxvirus vector is a derivative of SEQ ID NO: 210. For example, as noted herein, the modified orthopoxvirus vector may be modified to express one or more transgenes as discussed herein.

[00644] In various embodiments, the sequence of the modified orthopoxvirus vector is the sequence depicted below in Table 43 as SEQ ID NO: 624. In some embodiments, the sequence of the modified orthopoxvirus vector is a derivative of SEQ ID NO: 624. For example, as noted herein, the modified orthopoxvirus vector may contain a deletion of the B8R sequence and/or may be modified to express one or more transgenes as discussed herein.

[00645] In various embodiments, the modified orthopoxvirus expresses at least one of three transgenes: IL-12-TM, FLT3-L and anti-CLTA4 antibody. Non-limiting examples of sequences of these transgenes and/or of amino acid sequences encoded by them are described below:

Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains	
Nucleotide SEQ ID NO: 214	ATGGAAACAGACACCCTATTATTATGGGTTTTGCTTCTATGGGTGCCAGGATCT ACGGGTCAGGTTCAGCTAGTCGAATCGGGTGGAGGAGTCGTGCAGCCGGGACGT TCCTTACGTTTATCTTGCGCAGCGTCTGGTTTTACTTTCTCGTCCTACACTATG CATTGGGTTCGTCAGGCTCCGGGAAAGGGATTGGAGTGGGTAACATTTATAAGT TACGACGGTAATAATAAATACTATGCAGACAGTGTGAAGGGACGTTTCACTATA TCTCGAGATAATAGTAAGAACACTTTGTATTTGCAGATGAATTCATTGAGAGCG GAAGATACAGCAATTTACTACTGCGCCAGAACCGGATGGTTGGGTCCCTTTGAC TATTGGGGACAGGGTACTCTTGTTACGGTGTCTTCTGCTTCAACAAAGGGTCCC TCTGTCTTCCCGCTTGCGCCCTCATCAAAATCGACGTCGGGTGGAACCGCTGCC TTGGGATGCTTGGTTAAGGACTATTTCCCCGAACCTGTCACCGTGTCTTGGAAT TCCGGTGCTCTAACGTCTGGTGTGCACACTTTCCCTGCCGTTTTACAAAGTTCC GGACTATATTCACTTTCGTCCGTAGTAACTGTTCCAAGTTCGTCCCTTGGAACA CAGACCTATATATGCAACGTAAACCACAAACCCTCCAATACCAAAGTCGATAAA AGAGTTGAGCCTAAATCCTGCGACAAAACACACACCTGCCCACCTTGCCCGGCC CCTGAACTTCTTGGAGGACCATCTGTATTCCTTTTCCCACCGAAGCCTAAGGAC ACCTTGATGATATCCAGAACTCCCGAAGTCACGTGCGTAGTAGTCGATGTGAGT CACGAAGATCCGGAAGTCAAGTTTAACTGGTATGTAGACGGAGTAGAGGTTCAT AACGCCAAGACCAAGCCAAGAGAAGAACAATATAACTCGACTTACAGAGTCGTG TCTGTATTAACCGTCTTGCATCAGGACTGGTTAAACGGTAAAGAGTACAAGTGC AAGGTCTCCAATAAAGCCCTACCTGCCCCCATCGAAAAAACCATATCCAAGGCT AAGGGTCAGCCTAGAGAACCTCAAGTTTACACATTACCGCCCAGTAGAGATGAA CTTACGAAGAATCAAGTGAGTCTAACCTGCCTTGTTAAAGGATTCTACCCCAGT GACATAGCGGTGGAGTGGGAGTCCAACGGTCAACCCGAGAACAATTATAAGACG ACACCGCCCGTTCTTGACAGTGACGGATCGTTCTTTCTATACTCTAAGTTGACT GTGGATAAATCCCGATGGCAGCAGGGAAACGTATTCTCTTGCTCAGTGATGCAT GAGGCGTTGCACAATCATTACACCCAAAAGTCTTTGTCGCTAAGTCCAGGTAAA CCGCGGGGCAGCGGAGAGGGCAGAGGAAGCCTGCTGACTTGTGGCGATGTGGAA GAGAACCCTGGCCCTAAGCTTATGGCTTGGACACCAGGAATCTTCATGGTACTT AGTTACTTGACAGGATCTTTCTCGGAAATAGTCTTAACTCAGTCACCGGGTACA CTTTCCCTTTCGCCCGGAGAGCGTGCGACCCTATCGTGTCGAGCTTCCCAGTCG GTTGGTTCTTCGTATCTTGCTTGGTATCAGCAGAAGCCCGGACAAGCTCCTCGT CTTTTGATCTACGGTGCGTTTTCGAGAGCGACTGGTATCCCGGATAGATTTTCT GGATCGGGTTCTGGTACTGATTTCACTTTAACGATTTCGAGACTAGAGCCCGAA GATTTTGCTGTGTATTATTGCCAGCAATATGGATCTAGTCCGTGGACGTTCGGT CAGGGTACCAAGGTCGAGATAAAAAGAACTGTGGCCGCACCCTCCGTGTTTATC TTTCCCCCTTCCGACGAACAGCTAAAGTCGGGTACTGCATCGGTGGTATGTTTA CTTAACAACTTTTACCCACGAGAGGCCAAGGTACAATGGAAGGTGGATAACGCC TTACAATCAGGAAACTCACAAGAGTCCGTCACCGAGCAAGATTCCAAGGACAGT ACATACTCGTTATCCTCGACATTAACATTGAGTAAGGCGGATTATGAGAAGCAT

	AAGGTTTACGCATGCGAAGTGACGCACCAAGGACTTTCATCCCCCGTCACCAAG TCTTTCAATCGTGGTGAGTGCTGA
Amino acid SEQ ID NO: 211	*METDTLLLWVLLLWVPGSTG***QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTM HWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRA EDTAIYYCARTGWLGPFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKPRGSGEGRGSLLTCGDVE ********** ********** **ENPG***PKLMAWTPGIFMVLSYLTGSFS***EIVLTQSPGTLSLSPGERATLSCRASQS ***** **VGSSYLAWYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPE DFAVYYCQQYGSSPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKH KVYACEVTHQGLSSPVTKSFNRGEC** (italicized: signal peptide sequence; sequence having * beneath the letters: T2A sequence (including a PRGSG (SEQ ID NO: 589) linker); bold: heavy chain sequence; bold and underlined: light chain sequence)
Heavy chain (amino acid) (SEQ ID NO: 217)	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYD GNNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYW GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGKPRGSGEGRGSLLTCGDVEENPG
Light chain (amino acid) (SEQ ID NO: 218)	EIVLTQSPGTLSLSPGERATLSCRASQSVGSSYLAWYQQKPGQAPRLLIYGAFS RATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
Anti-CTLA-4 (human single chain)	
Nucleotide SEQ ID NO: 579	ATGGAGACAGATACTCTATTGCTATGGGTTTTGTTATTATGGGTGCCGGGTTCC ACGGGAATTCGTCGTGCTGACATTGTTTTAACACAGTCTCCAGGTACCCTATCA TTGTCCCCTGGTGAGCGTGCCACGCTTAGTTGCAGAGCCTCTCAGTCTGTGGGA TCAAGTTATTTAGCTTGGTATCAACAAAAACCTGGACAAGCACCTCGTTTGTTA ATATATGGTGCATTCAGTAGAGCAACTGGAATTCCTGATCGATTCTCAGGATCT GGATCTGGAACAGACTTCACACTTACCATCTCACGTCTTGAACCCGAGGACTTT GCGGTCTACTACTGCCAGCAGTATGGTTCGTCGCCTTGGACTTTCGGACAAGGA

	ACCAAAGTTGAAATCAAGCGAGGAGGAGGTGGATCGGGTGGTGGAGGATCCGGT GGAGGTGGAAGTGAAGCGAAGCTAGTCGAATCTGGAGGTGGTGTAGTGCAGCCT GGACGTTCGCTTCGACTATCCTGTGCTGCTTCAGGATTTACCTTTTCATCTTAC ACGATGCACTGGGTGCGTCAAGCGCCTGGTAAAGGACTAGAGTGGGTCACGTTT ATCTCATACGACGGTAATAACAAGTATTATGCTGATTCCGTAAAGGGACGTTTC ACCATATCGCGTGACAATTCTAAGAATACCTTGTATCTTCAAATGAATAGTCTT AGAGCTGAAGACACTGCCATTTACTATTGTGCACGAACGGGATGGCTTGGACCT TTTGATTATTGGGGTCAGGGTACTTTGGTCACCGTCTCCACAGCGAAGACAACA CCTCCCTCAGTCTATCCACTTGCTCCGCGTAGTTAA
Amino acid SEQ ID NO: 580	METDTLLLWVLLLWVPGSTGIRRADIVLTQSPGTLSLSPGERATLSCRASQSVG SSYLAWYQQKPGQAPRLLIYGAFSRATGIPDRFSGSGSGTDFTLTISRLEPEDF AVYYCQQYGSSPWTFGQGTKVEIKRGGGGSGGGGSGGGGSEAKLVESGGGVVQP GRSLRLSCAASGFTFSSYTMHWVRQAPGKGLEWVTFISYDGNNKYYADSVKGRF TISRDNSKNTLYLQMNSLRAEDTAIYYCARTGWLGPFDYWGQGTLVTVSTAKTT PPSVYPLAPRS
Anti-CTLA-4 (mouse single chain)	
Nucleotide SEQ ID NO: 581	ATGGAAACCGATACTTTGCTTCTATGGGTCCTTTTGCTATGGGTGCCCGGATCA ACCGGAATAAGACGTGCTGATATCGTTATGACCCAGACCACGCTATCATTACCA GTTAGTCTAGGTGACCAGGCCAGTATCAGTTGCCGTTCATCTCAGTCCATTGTA CACTCAAACGGAAACACCTACTTGGAGTGGTATCTTCAGAAACCTGGTCAATCT CCCAAGCTTCTAATTTACAAAGTGTCTAACCGATTTTCTGGTGTGCCGGATCGA TTTTCGGGTTCTGGTAGTGGAACGGATTTCACGCTAAAAATATCCCGAGTCGAA GCTGAAGACCTAGGAGTATATTATTGCTTTCAAGGATCTCACGTCCCGTACACC TTTGGTGGAGGAACCAAGCTTGAAATAAAGCGAGGAGGTGGAGGATCAGGAGGA GGTGGTTCGGGTGGTGGTGGTTCCGAGGCGAAGTTACAGGAGTCGGGACCCGTA TTAGTGAAGCCTGGTGCGAGTGTCAAAATGAGTTGCAAAGCCAGTGGTTACACC TTCACAGACTATTACATGAACTGGGTGAAGCAGTCTCACGGAAAATCTTTAGAG TGGATAGGAGTAATTAACCCGTACAATGGTGATACGAGTTACAACCAGAAGTTC AAAGGTAAGGCGACCTTGACGGTCGATAAATCCTCTAGTACTGCGTACATGGAA CTAAACTCTTTAACCTCTGAGGATTCTGCCGTATATTATTGTGCCAGATATTAT GGTTCGTGGTTCGCATATTGGGGACAGGGAACTTTAATTACGGTCTCGACAGCC AAAACGACTCCCCCCTCAGTTTATCCCCTTGCTCCTAGAAGTTAA
Amino acid SEQ ID NO: 582	METDTLLLWVLLLWVPGSTGIRRADIVMTQTTLSLPVSLGDQASISCRSSQSIV HSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVE AEDLGVYYCFQGSHVPYTFGGGTKLEIKRGGGGSGGGGSGGGGSEAKLQESGPV LVKPGASVKMSCKASGYTFTDYYMNWVKQSHGKSLEWIGVINPYNGDTSYNQKF KGKATLTVDKSSSTAYMELNSLTSEDSAVYYCARYYGSWFAYWGQGTLITVSTA KTTPPSVYPLAPRS
Human IL-12 TM p35	
Nucleotide SEQ ID NO: 215	ATGTGTCCCGCGCGATCGTTATTGTTAGTTGCGACGTTGGTCCTACTTGACCAT CTATCACTAGCGCGTAATTTGCCCGTTGCCACACCAGATCCCGGAATGTTTCCT TGCTTACATCATAGTCAGAACTTACTTCGTGCAGTCTCCAACATGTTACAGAAA GCCCGACAGACCTTAGAGTTCTATCCCTGTACTTCCGAAGAGATAGATCACGAG GACATAACGAAAGACAAAACATCGACCGTTGAAGCGTGCTTACCCTTAGAACTA ACCAAAAATGAAAGTTGTCTAAACTCTAGAGAAACGAGTTTTATCACCAATGGA AGTTGCTTGGCGTCTAGAAAAACATCATTTATGATGGCCTTGTGTCTTTCCTCC ATATACGAGGACTTGAAGATGTATCAGGTCGAGTTCAAGACAATGAACGCGAAA TTGCTTATGGACCCCAAACGACAGATATTTTTGGACCAAAACATGTTAGCTGTT

	ATAGACGAATTGATGCAGGCGCTAAACTTCAATTCGGAAACTGTGCCACAGAAG TCATCCTTAGAGGAGCCCGATTTTTACAAGACAAAAATCAAGTTATGCATTCTT CTTCACGCGTTTAGAATTCGTGCCGTTACGATTGATAGAGTAATGTCGTACTTG AATGCGTCGGGTGGAGGAGGTTCCGGAGGAGGAGGATCCGGAGGAGGTGGATCC **TTACTTCCTTCGTGGGCTATAACATTAATCTCCGTTAATGGTATCTTCGTGATT** **TGCTGTCTAACATACTGCTTTGCA**TGA (Underlined and bold: B7-1 transmembrane domain; Bold: B7-1 cytoplasmic domain.)
Amino acid: SEQ ID NO: 212	MCPARSLLLVATLVLLDHLSLARNLPVATPDPGMFPCLHHSQNLLRAVSNMLQK ARQTLEFYPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNG SCLASRKTSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAV IDELMQALNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYL NASGGGGSGGGGSGGGGS**LLPSWAITLISVNGIFVICCLTYCFA** (Underlined and bold: B7-1 transmembrane domain; Bold: B7-1 cytoplasmic domain.)
Human IL-12 TM p70	
Nucleotide SEQ ID NO: 583	ATGTGTCACCAGCAGTTGGTCATCTCTTGGTTTTCCCTGGTTTTTCTGGCATCT CCCCTCGTGGCCATATGGGAACTGAAGAAAGATGTTTATGTCGTAGAATTGGAT TGGTATCCGGATGCCCCTGGAGAAATGGTGGTCCTCACCTGTGACACCCCTGAA GAAGATGGTATCACCTGGACCTTGGACCAGAGCAGTGAGGTCTTAGGCTCTGGC AAAACCCTGACCATCCAAGTCAAAGAGTTTGGAGATGCTGGCCAGTACACCTGT CACAAAGGAGGCGAGGTTCTAAGCCATTCGCTCCTGCTGCTTCACAAAAAGGAA GATGGAATTTGGTCCACTGATATTTTAAAGGACCAGAAAGAACCCAAAAATAAG ACCTTTCTAAGATGCGAGGCCAAGAATTATTCTGGACGTTTCACCTGCTGGTGG CTGACGACAATCAGTACTGATTTGACATTCAGTGTCAAAAGCAGCAGAGGCTCT TCTGACCCCCAAGGGGTGACGTGCGGAGCTGCTACACTCTCTGCAGAGAGAGTC AGAGGGGACAACAAGGAGTATGAGTACTCAGTGGAGTGCCAGGAGGACAGTGCC TGCCCAGCTGCTGAGGAGAGTCTGCCCATTGAGGTCATGGTGGATGCCGTTCAC AAGCTCAAGTATGAAAACTACACCAGCAGCTTCTTCATCAGGGACATCATCAAA CCTGACCCACCCAAGAACTTGCAGCTGAAGCCATTAAAGAATTCTCGGCAGGTG GAGGTCAGCTGGGAGTACCCTGACACCTGGAGTACTCCACATTCCTACTTCTCC CTGACATTCTGCGTTCAGGTCCAGGGCAAGAGCAAGAGAGAAAAGAAAGATAGA GTCTTCACGGACAAGACCTCAGCCACGGTCATCTGCCGCAAAAATGCCAGCATT AGCGTGCGGGCCCAGGACCGCTACTATAGCTCATCTTGGAGCGAATGGGCATCT GTGCCCTGCAGTGTTCCTGGAGTAGGGGTACCTGGGGTGGGCGCCAGAAACCTC CCCGTGGCCACTCCAGACCCAGGAATGTTCCCATGCCTTCACCACTCCCAAAAC CTGCTGAGGGCCGTCAGCAACATGCTCCAGAAGGCCAGACAAACTCTAGAATTT TACCCTTGCACTTCTGAAGAGATTGATCATGAAGATATCACAAAAGATAAAACC AGCACAGTGGAGGCCTGTTTACCATTGGAATTAACCAAGAATGAGAGTTGCCTA AATTCCAGAGAGACCTCTTTCATAACTAATGGGAGTTGCCTGGCCTCCAGAAAG ACCTCTTTTATGATGGCCCTGTGCCTTAGTAGTATTTATGAAGACTTGAAGATG TACCAGGTGGAGTTCAAGACCATGAATGCAAAGCTGCTGATGGACCCTAAGAGG CAGATCTTTCTAGATCAAAACATGCTGGCAGTTATTGATGAGCTGATGCAGGCC CTGAATTTCAACAGTGAGACTGTGCCACAAAAATCCTCCCTTGAAGAACCGGAT TTTTATAAAACTAAAATCAAGCTCTGCATACTTCTTCATGCTTTCAGAATTCGG GCAGTGACTATTGATAGAGTGATGAGCTATCTGAATGCTTCCGGAGGAGGTGGA TCGGGTGGTGGAGGATCTGGTGGAGGTGGAAGT**CTGCTCCCATCCTGGGCCATT**

	ACCTTAATCTCAGTAAATGGAATTTTTGTGATATGCTGCCTGACCTACTGCTTT GCCTAA (Underlined and bold: B7-1 transmembrane domain; Bold: B7-1 cytoplasmic domain.)
Amino acid: SEQ ID NO: 584	MCHQQLVISWFSLVFLASPLVAIWELKKDVYVVELDWYPDAPGEMVVLTCDTPE EDGITWTLDQSSEVLGSGKTLTIQVKEFGDAGQYTCHKGGEVLSHSLLLLHKKE DGIWSTDILKDQKEPKNKTFLRCEAKNYSGRFTCWWLTTISTDLTFSVKSSRGS SDPQGVTCGAATLSAERVRGDNKEYEYSVECQEDSACPAAEESLPIEVMVDAVH KLKYENYTSSFFIRDIIKPDPPKNLQLKPLKNSRQVEVSWEYPDTWSTPHSYFS LTFCVQVQGKSKREKKDRVFTDKTSATVICRKNASISVRAQDRYYSSSWSEWAS VPCSVPGVGVPGVGARNLPVATPDPGMFPCLHHSQNLLRAVSNMLQKARQTLEF YPCTSEEIDHEDITKDKTSTVEACLPLELTKNESCLNSRETSFITNGSCLASRK TSFMMALCLSSIYEDLKMYQVEFKTMNAKLLMDPKRQIFLDQNMLAVIDELMQA LNFNSETVPQKSSLEEPDFYKTKIKLCILLHAFRIRAVTIDRVMSYLNASGGGG SGGGGSGGGGS**LLPSWAITLISVNGIFVICCLTYCFA** (Underlined and bold: B7-1 transmembrane domain; Bold: B7-1 cytoplasmic domain.)
Mouse IL-12 TM p35	
Nucleotide SEQ ID NO: 585	ATGTGTCAGTCTCGATACCTTCTTTTCCTAGCAACCTTAGCGTTATTGAATCAT CTTTCATTAGCGCGTGTCATTCCGGTCTCCGGTCCCGCCCGTTGCCTTTCGCAA AGTCGTAACTTGCTTAAGACTACGGATGATATGGTCAAAACTGCTAGAGAAAAG TTAAAACACTACTCGTGTACGGCTGAAGACATAGACCACGAAGACATCACGCGA GATCAAACAAGTACCCTAAAGACTTGCTTACCGCTAGAGCTTCATAAAAACGAG AGTTGCCTAGCGACCCGAGAGACATCTTCAACAACCAGAGGATCTTGTCTACCC CCTCAGAAGACTTCTCTAATGATGACCTTGTGCCTTGGTAGTATATATGAAGAT TTAAAGATGTACCAGACTGAATTTCAGGCAATCAATGCGGCATTACAAAACCAC AACCATCAGCAGATAATATTAGATAAAGGAATGCTTGTAGCCATTGACGAACTT ATGCAGTCTCTAAACCACAACGGTGAGACACTTCGTCAGAAACCTCCGGTTGGT GAGGCAGATCCTTACCGTGTGAAAATGAAGTTGTGCATTCTATTGCATGCATTT TCGACGCGTGTGGTCACCATCAACAGAGTCATGGGTTATCTAAGTTCTGCTGGT GGAGGTGGAAGTGGAGGTGGAGGAAGTGGTGGAGGAGGAAGT**ACCTTAGTGTTG TTTGGAGCAGGTTTCGGTGCAGTCATAACGGTTGTCGTTATCGTGGTGATCATA AAATGTTTCTGCAAG**TGA (Underlined and bold: transmembrane and cytoplasmic domain.)
Amino acid: SEQ ID NO: 586	MCQSRYLLFLATLALLNHLSLARVIPVSGPARCLSQSRNLLKTTDDMVKTAREK LKHYSCTAEDIDHEDITRDQTSTLKTCLPLELHKNESCLATRETSSTTRGSCLP PQKTSLMMTLCLGSIYEDLKMYQTEFQAINAALQNHNHQQIILDKGMLVAIDEL MQSLNHNGETLRQKPPVGEADPYRVKMKLCILLHAFSTRVVTINRVMGYLSSAG GGGSGGGGSGGGGS**TLVLFGAGFGAVITVVVIVVIIKCFCK** (Underlined and bold: transmembrane and cytoplasmic domain.)
Mouse IL-12 TM p70	

Nucleotide SEQ ID NO: 587	ATGTGCCCCCAAAAGTTGACCATCTCATGGTTCGCAATTGTACTACTAGTGAGT CCCTTGATGGCAATGTGGGAGCTTGAAAAGGACGTCTATGTGGTGGAGGTTGAC TGGACGCCCGATGCGCCAGGAGAAACAGTGAATCTAACTTGCGACACACCTGAA GAGGATGACATAACGTGGACATCTGATCAAAGACATGGTGTGATAGGTTCTGGT AAGACACTTACGATTACCGTCAAGGAATTTTTGGACGCTGGACAATACACTTGT CACAAAGGAGGTGAAACACTATCGCATTCACACCTACTTTTACACAAGAAGGAA AATGGTATTTGGAGTACGGAGATCCTAAAGAATTTTAAAAATAAGACCTTTTTA AAGTGCGAAGCACCAAATTATTCCGGACGATTTACATGTTCATGGTTAGTTCAA CGAAATATGGATTTAAAATTCAATATCAAGTCAAGTTCTAGTTCCCCGGATTCC CGAGCGGTTACTTGCGGTATGGCCAGTTTGAGTGCCGAGAAAGTCACACTAGAC CAGCGAGATTATGAGAAATATTCCGTTTCCTGCCAGGAGGACGTAACTTGTCCG ACTGCCGAGGAGACTTTGCCGATAGAGCTTGCCTTAGAGGCCCGACAGCAGAAT AAGTACGAGAATTACTCTACCTCTTTTTTCATCCGAGACATCATCAAACCTGAC CCACCAAAGAATTTGCAAATGAAACCCTTAAAAAACTCACAGGTGGAGGTGTCC TGGGAATATCCTGACTCTTGGTCTACCCCCCATTCTTACTTTTCCCTTAAGTTC TTCGTTAGAATACAACGTAAAAAAGAGAAGATGAAAGAAACGGAAGAAGGTTGC AACCAGAAAGGAGCATTTCTAGTTGAAAAGACCTCTACGGAAGTCCAGTGTAAA GGTGGAAATGTGTGTGTGCAAGCCCAGGACCGATATTACAACAGTTCGTGTTCG AAGTGGGCTTGCGTGCCGTGTCGTGTCCGATCTGTACCAGGAGTCGGAGTTCCT GGAGTAGGTCGTGTAATACCGGTATCCGGACCAGCTCGTTGCTTATCTCAATCG CGAAACCTACTTAAAACAACCGATGACATGGTGAAGACAGCGAGAGAAAAGCTT AAACATTATTCCTGTACCGCCGAAGACATCGATCATGAGGATATCACGAGAGAC CAGACCTCGACACTTAAGACATGCTTGCCACTAGAACTTCATAAAAATGAGTCT TGCTTAGCAACGCGAGAAACGTCGTCTACGACGCGTGGTTCATGTTTGCCGCCC CAAAAGACATCCTTGATGATGACGTTGTGTCTTGGATCCATCTATGAGGATTTA AAAATGTACCAGACAGAATTTCAGGCTATCAATGCAGCTCTACAGAATCATAAT CACCAGCAGATTATCTTAGACAAGGGAATGTTAGTAGCAATCGATGAGCTTATG CAATCCTTGAATCATAACGGAGAAACATTACGACAAAAGCCTCCGGTCGGTGAA GCGGATCCATATCGTGTGAAGATGAAATTATGTATATTGTTGCACGCCTTTAGT ACGCGTGTGGTCACCATAAACCGAGTAATGGGATACTTGTCCTCGGCGGGAGGT GGTGGTTCTGGTGGAGGTGGATCAGGTGGTGGTGGTTCA**ACCTTGGTTCTTTTT GGTGCGGGTTTCGGTGCCGTGATTACTGTCGTCGTCATAGTCGTCATTATTAAA TGTTTTTGTAAG**TAA (Underlined and bold: transmembrane and cytoplasmic domain.)
Amino acid: SEQ ID NO: 588	MCPQKLTISWFAIVLLVSPLMAMWELEKDVYVVEVDWTPDAPGETVNLTCDTPE EDDITWTSDQRHGVIGSGKTLTITVKEFLDAGQYTCHKGGETLSHSHLLLHKKE NGIWSTEILKNFKNKTFLKCEAPNYSGRFTCSWLVQRNMDLKFNIKSSSSSPDS RAVTCGMASLSAEKVTLDQRDYEKYSVSCQEDVTCPTAEETLPIELALEARQQN KYENYSTSFFIRDIIKPDPPKNLQMKPLKNSQVEVSWEYPDSWSTPHSYFSLKF FVRIQRKKEKMKETEEGCNQKGAFLVEKTSTEVQCKGGNVCVQAQDRYYNSSCS KWACVPCRVRSVPGVGVPGVGRVIPVSGPARCLSQSRNLLKTTDDMVKTAREKL KHYSCTAEDIDHEDITRDQTSTLKTCLPLELHKNESCLATRETSSTTRGSCLPP QKTSLMMTLCLGSIYEDLKMYQTEFQAINAALQNHNHQQIILDKGMLVAIDELM QSLNHNGETLRQKPPVGEADPYRVKMKLCILLHAFSTRVVTINRVMGYLSSAGG GGSGGGGSGGGGS**TLVLFGAGFGAVITVVVIVVIIKCFCK**

	(Underlined and bold: transmembrane and cytoplasmic domain.)
Human FLT3-L	
Nucleotide SEQ ID NO: 216	ATGACAGTCTTAGCGCCAGCTTGGAGTCCTACCACATATTTACTACTATTATTG CTTTTATCTAGTGGTTTATCAGGAACGCAAGACTGCTCATTCCAACATTCACCG ATCAGTTCCGACTTTGCAGTTAAGATTCGAGAACTATCAGACTACCTATTGCAA GACTATCCGGTGACGGTAGCATCGAATCTTCAAGACGAAGAGCTTTGTGGTGGA CTATGGCGTCTTGTACTTGCCCAAAGATGGATGGAGCGACTAAAAACCGTTGCC GGTTCAAAGATGCAGGGTTTACTAGAGCGTGTGAATACGGAAATTCATTTTGTT ACGAAATGTGCGTTCCAACCCCCACCCAGTTGCTTGCGTTTCGTGCAGACTAAT ATCTCTCGTTTACTACAAGAAACATCCGAGCAACTAGTGGCGCTAAAGCCCTGG ATAACACGTCAAAACTTTAGTCGTTGCTTGGAGTTACAGTGCCAACCCGGTGCC CCACGACCTCAAAGTCCTGGTCCAGCGGCTTGCGGAGCCCTTACCTGGCCTCGA CCGCATCCGGCCGAACCATGA
Amino acid SEQ ID NO: 213	MTVLAPAWSPTTYLLLLLLLSSGLSGTQDCSFQHSPISSDFAVKIRELSDYLLQ DYPVTVASNLQDEELCGGLWRLVLAQRWMERLKTVAGSKMQGLLERVNTEIHFV TKCAFQPPPSCLRFVQTNISRLLQETSEQLVALKPWITRQNFSRCLELQCQPGA PRPQSPGPAACGALTWPRPHPAEP

[00646] See Example 32 in Section 6.32 for exemplary methods of generating a recombinant vaccinia virus described herein.

5.4. Virus Propagation

[00647] The present invention features recombinant orthopoxviruses, including those constructed with one or more gene deletions compared to wild-type, such that the virus exhibits desirable properties for use against cancer cells, while being less toxic or non-toxic to non-cancer cells. This section summarizes various protocols, by way of example, for producing recombinant orthopoxviruses described herein, such as methods for generating mutated viruses through the use of recombinant DNA technology.

[00648] For example, to generate mutations in the orthopoxvirus genome, native and modified polypeptides may be encoded by a nucleic acid molecule comprised in a vector. Vectors may include, for example, plasmids, cosmids, viruses (bacteriophage, animal viruses, and plant viruses), and artificial chromosomes (*e.g.*, YACs). One of skill in the art would be well equipped to construct a vector through standard recombinant techniques, which are described in Sambrook *et al.*, (1989) and Ausubel *et al.*, 1994, both incorporated herein by reference in their entirety. In addition to encoding a modified polypeptide, a vector may encode non-modified polypeptide sequences such as a tag or targeting molecule.

[00649] In order to propagate a vector in a host cell, it may contain one or more origins of replication sites (often termed "ori"), which is a specific nucleic acid sequence at which replication is initiated. Alternatively, an autonomously replicating sequence (ARS) can be employed if the host cell is yeast.

[00650] In the context of expressing a heterologous nucleic acid sequence, "host cell" refers to a prokaryotic or eukaryotic cell, and it includes any transformable organism that is capable of replicating a vector and/or expressing a heterologous gene encoded by a vector. A host cell can, and has been, used as a recipient for vectors or viruses (which qualify as a vector if they express an exogenous polypeptide). A host cell may be "transfected" or "transformed," which refers to a process by which exogenous nucleic acid, such as a modified protein-encoding sequence, is transferred or introduced into the host cell. A transformed cell includes the primary subject cell and its progeny. Host cells may be derived from prokaryotes or eukaryotes, including yeast cells, insect cells, and mammalian cells, depending upon whether the desired result is replication of the vector or expression of part or all of the vector-encoded nucleic acid sequences. Numerous cell lines and cultures are available for use as a host cell, and they can be obtained through the American Type Culture Collection (ATCC), which is an organization that serves as an archive for living cultures and genetic materials (www.atcc.org). An appropriate host can be determined by one of skill in the art based on the vector backbone and the desired result. A plasmid or cosmid, for example, can be introduced into a prokaryote host cell for replication of many vectors. Bacterial cells used as host cells for vector replication and/or expression include DH5α, JM109, and KCB, as well as a number of commercially available bacterial hosts such as SURE® Competent Cells and SOLOPACK™ Gold Cells (STRATAGENE®, La Jolla, Calif.). Alternatively, bacterial cells such as E. coli LE392 could be used as host cells for phage viruses. Appropriate yeast cells include *Saccharomyces cerevisiae*, *Saccharomyces pombe*, and *Pichia pastoris*. Examples of eukaryotic host cells for replication and/or expression of a vector include HeLa, NIH3T3, Jurkat, 293, COS, CHO, Saos, and PC12. Many host cells from various cell types and organisms are available and would be known to one of skill in the art. Similarly, a viral vector may be used in conjunction with either a eukaryotic or prokaryotic host cell, particularly one that is permissive for replication or expression of the vector. Some vectors may employ control sequences that allow it to be replicated and/or expressed in both prokaryotic and eukaryotic cells. One of skill in the art would further understand the conditions under which to incubate all of the above described

host cells to maintain them and to permit replication of a vector. Also understood and known are techniques and conditions that would allow large-scale production of vectors, as well as production of the nucleic acids encoded by vectors and their cognate polypeptides, proteins, or peptides.

[00651] Also provided herein are methods of propagating a virus described in Section 5.2.4 using a cell, a cell line, or a packaging cell line described in Sections 5.2.6 and 5.4. In one aspect, provided herein is a method of propagating a virus, comprising culturing a cell, a cell line, or a packaging cell line infected with a virus described herein. In some embodiments, the virus is isolated or purified after propagation. See examples in Section 6 for exemplary methods and techniques for propagating viruses.

5.5. Methods of Treatment

5.5.1. Pharmaceutical Composition, Administration, and Doses

[00652] Also provided herein are pharmaceutical composition comprising a virus described in Section 5.2.4 and a physiologically acceptable carrier. In certain embodiments, the pharmaceutical composition provided herein comprises a therapeutically effective amount of the virus. In certain embodiments, the pharmaceutical composition provided herein is to be used in a method of treatment described herein.

[00653] Therapeutic compositions containing recombinant orthopoxvirus vectors of the invention can be prepared using methods known in the art. For example, such compositions can be prepared using, e.g., physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980); incorporated herein by reference), and in a desired form, e.g., in the form of lyophilized formulations or aqueous solutions.

[00654] To induce oncolysis, kill cells, inhibit growth, inhibit metastases, decrease tumor size and otherwise reverse or reduce the malignant phenotype of tumor cells, using the methods and compositions of the present invention, one may contact a tumor with the modified orthopoxvirus, *e.g.*, by administration of the orthopoxvirus to a patient having cancer by way of, for instance, one or more of the routes of administration described herein. The route of administration may vary with the location and nature of the cancer, and may include, *e.g.*, intradermal, transdermal, parenteral, intravenous, intramuscular, intranasal, subcutaneous, regional (*e.g.*, in the proximity of a tumor, particularly with the vasculature or adjacent vasculature of a tumor), percutaneous, intratracheal, intraperitoneal, intraarterial,

intravesical, intratumoral, inhalation, perfusion, lavage, and oral administration and formulation. In specific embodiments, the pharmaceutical composition provided herein is formulated so that it is suitable for the route of administration to be employed.

[00655] The term "intravascular" is understood to refer to delivery into the vasculature of a patient, meaning into, within, or in a vessel or vessels of the patient. In certain embodiments, the administration is into a vessel considered to be a vein (intravenous), while in others administration is into a vessel considered to be an artery. Veins include, but are not limited to, the internal jugular vein, a peripheral vein, a coronary vein, a hepatic vein, the portal vein, great saphenous vein, the pulmonary vein, superior vena cava, inferior vena cava, a gastric vein, a splenic vein, inferior mesenteric vein, superior mesenteric vein, cephalic vein, and/or femoral vein. Arteries include, but are not limited to, coronary artery, pulmonary artery, brachial artery, internal carotid artery, aortic arch, femoral artery, peripheral artery, and/or ciliary artery. It is contemplated that delivery may be through or to an arteriole or capillary.

[00656] Intratumoral injection, or injection directly into the tumor vasculature is specifically contemplated for discrete, solid, accessible tumors. Local, regional or systemic administration also may be appropriate. The viral particles may advantageously be contacted by administering multiple injections to the tumor, spaced, for example, at approximately 1 cm intervals. In the case of surgical intervention, the present invention may be used preoperatively, such as to render an inoperable tumor subject to resection. Continuous administration also may be applied where appropriate, for example, by implanting a catheter into a tumor or into tumor vasculature. Such continuous perfusion may take place, for example, for a period of from about 1-2 hours, to about 2-6 hours, to about 6-12 hours, or about 12-24 hours following the initiation of treatment. Generally, the dose of the therapeutic composition via continuous perfusion may be equivalent to that given by a single or multiple injections, adjusted over a period of time during which the perfusion occurs. It is further contemplated that limb perfusion may be used to administer therapeutic compositions of the present invention, particularly in the treatment of melanomas and sarcomas.

[00657] Treatment regimens may vary, and often depend on tumor type, tumor location, disease progression, and health and age of the patient. Certain types of tumor will require more aggressive treatment, while at the same time, certain patients cannot tolerate more taxing protocols. The clinician will be best suited to make such decisions based on the known efficacy and toxicity (if any) of the therapeutic formulations. In certain embodiments, the tumor being treated may not, at least initially, be resectable. Treatments with the

therapeutic agent of the disclosure may increase the resectability of the tumor due to shrinkage at the margins or by elimination of certain particularly invasive portions. Following treatments, resection may be possible. Additional treatments subsequent to resection will serve to eliminate microscopic residual disease at the tumor site.

[00658] The treatments may include various "unit doses." Unit dose is defined as containing a predetermined-quantity of the therapeutic composition. The quantity to be administered, and the particular route and formulation, are within the skill of those in the clinical arts. A unit dose need not be administered as a single injection but may comprise continuous infusion over a set period of time. Unit dose of the present invention may conveniently be described in terms of plaque forming units (pfu) for a viral construct. Unit doses may range from 10^3, 10^4, 10^5, 10^6, 10^7, 10^8, 10^9, 10^{10}, 10^{11}, 10^{12}, to 10^{13} pfu and higher. Additionally or alternatively, depending on the kind of virus and the titer attainable, one may deliver 1 to 100, 10 to 50, 100-1000, or up to about or at least about 1×10^4, 1×10^5, 1×10^6, 1×10^7, 1×10^8, 1×10^9, 1×10^{10}, 1×10^{11}, 1×10^{12}, 1×10^{13}, 1×10^{14}, or 1×10^{15} or higher infectious viral particles (vp), including all values and ranges there between, to the tumor or tumor site.

[00659] Another method of delivery of the recombinant orthopoxvirus genome disclosed herein to cancer or tumor cells may be via intratumoral injection. However, the pharmaceutical compositions disclosed herein may alternatively be administered parenterally, intravenously, intradermally, intramuscularly, transdermally or even intraperitoneally as described in U.S. Pat. No. 5,543,158; U.S. Pat. No. 5,641,515 and U.S. Pat. No. 5,399,363 (each specifically incorporated herein by reference in its entirety). Injection of nucleic acid constructs may be delivered by syringe or any other method used for injection of a solution, as long as the expression construct can pass through the particular gauge of needle required for injection. An exemplary needleless injection system that may be used for the administration of recombinant orthopoxviruses described herein is exemplified in U.S. Pat. No. 5,846,233. This system features a nozzle defining an ampule chamber for holding the solution and an energy device for pushing the solution out of the nozzle to the site of delivery. Another exemplary syringe system is one that permits multiple injections of predetermined quantities of a solution precisely at any depth (U.S. Pat. No. 5,846,225).

[00660] Mixtures of the viral particles or nucleic acids described herein may be prepared in water suitably mixed with one or more excipients, carriers, or diluents. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations may contain a preservative to

prevent the growth of microorganisms. The pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (U.S. Pat. No. 5,466,468, specifically incorporated herein by reference in its entirety). In all cases the form may be sterile and may be fluid to the extent that easy syringability exists. It may be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (*e.g.*, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

[00661] For parenteral administration in an aqueous solution, for example, the solution may be suitably buffered if necessary and the liquid diluent first rendered isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous, intratumoral and intraperitoneal administration. In this connection, sterile aqueous media that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml of hypodermoclysis fluid or injected at the proposed site of infusion. Some variation in dosage will necessarily occur depending on the condition of the subject being treated. The person responsible for administration will, in any event, determine the appropriate dose for the individual subject. Moreover, for human administration, preparations should meet sterility, pyrogenicity, general safety, and purity standards as required by FDA Office of Biologics standards.

[00662] As used herein, "carrier" includes any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as

any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase "pharmaceutically acceptable" or "pharmacologically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human. The preparation of an aqueous composition that contains a protein as an active ingredient is well understood in the art. Typically, such compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection can also be prepared.

5.5.2. Methods of Treatment

[00663] Also provided herein are methods of treating a cell proliferation disorder, such as cancer in a patient (*e.g.*, a mammalian patient, such as a human patient).

[00664] In one aspect, provided herein is a method of treating a cell proliferation disorder, such as cancer in a patient (*e.g.*, a mammalian patient, such as a human patient), the method comprising administering to the patient (*e.g.*, a mammalian patient, such as a human patient) a therapeutically effective amount of a virus described in Section 5.2.4.

[00665] In another aspect, provided herein is a method of treating a cell proliferation disorder, such as cancer in a patient (*e.g.*, a mammalian patient, such as a human patient), the method comprising administering to the patient (*e.g.*, a mammalian patient, such as a human patient) a therapeutically effective amount of a pharmaceutical composition described in Section 5.5.1.

[00666] In a specific embodiment of the method of treating described herein, the mammalian patient is a human patient.

[00667] In certain embodiments of the method of treating described herein, the cancer is selected from the group consisting of leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, and throat cancer.

[00668] In certain embodiments of the method of treating described herein, the cancer is selected from the group consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia

(CML), adrenocortical carcinoma, AIDS-related lymphoma, primary CNS lymphoma, anal cancer, appendix cancer, astrocytoma, atypical teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, extrahepatic cancer, Ewing sarcoma family, osteosarcoma and malignant fibrous histiocytoma, central nervous system embryonal tumors, central nervous system germ cell tumors, craniopharyngioma, ependymoma, bronchial tumors, Burkitt lymphoma, carcinoid tumor, primary lymphoma, chordoma, chronic myeloproliferative neoplasms, colon cancer, extrahepatic bile duct cancer, ductal carcinoma in situ (DCIS), endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, extracranial germ cell tumor, extragonadal germ cell tumor, fallopian tube cancer, fibrous histiocytoma of bone, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), testicular germ cell tumor, gestational trophoblastic disease, glioma, childhood brain stem glioma, hairy cell leukemia, hepatocellular cancer, Langerhans cell histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, islet cell tumors, pancreatic neuroendocrine tumors, Wilms tumor and other childhood kidney tumors, Langerhans cell histiocytosis, small cell lung cancer, cutaneous T cell lymphoma, intraocular melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer, midline tract carcinoma, multiple endocrine neoplasia syndromes, multiple myeloma/plasma cell neoplasm, myelodysplastic syndromes, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin's lymphoma (NHL), non-small cell lung cancer (NSCLC), epithelial ovarian cancer, germ cell ovarian cancer, low malignant potential ovarian cancer, pancreatic neuroendocrine tumors, papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pituitary tumor, pleuropulmonary blastoma, primary peritoneal cancer, rectal cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, Kaposi's sarcoma, rhabdomyosarcoma, Sézary syndrome, small intestine cancer, soft tissue sarcoma, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, urethral cancer, endometrial uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, and Waldenström macroglobulinemia.

[00669] In some embodiments of the method of treating described herein, the virus and the pharmaceutical composition are not administered in combination with another agent for treating the cell proliferation disorder (such as cancer).

[00670] In other embodiments of the method of treating described herein, the virus or the pharmaceutical composition is administered in combination with one or more additional

agents for treating the cell proliferation disorder (such as cancer), for example, the one or more additional agents described in Section 5.5.3.

[00671] The recombinant orthopoxvirus and the pharmaceutical composition disclosed herein can be administered to a subject, *e.g.*, a mammalian subject, such as a human, suffering from a cell proliferation disorder, such as cancer, e.g., to kill cancer cells directly by oncolysis and/or to enhance the effectiveness of the adaptive immune response against the target cancer cells. In some embodiments, the cell proliferation disorder is a cancer, such as leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, or throat cancer. In particular cases, the cell proliferation disorder may be a cancer selected from the group consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), adrenocortical carcinoma, AIDS-related lymphoma, primary CNS lymphoma, anal cancer, appendix cancer, astrocytoma, atypical teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, extrahepatic cancer, ewing sarcoma family, osteosarcoma and malignant fibrous histiocytoma, central nervous system embryonal tumors, central nervous system germ cell tumors, craniopharyngioma, ependymoma, bronchial tumors, burkitt lymphoma, carcinoid tumor, primary lymphoma, chordoma, chronic myeloproliferative neoplasms, colon cancer, extrahepatic bile duct cancer, ductal carcinoma in situ (DCIS), endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, extracranial germ cell tumor, extragonadal germ cell tumor, fallopian tube cancer, fibrous histiocytoma of bone, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), testicular germ cell tumor, gestational trophoblastic disease, glioma, childhood brain stem glioma, hairy cell leukemia, hepatocellular cancer, langerhans cell histiocytosis, hodgkin lymphoma, hypopharyngeal cancer, islet cell tumors, pancreatic neuroendocrine tumors, wilms tumor and other childhood kidney tumors, langerhans cell histiocytosis, small cell lung cancer, cutaneous T-cell lymphoma, intraocular melanoma, merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer, midline tract carcinoma, multiple endocrine neoplasia syndromes, multiple myeloma/plasma cell neoplasm, myelodysplastic syndromes, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-hodgkin lymphoma (NHL), non-small cell lung cancer (NSCLC), epithelial ovarian cancer, germ cell

ovarian cancer, low malignant potential ovarian cancer, pancreatic neuroendocrine tumors, papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pituitary tumor, pleuropulmonary blastoma, primary peritoneal cancer, rectal cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, kaposi sarcoma, rhabdomyosarcoma, sézary syndrome, small intestine cancer, soft tissue sarcoma, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, urethral cancer, endometrial uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, and Waldenström macroglobulinemia.

[00672] A physician having ordinary skill in the art can readily determine an effective amount of the recombinant orthopoxvirus vector for administration to a subject, *e.g.*, a mammalian subject (*e.g.*, a human) in need thereof. For example, a physician may start prescribing doses of recombinant orthopoxvirus vector at levels lower than that required in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved. Alternatively, a physician may begin a treatment regimen by administering a dose of recombinant orthopoxvirus vector and subsequently administer progressively lower doses until a therapeutic effect is achieved (*e.g.*, a reduction in the volume of one or more tumors). In general, a suitable daily dose of a recombinant orthopoxvirus vector of the invention will be an amount of the recombinant orthopoxvirus vector which is the lowest dose effective to produce a therapeutic effect. A daily dose of a therapeutic composition of the recombinant orthopoxvirus vector of the invention may be administered as a single dose or as two, three, four, five, six or more doses administered separately at appropriate intervals throughout the day, week, month, or year, optionally, in unit dosage forms. While it is possible for the recombinant orthopoxvirus vector of the invention to be administered alone, it may also be administered as a pharmaceutical formulation in combination with excipients, carriers, and optionally, additional therapeutic agents.

[00673] Recombinant orthopoxvirus vectors of the invention can be monitored for their ability to attenuate the progression of a cell proliferation disease, such as cancer, by any of a variety of methods known in the art. For instance, a physician may monitor the response of a subject, *e.g.*, a mammalian subject (*e.g.*, a human) to treatment with recombinant orthopoxvirus vector of the invention by analyzing the volume of one or more tumors in the patient. Alternatively, a physician may monitor the responsiveness of a subject (*e.g.*, a human) t to treatment with recombinant orthopoxvirus vector of the invention by analyzing

the T-reg cell population in the lymph of a particular subject. For instance, a physician may withdraw a sample from a subject, *e.g.*, a mammalian subject (*e.g.*, a human) and determine the quantity or density of cancer cells using established procedures, such as fluorescence activated cell sorting. A finding that the quantity of cancer cells in the sample has decreased (*e.g.*, by 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99%, or more) relative to the quantity of cancer cells in a sample obtained from the subject prior to administration of the recombinant orthopoxvirus may be an indication that the orthopoxvirus administration is effectively treating the cancer.

5.5.3. Combination Therapy

[00674] The recombinant orthopoxvirus vectors described herein may be administered with one or more additional agents, such as an immune checkpoint inhibitor. For instance, the recombinant orthopoxvirus vector can be administered simultaneously with, admixed with, or administered separately from an immune checkpoint inhibitor. Exemplary immune checkpoint inhibitors for use in conjunction with the compositions and methods of the invention include but are not limited to OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof. Additionally or alternatively, a vector of the invention can be administered simultaneously with, admixed with, or administered separately from an interleukin (IL). For instance, the recombinant orthopoxvirus vector can be administered simultaneously with, admixed with, or administered separately from an interleukin. Exemplary interleukins for use in conjunction with the compositions and methods of the invention include but are not limited to IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23. Additionally or alternatively, a vector of the invention can be administered simultaneously with, admixed with, or administered separately from an interferon. For instance, the recombinant orthopoxvirus vector can be administered simultaneously with, admixed with, or administered separately from an interferon. Exemplary interferons for use in conjunction with the compositions and methods of the invention include but are not limited to IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma. Additionally or alternatively, a

vector of the invention can be administered simultaneously with, admixed with, or administered separately from a TNF superfamily member protein. For instance, the recombinant orthopoxvirus vector can be administered simultaneously with, admixed with, or administered separately from a TNF superfamily member protein. Exemplary TNF superfamily member proteins for use in conjunction with the compositions and methods of the invention include but are not limited to TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand. Additionally or alternatively, a vector of the invention can be administered simultaneously with, admixed with, or administered separately from a cytokine. For instance, the recombinant orthopoxvirus vector can be administered simultaneously with, admixed with, or administered separately from a cytokine. Exemplary cytokines for use in conjunction with the compositions and methods of the invention includes but are not limited to GM-CSF, Flt3 ligand, CD40 ligand, anti-TGF-beta, anti-VEGF-R2, and cGAS (guanyl adenylate cyclase).

[00675] Additionally or alternatively, immune checkpoint inhibitors may be expressed in the orthopoxvirus itself. For instance, the recombinant orthopoxvirus vector can include a transgene encoding an immune checkpoint inhibitor. Exemplary immune checkpoint inhibitors for expression by the orthopoxvirus of the compositions and methods of the invention include but are not limited to OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof. Additionally or alternatively, interleukins may be expressed in the orthopoxvirus itself. For instance, the recombinant orthopoxvirus vector can include a transgene encoding an interleukin. Exemplary immune checkpoint inhibitors for expression by the orthopoxvirus of the compositions and methods of the invention include but are not limited to IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23. Additionally or alternatively, interferons may be expressed in the orthopoxvirus itself. For instance, the recombinant orthopoxvirus vector can include a transgene encoding an interferon. Exemplary interferons for expression by the orthopoxvirus of the compositions and methods of the invention include but are not limited to IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma. Additionally or alternatively, TNF superfamily member proteins may be expressed in the

orthopoxvirus itself. For instance, the recombinant orthopoxvirus vector can include a transgene encoding a TNF superfamily member protein. Exemplary TNF superfamily member proteins for expression by the orthopoxvirus of the compositions and methods of the invention include but are not limited to TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand. Additionally or alternatively, cytokines may be expressed in the orthopoxvirus itself. For instance, the recombinant orthopoxvirus vector can include a transgene encoding a cytokine. Exemplary cytokines for expression by the orthopoxvirus of the compositions and methods of the invention include but are not limited to GM-CSF, fms-related tyrosine kinase 3 (Flt3) ligand, CD40 ligand, TGF-beta, VEGF-R2, and c-KIT.

[00676] Additionally or alternatively, tumor-associated antigens may be expressed in the orthopoxvirus itself. For instance, the recombinant orthopoxvirus vector can include a transgene encoding a tumor-associated antigen. Exemplary tumor-associated antigens for expression by the orthopoxvirus of the compositions and methods of the invention include but are not limited to CD19, CD33, EpCAM, CEA, PSMA, EGFRvIII, CD133, EGFR, CDH19, ENPP3, DLL3, MSLN, ROR1, HER2, HLAA2, EphA2, EphA3, MCSP, CSPG4, NG2, RON, FLT3, BCMA, CD20, FAPα, FRα, CA-9, PDGFRα, PDGFRβ, FSP1, S100A4, ADAM12m, RET, MET, FGFR, INSR, NTRK, MAGE-A3, NY-ESO-1, one or more human papillomavirus (HPV) proteins, E6 and E7 proteins of HPV16, E6 and E7 proteins of HPV18, brachyury, or prostatic acid phosphatase, or one or more fragments thereof. Additional examples of tumor-associated antigens for use in conjunction with the compositions and methods described herein include, but are not limited to, those listed in Tables 3-30

[00677] In certain embodiments of the method of treating described herein, the method further comprises administering to the patient (*e.g.*, a mammalian patient, such as a human patient) an immune checkpoint inhibitor. In specific embodiments, the immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof. In a specific embodiment, the immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof. In another specific embodiment, the immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof. In

another specific embodiment, the immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof. In another specific embodiment, the immune checkpoint inhibitor is an anti-PD-L1 antibody or antigen-binding fragment thereof. In a specific embodiment, the immune checkpoint inhibitor is ipilimumab. In another specific embodiment, the immune checkpoint inhibitor is tremelimumab. In another specific embodiment, the immune checkpoint inhibitor is nivolumab. In another specific embodiment, the immune checkpoint inhibitor is pembrolizumab. In another specific embodiment, the immune checkpoint inhibitor is cemiplimab. In another specific embodiment, the immune checkpoint inhibitor is atezolizumab. In another specific embodiment, the immune checkpoint inhibitor is avelumab. In another specific embodiment, the immune checkpoint inhibitor is durvalumab.

[00678] In certain embodiments of the method of treating described herein, the method further comprises administering to the patient (*e.g.*, a mammalian patient, such as a human patient) an interleukin. In specific embodiments, the interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23. In specific embodiments, the interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70. In specific embodiments, the interleukin is membrane-bound.

[00679] In certain embodiments of the method of treating described herein, the method further comprises administering to the patient (*e.g.*, a mammalian patient, such as a human patient) an interferon. In specific embodiments, the interferon is selected from the group consisting of IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

[00680] In certain embodiments of the method of treating described herein, the method further comprises administering to the patient (*e.g.*, a mammalian patient, such as a human patient) a cytokine. In specific embodiments, the cytokine is a TNF superfamily member protein. In a specific embodiment, the TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand. In specific embodiments, the cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, TGF-beta, VEGF-R2, and cKit. In a specific embodiment, the cytokine is Flt3 ligand.

5.6. Kits

[00681] Also provided herein are kits that can be used in accordance with the invention.

[00682] In one aspect, provided herein is a kit comprising a nucleic acid described in Section 5.2.3 and a package insert instructing a user of the kit to express the nucleic acid in a host cell.

[00683] In another aspect, provided herein is a kit comprising a virus described in Section 5.2.4 and a package insert instructing a user of the kit to express the virus in a host cell.

[00684] In another aspect, provided herein is a kit comprising a virus described in Section 5.2.4 and a package insert instructing a user to administer a therapeutically effective amount of the virus to a patient (*e.g.*, a mammalian patient, such as a human patient) having cancer, thereby treating the cancer. In certain embodiments, the mammalian patient is a human patient. The cancer to be treated can be a cancer described in Section 5.5.

[00685] In preferred embodiments, the nucleic acid or the virus is stored in one or more containers suitable for storing the nucleic acid or the virus. In certain embodiments, the kits provided herein further comprise controls suitable for their intended use.

5.7. Illustrative Embodiments

5.7.1. Set 1

1. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

2. The nucleic acid of embodiment 1, wherein said deletion comprises at least 3 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

3. The nucleic acid of embodiment 2, wherein said deletion comprises at least 4 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

4. The nucleic acid of embodiment 3, wherein said deletion comprises at least 5 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R,

C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

5. The nucleic acid of embodiment 4, wherein said deletion comprises at least 6 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

6. The nucleic acid of embodiment 5, wherein said deletion comprises at least 7 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

7. The nucleic acid of embodiment 6, wherein said deletion comprises at least 8 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

8. The nucleic acid of embodiment 7, wherein said deletion comprises at least 9 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

9. The nucleic acid of embodiment 8, wherein said deletion comprises at least 10 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

10. The nucleic acid of embodiment 9, wherein said deletion comprises at least 11 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

11. The nucleic acid of embodiment 10, wherein said deletion comprises at least 12 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

12. The nucleic acid of embodiment 11, wherein said deletion comprises at least 13 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L,

K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

13. The nucleic acid of embodiment 12, wherein said deletion comprises at least 14 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

14. The nucleic acid of embodiment 13, wherein said deletion comprises at least 15 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

15. The nucleic acid of embodiment 14, wherein said deletion comprises at least 16 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

16. The nucleic acid of embodiment 15, wherein said deletion comprises at least 17 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

17. The nucleic acid of embodiment 16, wherein said deletion comprises at least 18 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

18. The nucleic acid of embodiment 17, wherein said deletion comprises at least 19 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

19. The nucleic acid of embodiment 18, wherein said deletion comprises at least 20 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

20. The nucleic acid of embodiment 19, wherein said deletion comprises at least 21 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L,

K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

21. The nucleic acid of embodiment 20, wherein said deletion comprises each of said F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R genes.

22. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

23. The nucleic acid of any one of embodiments 1-22, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

24. The nucleic acid of embodiment 23, wherein said deletion comprises at least 2 genes, each independently selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

25. The nucleic acid of embodiment 24, wherein said deletion comprises at least 3 genes, each independently selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

26. The nucleic acid of embodiment 25, wherein said deletion comprises at least 4 genes, each independently selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

27. The nucleic acid of embodiment 26, wherein said deletion comprises at least 5 genes, each independently selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

28. The nucleic acid of embodiment 27, wherein said deletion comprises each of said B14R, B16R, B17L, B18R, B19R, and B20R genes.

29. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

30. The nucleic acid of any one of embodiments 1-29, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

31. The nucleic acid of embodiment 30, wherein said deletion comprises at least 2 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

32. The nucleic acid of embodiment 31, wherein said deletion comprises at least 3 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

33. The nucleic acid of embodiment 32, wherein said deletion comprises at least 4 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

34. The nucleic acid of embodiment 33, wherein said deletion comprises at least 5 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

35. The nucleic acid of embodiment 34, wherein said deletion comprises at least 6 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

36. The nucleic acid of embodiment 35, wherein said deletion comprises at least 7 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

37. The nucleic acid of embodiment 36, wherein said deletion comprises at least 8 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

38. The nucleic acid of embodiment 37, wherein said deletion comprises at least 9 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

39. The nucleic acid of embodiment 38, wherein said deletion comprises at least 10 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

40. The nucleic acid of embodiment 39, wherein said deletion comprises each of said C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L genes.

41. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a caspase-9 inhibitor.

42. The nucleic acid of any one of embodiments 1-41, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a caspase-9 inhibitor.

43. The nucleic acid of embodiment 41 or 42, wherein said gene that encodes a caspase-9 inhibitor is F1L.

44. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a BCL-2 inhibitor.

45. The nucleic acid of any one of embodiments 1-44, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a BCL-2 inhibitor.

46. The nucleic acid of embodiment 44 or 45, wherein said gene that encodes a BCL-2 inhibitor is N1L.

47. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a dUTPase.

48. The nucleic acid of any one of embodiments 1-47, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a dUTPase.

49. The nucleic acid of embodiment 46 or 47, wherein said gene that encodes a dUTPase is F2L.

50. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a IFN-alpha/beta-receptor-like secreted glycoprotein.

51. The nucleic acid of any one of embodiments 1-50, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a IFN-alpha/beta-receptor-like secreted glycoprotein.

52. The nucleic acid of embodiment 50 or 51, wherein said gene that encodes a IFN-alpha/beta-receptor-like secreted glycoprotein is B19R.

53. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes an IL-1-beta-inhibitor.

54. The nucleic acid of any one of embodiments 1-53, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes an IL-1-beta-inhibitor.

55. The nucleic acid of embodiment 53 or 54, wherein said gene that encodes an IL-1-beta-inhibitor is B16R.

56. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a phospholipase-D.

57. The nucleic acid of any one of embodiments 1-56, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a phospholipase-D.

58. The nucleic acid of embodiment 56 or 57, wherein said gene that encodes a phospholipase-D is K4L.

59. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a PKR inhibitor.

60. The nucleic acid of any one of embodiments 1-59, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a PKR inhibitor.

61. The nucleic acid of embodiment 59 or 60, wherein said gene that encodes a PKR inhibitor is K3L.

62. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a serine protease inhibitor.

63. The nucleic acid of any one of embodiments 1-62, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a serine protease inhibitor.

64. The nucleic acid of embodiment 62 or 63, wherein said gene that encodes a serine protease inhibitor is K2L.

65. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a TLR signaling inhibitor.

66. The nucleic acid of any one of embodiments 1-65, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a TLR signaling inhibitor.

67. The nucleic acid of embodiment 65 or 66, wherein said gene that encodes a TLR signaling inhibitor is N2L.

68. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a kelch-like protein.

69. The nucleic acid of any one of embodiments 1-68, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a kelch-like protein.

70. The nucleic acid of embodiment 69, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes that each encodes a kelch-like protein.

71. The nucleic acid of any one of embodiments 68-70, wherein said genes that encode a kelch-like protein are, independently, selected from the group consisting of F3L and C2L.

72. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a monoglyceride lipase.

73. The nucleic acid of any one of embodiments 1-72, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a monoglyceride lipase.

74. The nucleic acid of embodiment 73, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes that each encodes a monoglyceride lipase.

75. The nucleic acid of any one of embodiments 72-74, wherein said genes that encode a monoglyceride lipase are, independently, selected from the group consisting of K5L and K6L.

76. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes an NF-κB inhibitor.

77. The nucleic acid of any one of embodiments 1-76, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes an NF-κB inhibitor.

78. The nucleic acid of embodiment 77, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes that each encodes an NF-κB inhibitor.

79. The nuclei acid of embodiment 78, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes that each encodes an NF-κB inhibitor.

80. The nucleic acid of any one of embodiments 76-79, wherein said genes that encode an NF-κB inhibitor are, independently, selected from the group consisting of K7R, K1L, and M2L.

81. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes an Ankyrin repeat protein.

82. The nucleic acid of any one of embodiments 1-81, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes an Ankyrin repeat protein.

83. The nucleic acid of embodiment 82, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes that each encodes an Ankyrin repeat protein.

84. The nuclei acid of embodiment 83, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes that each encodes an Ankyrin repeat protein.

85. The nucleic acid of any one of embodiments 81-84, wherein said genes that encode an Ankyrin repeat protein are, independently, selected from the group consisting of B18R, B20R, and M1L.

86. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of B15R, B17R, and B14R.

87. The nucleic acid of any one of embodiments 1-86, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of B15R, B17R, and B14R.

88. The nucleic acid of embodiment 87, wherein said deletion comprises at least 2 genes, each independently selected from the group consisting of B15R, B17R, and B14R.

89. The nucleic acid of embodiment 88, wherein said deletion comprises each of said B15R, B17R, and B14R genes.

90. The nucleic acid of any one of embodiments 1-89, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

91. The nucleic acid of embodiment 90, wherein said deletion comprises at least 2 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

92. The nucleic acid of embodiment 91, wherein said deletion comprises at least 3 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

93. The nucleic acid of embodiment 92, wherein said deletion comprises at least 4 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

94. The nucleic acid of embodiment 93, wherein said deletion comprises at least 5 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

95. The nucleic acid of embodiment 94, wherein said deletion comprises at least 6 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

96. The nucleic acid of embodiment 95, wherein said deletion comprises at least 7 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

97. The nucleic acid of embodiment 96, wherein said deletion comprises at least 8 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

98. The nucleic acid of embodiment 97, wherein said deletion comprises each of said B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R genes.

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102. The nucleic acid of embodiment 101, wherein said vaccinia virus is a strain selected from the group consisting of Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16m8, LC16mO, Tashkent, Tian Tan, and WAU86/88-1.

103. The nucleic acid of embodiment 101, wherein said vaccinia virus is a strain selected from the group consisting of Copenhagen, Western Reserve, Tian Tan, Wyeth, and Lister.

104. The nucleic acid of embodiment 101, wherein said vaccinia virus is a Copenhagen strain vaccinia virus.

105. The nucleic acid of any one of embodiments 1-104, wherein each of said deletions is a deletion of the entire polynucleotide encoding the corresponding gene.

106. The nucleic acid of any one of embodiments 1-104, wherein each of said deletions is a deletion of a portion of the polynucleotide encoding the corresponding gene, and wherein said deletion is sufficient to render said gene nonfunctional upon introduction into a host cell.

107. The nucleic acid of any one of embodiments 1-106, wherein said nucleic acid further comprises a transgene encoding a tumor-associated antigen.

108. The nucleic acid of embodiment 107, wherein said tumor-associated antigen is a tumor-associated antigen listed in any one of Tables 3-30.

109. The nucleic acid of embodiment 107, wherein said tumor-associated antigen is a tumor-associated antigen selected from the group consisting of CD19, CD33, EpCAM, CEA, PSMA, EGFRvIII, CD133, EGFR, CDH19, ENPP3, DLL3, MSLN, ROR1, HER2, HLAA2, EpHA2, EpHA3, MCSP, CSPG4, NG2, RON, FLT3, BCMA, CD20, FAPα, FRα, CA-9, PDGFRα, PDGFRβ, FSP1, S100A4, ADAM12m, RET, MET, FGFR, INSR, and NTRK.

110. The nucleic acid of embodiment 107, wherein said tumor-associated antigen comprises MAGE-A3, or one or more fragments thereof.

111. The nucleic acid of embodiment 107, wherein said tumor-associated antigen comprises NY-ESO-1, or one or more fragments thereof.

112. The nucleic acid of embodiment 107, wherein said tumor-associated antigen comprises one or more human papillomavirus (HPV) proteins, or fragments thereof.

113. The nucleic acid of embodiment 107, wherein said tumor-associated antigen comprises (i) E6 and E7 proteins, or fragments thereof, of HPV16 and (ii) E6 and E7 proteins, or fragments thereof, of HPV18.

114. The nucleic acid of embodiment 107, wherein said tumor-associated antigen comprises brachyury or one or more fragments thereof.

115. The nucleic acid of embodiment 107, wherein said tumor-associated antigen comprises prostatic acid phosphatase, or one or more fragments thereof.

116. A method of producing the nucleic acid of any one of embodiments 107-115, said method comprising:

a. introducing a transposon insertion site into the nucleic acid of any one of embodiments 1-106;
b. contacting the nucleic acid formed in (a) with a transposable element comprising a gene encoding said tumor-associated antigen, thereby introducing said gene into said nucleic acid; and
c. recovering the nucleic acid formed in (b).

117. The nucleic acid of any one of embodiments 1-115, wherein said nucleic acid further comprises a transgene encoding an immune checkpoint inhibitor.

118. The nucleic acid of embodiment 117, wherein said immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof.

119. The nucleic acid of embodiment 117, wherein said immune checkpoint inhibitor is an anti-PD-L1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof.

120. The nucleic acid of embodiment 117, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof.

121. The nucleic acid of embodiment 117, wherein said immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

122. A method of producing the nucleic acid of any one of embodiments 117-121, said method comprising:

a. introducing a transposon insertion site into the nucleic acid of any one of embodiments 1-116;
b. contacting the nucleic acid formed in (a) with a transposable element comprising a gene encoding said immune checkpoint inhibitor, thereby introducing said gene into said nucleic acid; and
c. recovering the nucleic acid formed in (b).

123. The nucleic acid of any one of embodiments 1-115 and 117-121, wherein said nucleic acid further comprises a transgene encoding an interleukin (IL).

124. The nucleic acid of embodiment 123, wherein said interleukin is selected from the group consisting of

IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23.

125. The nucleic acid of embodiment 123, wherein said interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70.

126. The nucleic acid of embodiment 125, wherein said interleukin is membrane-bound.

127. A method of producing the nucleic acid of one of embodiments 123-126, said method comprising:

a. introducing a transposon insertion site into the nucleic acid of any one of embodiments 1-115 and 117-121;
b. contacting the nucleic acid formed in (a) with a transposable element comprising a gene encoding said interleukin, thereby introducing said gene into said nucleic acid; and
c. recovering the nucleic acid formed in (b).

128. The nucleic acid of any one of embodiments 1-115, 117-121, and 123-126, wherein said nucleic acid further comprises a transgene encoding an interferon (IFN).

129. The nucleic acid of embodiment 128, wherein said interferon is selected from the group consisting of IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

130. A method of producing the nucleic acid of embodiment 128 or 129, said method comprising:

a. introducing a transposon insertion site into the nucleic acid of any one of embodiments 1-115, 117-121, and 123-126;
b. contacting the nucleic acid formed in (a) with a transposable element comprising a gene encoding said interferon, thereby introducing said gene into said nucleic acid; and
c. recovering the nucleic acid formed in (b).

131. The nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, and 129, wherein said nucleic acid further comprises a transgene encoding a TNF superfamily member protein.

132. The nucleic acid of embodiment 131, wherein said TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

133. A method of producing the nucleic acid of embodiment 131 or 132, said method comprising:

a. introducing a transposon insertion site into the nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, and 129;

b. contacting the nucleic acid formed in (a) with a transposable element comprising a gene encoding said TNF superfamily member protein, thereby introducing said gene into said nucleic acid; and

c. recovering the nucleic acid formed in (b).

134. The nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, and 132 wherein said nucleic acid further comprises a transgene encoding a cytokine.

135. The nucleic acid of embodiment 134, wherein said cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, anti-TGF-beta, anti-VEGF-R2, and cGAS (guanyl adenylate cyclase).

136. The nucleic acid of embodiment 134, wherein said cytokine is Flt3 ligand.

137. A method of producing the nucleic acid of embodiment 135 or 136, said method comprising:

a. introducing a transposon insertion site into the nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, and 132;

b. contacting the nucleic acid formed in (a) with a transposable element comprising a gene encoding said cytokine, thereby introducing said gene into said nucleic acid; and

c. recovering the nucleic acid formed in (b).

138. The nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, and 134-136, wherein said nucleic acid further comprises a transgene encoding microRNA (miRNA).

139. The nucleic acid of embodiment 138, wherein said miRNA is mir-6.

140. A method of producing the nucleic acid of embodiment 138 or 139, said method comprising:

a. introducing a transposon insertion site into the nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, and 134-136;

b. contacting the nucleic acid formed in (a) with a transposable element comprising a gene encoding said miRNA, thereby introducing said gene into said nucleic acid; and

c. recovering the nucleic acid formed in (b).

141. A recombinant orthopoxvirus vector comprising a deletion of at least 2 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L,

N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

142. The recombinant orthopoxvirus vector of embodiment 141, wherein said deletion comprises at least 3 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

143. The recombinant orthopoxvirus vector of embodiment 142, wherein said deletion comprises at least 4 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

144. The recombinant orthopoxvirus vector of embodiment 143, wherein said deletion comprises at least 5 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

145. The recombinant orthopoxvirus vector of embodiment 144, wherein said deletion comprises at least 6 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

146. The recombinant orthopoxvirus vector of embodiment 145, wherein said deletion comprises at least 7 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

147. The recombinant orthopoxvirus vector of embodiment 146, wherein said deletion comprises at least 8 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

148. The recombinant orthopoxvirus vector of embodiment 147, wherein said deletion comprises at least 9 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

149. The recombinant orthopoxvirus vector of embodiment 148, wherein said deletion comprises at least 10 genes, each independently selected from the group consisting of F1L,

N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

150. The recombinant orthopoxvirus vector of embodiment 149, wherein said deletion comprises at least 11 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

151. The recombinant orthopoxvirus vector of embodiment 150, wherein said deletion comprises at least 12 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

152. The recombinant orthopoxvirus vector of embodiment 151, wherein said deletion comprises at least 13 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

153. The recombinant orthopoxvirus vector of embodiment 152, wherein said deletion comprises at least 14 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

154. The recombinant orthopoxvirus vector of embodiment 153, wherein said deletion comprises at least 15 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

155. The recombinant orthopoxvirus vector of embodiment 154, wherein said deletion comprises at least 16 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

156. The recombinant orthopoxvirus vector of embodiment 155, wherein said deletion comprises at least 17 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

157. The recombinant orthopoxvirus vector of embodiment 156, wherein said deletion comprises at least 18 genes, each independently selected from the group consisting of F1L,

N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

158. The recombinant orthopoxvirus vector of embodiment 157, wherein said deletion comprises at least 19 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

159. The recombinant orthopoxvirus vector of embodiment 158, wherein said deletion comprises at least 20 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

160. The recombinant orthopoxvirus vector of embodiment 159, wherein said deletion comprises at least 21 genes, each independently selected from the group consisting of F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R.

161. The recombinant orthopoxvirus vector of embodiment 160, wherein said deletion comprises each of said F1L, N1L, B14R, M2L, K1L, K7R, C2L, N2L, M1L, K2L, K3L, F3L, B16R, B19R, K4L, K5L, K6L, F2L, B15R, B17L, B18R, and B20R genes.

162. A recombinant orthopoxvirus vector comprising a deletion of at least 1 gene selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

163. The recombinant orthopoxvirus vector of any one of embodiments 141-162, wherein said vector comprises a deletion of at least 1 gene selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

164. The vector of embodiment 163, wherein said deletion comprises at least 2 genes, each independently selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

165. The vector of embodiment 164, wherein said deletion comprises at least 3 genes, each independently selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

166. The vector of embodiment 165, wherein said deletion comprises at least 4 genes, each independently selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

167. The vector of embodiment 166, wherein said deletion comprises at least 5 genes, each independently selected from the group consisting of B14R, B16R, B17L, B18R, B19R, and B20R.

168. The vector of embodiment 167, wherein said deletion comprises each of B14R, B16R, B17L, B18R, B19R, and B20R.

169. A recombinant orthopoxvirus vector comprising a deletion of at least 1 gene selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

170. The recombinant orthopoxvirus vector of any one of embodiments 141-169, wherein said vector comprises a deletion of at least 1 gene selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

171. The vector of embodiment 170, wherein said deletion comprises at least 2 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

172. The vector of embodiment 171, wherein said deletion comprises at least 3 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

173. The vector of embodiment 172, wherein said deletion comprises at least 4 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

174. The vector of embodiment 173, wherein said deletion comprises at least 5 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

175. The vector of embodiment 174, wherein said deletion comprises at least 6 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

176. The vector of embodiment 175, wherein said deletion comprises at least 7 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

177. The vector of embodiment 176, wherein said deletion comprises at least 8 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

178. The vector of embodiment 177, wherein said deletion comprises at least 9 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

179. The vector of embodiment 178, wherein said deletion comprises at least 10 genes, each independently selected from the group consisting of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

180. The vector of embodiment 179, wherein said deletion comprises each of C2L, C1L, N1L, N2L, M1L, K1L, K2L, K3L, K4L, K7R, and F2L.

181. A recombinant orthopoxvirus vector comprising a deletion of at least 1 gene that encodes a caspase-9 inhibitor.

182. The recombinant orthopoxvirus vector of any one of embodiments 141-181, wherein said vector comprises a deletion of at least 1 gene that encodes a caspase-9 inhibitor.

183. The vector of embodiment 181 or 182, wherein said gene that encodes a caspase-9 inhibitor is F1L.

184. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a BCL-2 inhibitor.

185. The recombinant orthopoxvirus vector of any one of embodiments 141-184, wherein said vector comprises a deletion of at least 1 gene that encodes a BCL-2 inhibitor.

186. The vector of embodiment 184 or 185, wherein said gene that encodes a BCL-2 inhibitor is N1L.

187. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a dUTPase.

188. The recombinant orthopoxvirus vector of any one of embodiments 141-187, wherein said vector comprises a deletion of at least 1 gene that encodes a dUTPase.

189. The vector of embodiment 187 or 188, wherein said gene that encodes a dUTPase is F2L.

190. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a IFN-alpha/beta-receptor-like secreted glycoprotein.

191. The recombinant orthopoxvirus vector of any one of embodiments 141-190, wherein said vector comprises a deletion of at least 1 gene that encodes a IFN-alpha/beta-receptor-like secreted glycoprotein.

192. The vector of embodiment 190 or 191, wherein said gene that encodes a IFN-alpha/beta-receptor-like secreted glycoprotein is B19R.

193. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes an IL-1-beta-inhibitor.

194. The recombinant orthopoxvirus vector of any one of embodiments 141-193, wherein said vector comprises a deletion of at least 1 gene that encodes an IL-1-beta-inhibitor.

195. The vector of embodiment 193 or 194, wherein said gene that encodes an IL-1-beta-inhibitor is B16R.

196. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a phospholipase-D.

197. The recombinant orthopoxvirus vector of any one of embodiments 141-196, wherein said vector comprises a deletion of at least 1 gene that encodes a phospholipase-D.

198. The vector of embodiment 196 or 197, wherein said gene that encodes a phospholipase-D is K4L.

199. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a PKR inhibitor.

200. The recombinant orthopoxvirus vector of any one of embodiments 141-199, wherein said vector comprises a deletion of at least 1 gene that encodes a PKR inhibitor.

201. The vector of embodiment 199 or 200, wherein said gene that encodes a PKR inhibitor is K3L.

202. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a serine protease inhibitor.

203. The recombinant orthopoxvirus vector of any one of embodiments 141-202, wherein said vector comprises a deletion of at least 1 gene that encodes a serine protease inhibitor.

204. The vector of embodiment 202 or 203, wherein said gene that encodes a serine protease inhibitor is K2L.

205. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a TLR signaling inhibitor.

206. The recombinant orthopoxvirus vector of any one of embodiments 141-205, wherein said vector comprises a deletion of at least 1 gene that encodes a TLR signaling inhibitor.

207. The vector of embodiment 205 or 206, wherein said gene that encodes a TLR signaling inhibitor is N2L.

208. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a kelch-like protein.

209. The recombinant orthopoxvirus vector of any one of embodiments 141-208, wherein said vector comprises a deletion of at least 1 gene that encodes a kelch-like protein.

210. The vector of embodiment 209, wherein said vector comprises a deletion of at least 2 genes that each encodes a kelch-like protein.

211. The vector of any one of embodiments 208-210, wherein said genes that encode a kelch-like protein are, independently, selected from the group consisting of F3L and C2L.

212. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes a monoglyceride lipase.

213. The recombinant orthopoxvirus vector of any one of embodiments 141-212, wherein said vector comprises a deletion of at least 1 gene that encodes a monoglyceride lipase.

214. The vector of embodiment 213, wherein said vector comprises a deletion of at least 2 genes that each encodes a monoglyceride lipase.

215. The vector of any one of embodiments 212-214, wherein said genes that encode a monoglyceride lipase are, independently, selected from the group consisting of K5L and K6L.

216. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes an NF-κB inhibitor.

217. The recombinant orthopoxvirus vector of any one of embodiments 141-216, wherein said vector comprises a deletion of at least 1 gene that encodes an NF-κB inhibitor.

218. The vector of embodiment 217, wherein said deletion comprises at least 2 genes that each encodes an NF-κB inhibitor.

219. The vector of embodiment 218, wherein said deletion comprises at least 3 genes that each encodes an NF-κB inhibitor.

220. The vector of any one of embodiments 216-219, wherein said genes that encode an NF-κB inhibitor are, independently, selected from the group consisting of K7R, K1L, and M2L.

221. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene that encodes an Ankyrin repeat protein.

222. The recombinant orthopoxvirus vector of any one of embodiments 141-221, wherein said vector comprises a deletion of at least 1 gene that encodes an Ankyrin repeat protein.

223. The vector of embodiment 222, wherein said deletion comprises at least 2 genes that each encodes an Ankyrin repeat protein.

224. The vector of embodiment 223, wherein said deletion comprises at least 3 genes that each encodes an Ankyrin repeat protein.

225. The recombinant orthopoxvirus vector of any one of embodiments 221-224, wherein said genes that encode an Ankyrin repeat protein are, independently, selected from the group consisting of B18R, B20R, and M1L.

226. A recombinant orthopoxvirus vector, wherein said vector comprises a deletion of at least 1 gene selected from the group consisting of B15R, B17R, and B14R.

227. The recombinant orthopoxvirus vector of any one of embodiments 1-226, wherein said vector comprises a deletion of at least 1 gene selected from the group consisting of B15R, B17R, and B14R.

228. The vector of embodiment 227, wherein said deletion comprises at least 2 genes, each independently selected from the group consisting of B15R, B17R, and B14R.

229. The vector of embodiment 228, wherein said deletion comprises each of said B15R, B17R, and B14R genes.

230. The recombinant orthopoxvirus vector of any one of embodiments 141-229, wherein said vector comprises a deletion of at least 1 gene selected from the group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

231. The vector of embodiment 230, wherein said deletion comprises at least 2 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

232. The vector of embodiment 231, wherein said deletion comprises at least 3 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

233. The vector of embodiment 232, wherein said deletion comprises at least 4 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

234. The vector of embodiment 233, wherein said deletion comprises at least 5 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

235. The vector of embodiment 234, wherein said deletion comprises at least 6 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

236. The vector of embodiment 235, wherein said deletion comprises at least 7 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

237. The vector of embodiment 236, wherein said deletion comprises at least 8 genes, each independently selected from said group of ITR genes consisting of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

238. The vector of embodiment 237, wherein said deletion comprises each of B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R.

239.

242. The recombinant orthopoxvirus vector of embodiment 241, wherein said vaccinia virus is a strain selected from the group consisting of Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16m8, LC16mO, Tashkent, Tian Tan, and WAU86/88-1.

243. The recombinant orthopoxvirus vector of embodiment 241, wherein said vaccinia virus is a strain selected from the group consisting of Copenhagen, Western Reserve, Tian Tan, Wyeth, and Lister.

244. The recombinant orthopoxvirus vector of embodiment 241, wherein said vaccinia virus is a Copenhagen strain vaccinia virus.

245. The recombinant orthopoxvirus vector of any one of embodiments 141-244, wherein said deletions is a deletion of the entire polynucleotide encoding the corresponding gene.

246. The recombinant orthopoxvirus vector of any one of embodiments 141-244, wherein each of said deletions is a deletion of a portion of the polynucleotide encoding the corresponding gene, and wherein said deletion is sufficient to render said gene nonfunctional upon introduction into a host cell.

247. The recombinant orthopoxvirus vector of any one of embodiments 14141-246, wherein said vector further comprises a transgene encoding a tumor-associated antigen.

248. The recombinant orthopoxvirus vector of any one of embodiments 141-247, wherein said recombinant orthopoxvirus vector further comprises a transgene encoding a tumor-associated antigen.

249. The recombinant orthopoxvirus vector of embodiment 248, wherein said tumor-associated antigen is a tumor-associated antigen listed in any one of Tables 3-30.

250. The recombinant orthopoxvirus vector of embodiment 248, wherein said tumor-associated antigen is a tumor-associated antigen selected from the group consisting of CD19,

CD33, EpCAM, CEA, PSMA, EGFRvIII, CD274, EGFR, CDH19, ENPP3, DLL3, MSLN, ROR1, HER2, HLAA2, EpHA2, EpHA3, MCSP, CSPG4, NG2, RON, FLT3, BCMA, CD20, FAPα, FRα, CA-9, PDGFRα, PDGFRβ, FSP1, S100A4, ADAM12m, RET, MET, FGFR, INSR, and NTRK.

251. The recombinant orthopoxvirus vector of embodiment 248, wherein said tumor-associated antigen comprises MAGE-A3, or one or more fragments thereof.

252. The recombinant orthopoxvirus vector of embodiment 248, wherein said tumor-associated antigen comprises NY-ESO-1, or one or more fragments thereof.

253. The recombinant orthopoxvirus vector of embodiment 248, wherein said tumor-associated antigen comprises one or more human papillomavirus (HPV) proteins, or fragments thereof.

254. The recombinant orthopoxvirus vector of embodiment 248, wherein said tumor-associated antigen comprises (i) E6 and E7 proteins, or fragments thereof, of HPV16 and (ii) E6 and E7 proteins, or fragments thereof, of HPV18.

255. The recombinant orthopoxvirus vector of embodiment 248, wherein said tumor-associated antigen comprises brachyury or one or more fragments thereof.

256. The recombinant orthopoxvirus vector of embodiment 248, wherein said tumor-associated antigen comprises prostatic acid phosphatase, or one or more fragments thereof.

257. A method of producing the recombinant orthopoxvirus vector of any one of embodiments 248-256, said method comprising:

d. introducing a transposon insertion site into the recombinant orthopoxvirus vector of any one of embodiments 141-247;
e. contacting the recombinant orthopoxvirus vector formed in (a) with a transposable element comprising a gene encoding said tumor-associated antigen, thereby introducing said gene into said recombinant orthopoxvirus vector; and
f. recovering the recombinant orthopoxvirus vector formed in (b).

258. The recombinant orthopoxvirus vector of any one of embodiments 141-256, wherein said recombinant orthopoxvirus vector further comprises a transgene encoding an immune checkpoint inhibitor.

259. The recombinant orthopoxvirus vector of embodiment 258, wherein said immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-

binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof.

260. The recombinant orthopoxvirus vector of embodiment 258, wherein said immune checkpoint inhibitor is an anti-PD-L1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof.

261. The recombinant orthopoxvirus vector of embodiment 258, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof.

262. The recombinant orthopoxvirus vector of embodiment 258, wherein said immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

263. A method of producing the recombinant orthopoxvirus vector of any one of embodiments 258-262, said method comprising:

d. introducing a transposon insertion site into the recombinant orthopoxvirus vector of any one of embodiments 141-257;
e. contacting the recombinant orthopoxvirus vector formed in (a) with a transposable element comprising a gene encoding said immune checkpoint inhibitor, thereby introducing said gene into said recombinant orthopoxvirus vector; and
f. recovering the recombinant orthopoxvirus vector formed in (b).

264. The recombinant orthopoxvirus vector of any one of embodiments 141-256 and 258-262, wherein said recombinant orthopoxvirus vector further comprises a transgene encoding an interleukin (IL).

265. The recombinant orthopoxvirus vector of embodiment 264, wherein said interleukin is selected from the group consisting of

IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23.

266. The recombinant orthopoxvirus vector of embodiment 264, wherein said interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70.

267. The recombinant orthopoxvirus vector of embodiment 266, wherein said interleukin is membrane-bound.

268. A method of producing the recombinant orthopoxvirus vector of one of embodiments 264-267, said method comprising:

d. introducing a transposon insertion site into the recombinant orthopoxvirus vector of any one of embodiments 141-256 and 258-262;
e. contacting the recombinant orthopoxvirus vector formed in (a) with a transposable element comprising a gene encoding said interleukin, thereby introducing said gene into said recombinant orthopoxvirus vector; and
f. recovering the recombinant orthopoxvirus vector formed in (b).

269. The recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, and 264-267, wherein said recombinant orthopoxvirus vector further comprises a transgene encoding an interferon (IFN).

270. The recombinant orthopoxvirus vector of embodiment 269, wherein said interferon is selected from the group consisting of IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

271. A method of producing the recombinant orthopoxvirus vector of embodiment 269 or 270, said method comprising:

d. introducing a transposon insertion site into the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, and 264-267;
e. contacting the recombinant orthopoxvirus vector formed in (a) with a transposable element comprising a gene encoding said interferon, thereby introducing said gene into said recombinant orthopoxvirus vector; and
f. recovering the recombinant orthopoxvirus vector formed in (b).

272. The recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, and 270, wherein said recombinant orthopoxvirus vector further comprises a transgene encoding a TNF superfamily member protein.

273. The recombinant orthopoxvirus vector of embodiment 272, wherein said TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

274. A method of producing the recombinant orthopoxvirus vector of embodiment 272 or 273, said method comprising:

d. introducing a transposon insertion site into the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, and 270;
e. contacting the recombinant orthopoxvirus vector formed in (a) with a transposable element comprising a gene encoding said TNF superfamily

member protein, thereby introducing said gene into said recombinant orthopoxvirus vector; and

f. recovering the recombinant orthopoxvirus vector formed in (b).

275. The recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, and 273 wherein said recombinant orthopoxvirus vector further comprises a transgene encoding a cytokine.

276. The recombinant orthopoxvirus vector of embodiment 275, wherein said cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, anti-TGF-beta, anti-VEGF-R2, and cGAS (guanyl adenylate cyclase).

277. The recombinant orthopoxvirus vector of embodiment 275, wherein said cytokine is Flt3 ligand.

278. A method of producing the recombinant orthopoxvirus vector of embodiment 276 or 277, said method comprising:

d. introducing a transposon insertion site into the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, and 273;

e. contacting the recombinant orthopoxvirus vector formed in (a) with a transposable element comprising a gene encoding said cytokine, thereby introducing said gene into said recombinant orthopoxvirus vector; and

f. recovering the recombinant orthopoxvirus vector formed in (b).

279. The recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, and 275-277, wherein said recombinant orthopoxvirus vector further comprises a transgene encoding microRNA (miRNA).

280. The recombinant orthopoxvirus vector of embodiment 279, wherein said miRNA is mir-6.

281. A method of producing the recombinant orthopoxvirus vector of embodiment 279 or 280, said method comprising:

d. introducing a transposon insertion site into the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, and 275-277;

e. contacting the recombinant orthopoxvirus vector formed in (a) with a transposable element comprising a gene encoding said miRNA, thereby introducing said gene into said recombinant orthopoxvirus vector; and

f. recovering the recombinant orthopoxvirus vector formed in (b).

282. The nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, and 139, or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, and 280, wherein said nucleic acid or said recombinant orthopoxvirus vector comprises the Thymidine Kinase (TK) gene.

283. The nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, 139, and 282, or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, 280, and 282, wherein said nucleic acid or said recombinant orthopoxvirus vector comprises the ribonucleotide reductase gene.

284. The nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, 139, 282, and 283, or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, 280, 282, and 283, wherein upon contacting a population of mammalian cells with said nucleic acid or said recombinant orthopoxvirus vector, the cells exhibit increased syncytia formation relative to a population of mammalian cells of the same type contacted with a form of the orthopoxvirus vector that does not comprise said deletions.

285. The nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, 139, and 282-284 or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, 280, and 282-284, wherein upon contacting a population of mammalian cells with said nucleic acid or said recombinant orthopoxvirus vector, the cells exhibit increased spreading of the orthopoxvirus vector relative to a population of mammalian cells of the same type contacted with a form of the orthopoxvirus vector that does not comprise said deletions.

286. The nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, 139, and 282-285, or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, 280, and 282-285, wherein said nucleic acid or said recombinant orthopoxvirus vector exerts an increased cytotoxic effect on a population of mammalian cells relative to that of a form of the orthopoxvirus vector that does not comprise said deletions.

287. The nucleic acid or the recombinant orthopoxvirus vector of any one of embodiments 284-286, wherein said mammalian cells are human cells.

288. The nucleic acid or the recombinant orthopoxvirus vector of embodiment 287, wherein said human cells are cancer cells.

289. The nucleic acid or the recombinant orthopoxvirus vector of any one of embodiments 284-286, wherein said mammalian cells are from a cell line selected from the group consisting of U2OS, 293, 293T, Vero, HeLa, A549, BHK, BSC40, CHO, OVCAR-8, 786-0, NCI-H23, U251, SF-295, T-47D, SKMEL2, BT-549, SK-MEL-28, MDA-MB-231, SK-OV-3, MCF7, M14, SF-268, CAKI-1, HPAV, OVCAR-4, HCT15, K-562, and HCT-116.

290. A packaging cell line comprising the nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, 139, and 282-289 or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, 280, and 282-289.

291. A method of treating cancer in a mammalian patient, said method comprising administering a therapeutically effective amount of the nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, 139, and 282-289, or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, 280, and 282-289 to said patient.

292. The method of embodiment 291, wherein said mammalian patient is a human patient.

293. The method of embodiment 291 or 292, wherein said cancer is selected from the group consisting of leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, and throat cancer.

294. The method of embodiment 291 or 292, wherein said cancer is selected from the group consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), adrenocortical carcinoma, AIDS-related lymphoma, primary CNS lymphoma, anal cancer, appendix cancer, astrocytoma, atypical teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, extrahepatic cancer, ewing sarcoma family, osteosarcoma and malignant fibrous histiocytoma, central nervous system embryonal tumors, central nervous system germ cell tumors, craniopharyngioma, ependymoma, bronchial tumors, burkitt lymphoma, carcinoid tumor, primary lymphoma, chordoma, chronic myeloproliferative neoplasms, colon cancer, extrahepatic bile duct cancer, ductal carcinoma in situ (DCIS), endometrial cancer,

ependymoma, esophageal cancer, esthesioneuroblastoma, extracranial germ cell tumor, extragonadal germ cell tumor, fallopian tube cancer, fibrous histiocytoma of bone, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), testicular germ cell tumor, gestational trophoblastic disease, glioma, childhood brain stem glioma, hairy cell leukemia, hepatocellular cancer, langerhans cell histiocytosis, hodgkin lymphoma, hypopharyngeal cancer, islet cell tumors, pancreatic neuroendocrine tumors, wilms tumor and other childhood kidney tumors, langerhans cell histiocytosis, small cell lung cancer, cutaneous T cell lymphoma, intraocular melanoma, merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer, midline tract carcinoma, multiple endocrine neoplasia syndromes, multiple myeloma/plasma cell neoplasm, myelodysplastic syndromes, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-hodgkin lymphoma (NHL), non-small cell lung cancer (NSCLC), epithelial ovarian cancer, germ cell ovarian cancer, low malignant potential ovarian cancer, pancreatic neuroendocrine tumors, papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pituitary tumor, pleuropulmonary blastoma, primary peritoneal cancer, rectal cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, kaposi sarcoma, rhabdomyosarcoma, sézary syndrome, small intestine cancer, soft tissue sarcoma, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, urethral cancer, endometrial uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, and Waldenström macroglobulinemia.

295. The method of any one of embodiments 291-294, wherein said method further comprises administering to said patient an immune checkpoint inhibitor.

296. The method of embodiment 295, wherein said immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof.

297. The method of embodiment 295, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof.

298. The method of embodiment 295, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof.

299. The method of embodiment 295, wherein said immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

300. The method of any one of embodiments 291-299, wherein said method further comprises administering to said patient an interleukin.

301. The method of embodiment 300, wherein said interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23.

302. The method of embodiment 300, wherein said interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70.

303. The method of embodiment 301 or 302, wherein said interleukin is membrane-bound.

304. The method of any one of embodiments 291-303, wherein said method further comprises administering to said patient an interferon.

305. The method of embodiment 304, wherein said interferon is selected from the group consisting of

IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

306. The method of any one of embodiments 291-305, wherein said method further comprises administering to said patient a TNF superfamily member protein.

307. The method of embodiment 306, wherein said TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

308. The method of any one of embodiments 291-307, wherein said method further comprises administering to said patient a cytokine.

309. The method of embodiment 308, wherein said cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, anti-TGF-beta, anti-VEGF-R2, and cGAS (guanyl adenylate cyclase).

310. The method of embodiment 308, wherein said cytokine is Flt3 ligand.

311. The method of any one of embodiments 291-310, wherein said method further comprises administering to said patient a miRNA.

312. The method of embodiment 311, wherein said miRNA is mir-6.

313. A kit comprising the nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, 139, and 282-289 or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, 280, and 282-289 and a package insert instructing a user of said kit to express said nucleic acid or said vector in a host cell.

314. A kit comprising the nucleic acid of any one of embodiments 1-115, 117-121, 123-126, 128, 129, 131, 132, 134-136, 138, 139, and 282-289 or the recombinant orthopoxvirus vector of any one of embodiments 141-256, 258-262, 264-267, 269, 270, 272, 273, 275-277, 279, 280, and 282-289 and a package insert instructing a user to administer a therapeutically effective amount of said nucleic acid or recombinant orthopoxvirus vector to a mammalian patient having cancer, thereby treating said cancer.

315. The kit of embodiment 314, wherein said mammalian patient is a human patient.

316. The orthopox virus of any of the preceding embodiments wherein the B8R gene is deleted.

317. The orthopox virus of embodiment 316, wherein at least one transgene is inserted into the locus of the deleted B8R gene.

318. The orthopox virus of embodiment 317, wherein at least two transgenes are inserted into the locus of the deleted B8R gene.

319. The orthopox virus of embodiment 318, wherein at least three transgenes are inserted into the locus of the deleted B8R gene.

320. The orthopox virus of any one of embodiments 316-319, wherein at least one additional transgene is inserted at locus that is not the locus of the B8R gene.

321. The orthopox virus of embodiment 320, wherein the locus is the boundary of the 5p deletion.

322. The orthopox virus of embodiment 321, wherein the locus is the boundary of the 3p deletion.

323. The orthopox virus of embodiments 316-322, wherein at least one of the following transgenes is inserted: IL-12TM, FLT3-L or anti-CLTA-4 antibody.

324. The orthopox virus of embodiment 323, wherein the IL-12-TM and FLT3-L genes are inserted into the locus of the deleted B8R gene.

325. The orthopox virus of any one of embodiments 323-324, wherein the anti-CLTA-4 antibody is inserted within the boundary of the 5p deletion.

326. The orthopox virus of anyone of embodiments 323-325, wherein the virus comprises the sequence of SEQ ID. NO: 210.

326. The orthopox virus of any one of embodiments 323-325 wherein the anti-CLTA antibody is SEQ ID NO: 211.

327. The orthopox virus of any one of embodiments 323-326, wherein the IL-12-TM is SEQ ID NO: 212.

328. The orthopox virus of any one of embodiments 323-327 wherein the FLT3-L is SEQ ID NO: 213.

329. An orthopox virus comprising a nucleic acid sequence wherein the nucleic acid sequence is a derivative of SEQ ID NO: 210,

wherein said derivative comprises a deletion of the B8R gene of SEQ ID NO: 210,

wherein, an IL-12-TM and an FLT3-L transgene are inserted into the locus of said deleted B8R gene,

wherein, genes encoding a heavy and a light chain of an anti-CLTA-4 antibody are inserted within the boundaries of the 5p deletion present in SEQ ID NO: 210;

wherein the IL-12-TM is SEQ ID NO: 212;

wherein the FLT3-L is SEQ ID NO: 213; and

wherein the anti-CLTA4 antibody is encoded by SEQ ID NO: 211.

5.7.2. Set 2

1. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

2. The nucleic acid of embodiment 1, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

3. The nucleic acid of embodiment 2, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes..

4. The nucleic acid of embodiment 3, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

5. The nucleic acid of embodiment 4, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

6. The nucleic acid of embodiment 5, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 7 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

7. The nucleic acid of embodiment 6, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 8 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

8. The nucleic acid of embodiment 7, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 9 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

9. The nucleic acid of embodiment 8, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 10 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

10. The nucleic acid of embodiment 9, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 11 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

11. The nucleic acid of embodiment 10, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 12 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

12. The nucleic acid of embodiment 11, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 13 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

13. The nucleic acid of embodiment 12, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 14 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

14. The nucleic acid of embodiment 13, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 15 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

15. The nucleic acid of embodiment 14, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 16 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

16. The nucleic acid of embodiment 15, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 17 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

17. The nucleic acid of embodiment 16, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 18 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

18. The nucleic acid of embodiment 17, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 19 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

19. The nucleic acid of embodiment 18, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 20 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

20. The nucleic acid of embodiment 19, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 21 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

21. The nucleic acid of embodiment 20, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 22 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

22. The nucleic acid of embodiment 21, wherein said recombinant orthopoxvirus genome comprises a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

23. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

24. The nucleic acid of embodiment 23, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

25. The nucleic acid of embodiment 24, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

26. The nucleic acid of embodiment 25, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

27. The nucleic acid of embodiment 26, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

28. The nucleic acid of embodiment 27, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

29. The nucleic acid of embodiment 28, wherein said recombinant orthopoxvirus genome comprises a deletion of each of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

30. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

31. The nucleic acid of embodiment 30, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

32. The nucleic acid of embodiment 31, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

33. The nucleic acid of embodiment 32, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

34. The nucleic acid of embodiment 33, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

35. The nucleic acid of embodiment 34, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

36. The nucleic acid of embodiment 35, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 7 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

37. The nucleic acid of embodiment 36, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 8 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

38. The nucleic acid of embodiment 37, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 9 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

39. The nucleic acid of embodiment 38, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 10 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

40. The nucleic acid of embodiment 39, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 11 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

41. The nucleic acid of embodiment 40, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 12 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

42. The nucleic acid of embodiment 41, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 13 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

43. The nucleic acid of embodiment 42, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 14 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

44. The nucleic acid of embodiment 43, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 15 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

45. The nucleic acid of embodiment 44, wherein said recombinant orthopoxvirus genome comprises a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

46. The nucleic acid comprising a recombinant orthopoxvirus genome of any one of embodiments 1-45, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a protein involved in host interaction.

47. The nucleic acid of embodiment 46, wherein said protein affects calcium-independent adhesion to the extracellular matrix.

48. The nucleic acid of embodiment 46, wherein said protein is an NF-κB inhibitor.

49. The nucleic acid of embodiment 48, wherein said protein is encoded by a gene selected from the group consisting of the C2L, N1L, M2L, K1L, and K7R genes.

50. The nucleic acid of embodiment 46, wherein said protein is an apoptosis inhibitor.

51. The nucleic acid of embodiment 47, wherein said apoptosis inhibitor is a caspase-9 inhibitor.

52. The nucleic acid of embodiment 51, wherein said caspase-9 inhibitor is encoded by the F1L gene.

53. The nucleic acid of embodiment 50, wherein said apoptosis inhibitor is a BCL-2-like protein.

54. The nucleic acid of embodiment 53, wherein said BCL-2-like protein is encoded by N1L.

55. The nucleic acid of embodiment 46, wherein said protein is an interferon regulatory factor 3 (IRF3) inhibitor.

56. The nucleic acid of embodiment 55, wherein said IRF3 inhibitor is encoded by N2L or K7R.

57. The nucleic acid of embodiment 46, wherein said protein is a serine protease inhibitor.

58. The nucleic acid of embodiment 46, wherein said protein prevents cell fusion.

59. The nucleic acid of embodiment 58, wherein said protein is encoded by K2L.

60. The nucleic acid of embodiment 46, wherein said protein is an RNA-activated protein kinase (PKR) inhibitor.

61. The nucleic acid of embodiment 60, wherein said protein is encoded by K1L or K3L.

62. The nucleic acid of embodiment 46, wherein said protein is a virulence factor.

63. The nucleic acid of embodiment 63, wherein said protein is encoded by F3L.

64. The nucleic acid of embodiment 46, wherein said protein is an IL-1-beta inhibitor.

65. The nucleic acid of embodiment 64, wherein said protein is encoded by B16R.

66. The nucleic acid of embodiment 46, wherein said protein is a secreted IFNα sequestor.

67. The nucleic acid of embodiment 67, wherein said protein is encoded by B19R.

68. The nucleic acid comprising a recombinant orthopoxvirus genome of any one of embodiments 1-67, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene encoding a protein involved in DNA replication.

69. The nucleic acid of embodiment 68, wherein said protein is a DNA modifying nuclease.

70. The nucleic acid of embodiment 69, wherein said protein is encoded by K4L.

71. The nucleic acid of embodiment 70, wherein said protein is a deoxyuridine triphosphatase (dUTPase).

72. The nucleic acid of embodiment 71, wherein the dUTPase is encoded by F2L.

73. The nucleic acid of any one of embodiments 1-72, wherein at least one deleted gene's entire nucleotide sequence is deleted.

74. The nucleic acid of any one of embodiments 1-72, wherein at least one deleted gene is only partially deleted, and wherein the partial deletion is sufficient to render said partially deleted gene nonfunctional upon introduction into a host cell.

75. The nucleic acid of any one of embodiments 1-74, wherein said recombinant orthopoxvirus genome comprises at least two copies of inverted terminal repeats (ITRs).

76. The nucleic acid of any one of embodiments 1-74, wherein said recombinant orthopoxvirus genome lacks any copies of ITRs.

77. The nucleic acid of any one of embodiments 1-74, wherein said recombinant orthopoxvirus genome comprises a deletion in at least one copy of an ITR selected from the group consisting of B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

78. The nucleic acid of any one of embodiments 1-74, wherein said recombinant orthopoxvirus genome comprises a deletion in at least all of the following copies of ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

79. The nucleic acid of any one of embodiments 1-78, wherein said recombinant orthopoxvirus genome comprises a deletion in the B8R gene.

80. The nucleic acid of any one of embodiments 1-78, wherein said recombinant orthopoxvirus genome comprises an intact B8R gene.

81. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises

(i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, B20R, and B8R genes; and

(ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

82. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises

(i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes; and

(ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR,

wherein said recombinant orthopoxvirus genome comprises an intact B8R gene.

83. The nucleic acid of any one of embodiments 1-82, further comprising at least one transgene selected from the group consisting of a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine.

84. The nucleic acid of embodiment 83, wherein the nucleic acid comprises at least two transgenes selected from the group consisting of a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine.

85. The nucleic acid of embodiment 84, wherein the nucleic acid comprises a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine.

86. The nucleic acid of any one of embodiment 83 or 84, wherein said nucleic acid comprises a transgene encoding an immune checkpoint inhibitor.

87. The nucleic acid of embodiment 85 or 86, wherein said immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof.

88. The nucleic acid of embodiment 87, wherein said immune checkpoint inhibitor is an anti-PD-L1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof.

89. The nucleic acid of embodiment 88, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof.

90. The nucleic acid of embodiment 88, wherein said immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

91. The nucleic acid of embodiment 83 or 84, wherein said nucleic acid comprises a transgene encoding an interleukin (IL).

92. The nucleic acid of embodiment 85 or 91, wherein said interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23.

93. The nucleic acid of embodiment 92, wherein said interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70.

94. The nucleic acid of embodiment 93, wherein said interleukin is membrane-bound.

95. The nucleic acid of embodiment 94, wherein said interleukin is membrane-bound IL-12 p70.

96. The nucleic acid of embodiment 83 or 84, wherein said nucleic acid comprises a transgene encoding a cytokine.

97. The nucleic acid of embodiment 96, wherein said cytokine is an interferon (IFN).

98. The nucleic acid of embodiment 97, wherein said interferon is selected from the group consisting of IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

99. The nucleic acid of embodiment 96, wherein said cytokine is a TNF superfamily member protein.

100. The nucleic acid of embodiment 99, wherein said TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

101. The nucleic acid of embodiment 96, wherein said cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, TGF-beta, VEGF-R2, and c-kit.

102. The nucleic acid of embodiment 101, wherein said cytokine is Flt3 ligand.

103. The nucleic acid of embodiment 83-102, wherein said recombinant orthopoxvirus genome comprises a deletion in the B8R gene and at least one transgene is inserted into the deletion in the B8R gene.

104. The nucleic acid of embodiment 103, wherein at least two transgenes are inserted into the deletion in the B8R gene.

105. The nucleic acid of embodiment 104, wherein at least three transgenes are inserted into the deletion in the B8R gene.

106. The nucleic acid of any one of embodiments 103-105, wherein at least one transgene is inserted in a locus that is not at the deletion in the B8R gene.

107. The nucleic acid of embodiment 106, wherein the locus is at the boundary of a deletion at the 5' end of the orthopoxvirus genome.

108. The nucleic acid of embodiment 106, wherein the locus is at the boundary of a deletion at the 3' end of the orthopoxvirus genome.

109. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises

(i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, B20R, and B8R genes;

(ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR;

(iii) an IL-12-TM transgene inserted into the deletion in the B8R gene;

(iv) an Flt3 ligand transgene inserted into the deletion in the B8R gene; and

(v) one of:

(a) a transgene encoding a single chain anti-CTLA-4 antibody or antigen-binding fragment thereof

or

(b) (i) a transgene encoding a heavy chain of an anti-CTLA-4 antibody or antigen-binding fragment thereof, and

(ii) a transgene encoding a light chain of an anti-CTLA-4 antibody or antigen-binding fragment thereof,

wherein the transgene(s) in part (v) is/are inserted within the boundaries of a 5p deletion present in the recombinant orthopoxvirus genome, and

wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is capable of binding CTLA-4.

110. The nucleic acid of embodiment 109, wherein the orthopoxvirus genome is derived from a sequence of SEQ ID NO: 210, wherein

(a) said derived sequence comprises a deletion of the B8R gene, and the IL-12-TM transgene, the Flt3 ligand transgene, and the transgene(s) encoding the single or double-chain anti-CTLA-4 antibody;

(b) the IL-12-TM transgene encodes a protein comprising an amino acid sequence of is SEQ ID NO: 212;

(c) the Flt3 ligand transgene encodes a protein comprising an amino acid sequence of SEQ ID NO: 213; and

(d) the anti-CTLA-4 antibody comprises an amino acid sequence of SEQ ID NO: 211.

111. A virus comprising the nucleic acid comprising the recombinant orthopoxvirus genome of any one of embodiments 1-110.

112. The virus of embodiment 111, wherein

a) said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes;

b) said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes; or

c) said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

113. The virus of embodiment 111 or 112, wherein said virus is derived from a vaccinia virus.

114. The virus of embodiment 113, wherein said vaccinia virus is derived from a strain selected from the group consisting of Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16mO, Tashkent, Tian Tan, and WAU86/88-1.

115. The virus of embodiment 114, wherein said vaccinia virus is derived from a strain selected from the group consisting of Copenhagen, Western Reserve, Tian Tan, Wyeth, and Lister.

116. The virus of embodiment 115, wherein said vaccinia virus is derived from a Copenhagen strain vaccinia virus.

117. The virus of any one of embodiments 111-116, wherein said recombinant orthopoxvirus genome further comprises a Thymidine Kinase (TK) gene.

118. The virus of any one of embodiments 111-117, wherein said recombinant orthopoxvirus genome further comprises a ribonucleotide reductase gene.

119. The virus of any one of embodiments 111-118, wherein upon contacting a population of mammalian cells with said virus, the population of mammalian cells exhibit increased syncytia formation relative to a population of mammalian cells of the same type contacted with a form of the virus that does not comprise said deletion.

120. The virus of any one of embodiments 111-119, wherein upon contacting a population of mammalian cells with said virus, the population of mammalian cells exhibit increased spreading of the virus relative to a population of mammalian cells of the same type contacted with a form of the virus that does not comprise said deletion.

121. The virus of any one of embodiments 111-120, wherein said virus exerts an increased cytotoxic effect on a population of mammalian cells relative to that of a form of the virus that does not comprise said deletion.

122. The virus of any one of embodiments 119-121, wherein said mammalian cells are human cells.

123. The virus of embodiment 122, wherein said human cells are cancer cells.

124. The virus of any one of embodiments 119-121, wherein said mammalian cells are from a cell line selected from the group consisting of U2OS, 293, 293T, Vero, HeLa, A549, BHK, BSC40, CHO, OVCAR-8, 786-0, NCI-H23, U251, SF-295, T-47D, SKMEL2, BT-549, SK-MEL-28, MDA-MB-231, SK-OV-3, MCF7, M14, SF-268, CAKI-1, HPAV, OVCAR-4, HCT15, K-562, and HCT-116.

125. The nucleic acid of any one of embodiments 1-110 or the virus of any one of embodiments 111-124, wherein said nucleic acid or said virus further comprises a transgene encoding a tumor-associated antigen.

126. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen is a tumor-associated antigen listed in any one of Tables 3-30.

127. The nucleic acid or the virus of embodiment 126, wherein said tumor-associated antigen is a tumor-associated antigen selected from the group consisting of CD19, CD33, EpCAM, CEA, PSMA, EGFRvIII, CD133, EGFR, CDH19, ENPP3, DLL3, MSLN, ROR1, HER2, HLAA2, EpHA2, EpHA3, MCSP, CSPG4, NG2, RON, FLT3, BCMA, CD20, FAPα, FRα, CA-9, PDGFRα, PDGFRβ, FSP1, S100A4, ADAM12m, RET, MET, FGFR, INSR, and NTRK.

128. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises MAGE-A3, or one or more fragments thereof.

129. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises NY-ESO-1, or one or more fragments thereof.

130. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises one or more human papillomavirus (HPV) proteins, or fragments thereof.

131. The nucleic acid or the virus of embodiment 125, wherein said HPV proteins or fragments thereof comprise one or more of (i) E6 and E7 proteins, or fragments thereof, of HPV16 and (ii) E6 and E7 proteins, or fragments thereof, of HPV18.

132. The nucleic acid or the virus of embodiment 131, wherein the sequences of said HPV proteins or fragments are disclosed in International Patent Publication WO/2014/127478, the contents of which are incorporated herein by reference.

133. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises brachyury or one or more fragments thereof.

134. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises prostatic acid phosphatase, or one or more fragments thereof.

135. A packaging cell line comprising the nucleic acid of any one of embodiments 1-110 or the virus of any one of embodiments 111-124.

136. A method of treating cancer in a mammalian patient, said method comprising administering a therapeutically effective amount of the virus of any one of embodiments 111-134 to said patient.

137. The method of embodiment 136, wherein said mammalian patient is a human patient.

138. The method of embodiment 136 or 137, wherein the virus is used as a prime in a prime:boost treatment.

139. The method of embodiment 136 or 137, wherein the virus is used as a boost in a prime:boost treatment.

140. The method of any one of embodiments 136-139, wherein said mammalian patient has cancer.

141. The method of embodiment 140, wherein said cancer is selected from the group consisting of leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, and throat cancer.

142. The method of embodiment 140, wherein said cancer is selected from the group consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), adrenocortical carcinoma, AIDS-related lymphoma, primary CNS lymphoma, anal cancer, appendix cancer, astrocytoma, atypical teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, extrahepatic cancer, Ewing sarcoma family, osteosarcoma and malignant fibrous histiocytoma, central nervous system embryonal tumors, central nervous system germ cell tumors, craniopharyngioma, ependymoma, bronchial tumors, Burkitt lymphoma, carcinoid tumor, primary lymphoma, chordoma, chronic myeloproliferative neoplasms, colon cancer, extrahepatic bile duct cancer, ductal carcinoma in situ (DCIS), endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, extracranial germ cell tumor, extragonadal germ cell tumor, fallopian tube cancer, fibrous histiocytoma of bone, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), testicular germ cell tumor, gestational trophoblastic disease, glioma, childhood brain stem glioma, hairy cell leukemia, hepatocellular cancer, Langerhans cell histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, islet cell tumors, pancreatic neuroendocrine tumors, Wilms tumor and other childhood kidney tumors, Langerhans cell histiocytosis, small cell lung cancer, cutaneous T cell lymphoma, intraocular melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer, midline tract carcinoma, multiple endocrine neoplasia syndromes, multiple myeloma/plasma cell neoplasm, myelodysplastic syndromes, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin's lymphoma (NHL), non-small cell lung cancer (NSCLC), epithelial ovarian cancer, germ cell ovarian cancer, low malignant potential ovarian cancer, pancreatic neuroendocrine tumors, papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pituitary tumor, pleuropulmonary

blastoma, primary peritoneal cancer, rectal cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, Kaposi's sarcoma, rhabdomyosarcoma, Sézary syndrome, small intestine cancer, soft tissue sarcoma, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, urethral cancer, endometrial uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, and Waldenström macroglobulinemia.

143. The method of any one of embodiments 136-142, wherein said method further comprises administering to said patient an immune checkpoint inhibitor.

144. The method of embodiment 143, wherein said immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof.

145. The method of embodiment 144, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof.

146. The method of embodiment 145, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof.

147. The method of embodiment 145, wherein said immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

148. The method of any one of embodiments 136-147, wherein said method further comprises administering to said patient an interleukin.

149. The method of embodiment 148, wherein said interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23.

150. The method of embodiment 149, wherein said interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70.

151. The method of embodiment 149 or 150, wherein said interleukin is membrane-bound.

152. The method of any one of embodiments 136-151, wherein said method further comprises administering to said patient an interferon.

153. The method of embodiment 152, wherein said interferon is selected from the group consisting of
IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

154. The method of any one of embodiments 136-153, wherein said method further comprises administering to said patient a cytokine.

155. The method of embodiment 154, wherein said cytokine is a TNF superfamily member protein.

156. The method of embodiment 155, wherein said TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

157. The method of embodiment 154, wherein said cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, TGF-beta, VEGF-R2, and cKit.

158. The method of embodiment 157, wherein said cytokine is Flt3 ligand.

159. A kit comprising the nucleic acid of any one of embodiments 1-110 or the virus of any one of embodiments 111-134 and a package insert instructing a user of said kit to express said nucleic acid or said virus in a host cell.

160. A kit comprising the virus of any one of embodiments 111-134 and a package insert instructing a user to administer a therapeutically effective amount of said virus to a mammalian patient having cancer, thereby treating said cancer.

161. The kit of embodiment 160, wherein said mammalian patient is a human patient.

162. The nucleic acid of embodiment 94, wherein said interleukin is membrane-bound IL-12 p35.

5.7.3. Set 3

1. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

2. The nucleic acid of embodiment 1, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the

C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

3. The nucleic acid of embodiment 2, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes..

4. The nucleic acid of embodiment 3, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

5. The nucleic acid of embodiment 4, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

6. The nucleic acid of embodiment 5, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 7 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

7. The nucleic acid of embodiment 6, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 8 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

8. The nucleic acid of embodiment 7, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 9 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

9. The nucleic acid of embodiment 8, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 10 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

10. The nucleic acid of embodiment 9, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 11 genes, each gene selected from the group consisting of the

C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

11. The nucleic acid of embodiment 10, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 12 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

12. The nucleic acid of embodiment 11, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 13 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

13. The nucleic acid of embodiment 12, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 14 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

14. The nucleic acid of embodiment 13, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 15 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

15. The nucleic acid of embodiment 14, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 16 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

16. The nucleic acid of embodiment 15, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 17 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

17. The nucleic acid of embodiment 16, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 18 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

18. The nucleic acid of embodiment 17, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 19 genes, each gene selected from the group consisting of the

C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

19. The nucleic acid of embodiment 18, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 20 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

20. The nucleic acid of embodiment 19, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 21 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

21. The nucleic acid of embodiment 20, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 22 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

22. The nucleic acid of embodiment 21, wherein said recombinant orthopoxvirus genome comprises a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

23. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

24. The nucleic acid of embodiment 23, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

25. The nucleic acid of embodiment 24, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

26. The nucleic acid of embodiment 25, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

27. The nucleic acid of embodiment 26, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

28. The nucleic acid of embodiment 27, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

29. The nucleic acid of embodiment 28, wherein said recombinant orthopoxvirus genome comprises a deletion of each of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes.

30. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

31. The nucleic acid of embodiment 30, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

32. The nucleic acid of embodiment 31, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 3 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

33. The nucleic acid of embodiment 32, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 4 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

34. The nucleic acid of embodiment 33, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 5 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

35. The nucleic acid of embodiment 34, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 6 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

36. The nucleic acid of embodiment 35, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 7 genes, each gene selected from the group consisting of the

C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

37. The nucleic acid of embodiment 36, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 8 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

38. The nucleic acid of embodiment 37, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 9 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

39. The nucleic acid of embodiment 38, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 10 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

40. The nucleic acid of embodiment 39, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 11 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

41. The nucleic acid of embodiment 40, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 12 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

42. The nucleic acid of embodiment 41, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 13 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

43. The nucleic acid of embodiment 42, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 14 genes, each gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

44. The nucleic acid of embodiment 43, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 15 genes, each gene selected from the group consisting of the

C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

45. The nucleic acid of embodiment 44, wherein said recombinant orthopoxvirus genome comprises a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

46. The nucleic acid comprising a recombinant orthopoxvirus genome of any one of embodiments 1-45, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene that encodes a protein involved in host interaction.

47. The nucleic acid of embodiment 46, wherein said protein affects calcium-independent adhesion to the extracellular matrix.

48. The nucleic acid of embodiment 46, wherein said protein is an NF-κB inhibitor.

49. The nucleic acid of embodiment 48, wherein said protein is encoded by a gene selected from the group consisting of the C2L, N1L, M2L, K1L, and K7R genes.

50. The nucleic acid of embodiment 46, wherein said protein is an apoptosis inhibitor.

51. The nucleic acid of embodiment 47, wherein said apoptosis inhibitor is a caspase-9 inhibitor.

52. The nucleic acid of embodiment 51, wherein said caspase-9 inhibitor is encoded by the F1L gene.

53. The nucleic acid of embodiment 50, wherein said apoptosis inhibitor is a BCL-2-like protein.

54. The nucleic acid of embodiment 53, wherein said BCL-2-like protein is encoded by N1L.

55. The nucleic acid of embodiment 46, wherein said protein is an interferon regulatory factor 3 (IRF3) inhibitor.

56. The nucleic acid of embodiment 55, wherein said IRF3 inhibitor is encoded by N2L or K7R.

57. The nucleic acid of embodiment 46, wherein said protein is a serine protease inhibitor.

58. The nucleic acid of embodiment 46, wherein said protein prevents cell fusion.

59. The nucleic acid of embodiment 58, wherein said protein is encoded by K2L.

60. The nucleic acid of embodiment 46, wherein said protein is an RNA-activated protein kinase (PKR) inhibitor.

61. The nucleic acid of embodiment 60, wherein said protein is encoded by K1L or K3L.

62. The nucleic acid of embodiment 46, wherein said protein is a virulence factor.

63. The nucleic acid of embodiment 63, wherein said protein is encoded by F3L.

64. The nucleic acid of embodiment 46, wherein said protein is an IL-1-beta inhibitor.

65. The nucleic acid of embodiment 64, wherein said protein is encoded by B16R.

66. The nucleic acid of embodiment 46, wherein said protein is a secreted IFNα sequestor.

67. The nucleic acid of embodiment 67, wherein said protein is encoded by B19R.

68. The nucleic acid comprising a recombinant orthopoxvirus genome of any one of embodiments 1-67, wherein said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene encoding a protein involved in DNA replication.

69. The nucleic acid of embodiment 68, wherein said protein is a DNA modifying nuclease.

70. The nucleic acid of embodiment 69, wherein said protein is encoded by K4L.

71. The nucleic acid of embodiment 70, wherein said protein is a deoxyuridine triphosphatase (dUTPase).

72. The nucleic acid of embodiment 71, wherein the dUTPase is encoded by F2L.

73. The nucleic acid of any one of embodiments 1-72, wherein at least one deleted gene's entire nucleotide sequence is deleted.

74. The nucleic acid of any one of embodiments 1-72, wherein at least one deleted gene is only partially deleted, and wherein the partial deletion is sufficient to render said partially deleted gene nonfunctional upon introduction into a host cell.

75. The nucleic acid of any one of embodiments 1-74, wherein said recombinant orthopoxvirus genome comprises at least two copies of inverted terminal repeats (ITRs).

76. The nucleic acid of any one of embodiments 1-74, wherein said recombinant orthopoxvirus genome lacks any copies of ITRs.

77. The nucleic acid of any one of embodiments 1-74, wherein said recombinant orthopoxvirus genome comprises a deletion in at least one copy of an ITR selected from the group consisting of B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

78. The nucleic acid of any one of embodiments 1-74, wherein said recombinant orthopoxvirus genome comprises a deletion in at least all of the following copies of ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

79. The nucleic acid of any one of embodiments 1-78, wherein said recombinant orthopoxvirus genome comprises a deletion in the B8R gene.

80. The nucleic acid of any one of embodiments 1-78, wherein said recombinant orthopoxvirus genome comprises an intact B8R gene.

81. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises

(i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, B20R, and B8R genes; and

(ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR.

82. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises

(i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes; and

(ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR,

wherein said recombinant orthopoxvirus genome comprises an intact B8R gene.

83. The nucleic acid of any one of embodiments 1-82, further comprising at least one transgene selected from the group consisting of a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine.

84. The nucleic acid of embodiment 83, wherein the nucleic acid comprises at least two transgenes selected from the group consisting of a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine.

85. The nucleic acid of embodiment 84, wherein the nucleic acid comprises a transgene encoding an immune checkpoint inhibitor, a transgene encoding an interleukin (IL), and a transgene encoding a cytokine.

86. The nucleic acid of any one of embodiment 83 or 84, wherein said nucleic acid comprises a transgene encoding an immune checkpoint inhibitor.

87. The nucleic acid of embodiment 85 or 86, wherein said immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment

thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof.

88. The nucleic acid of embodiment 87, wherein said immune checkpoint inhibitor is an anti-PD-L1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof.

89. The nucleic acid of embodiment 88, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof.

90. The nucleic acid of embodiment 88, wherein said immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

91. The nucleic acid of embodiment 83 or 84, wherein said nucleic acid comprises a transgene encoding an interleukin (IL).

92. The nucleic acid of embodiment 85 or 91, wherein said interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23.

93. The nucleic acid of embodiment 92, wherein said interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70.

94. The nucleic acid of embodiment 93, wherein said interleukin is membrane-bound.

95. The nucleic acid of embodiment 94, wherein said interleukin is membrane-bound IL-12 p70.

96. The nucleic acid of embodiment 83 or 84, wherein said nucleic acid comprises a transgene encoding a cytokine.

97. The nucleic acid of embodiment 96, wherein said cytokine is an interferon (IFN).

98. The nucleic acid of embodiment 97, wherein said interferon is selected from the group consisting of IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

99. The nucleic acid of embodiment 96, wherein said cytokine is a TNF superfamily member protein.

100. The nucleic acid of embodiment 99, wherein said TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

101. The nucleic acid of embodiment 96, wherein said cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, TGF-beta, VEGF-R2, and c-kit.

102. The nucleic acid of embodiment 101, wherein said cytokine is Flt3 ligand.

103. The nucleic acid of embodiment 83-102, wherein said recombinant orthopoxvirus genome comprises a deletion in the B8R gene and at least one transgene is inserted into the deletion in the B8R gene.

104. The nucleic acid of embodiment 103, wherein at least two transgenes are inserted into the deletion in the B8R gene.

105. The nucleic acid of embodiment 104, wherein at least three transgenes are inserted into the deletion in the B8R gene.

106. The nucleic acid of any one of embodiments 103-105, wherein at least one transgene is inserted in a locus that is not at the deletion in the B8R gene.

107. The nucleic acid of embodiment 106, wherein the locus is at the boundary of a deletion at the 5' end of the orthopoxvirus genome.

108. The nucleic acid of embodiment 106, wherein the locus is at the boundary of a deletion at the 3' end of the orthopoxvirus genome.

109. A nucleic acid comprising a recombinant orthopoxvirus genome, wherein said recombinant orthopoxvirus genome comprises

(i) a deletion of each of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, B20R, and B8R genes;

(ii) a deletion in each copy of the following ITRs: B21R-ITR, B22R-ITR, B23R-ITR, B24R-ITR, B25R-ITR, B26R-ITR, B27R-ITR, B28R-ITR, and B29R-ITR;

(iii) an IL-12-TM transgene inserted into the deletion in the B8R gene;

(iv) an Flt3 ligand transgene inserted into the deletion in the B8R gene; and

(v) one of:

(a) a transgene encoding a single chain anti-CTLA-4 antibody or antigen-binding fragment thereof

or

(b) (i) a transgene encoding a heavy chain of an anti-CTLA-4 antibody or antigen-binding fragment thereof, and

(ii) a transgene encoding a light chain of an anti-CTLA-4 antibody or antigen-binding fragment thereof,

wherein the transgene(s) in part (v) is/are inserted within the boundaries of a 5p deletion present in the recombinant orthopoxvirus genome, and

wherein the anti-CTLA-4 antibody or antigen-binding fragment thereof is capable of binding CTLA-4.

110. The nucleic acid of embodiment 109, wherein the orthopoxvirus genome is derived from a sequence of SEQ ID NO: 210, wherein

(a) said derived sequence comprises a deletion of the B8R gene, and the IL-12-TM transgene, the Flt3 ligand transgene, and the transgene(s) encoding the single or double-chain anti-CTLA-4 antibody;

(b) the IL-12-TM transgene encodes a protein comprising an amino acid sequence of is SEQ ID NO: 212;

(c) the Flt3 ligand transgene encodes a protein comprising an amino acid sequence of SEQ ID NO: 213; and

(d) the anti-CTLA-4 antibody comprises an amino acid sequence of SEQ ID NO: 211.

111. A virus comprising the nucleic acid comprising the recombinant orthopoxvirus genome of any one of embodiments 1-110.

112. The virus of embodiment 111, wherein

a) said recombinant orthopoxvirus genome comprises a deletion of at least 2 genes selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes;

b) said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes; or

c) said recombinant orthopoxvirus genome comprises a deletion of at least 1 gene selected from the group consisting of the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes.

113. The virus of embodiment 111 or 112, wherein said virus is derived from a vaccinia virus.

114. The virus of embodiment 113, wherein said vaccinia virus is derived from a strain selected from the group consisting of Copenhagen, Western Reserve, Wyeth, Lister, EM63, ACAM2000, LC16m8, CV-1, modified vaccinia Ankara (MVA), Dairen I, GLV-1h68, IHD-J, L-IVP, LC16mO, Tashkent, Tian Tan, and WAU86/88-1.

115. The virus of embodiment 114, wherein said vaccinia virus is derived from a strain selected from the group consisting of Copenhagen, Western Reserve, Tian Tan, Wyeth, and Lister.

116. The virus of embodiment 115, wherein said vaccinia virus is derived from a Copenhagen strain vaccinia virus.

117. The virus of any one of embodiments 111-116, wherein said recombinant orthopoxvirus genome further comprises a Thymidine Kinase (TK) gene.

118. The virus of any one of embodiments 111-117, wherein said recombinant orthopoxvirus genome further comprises a ribonucleotide reductase gene.

119. The virus of any one of embodiments 111-118, wherein upon contacting a population of mammalian cells with said virus, the population of mammalian cells exhibit increased syncytia formation relative to a population of mammalian cells of the same type contacted with a form of the virus that does not comprise said deletion.

120. The virus of any one of embodiments 111-119, wherein upon contacting a population of mammalian cells with said virus, the population of mammalian cells exhibit increased spreading of the virus relative to a population of mammalian cells of the same type contacted with a form of the virus that does not comprise said deletion.

121. The virus of any one of embodiments 111-120, wherein said virus exerts an increased cytotoxic effect on a population of mammalian cells relative to that of a form of the virus that does not comprise said deletion.

122. The virus of any one of embodiments 119-121, wherein said mammalian cells are human cells.

123. The virus of embodiment 122, wherein said human cells are cancer cells.

124. The virus of any one of embodiments 119-121, wherein said mammalian cells are from a cell line selected from the group consisting of U2OS, 293, 293T, Vero, HeLa, A549, BHK, BSC40, CHO, OVCAR-8, 786-0, NCI-H23, U251, SF-295, T-47D, SKMEL2, BT-549, SK-MEL-28, MDA-MB-231, SK-OV-3, MCF7, M14, SF-268, CAKI-1, HPAV, OVCAR-4, HCT15, K-562, and HCT-116.

125. The nucleic acid of any one of embodiments 1-110 or the virus of any one of embodiments 111-124, wherein said nucleic acid or said virus further comprises a transgene encoding a tumor-associated antigen.

126. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen is a tumor-associated antigen listed in any one of Tables 3-30.

127. The nucleic acid or the virus of embodiment 126, wherein said tumor-associated antigen is a tumor-associated antigen selected from the group consisting of CD19, CD33, EpCAM, CEA, PSMA, EGFRvIII, CD133, EGFR, CDH19, ENPP3, DLL3, MSLN, ROR1, HER2, HLAA2, EpHA2, EpHA3, MCSP, CSPG4, NG2, RON, FLT3, BCMA, CD20, FAPα, FRα, CA-9, PDGFRα, PDGFRβ, FSP1, S100A4, ADAM12m, RET, MET, FGFR, INSR, and NTRK.

128. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises MAGE-A3, or one or more fragments thereof.

129. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises NY-ESO-1, or one or more fragments thereof.

130. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises one or more human papillomavirus (HPV) proteins, or fragments thereof.

131. The nucleic acid or the virus of embodiment 125, wherein said HPV proteins or fragments thereof comprise one or more of (i) E6 and E7 proteins, or fragments thereof, of HPV16 and (ii) E6 and E7 proteins, or fragments thereof, of HPV18.

132. The nucleic acid or the virus of embodiment 131, wherein the sequences of said HPV proteins or fragments are disclosed in International Patent Publication WO/2014/127478, the contents of which are incorporated herein by reference.

133. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises brachyury or one or more fragments thereof.

134. The nucleic acid or the virus of embodiment 125, wherein said tumor-associated antigen comprises prostatic acid phosphatase, or one or more fragments thereof.

135. A packaging cell line comprising the nucleic acid of any one of embodiments 1-110 or the virus of any one of embodiments 111-124.

136. A method of treating cancer in a mammalian patient, said method comprising administering a therapeutically effective amount of the virus of any one of embodiments 111-134 to said patient.

137. The method of embodiment 136, wherein said mammalian patient is a human patient.

138. The method of embodiment 136 or 137, wherein the virus is used as a prime in a prime:boost treatment.

139. The method of embodiment 136 or 137, wherein the virus is used as a boost in a prime:boost treatment.

140. The method of any one of embodiments 136-139, wherein said mammalian patient has cancer.

141. The method of embodiment 140, wherein said cancer is selected from the group consisting of leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, and throat cancer.

142. The method of embodiment 140, wherein said cancer is selected from the group consisting of acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), adrenocortical carcinoma, AIDS-related lymphoma, primary CNS lymphoma, anal cancer, appendix cancer, astrocytoma, atypical teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, extrahepatic cancer, Ewing sarcoma family, osteosarcoma and malignant fibrous histiocytoma, central nervous system embryonal tumors, central nervous system germ cell tumors, craniopharyngioma, ependymoma, bronchial tumors, Burkitt lymphoma, carcinoid tumor, primary lymphoma, chordoma, chronic myeloproliferative neoplasms, colon cancer, extrahepatic bile duct cancer, ductal carcinoma in situ (DCIS), endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, extracranial germ cell tumor, extragonadal germ cell tumor, fallopian tube cancer, fibrous histiocytoma of bone, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), testicular germ cell tumor, gestational trophoblastic disease, glioma, childhood brain stem glioma, hairy cell leukemia, hepatocellular cancer, Langerhans cell histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, islet cell tumors, pancreatic neuroendocrine tumors, Wilms tumor and other childhood kidney tumors, Langerhans cell histiocytosis, small cell lung cancer, cutaneous T cell lymphoma, intraocular melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer, midline tract carcinoma, multiple endocrine neoplasia syndromes, multiple myeloma/plasma cell neoplasm, myelodysplastic syndromes, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin's lymphoma (NHL), non-small cell lung cancer (NSCLC), epithelial ovarian cancer, germ cell ovarian cancer, low malignant potential ovarian cancer, pancreatic neuroendocrine tumors, papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pituitary tumor, pleuropulmonary

blastoma, primary peritoneal cancer, rectal cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, Kaposi's sarcoma, rhabdomyosarcoma, Sézary syndrome, small intestine cancer, soft tissue sarcoma, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, urethral cancer, endometrial uterine cancer, uterine sarcoma, vaginal cancer, vulvar cancer, and Waldenström macroglobulinemia.

143. The method of any one of embodiments 136-142, wherein said method further comprises administering to said patient an immune checkpoint inhibitor.

144. The method of embodiment 143, wherein said immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof.

145. The method of embodiment 144, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof.

146. The method of embodiment 145, wherein said immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof.

147. The method of embodiment 145, wherein said immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

148. The method of any one of embodiments 136-147, wherein said method further comprises administering to said patient an interleukin.

149. The method of embodiment 148, wherein said interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23.

150. The method of embodiment 149, wherein said interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70.

151. The method of embodiment 149 or 150, wherein said interleukin is membrane-bound.

152. The method of any one of embodiments 136-151, wherein said method further comprises administering to said patient an interferon.

153. The method of embodiment 152, wherein said interferon is selected from the group consisting of
IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

154. The method of any one of embodiments 136-153, wherein said method further comprises administering to said patient a cytokine.

155. The method of embodiment 154, wherein said cytokine is a TNF superfamily member protein.

156. The method of embodiment 155, wherein said TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

157. The method of embodiment 154, wherein said cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, TGF-beta, VEGF-R2, and cKit.

158. The method of embodiment 157, wherein said cytokine is Flt3 ligand.

159. A kit comprising the nucleic acid of any one of embodiments 1-110 or the virus of any one of embodiments 111-134 and a package insert instructing a user of said kit to express said nucleic acid or said virus in a host cell.

160. A kit comprising the virus of any one of embodiments 111-134 and a package insert instructing a user to administer a therapeutically effective amount of said virus to a mammalian patient having cancer, thereby treating said cancer.

161. The kit of embodiment 160, wherein said mammalian patient is a human patient.

162. The nucleic acid of embodiment 94, wherein said interleukin is membrane-bound IL-12 p35.

5.7.4. Set 4

1. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
   (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;
   (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214;

(c) a second transgene comprising a second nucleotide sequence encoding an Interleukin 12 (IL-12) polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215; and

(d) a third transgene comprising a third nucleotide sequence encoding FMS-like tyrosine kinase 3 ligand (FLT3L), wherein the third nucleotide sequence is set forth in SEQ ID NO: 216.

2. The nucleic acid of embodiment 1, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.
3. The nucleic acid of embodiment 1 or 2, further comprising a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody.
4. The nucleic acid of embodiment 3, wherein the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an H5R promoter, a pS promoter, or a LEO promoter.
5. The nucleic acid of embodiment 3, wherein the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an H5R promoter.
6. The nucleic acid of any one of embodiments 1-5, further comprising a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide.
7. The nucleic acid of embodiment 6, wherein the at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide is a late promoter.
8. The nucleic acid of embodiment 7, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.
9. The nucleic acid of embodiment 7, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.
10. The nucleic acid of any one of embodiments 1-9, further comprising a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence encoding FLT3L.

11. The nucleic acid of embodiment 10, wherein the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.
12. The nucleic acid of embodiment 10, wherein the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter.
13. The nucleic acid of embodiment 10, wherein the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B19R promoter.
14. The nucleic acid of embodiment 10, wherein the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter and a B19R promoter.
15. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
16. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
17. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
18. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present in the locus of the deletion in the B8R gene.
19. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present in the locus of the deletion in the B8R gene.
20. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present in the locus of the deletion in the B8R gene.
21. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
22. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
23. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
24. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the second transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
25. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the second transgene are present in the locus of the deletion in the B8R gene.

26. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the second transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
27. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
28. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the third transgene are present in the locus of the deletion in the B8R gene.
29. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
30. The nucleic acid of any one of embodiments 1-14, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
31. The nucleic acid of any one of embodiments 1-14, wherein the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.
32. The nucleic acid of any one of embodiments 1-14, wherein the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
33. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present in the locus of the deletion in the B8R gene.
34. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present in the locus of the deletion in the B8R gene.
35. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present in the locus of the deletion in the B8R gene.
36. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present in the locus of the deletion in the B8R gene.

37. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present in the locus of the deletion in the B8R gene.
38. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present in the locus of the deletion in the B8R gene.
39. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
40. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
41. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
42. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
43. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
44. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
45. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

46. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
47. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
48. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
49. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
50. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
51. The nucleic acid of any one of embodiments 1-14, wherein the first transgene, the second transgene, and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
52. The nucleic acid of any one of embodiments 1-14, wherein the first transgene, the second transgene, and the third transgene are present in the locus of the deletion in the B8R gene.
53. The nucleic acid of any one of embodiments 1-14, wherein the first transgene, the second transgene, and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
54. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.
55. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene and the third transgene are present in the locus of the deletion in the B8R gene.

56. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene and the second transgene are present in the locus of the deletion in the B8R gene.
57. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the second transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present in the locus of the deletion in the B8R gene.
58. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present in the locus of the deletion in the B8R gene.
59. The nucleic acid of any one of embodiments 1-14, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present in the locus of the deletion in the B8R gene.
60. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
61. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
62. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene and the second transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
63. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the second transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

64. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
65. The nucleic acid of any one of embodiments 1-14, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
66. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
67. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
68. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene and the second transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
69. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the second transgene are present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
70. The nucleic acid of any one of embodiments 1-14, wherein the first transgene and the third transgene are present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
71. The nucleic acid of any one of embodiments 1-14, wherein the second transgene and the third transgene are present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

72. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the second transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
73. The nucleic acid of any one of embodiments 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the third transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
74. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the first transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
75. The nucleic acid of any one of embodiments 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
76. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
77. The nucleic acid of any one of embodiments 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the second transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
78. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

79. The nucleic acid of embodiment 78, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

80. The nucleic acid of embodiment 78 or 79, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.

81. The nucleic acid of embodiment 78 or 79, wherein the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.
82. The nucleic acid of embodiment 80 or 81, wherein the third transgene is upstream of the second transgene.
83. The nucleic acid of embodiment 80 or 81, wherein the third transgene is downstream of the second transgene.
84. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;
(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes the vaccinia virus nucleotide sequence of SEQ ID NO: 210;
(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and
(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;
wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

85. The nucleic acid of embodiment 84, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.
86. The nucleic acid of embodiment 85, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.
87. The nucleic acid of any one of embodiments 84-86, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.
88. The nucleic acid of embodiment 87, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.
89. The nucleic acid of embodiment 88, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.
90. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the

first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

91. The nucleic acid of embodiment 90, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

92. The nucleic acid of embodiment 91, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

93. The nucleic acid of any one of embodiments 90-92, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.
94. The nucleic acid of embodiment 93, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.
95. The nucleic acid of embodiment 94, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.
96. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;
(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210;
(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and
(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;
wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

97. The nucleic acid of embodiment 96, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

98. The nucleic acid of embodiment 97, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

99. The nucleic acid of any one of embodiments 96-98, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

100. The nucleic acid of embodiment 99, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

101. The nucleic acid of embodiment 100, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

102. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the

first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

103. The nucleic acid of embodiment 102, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

104. The nucleic acid of embodiment 103, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

105. The nucleic acid of any one of embodiments 102-104, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

106. The nucleic acid of embodiment 105, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

107. The nucleic acid of embodiment 106, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

108. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

109. The nucleic acid of embodiment 108, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

110. The nucleic acid of embodiment 109, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

111. The nucleic acid of any one of embodiments 108-110, wherein the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

112. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second

transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

113. The nucleic acid of embodiment 112, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

114. The nucleic acid of embodiment 113, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

115. The nucleic acid of any one of embodiments 112-114, wherein the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

116. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

117. The nucleic acid of embodiment 116, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

118. The nucleic acid of embodiment 117, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

119. The nucleic acid of any one of embodiments 116-118, wherein the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

120. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

121. The nucleic acid of embodiment 120, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

122. The nucleic acid of embodiment 121, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

123. The nucleic acid of any one of embodiments 120-122, wherein the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

124. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

125. The nucleic acid of embodiment 124, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

126. The nucleic acid of embodiment 125, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

127. The nucleic acid of any one of embodiments 124-126, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

128. The nucleic acid of embodiment 127, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

129. The nucleic acid of embodiment 128, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

130. The nucleic acid of any one of embodiments 124-129, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

131. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene, of the vaccinia virus nucleotide sequence of SEQ ID NO: 210 and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

132. The nucleic acid of embodiment 131, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

133. The nucleic acid of embodiment 132, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

134. The nucleic acid of any one of embodiments 131-133, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

135. The nucleic acid of embodiment 134, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

136. The nucleic acid of embodiment 135, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

137. The nucleic acid of any one of embodiments 131-136, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

138. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous

vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

139. The nucleic acid of embodiment 138, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

140. The nucleic acid of embodiment 139, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

141. The nucleic acid of any one of embodiments 138-140, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

142. The nucleic acid of embodiment 141, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

143. The nucleic acid of embodiment 142, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

144. The nucleic acid of any one of embodiments 138-143, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

145. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

146. The nucleic acid of embodiment 145, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

147. The nucleic acid of embodiment 146, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

148. The nucleic acid of any one of embodiments 145-147, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

149. The nucleic acid of embodiment 148, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

150. The nucleic acid of embodiment 149, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

151. The nucleic acid of any one of embodiments 145-150, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

152. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

153. The nucleic acid of embodiment 152, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

154. The nucleic acid of embodiment 153, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

155. The nucleic acid of embodiment 154, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

156. The nucleic acid of any one of embodiments 152-155, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

157. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

158. The nucleic acid of embodiment 157, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

159. The nucleic acid of embodiment 158, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

160. The nucleic acid of embodiment 159, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

161. The nucleic acid of any one of embodiments 157-160, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

162. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus

genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

163. The nucleic acid of embodiment 162, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

164. The nucleic acid of embodiment 163, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

165. The nucleic acid of embodiment 164, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

166. The nucleic acid of any one of embodiments 162-165, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

167. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation

as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

168. The nucleic acid of embodiment 167, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

169. The nucleic acid of embodiment 168, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

170. The nucleic acid of embodiment 169, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

171. The nucleic acid of any one of embodiments 167-170, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

172. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

173. The nucleic acid of embodiment 172, wherein the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

174. The nucleic acid of embodiment 172 or 173, wherein the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

175. The nucleic acid of any one of embodiments 172-174, wherein the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

176. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus

genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

177. The nucleic acid of embodiment 176, wherein the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

178. The nucleic acid of embodiment 176 or 177, wherein the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

179. The nucleic acid of any one of embodiments 176-178, wherein the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

180. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

181. The nucleic acid of embodiment 180, wherein the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

182. The nucleic acid of embodiment 170 or 181, wherein the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

183. The nucleic acid of any one of embodiments 180-182, wherein the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

184. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

185. The nucleic acid of embodiment 184, wherein the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

186. The nucleic acid of embodiment 174 or 185, wherein the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

187. The nucleic acid of any one of embodiments 184-186, wherein the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

188. A virus comprising the nucleic acid comprising a recombinant vaccinia virus genome of any one of embodiments 1-187.

189. A packaging cell line comprising the nucleic acid of any one of embodiments 1-187.

190. A packaging cell line comprising the virus of embodiment 188.

191. A pharmaceutical composition comprising the virus of embodiment 188 and a physiologically acceptable carrier.

192. A kit comprising the nucleic acid of any one of embodiments 1-187 and a package insert instructing a user of the kit to express the nucleic acid in a host cell.

193. A kit comprising the virus of embodiment 188 and a package insert instructing a user of the kit to express the virus in a host cell.

194. A kit comprising the virus of embodiment 188 and a package insert instructing a user to administer a therapeutically effective amount of the virus to a mammalian patient having cancer, thereby treating the cancer.

195. The kit of embodiment 194, wherein the mammalian patient is a human patient.

196. A method of treating cancer in a mammalian patient, the method comprising administering to the mammalian patient a therapeutically effective amount of the virus of embodiment 188.

197. A method of treating cancer in a mammalian patient, the method comprising administering to the mammalian patient a therapeutically effective amount of the pharmaceutical composition of embodiment 191.

198. The method of embodiment 196 or 197, wherein the mammalian patient is a human patient.

199. The method of any one of embodiments 196-198, wherein the cancer is selected from the group consisting of leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, and throat cancer.

200. The method of embodiment 199, wherein the method further comprises administering to the mammalian patient an anti-PD1 antibody or an anti-PD-L1 antibody.

5.7.5. Set 5

1. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
   (a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R;
   (b) deletions in the following genes in the 3′ inverted terminal repeat (ITR): B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and
   (c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4);
   wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.
2. The nucleic acid of embodiment 1, further comprising a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence.
3. The nucleic acid of embodiment 2, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter.
4. The nucleic acid of embodiment 2, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.
5. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and

(d) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

6. The nucleic acid of embodiment 5, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.
7. The nucleic acid of any one of embodiments 1-6, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence.
8. The nucleic acid of any one of embodiments 1-7, wherein the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211.
9. The nucleic acid of any one of embodiments 1-8, wherein the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214.
10. The nucleic acid of any one of embodiments 1-8, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214.
11. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and

(c) a second transgene comprising a second nucleotide sequence encoding an Interleukin 12 (IL-12) polypeptide;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

12. The nucleic acid of embodiment 11, further comprising a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence.
13. The nucleic acid of embodiment 12, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter.
14. The nucleic acid of embodiment 13, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.
15. The nucleic acid of embodiment 13, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.
16. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;
(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;
(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and
(d) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter;
wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.
17. The nucleic acid of embodiment 16, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.
18. The nucleic acid of embodiment 16, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.
19. The nucleic acid of any one of embodiments 11-18, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence.
20. The nucleic acid of any one of embodiments 11-19, wherein the IL-12 polypeptide is membrane-bound.

21. The nucleic acid of any one of embodiments 11-20, wherein the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70.
22. The nucleic acid of any one of embodiments 11-21, wherein the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212.
23. The nucleic acid of any one of embodiments 11-22, wherein the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215.
24. The nucleic acid of any one of embodiments 11-22, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215.
25. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R;
(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R; and
(c) a third transgene comprising a third nucleotide sequence encoding FMS-like tyrosine kinase 3 ligand (FLT3L);
wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.
26. The nucleic acid of embodiment 25, further comprising a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence.
27. The nucleic acid of embodiment 26, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.
28. The nucleic acid of embodiment 26, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter.
29. The nucleic acid of embodiment 26, wherein the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter.
30. The nucleic acid of embodiment 26, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.
31. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a third transgene comprising a third nucleotide sequence encoding FLT3L; and

(d) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

32. The nucleic acid of embodiment 31, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter.
33. The nucleic acid of embodiment 31, wherein the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter.
34. The nucleic acid of embodiment 31, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.
35. The nucleic acid of any one of embodiments 25-34, wherein the third nucleotide sequence is the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.
36. The nucleic acid of any one of embodiments 25-35, wherein the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213.
37. The nucleic acid of any one of embodiments 25-36, wherein the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216.
38. The nucleic acid of any one of embodiments 25-36, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216.
39. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

40. The nucleic acid of embodiment 39, further comprising a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence.
41. The nucleic acid of embodiment 40, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter.
42. The nucleic acid of embodiment 40, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.
43. The nucleic acid of any one of embodiments 39-42, further comprising a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence.
44. The nucleic acid of embodiment 43, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter.
45. The nucleic acid of embodiment 44, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.
46. The nucleic acid of embodiment 44, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.
47. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; and/or
(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter.

48. The nucleic acid comprising embodiment 47, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.
49. The nucleic acid comprising embodiment 47 or 48, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.
50. The nucleic acid of embodiment 47 or 48, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.
51. The nucleic acid of any one of embodiments 39-50, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence.
52. The nucleic acid of any one of embodiments 39-51, wherein the IL-12 polypeptide is membrane-bound.
53. The nucleic acid of any one of embodiments 39-52, wherein the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70.
54. The nucleic acid of any one of embodiments 39-53, wherein the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211.
55. The nucleic acid of any one of embodiments 39-54, wherein the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214.
56. The nucleic acid of any one of embodiments 39-54, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214.
57. The nucleic acid of any one of embodiments 39-56, wherein the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212.
58. The nucleic acid of any one of embodiments 39-57, wherein the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215.

59. The nucleic acid of any one of embodiments 39-57, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215.
60. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R;
(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;
(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and
(d) a third transgene comprising a third nucleotide sequence encoding FLT3L;
wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.
61. The nucleic acid of embodiment 60, further comprising a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence.
62. The nucleic acid of embodiment 61, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter.
63. The nucleic acid of embodiment 61, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.
64. The nucleic acid of any one of embodiments 60-63, further comprising a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence.
65. The nucleic acid of embodiment 64, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.
66. The nucleic acid of embodiment 64, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter.
67. The nucleic acid of embodiment 64, wherein the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter.
68. The nucleic acid of embodiment 64, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.
69. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter; and/or

(ii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.

70. The nucleic acid of embodiment 69, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.
71. The nucleic acid of embodiment 69 or 70, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter.
72. The nucleic acid of embodiment 69 or 70, wherein the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter.
73. The nucleic acid of embodiment 69 or 70, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.
74. The nucleic acid of any one of embodiments 60-73, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.
75. The nucleic acid of any one of embodiments 60-74, wherein the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211.

76. The nucleic acid of any one of embodiments 60-75, wherein the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214.
77. The nucleic acid of any one of embodiments 60-75, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214.
78. The nucleic acid of any one of embodiments 60-77, wherein the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213.
79. The nucleic acid of any one of embodiments 60-78, wherein the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216.
80. The nucleic acid of any one of embodiments 60-78, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216.
81. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R;
(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;
(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and
(d) a third transgene comprising a third nucleotide sequence encoding FLT3L;
wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.
82. The nucleic acid of embodiment 81, further comprising a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence.
83. The nucleic acid of embodiment 82, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter.
84. The nucleic acid of embodiment 83, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.
85. The nucleic acid of embodiment 83, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.
86. The nucleic acid of any one of embodiments 81-85, further comprising a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence.

87. The nucleic acid of embodiment 86, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.
88. The nucleic acid of embodiment 86, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter.
89. The nucleic acid of embodiment 86, wherein the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter.
90. The nucleic acid of embodiment 86, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.
91. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;
(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;
(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and
(d) a third transgene comprising a third nucleotide sequence encoding FLT3L;
wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and
wherein the nucleic acid further comprises:
(i) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter; and/or
(ii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.
92. The nucleic acid of embodiment 91, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.
93. The nucleic acid of embodiment 91, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.

94. The nucleic acid of any one of embodiments 91-93, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter.
95. The nucleic acid of any one of embodiments 91-93, wherein the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter.
96. The nucleic acid of any one of embodiments 91-93, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.
97. The nucleic acid of any one of embodiments 81-96, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia genes that flank the third nucleotide sequence.
98. The nucleic acid of any one of embodiments 81-97, wherein the IL-12 polypeptide is membrane-bound.
99. The nucleic acid of any one of embodiments 81-98, wherein the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70.
100. The nucleic acid of any one of embodiments 81-99, wherein the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212.
101. The nucleic acid of any one of embodiments 81-100, wherein the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215.
102. The nucleic acid of any one of embodiments 81-100, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215.
103. The nucleic acid of any one of embodiments 81-102, wherein the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213.
104. The nucleic acid of any one of embodiments 81-103, wherein the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216.
105. The nucleic acid of any one of embodiments 81-103, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216.
106. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B8R, B14R, B15R, B16R, B17L, B18R, B19R, and B20R;
(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4;

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and

(e) a third transgene comprising a third nucleotide sequence encoding FLT3L;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions.

107. The nucleic acid of embodiment 106, further comprising a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence.

108. The nucleic acid of embodiment 107, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter.

109. The nucleic acid of embodiment 107, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

110. The nucleic acid of any one of embodiments 106-109, further comprising a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence.

111. The nucleic acid of embodiment 110, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter.

112. The nucleic acid of embodiment 111, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.

113. The nucleic acid of embodiment 111, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.

114. The nucleic acid of any one of embodiments 106-113, further comprising a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence.

115. The nucleic acid of embodiment 114, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.

116. The nucleic acid of embodiment 114, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter.

117. The nucleic acid of embodiment 114, wherein the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter.

118. The nucleic acid of embodiment 114, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

119. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4;

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and

(e) a third transgene comprising a third nucleotide sequence encoding FLT3L;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter, a pS promoter, or a LEO promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter; and/or

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.

120. The nucleic acid of embodiment 119, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter.

121. The nucleic acid of embodiment 119 or 120, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.

122. The nucleic acid of embodiment 119 or 120, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.

123. The nucleic acid of any one of embodiments 119-122, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter.

124. The nucleic acid of any one of embodiments 119-122, wherein the at least one promoter operably linked to the third nucleotide sequence is a B19R promoter.

125. The nucleic acid of any one of embodiments 119-122, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

126. The nucleic acid of any one of embodiments 106-125, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

127. The nucleic acid of any one of embodiments 106-126, wherein the IL-12 polypeptide is membrane-bound.

128. The nucleic acid of any one of embodiments 106-127, wherein the IL-12 polypeptide comprises IL-12 p35 or IL-12 p70.

129. The nucleic acid of any one of embodiments 106-128, wherein the first nucleotide sequence encodes an amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 211.

130. The nucleic acid of any one of embodiments 106-129, wherein the first nucleotide sequence comprises the sequence set forth in SEQ ID NO: 214.

131. The nucleic acid of any one of embodiments 106-129, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214.

132. The nucleic acid of any one of embodiments 106-131, wherein the IL-12 polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 212.

133. The nucleic acid of any one of embodiments 106-132, wherein the second nucleotide sequence comprises the sequence set forth in SEQ ID NO: 215.

134. The nucleic acid of any one of embodiments 106-132, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215.

135. The nucleic acid of any one of embodiments 106-134, wherein the FLT3L comprises the amino acid sequence set forth in SEQ ID NO: 213.

136. The nucleic acid of any one of embodiments 106-135, wherein the third nucleotide sequence comprises the sequence set forth in SEQ ID NO: 216.

137. The nucleic acid of any one of embodiments 106-135, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216.

138. The nucleic acid of any one of embodiments 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.

139. The nucleic acid of embodiment 138, wherein the third transgene is upstream of the second transgene.

140. The nucleic acid of any one of embodiments 1-10, 39-80, and 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes.

141. The nucleic acid of any one of embodiments 11-24, 39-59, and 81-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes.

142. The nucleic acid of any one of embodiments 25-38 and 60-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes.

143. The nucleic acid of any one of embodiments 1-10, 39-80, and 106-137, wherein the first transgene is present in the locus of the deletion in the B8R gene.

144. The nucleic acid of any one of embodiments 11-24, 39-59, and 81-137, wherein the second transgene is present in the locus of the deletion in the B8R gene.

145. The nucleic acid of any one of embodiments 25-38 and 60-137, wherein the third transgene is present in the locus of the deletion in the B8R gene.

146. The nucleic acid of any one of embodiments 1-10, 39-80, and 106-137, wherein the first transgene is present between the partial B14R and B29R vaccinia genes.

147. The nucleic acid of any one of embodiments 11-24, 39-59, and 81-137, wherein the second transgene is present between the partial B14R and B29R vaccinia genes.

148. The nucleic acid of any one of embodiments 25-38 and 60-137, wherein the third transgene is present between the partial B14R and B29R vaccinia genes.

149. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the first transgene and the second transgene are present between the partial C2L and F3L vaccinia genes.

150. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the first transgene and the second transgene are present in the locus of the deletion in the B8R gene.

151. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the first transgene and the second transgene are present between the partial B14R and B29R vaccinia genes.

152. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes.

153. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the first transgene and the third transgene are present in the locus of the deletion in the B8R gene.

154. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes.

155. The nucleic acid of any one of embodiments 81-137, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes.

156. The nucleic acid of any one of embodiments 81-137, wherein the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.

157. The nucleic acid of any one of embodiments 81-137, wherein the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes.

158. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, and the second transgene is present in the locus of the deletion in the B8R gene.

159. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes, and the first transgene is present in the locus of the deletion in the B8R gene.

160. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, and the third transgene is present in the locus of the deletion in the B8R gene.

161. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes, and the first transgene is present in the locus of the deletion in the B8R gene.

162. The nucleic acid of any one of embodiments 81-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes, and the third transgene is present in the locus of the deletion in the B8R gene.

163. The nucleic acid of any one of embodiments 81-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes, and the second transgene is present in the locus of the deletion in the B8R gene.

164. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, and the second transgene is present between the partial B14R and B29R vaccinia genes.

165. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes, and the first transgene is present between the partial B14R and B29R vaccinia genes.

166. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, and the third transgene is present between the partial B14R and B29R vaccinia genes.

167. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes, and the first transgene is present between the partial B14R and B29R vaccinia genes.

168. The nucleic acid of any one of embodiments 81-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes, and the third transgene is present between the partial B14R and B29R vaccinia genes.

169. The nucleic acid of any one of embodiments 81-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes, and the second transgene is present between the partial B14R and B29R vaccinia genes.

170. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes.

171. The nucleic acid of any one of embodiments 39-59 and 106-137, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes.

172. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes.

173. The nucleic acid of any one of embodiments 60-80 and 106-137, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes.

174. The nucleic acid of any one of embodiments 81-137, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes.

175. The nucleic acid of any one of embodiments 81-137, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes.

176. The nucleic acid of any one of embodiments 106-137, wherein the first transgene, the second transgene, and the third transgene are present between the partial C2L and F3L vaccinia genes.

177. The nucleic acid of any one of embodiments 106-137, wherein the first transgene, the second transgene, and the third transgene are present in the locus of the deletion in the B8R gene.

178. The nucleic acid of any one of embodiments 106-137, wherein the first transgene, the second transgene, and the third transgene are present between the partial B14R and B29R vaccinia genes.

179. The nucleic acid of any one of embodiments 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.

180. The nucleic acid of any one of embodiments 106-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes, and the first

transgene and the third transgene are present in the locus of the deletion in the B8R gene.

181. The nucleic acid of any one of embodiments 106-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes, and the first transgene and the second transgene are present in the locus of the deletion in the B8R gene.

182. The nucleic acid of any one of embodiments 106-137, wherein the first transgene and the second transgene are present between the partial C2L and F3L vaccinia genes, and the third transgene is present in the locus of the deletion in the B8R gene.

183. The nucleic acid of any one of embodiments 106-137, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes, and the second transgene is present in the locus of the deletion in the B8R gene.

184. The nucleic acid of any one of embodiments 106-137, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes, and the first transgene is present in the locus of the deletion in the B8R gene.

185. The nucleic acid of any one of embodiments 106-137, wherein the first transgene is present within between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes.

186. The nucleic acid of any one of embodiments 106-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes, and the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes.

187. The nucleic acid of any one of embodiments 106-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes, and the first transgene and the second transgene are present between the partial B14R and B29R vaccinia genes.

188. The nucleic acid of any one of embodiments 106-137, wherein the first transgene and the second transgene are present between the partial C2L and F3L

vaccinia genes, and the third transgene is present between the partial B14R and B29R vaccinia genes.

189. The nucleic acid of any one of embodiments 106-137, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes, and the second transgene is present between the partial B14R and B29R vaccinia genes.

190. The nucleic acid of any one of embodiments 106-137, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes, and the first transgene is present between the partial B14R and B29R vaccinia genes.

191. The nucleic acid of any one of embodiments 106-137, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes.

192. The nucleic acid of any one of embodiments 106-137, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes.

193. The nucleic acid of any one of embodiments 106-137, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene and the second transgene are present between the partial B14R and B29R vaccinia genes.

194. The nucleic acid of any one of embodiments 106-137, wherein the first transgene and the second transgene are present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes.

195. The nucleic acid of any one of embodiments 106-137, wherein the first transgene and the third transgene are present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes.

196. The nucleic acid of any one of embodiments 106-137, wherein the second transgene and the third transgene are present in the locus of the deletion in the B8R

gene, and the first transgene is present between the partial B14R and B29R vaccinia genes.

197. The nucleic acid of any one of embodiments 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, the second transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes.

198. The nucleic acid of any one of embodiments 106-137, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, the third transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes.

199. The nucleic acid of any one of embodiments 106-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes, the first transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes.

200. The nucleic acid of any one of embodiments 106-137, wherein the second transgene is present between the partial C2L and F3L vaccinia genes, the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes.

201. The nucleic acid of any one of embodiments 106-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes, the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes.

202. The nucleic acid of any one of embodiments 106-137, wherein the third transgene is present between the partial C2L and F3L vaccinia genes, the second transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes.

203. The nucleic acid of any one of embodiments 1-202, wherein the deletion in the B8R gene is a deletion of at least 50% of the B8R gene sequence.

204. The nucleic acid of any one of embodiments 1-202, wherein the deletion in the B8R gene is a deletion of at least 60% of the B8R gene sequence.

205. The nucleic acid of any one of embodiments 1-202, wherein the deletion in the B8R gene is a deletion of at least 70% of the B8R gene sequence.

206. The nucleic acid of any one of embodiments 1-202, wherein the deletion in the B8R gene is a deletion of at least 80% of the B8R gene sequence.

207. The nucleic acid of any one of embodiments 1-202, wherein the deletion in the B8R gene is a deletion of about 75% of the B8R gene sequence.

208. The nucleic acid of any one of embodiments 1-202, wherein the deletion in the B8R gene is a deletion of about 80% of the B8R gene sequence.

209. The nucleic acid of any one of embodiments 1-208, wherein the recombinant vaccinia virus genome is derived from the genome of a Copenhagen strain vaccinia virus.

210. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4;

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide; and

(e) a third transgene comprising a third nucleotide sequence encoding FLT3L;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

211. The nucleic acid of embodiment 210, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

212. The nucleic acid of embodiment 210 or 211, wherein the first transgene is present between the partial C2L and F3L vaccinia genes, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.

213. The nucleic acid of embodiment 210 or 211, wherein the first transgene is present between the partial B14R and B29R vaccinia genes, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.

214. The nucleic acid of embodiment 212 or 213, wherein the third transgene is upstream of the second transgene.

215. The nucleic acid of embodiment 212 or 213, wherein the third transgene is downstream of the second transgene.

216. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is present between the partial C2L and F3L vaccinia genes;

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and wherein the second transgene is present in the locus of the deletion in the B8R gene; and

(e) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is present in the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions; and

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

217. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is present between the partial C2L and F3L vaccinia genes;

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and

wherein the second transgene is present in the locus of the deletion in the B8R gene; and

(e) a third transgene comprising a third nucleotide sequence encoding FLT3L;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is present in the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; and

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

218. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is present between the partial B14R and B29R vaccinia genes;

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and

wherein the second transgene is present in the locus of the deletion in the B8R gene; and

(e) a third transgene comprising a third nucleotide sequence encoding FLT3L;

wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is present in the locus of the deletion in the B8R gene, and wherein the third transgene is upstream of the second transgene; and

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

219. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) deletions in the following genes: C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R, and optionally a deletion in the B8R gene;

(b) deletions in the following genes in the 3′ ITR: B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R;

(c) a first transgene comprising a first nucleotide sequence encoding an antibody or antigen-binding fragment thereof that specifically binds to CTLA-4, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, and wherein the first transgene is present between the partial B14R and B29R vaccinia genes;

(d) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and

wherein the second transgene is present in the locus of the deletion in the B8R gene; and

(e) a third transgene comprising a third nucleotide sequence encoding FLT3L; wherein the deletions in the C2L, F3L, B14R, and B29R vaccinia genes are partial deletions, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence, wherein the third transgene is present in the locus of the deletion in the B8R gene, and wherein the third transgene is downstream of the second transgene; and

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

220. The nucleic acid of any one of embodiments 1-219, wherein the recombinant vaccinia virus genome comprises a vaccinia virus nucleotide sequence of SEQ ID NO: 624.

221. The nucleic acid of any one of embodiments 1-105, wherein the recombinant vaccinia virus genome comprises a vaccinia virus nucleotide sequence of SEQ ID NO: 210.

222. A virus comprising the nucleic acid comprising a recombinant vaccinia virus genome of any one of embodiments 1-221.

223. A packaging cell line comprising the nucleic acid of any one of embodiments 1-221.

224. A packaging cell line comprising the virus of embodiment 222.

225. A pharmaceutical composition comprising the virus of embodiment 222 and a physiologically acceptable carrier.

226. A kit comprising the nucleic acid of any one of embodiments 1-221 and a package insert instructing a user of the kit to express the nucleic acid in a host cell.

227. A kit comprising the virus of embodiment 222 and a package insert instructing a user of the kit to express the virus in a host cell.

228. A kit comprising the virus of embodiment 222 and a package insert instructing a user to administer a therapeutically effective amount of the virus to a mammalian patient having cancer, thereby treating the cancer.

229. The kit of embodiment 228, wherein the mammalian patient is a human patient.

230. A method of treating cancer in a mammalian patient, the method comprising administering to the mammalian patient a therapeutically effective amount of the virus of embodiment 222.

231. A method of treating cancer in a mammalian patient, the method comprising administering to the mammalian patient a therapeutically effective amount of the pharmaceutical composition of embodiment 225.

232. The method of embodiment 230 or 231, wherein the mammalian patient is a human patient.

233. The method of any one of embodiments 230-232, wherein the cancer is selected from the group consisting of leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, and throat cancer.

234. The method of any one of embodiments 230-233, wherein the method further comprises administering to the mammalian patient an immune checkpoint inhibitor.

235. The method of embodiment 234, wherein the immune checkpoint inhibitor is selected from the group consisting of OX40 ligand, ICOS ligand, anti-CD47 antibody or antigen-binding fragment thereof, anti-CD40/CD40L antibody or antigen-binding fragment thereof, anti-Lag3 antibody or antigen-binding fragment thereof, anti-CTLA-4 antibody or antigen-binding fragment thereof, anti-PD-L1 antibody or antigen-binding fragment thereof, anti-PD1 antibody or antigen-binding fragment thereof, and anti-Tim-3 antibody or antigen-binding fragment thereof.

236. The method of embodiment 234, wherein the immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof or an anti-CTLA-4 antibody or antigen-binding fragment thereof.

237. The method of embodiment 234, wherein the immune checkpoint inhibitor is an anti-PD1 antibody or antigen-binding fragment thereof.

238. The method of embodiment 234, wherein the immune checkpoint inhibitor is an anti-CTLA-4 antibody or antigen-binding fragment thereof.

239. The method of embodiment 234, wherein the immune checkpoint inhibitor is an anti-PD-L1 antibody or antigen-binding fragment thereof.

240. The method of any one of embodiments 219-228, wherein the method further comprises administering to the mammalian patient an interleukin.

241. The method of embodiment 240, wherein the interleukin is selected from the group consisting of IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-7, IL-10, IL-12 p35, IL-12 p40, IL-12 p70, IL-15, IL-18, IL-21, and IL-23.

242. The method of embodiment 240, wherein the interleukin is selected from the group consisting of IL-12 p35, IL-12 p40, and IL-12 p70.

243. The method of any one of embodiments 240-242, wherein the interleukin is membrane-bound.

244. The method of any one of embodiments 230-243, wherein the method further comprises administering to the mammalian patient an interferon.

245. The method of embodiment 244, wherein the interferon is selected from the group consisting of IFN-alpha, IFN-beta, IFN-delta, IFN-epsilon, IFN-tau, IFN-omega, IFN-zeta, and IFN-gamma.

246. The method of any one of embodiments 230-245, wherein the method further comprises administering to the mammalian patient a cytokine.

247. The method of embodiment 246, wherein the cytokine is a TNF superfamily member protein.

248. The method of embodiment 247, wherein the TNF superfamily member protein is selected from the group consisting of TRAIL, Fas ligand, LIGHT (TNFSF-14), TNF-alpha, and 4-1BB ligand.

249. The method of embodiment 246, wherein the cytokine is selected from the group consisting of GM-CSF, Flt3 ligand, CD40 ligand, TGF-beta, VEGF-R2, and cKit.

250. The method of embodiment 246, wherein the cytokine is Flt3 ligand.

5.8. Tables 3-45 Referenced in the Application

Table 3. Ovarian cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*Kallikrein 4*	FLGYLILGV (SEQ ID NO: 410); SVSESDTIRSISIAS (SEQ ID NO: 199); LLANGRMPTVLQCVN (SEQ ID NO: 209); and RMPTVLQCVNVSVVS (SEQ ID NO: 220)	Wilkinson *et al.* Cancer Immunol. Immunother. 61(2):169-79 (2012). Hural *et al.* J. Immunol. 169(1):557-65 (2002).
2	*PBF*	CTACRWKKACQR (SEQ ID NO: 221)	Tsukahara *et al.* Cancer Res. 64(15):5442-8 (2004).
3	*PRAME*	VLDGLDVLL (SEQ ID NO: 222); SLYSFPEPEA (SEQ ID NO: 223); ALYVDSLFFL (SEQ ID NO: 224); SLLQHLIGL (SEQ ID NO: 225); and LYVDSLFFL (SEQ ID NO: 226)	Kessler *et al.* J. Exp. Med. 193(1):73-88 (2001). Ikeda *et al.* Immunity 6(2):199-208 (1997).
4	*WT1*	TSEKRPFMCAY (SEQ ID NO: 227); CMTWNQMNL (SEQ ID NO: 228); LSHLQMHSRKH (SEQ ID NO: 229); KRYFKLSHLQMHSRKH (SEQ ID NO: 230); and KRYFKLSHLQMHSRKH (SEQ ID NO: 230)	Asemissen *et al.* Clin. Cancer Res. 12(24):7476-82 (2006) Ohminami *et al.* Blood. 95(1):286-93 (2000). Guo *et al.* Blood. 106(4):1415-8 (2005). Lin *et al.* J. Immunother. 36(3):159-70 (2013). Fujiki *et al.* J. Immunother. 30(3):282-93 (2007).
5	*HSDL1*	CYMEAVAL (SEQ ID NO: 231)	Wick *et al.* Clin. Cancer Res. 20(5):1125-34 (2014).
6	*Mesothelin*	SLLFLLFSL (SEQ ID NO: 232) VLPLTVAEV (SEQ ID NO: 233)	Hassan *et al.* Appl. Immunohistochem. Mol. Morphol. 13(3):243-7 (2005). Thomas et al J Exp Med. 2004 Aug 2; 200(3): 297–306.

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		ALQGGGPPY (SEQ ID NO: 234) LYPKARLAF (SEQ ID NO: 235) AFLPWHRLF (SEQ ID NO: 236)	
7	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAE LARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIR LTAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAA EVPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIR LT (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQ L (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIR LTAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAE LARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
8	*CEA/PMEL or gp100*	TYYRPGVNLSLSC (SEQ ID NO: 265) EIIYPNASLLIQN (SEQ ID NO: 266) YACFVSNLATGRNNS (SEQ ID NO: 267)	Galanis *et al.* Cancer Res. 70(3):875-82 (2010). Bast *et al.* Am. J. Obstet. Gynecol. 149(5):553-9 (1984). Crosti *et al.* J Immunol. 176(8):5093-9 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LWWVNNQSLPVSP (SEQ ID NO: 268) LWWVNNQSLPVSP (SEQ ID NO: 268) LWWVNNQSLPVSP (SEQ ID NO: 268) EIIYPNASLLIQN (SEQ ID NO: 266) NSIVKSITVSASG (SEQ ID NO: 269) KTWGQYWQV (SEQ ID NO: 270) AMLGTHTMEV (SEQ ID NO: 271) MLGTHTMEV (SEQ ID NO: 627) ITDQVPFSV (SEQ ID NO: 272) YLEPGPVTA (SEQ ID NO: 273) LLDGTATLRL (SEQ ID NO: 274) VLYRYGSFSV (SEQ ID NO: 275) SLADTNSLAV (SEQ ID NO: 276) RLMKQDFSV (SEQ ID NO: 277) RLPRIFCSC (SEQ ID NO: 278) LIYRRRLMK (SEQ ID NO: 279) ALLAVGATK (SEQ ID NO: 280) IALNFPGSQK (SEQ ID NO: 281) RSYVPLAHR (SEQ ID NO: 282)	Kobayashi *et al.* Clin Cancer Res. 8(10):3219-25 (2002). Campi *et al.* Cancer Res. 63(23):8481-6 (2003). Bakker *et al.* Int J Cancer. 62(1):97-102 (1995). Tsai *et al.* J Immunol. 158(4):1796-802 (1997). Kawakami *et al.* J Immunol. 154(8):3961-8 (1995). Cox *et al.* Science. 264(5159):716-9 (1994). Kawakami *et al.* J Immunol. 154(8):3961-8 (1995). Kawakami *et al.* J Immunol. 161(12):6985-92 (1998). Skipper *et al.* J Immunol. 157(11):5027-33 (1996). Michaux *et al.* J Immunol. 192(4):1962-71 (2014).
9	*p53*	VVPCEPPEV (SEQ ID NO: 283)	Hung *et al.* Immunol. Rev. 222:43-69 (2008).
10	*Her2/Neu*	HLYQGCQVV (SEQ ID NO: 284)	Nakatsuka *et al.* Mod. Pathol. 19(6):804-814 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		YLVPQQGFFC (SEQ ID NO: 285) PLQPEQLQV (SEQ ID NO: 286) TLEEITGYL (SEQ ID NO: 287) ALIHHNTHL (SEQ ID NO: 288) PLTSIISAV (SEQ ID NO: 289) VLRENTSPK (SEQ ID NO: 290) TYLPTNASL (SEQ ID NO: 291)	Pils *et al.* Br. J. Cancer 96(3):485-91 (2007). Scardino *et al.* Eur J Immunol. 31(11):3261-70 (2001). Scardino *et al.* J Immunol. 168(11):5900-6 (2002). Kawashima *et al.* Cancer Res. 59(2):431-5 (1999). Okugawa *et al.* Eur J Immunol. 30(11):3338-46 (2000).
11	*EpCAM*	RYQLDPKFI (SEQ ID NO: 292)	Spizzo *et al.* Gynecol. Oncol. 103(2):483-8 (2006). Tajima *et al.* Tissue Antigens. 64(6):650-9 (2004).
12	*CA125*	ILFTINFTI (SEQ ID NO: 293) VLFTINFTI (SEQ ID NO: 294) TLNFTITNL (SEQ ID NO: 295) VLQGLLKPL (SEQ ID NO: 296) VLQGLLRPV (SEQ ID NO: 297) RLDPKSPGV (SEQ ID NO: 298) QLYWELSKL (SEQ ID NO: 299) KLTRGIVEL (SEQ ID NO: 300) QLTNGITEL (SEQ ID NO: 301) QLTHNITEL (SEQ ID NO: 302) TLDRNSLYV (SEQ ID NO: 303)	Bast *et al.* Cancer 116(12):2850-2853 (2010).
13	*Folate receptor α*	FLLSLALML (SEQ ID NO: 304)	Bagnoli *et al.* Gynecol. Oncol. 88:S140-4 (2003).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		NLGPWIQQV (SEQ ID NO: 305)	Pampeno *et al.* (2016) High-ranking *In Silico* epitopes [determined by 3 algorithms: BISMAS, IEDB, RANKPEP] unpublished
14	*Sperm protein 17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Inernati *et al.* J. Immunother. 31(8):693-703 (2008).
15	*TADG-12*	YLPKSWTIQV (SEQ ID NO: 307) WIHEQMERDLKT (SEQ ID NO: 308)	Bellone *et al.* Cancer 115(4):800-11 (2009). Underwood *et al.* BBA Mol. Basis of Disease. 1502(3):337-350 (2000).
16	*MUC-16*	ILFTINFTI (SEQ ID NO: 293) VLFTINFTI (SEQ ID NO: 294) TLNFTITNL (SEQ ID NO: 295) VLQGLLKPL (SEQ ID NO: 296) VLQGLLRPV (SEQ ID NO: 297) RLDPKSPGV (SEQ ID NO: 298) QLYWELSKL (SEQ ID NO: 299) KLTRGIVEL (SEQ ID NO: 300) QLTNGITEL (SEQ ID NO: 301) QLTHNITEL (SEQ ID NO: 302) TLDRNSLYV (SEQ ID NO: 303)	Chekmasova *et al.* Clin. Cancer Res. 16(14):3594-606 (2010).
17	*L1CAM*	LLANAYIYV (SEQ ID NO: 309) YLLCKAFGA (SEQ ID NO: 310) KLSPYVHYT (SEQ ID NO: 311)	Hong *et al.* J. Immunother. 37(2):93-104 (2014). Pampeno *et al.* (2016) High-ranking *In Silico* epitopes [determined by 3 algorithms: BISMAS, IEDB, RANKPEP] unpublished
18	*Mannan-MUC-1*	PDTRPAPGSTAPPAHGV TSA (SEQ ID NO: 312) STAPPVHNV (SEQ ID NO: 313)	Loveland *et al.* Clin. Cancer Res. 12(3 Pt 1):869-77 (2006). Godelaine *et al.* Cancer Immunol Immunother. 56(6):753-9 (2007).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LLLLTVLTV (SEQ ID NO: 314) PGSTAPPAHGVT (SEQ ID NO: 315)	Ma *et al.* Int J Cancer. 129(10):2427-34 (2011). Wen *et al.* Cancer Sci. 102(8):1455-61 (2011). Jerome *et al.* J Immunol. 151(3):1654-62 (1993). Brossart *et al.* Blood. 93(12):4309-17 (1999). Hiltbold *et al.* Cancer Res. 58(22):5066-70 (1998).
19	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
20	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
21	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(19 Pt 1): 6047-57 (2004).
22	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAA EVPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQ L (SEQ ID NO: 260) CLSRRPWKRSWSAGSCP GMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
23	*MAGE-A4*	EVDPASNTY (SEQ ID NO: 325) GVYDGREHTV (SEQ ID NO: 326) NYKRCFPVI (SEQ ID NO: 327) SESLKMIF (SEQ ID NO: 328)	Kobayashi *et al.* Tissue Antigens. 62(5):426-32 (2003). Duffour *et al.* Eur J Immunol. 29(10):3329-37 (1999). Miyahara *et al.* Clin Cancer Res. 11(15):5581-9 (2005). Ottaviani *et al.* Cancer Immunol Immunother. 55(7):867-72 (2006) Zhang *et al.* Tissue Antigens. 60(5):365-71 (2002).
24	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).
25	*SSX-4*	INKTSGPKRGKHAWTHRLRE (SEQ ID NO: 329) YFSKKEWEKMKSSEKIVYVY (SEQ ID NO: 330) MKLNYEVMTKLGFKVTLPPF (SEQ ID NO: 331) KHAWTHRLRERKQLVVYEEI (SEQ ID NO: 332) LGFKVTLPPFMRSKRAADFH (SEQ ID NO: 333) KSSEKIVYVYMKLNYEVMTK (SEQ ID NO: 334) KHAWTHRLRERKQLVVYEEI (SEQ ID NO: 332)	Ayyoub *et al.* Clin Immunol. 114(1):70-8 (2005). Valmori *et al.* Clin Cancer Res. 12(2):398-404 (2006).
26	*TAG-1*	SLGWLFLLL (SEQ ID NO: 335) LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
27	*TAG-2*	LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).

Table 4. Breast cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*ENAH (hMena)*	TMNGSKSPV (SEQ ID NO: 337)	Di Modugno *et al.* Int. J. Cancer. 109(6):909-18 (2004).
2	*mammaglobin-A*	PLLENVISK (SEQ ID NO: 338)	Jaramillo *et al.* Int. J. Cancer. 102(5):499-506 (2002).
3	*NY-BR-1*	SLSKILDTV (SEQ ID NO: 339)	Wang *et al.* Cancer Res. 66(13):6826-33 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
4	*EpCAM*	RYQLDPKFI (SEQ ID NO: 292)	Gastl *et al.* Lancet 356(9246):1981-2 (2000). Tajima, 2004
5	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRL T (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
6	*BAGE-1*	AARAVFLAL (SEQ ID NO: 340)	Boel *et al.* Immunity. 2(2):167-75 (1995).
7	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
8	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
9	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
10	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCPGMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
11	*MAGE-A1*	EADPTGHSY (SEQ ID NO: 341) KVLEYVIKV (SEQ ID NO: 342) SLFRAVITK (SEQ ID NO: 343) EVYDGREHSA (SEQ ID NO: 344) RVRFFFPSL (SEQ ID NO: 345) EADPTGHSY (SEQ ID NO: 341) REPVTKAEML (SEQ ID NO: 346) KEADPTGHSY (SEQ ID NO: 347)	Traversari *et al.* J Exp Med. 176(5):1453-7 (1992). Ottaviani *et al.* Cancer Immunol Immunother. 54(12):1214-20 (2005). Pascolo *et al.* Cancer Res. 61(10):4072-7 (2001). Chaux *et al.* J Immunol. 163(5):2928-36 (1999). Luiten *et al.* Tissue Anitgens. 55(2):49-52 (2000). Luiten *et al.* Tissue Antigens. 56(1):77-81 (2000). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Stroobant *et al.* Eur J Immunol. 42(6):1417-28 (2012).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		DPARYEFLW (SEQ ID NO: 348) ITKKVADLVGF (SEQ ID NO: 349) SAFPTTINF (SEQ ID NO: 350) SAYGEPRKL (SEQ ID NO: 351) RVRFFFPSL (SEQ ID NO: 345) TSCILESLFRAVITK (SEQ ID NO: 352) PRALAETSYVKVLEY (SEQ ID NO: 353) FLLLKYRAREPVTKAE (SEQ ID NO: 354) EYVIKVSARVRF (SEQ ID NO: 355)	Corbière *et al.* Tissue Antigens. 63(5):453-7 (2004). Goodyear *et al.* Cancer Immunol Immunother. 60(12):1751-61 (2011). van der Bruggen *et al.* Eur J Immunol. 24(9):2134-40 (1994). Wang *et al.* Cancer Immunol Immunother. 56(6):807-18 (2007). Chaux *et al.* J Exp Med. 189(5):767-78 (1999). Chaux *et al.* Eur J Immunol. 31(6): 1910-6 (2001).
12	*MAGE-A2*	YLQLVFGIEV (SEQ ID NO: 356) EYLQLVFGI (SEQ ID NO: 357) REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358) LLKYRAREPVTKAE (SEQ ID NO: 359)	Kawashima *et al.* Hum Immunol. 59(1):1-14 (1998). Tahara *et al.* Clin Cancer Res. 5(8):2236-41 (1999). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Chaux *et al.* J Exp Med. 89(5):767-78 (1999).
13	*mucink*	PDTRPAPGSTAPPAHGVT SA (SEQ ID NO: 312)	Jerome *et al.* J Immunol. 151(3):1654-62 (1993).
14	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).
15	*SSX-2*	KASEKIFYV (SEQ ID NO: 360) EKIQKAFDDIAKYFSK (SEQ ID NO: 361) FGRLQGISPKI (SEQ ID NO: 362) WEKMKASEKIFYVYMKR K (SEQ ID NO: 363) KIFYVYMKRKYEAMT (SEQ ID NO: 364)	Ayyoub *et al.* J Immunol. 168(4):1717-22 (2002). Ayyoub *et al.* J Immunol. 172(11):7206-11 (2004). Neumann *et al.* Cancer Immunol Immunother. 60(9):1333-46 (2011). Ayyoub *et al.* Clin Immunol. 114(1):70-8 (2005). Neumann *et al.* Int J Cancer. 112(4):661-8 (2004).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		KIFYVYMKRKYEAM (SEQ ID NO: 365)	Ayyoub *et al.* J Clin Invest. 113(8):1225-33 (2004).
16	*TAG-1*	SLGWLFLLL (SEQ ID NO: 335) LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
17	*TAG-2*	LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
18	*TRAG-3*	CEFHACWPAFTVLGE (SEQ ID NO: 366)	Janjic *et al.* J Immunol. 177(4):2717-27 (2006).
19	*Her2/Neu*	HLYQGCQVV (SEQ ID NO: 284) YLVPQQGFFC (SEQ ID NO: 285) PLQPEQLQV (SEQ ID NO: 286) TLEEITGYL (SEQ ID NO: 287) ALIHHNTHL (SEQ ID NO: 288) PLTSIISAV (SEQ ID NO: 289) VLRENTSPK (SEQ ID NO: 290) TYLPTNASL (SEQ ID NO: 291)	Nakatsuka *et al.* Mod. Pathol. 19(6):804-814 (2006). Pils *et al.* Br. J. Cancer 96(3):485-91 (2007). Scardino *et al.* Eur J Immunol. 31(11):3261-70 (2001). Scardino *et al.* J Immunol. 168(11):5900-6 (2002). Kawashima *et al.* Cancer Res. 59(2):431-5 (1999). Okugawa *et al.* Eur J Immunol. 30(11):3338-46 (2000).
20	*c-myc*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
21	*cyclin B1*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
22	*MUC1*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
23	*p53*	VVPCEPPEV (SEQ ID NO: 283)	Hung *et al.* Immunol. Rev. 222:43-69 (2008). http://cancerimmunity.org/peptide/mutations/
24	*p62*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
25	*Survivin*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)

Table 5. Testicular cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*CD45*	KFLDALISL (SEQ ID NO: 367)	Tomita *et al.* Cancer Sci. 102(4):697-705 (2011).
2	*DKK1*	ALGGHPLLGV (SEQ ID NO: 368)	Qian *et al.* Blood. (5):1587-94 (2007).
3	*PRAME*	VLDGLDVLL (SEQ ID NO: 222), SLYSFPEPEA (SEQ ID NO: 223), ALYVDSLFFL (SEQ ID NO: 224), SLLQHLIGL (SEQ ID NO: 225), LYVDSLFFL (SEQ ID NO: 226)	Kessler *et al.* J Exp Med. 193(1):73-88 (2001). Ikeda *et al.* Immunity 6(2):199-208 (1997).
4	*RU2AS*	LPRWPPPQL (SEQ ID NO: 369)	Van Den Eynde *et al.* J. Exp. Med. 190(12):1793-800 (1999).
5	*Telomerase*	ILAKFLHWL (SEQ ID NO: 370); RLVDDFLLV (SEQ ID NO: 371); RPGLLGASVLGLDDI (SEQ ID NO: 372); and LTDLQPYMRQFVAHL (SEQ ID NO: 373)	Vonderheide *et al.* Immunity 10(6):673-9 (1999). Miney *et al.* Proc. Natl. Acad. Sci. U.S.A. 97(9):4796-801 (2000). Schroers *et al.* Cancer Res. 62(9):2600-5 (2002). Schroers *et al.* Clin. Cancer Res. 9(13):4743-55 (2003).

Table 6. Pancreatic cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*ENAH (hMena)*	TMNGSKSPV (SEQ ID NO: 337)	Di Modugno *et al.* Int. J. Cancer. 109(6):909-18 (2004).
2	*PBF*	CTACRWKKACQR (SEQ ID NO: 221)	Tsukahara *et al.* Cancer Res. 64(15):5442-8 (2004).
3	*K-ras*	VVVGAVGVG (SEQ ID NO: 374)	Gjertsen *et al.* Int. J. Cancer. 72(5):784-90 (1997).
4	*Mesothelin*	SLLFLLFSL (SEQ ID NO: 232)	Le *et al.* Clin. Cancer Res. 18(3):858-68 (2012).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		VLPLTVAEV (SEQ ID NO: 233) ALQGGGPPY (SEQ ID NO: 234) LYPKARLAF (SEQ ID NO: 235) AFLPWHRLF (SEQ ID NO: 236)	Hassan *et al.* Appl. Immunohistochem. Mol. Morphol. 13(3):243-7 (2005). Thomas et al J Exp Med. 2004 Aug 2; 200(3): 297–306.
5	*mucink*	PDTRPAPGSTAPPAHGVTSA (SEQ ID NO: 312)	Jerome *et al.* J Immunol. 151(3):1654-62 (1993).

Table 7. Liver cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*G250 / MN / CAIX*	HLSTAFARV (SEQ ID NO: 375); KIFGSLAFL (SEQ ID NO: 376); IISAVVGIL (SEQ ID NO: 377); ALCRWGLLL (SEQ ID NO: 378); ILHNGAYSL (SEQ ID NO: 379); RLLQETELV (SEQ ID NO: 380); VVKGVVFGI (SEQ ID NO: 381); and YMIMVKCWMI (SEQ ID NO: 382)	Vissers *et al.* Cancer Res. 59(21):5554-9 (1999). Fisk *et al.* J Exp Med. 181(6):2109-17 (1995). Brossart *et al.* Cancer Res. 58(4):732-6 (1998). Kawashima *et al.* Hum Immunol. 59(1):1-14 (1998). Rongcun *et al.* J Immunol. 163(2):1037-44 (1999).
2	*Hepsin*	SLLSGDWVL (SEQ ID NO: 383); GLQLGVQAV (SEQ ID NO: 384); and PLTEYIQPV (SEQ ID NO: 385)	Guo *et al.* Scand J Immunol. 78(3):248-57 (2013).
3	*Intestinal carboxyl esterase*	SPRWWPTCL (SEQ ID NO: 386)	Ronsin *et al.* J Immunol. 163(1):483-90 (1999).
4	*alpha-foetoprotein*	GVALQTMKQ (SEQ ID NO: 387); FMNKFIYEI (SEQ ID NO: 388); and QLAVSVILRV (SEQ ID NO: 389)	Butterfield *et al.* Cancer Res. 59(13):3134-42 (1999). Pichard *et al.* J Immunother. 31(3):246-53 (2008) Alisa *et al.* Clin. Cancer Res. 11(18):6686-94 (2005).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
5	*M-CSF*	LPAVVGLSPGEQEY (SEQ ID NO: 390)	Probst-Kepper *et al.* J Exp Med. 193(10):1189-98 (2001).
6	*PBF*	CTACRWKKACQR (SEQ ID NO: 221)	Tsukahara *et al.* Cancer Res. 64(15):5442-8 (2004).
7	*PSMA*	NYARTEDFF (SEQ ID NO: 391)	Horiguchi *et al.* Clin Cancer Res. 8(12):3885-92 (2002).
8	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LLEFYLAMPFATPMEAELAR RSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRLTA ADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAEVP R (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRLT (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRLTA ADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAELAR RSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
9	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCPGMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
10	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
11	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
12	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
13	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).
14	*c-myc*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
15	*cyclin B1*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
16	*p53*	VVPCEPPEV (SEQ ID NO: 283)	Hung *et al.* Immunol. Rev. 222:43-69 (2008). http://cancerimmunity.org/peptide/mutations/
17	*p62*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
18	*Survivin*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)

Table 8. Colorectal cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*ENAH (hMena)*	TMNGSKSPV (SEQ ID NO: 337)	Di Modugno *et al.* Int. J Cancer. 109(6):909-18 (2004).
2	*Intestinal carboxyl esterase*	SPRWWPTCL (SEQ ID NO: 386)	Ronsin *et al.* J Immunol. 163(1):483-90 (1999).
3	*CASP-5*	FLIIWQNTM (SEQ ID NO: 392)	Schwitalle *et al.* Cancer Immun. 4: 14 (2004).
4	*COA-1*	TLYQDDTLTLQAAG (SEQ ID NO: 393)	Maccalli *et al.* Cancer Res. 63(20):6735-43 (2003).
5	*OGT*	SLYKFSPFPL (SEQ ID NO: 394)	Ripberger. J Clin Immunol. 23(5):415-23 (2003).
6	*OS-9*	KELEGILLL (SEQ ID NO: 395)	Vigneron *et al.* Cancer Immun. 2: 9 (2002).
7	*TGF-betaRII*	RLSSCVPVA (SEQ ID NO: 396)	Linnebacher *et al.* Int. J. Cancer. 93(1):6-11 (2001).
8	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAELAR RSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRLTA ADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAEVP R (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRLT (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRLTA ADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAELAR RSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
9	*CEA/PMEL or gp100*	TYYRPGVNLSLSC (SEQ ID NO: 265) EIIYPNASLLIQN (SEQ ID NO: 266) YACFVSNLATGRNNS (SEQ ID NO: 267) LWWVNNQSLPVSP (SEQ ID NO: 268) LWWVNNQSLPVSP (SEQ ID NO: 268) LWWVNNQSLPVSP (SEQ ID NO: 268) EIIYPNASLLIQN (SEQ ID NO: 266) NSIVKSITVSASG (SEQ ID NO: 269) KTWGQYWQV (SEQ ID NO: 270) AMLGTHTMEV (SEQ ID NO: 271) MLGTHTMEV (SEQ ID NO: 627) ITDQVPFSV (SEQ ID NO: 272) YLEPGPVTA (SEQ ID NO: 273) LLDGTATLRL (SEQ ID NO: 274) VLYRYGSFSV (SEQ ID NO: 275) SLADTNSLAV (SEQ ID NO: 276) RLMKQDFSV (SEQ ID NO: 277) RLPRIFCSC (SEQ ID NO: 278) LIYRRRLMK (SEQ ID NO: 279) ALLAVGATK (SEQ ID NO: 280) IALNFPGSQK (SEQ ID NO: 281)	Duffy, Clin. Chem. 47(4):624-30 (2001). Parkhurst *et al.* Mol. Ther. 19(3):620-6 (2011). Galanis *et al.* Cancer Res. 70(3):875-82 (2010). Bast *et al.* Am. J. Obstet. Gynecol. 149(5):553-9 (1984). Crosti *et al.* J Immunol. 176(8):5093-9 (2006). Kobayashi *et al.* Clin Cancer Res. 8(10):3219-25 (2002). Campi *et al.* Cancer Res. 63(23):8481-6 (2003). Bakker *et al.* Int J Cancer. 62(1):97-102 (1995). Tsai *et al.* J Immunol. 158(4):1796-802 (1997). Kawakami *et al.* J Immunol. 154(8):3961-8 (1995). Cox *et al.* Science. 264(5159):716-9 (1994). Kawakami *et al.* J Immunol. 154(8):3961-8 (1995). Kawakami *et al.* J Immunol. 161(12):6985-92 (1998). Skipper *et al.* J Immunol. 157(11):5027-33 (1996). Michaux *et al.* J Immunol. 192(4):1962-71 (2014).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		RSYVPLAHR (SEQ ID NO: 282)	
10	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
11	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
12	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
13	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCPGMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
14	*MAGE-A2*	YLQLVFGIEV (SEQ ID NO: 356) EYLQLVFGI (SEQ ID NO: 357) REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358)	Kawashima *et al.* Hum Immunol. 59(1):1-14 (1998). Tahara *et al.* Clin Cancer Res. 5(8):2236-41 (1999). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LLKYRAREPVTKAE (SEQ ID NO: 359)	Chaux *et al.* J Exp Med. 89(5):767-78 (1999).
15	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).
16	*TAG-1*	SLGWLFLLL (SEQ ID NO: 335) LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
17	*TAG-2*	LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
18	*c-myc*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
19	*cyclin B1*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
20	*MUC1*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
21	*p53*	VVPCEPPEV (SEQ ID NO: 283)	Hung *et al.* Immunol. Rev. 222:43-69 (2008). http://cancerimmunity.org/peptide/mutations/
22	*p62*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
23	*Survivin*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
24	*gp70*		Castle *et al.*, BMC Genomics 15:190 (2014)

Table 9. Thyroid cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*CALCA*	VLLQAGSLHA (SEQ ID NO: 397)	El Hage *et al.* Proc. Natl. Acad. Sci. U.S.A. 105(29):10119-24 (2008).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
2	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAELARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRLTAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRLT (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRLTAADHR (SEQ ID NO: 254)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LLEFYLAMPFATPMEAELARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
3	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
4	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
5	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
6	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCPGMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
7	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).

Table 10. Lung cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*CD274*	LLNAFTVTV (SEQ ID NO: 398)	Munir *et al.* Cancer Res. 73(6):1764-76 (2013).
2	*mdm-2*	VLFYLGQY (SEQ ID NO: 399)	Asai *et al.* Cancer Immun. 2: 3 (2002).
3	*alpha-actinin-4*	FIASNGVKLV (SEQ ID NO: 400)	Echchakir *et al.* Cancer Res. 61(10):4078-83 (2001).
4	*Elongation factor 2* **(squamous cell carcinoma**	ETVSEQSNV (SEQ ID NO: 401)	Hogan *et al.* Cancer Res. 58(22):5144-50 (1998).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
	of the lung)		
5	*ME1* **(non-small cell lung carcinoma)**	FLDEFMEGV (SEQ ID NO: 402)	Karanikas *et al.* Cancer Res. 61(9):3718-24 (2001).
6	*NFYC* **(squamous cell carcinoma of the lung)**	QQITKTEV (SEQ ID NO: 403)	Takenoyama *et al.* Int. J Cancer. 118(8):1992-7 (2006).
7	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAELAR RSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRLTA ADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAEVP R (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRLT (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRLTA ADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAELAR RSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
8	*GAGE-1,2,8*	YRPRPRRY (SEQ ID NO: 404)	Van den Eynde *et al.* J Exp Med. 182(3):689-98 (1995).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
9	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
10	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
11	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
12	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCPGMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
13	*MAGE-A2*	YLQLVFGIEV (SEQ ID NO: 356) EYLQLVFGI (SEQ ID NO: 357) REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358) LLKYRAREPVTKAE (SEQ ID NO: 359)	Kawashima *et al.* Hum Immunol. 59(1):1-14 (1998). Tahara *et al.* Clin Cancer Res. 5(8):2236-41 (1999). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Chaux *et al.* J Exp Med. 89(5):767-78 (1999).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
14	*MAGE-A6* (squamous cell lung carcinoma)	MVKISGGPR (SEQ ID NO: 529) EVDPIGHVY (SEQ ID NO: 530) REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358) ISGGPRISY (SEQ ID NO: 406) LLKYRAREPVTKAE (SEQ ID NO: 359)	Zorn *et al.* Eur J Immunol. 29(2):602-7 (1999). Benlalam *et al.* J Immunol. 171(11):6283-9 (2003). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Vantomme *et al.* Cancer Immun. 3:17 (2003). Chaux *et al.* J Exp Med. 189(5):767-78 (1999).
15	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).
16	*TAG-1*	SLGWLFLLL (SEQ ID NO: 335) LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
17	*TAG-2*	LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
18	*TRAG-3*	CEFHACWPAFTVLGE (SEQ ID NO: 366)	Janjic *et al.* J Immunol. 177(4):2717-27 (2006).
19	*XAGE-1b/GAGED2a* (non-small cell lung cancer)	RQKKIRIQL (SEQ ID NO: 407) HLGSRQKKIRIQLRSQ (SEQ ID NO: 408) CATWKVICKSCISQTPG (SEQ ID NO: 409)	Ohue *et al.* Int J Cancer. 131(5):E649-58 (2012). Shimono *et al.* Int J Oncol. 30(4):835-40 (2007).
20	*c-myc*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
21	*cyclin B1*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
22	*Her2/Neu*	HLYQGCQVV (SEQ ID NO: 284) YLVPQQGFFC (SEQ ID NO: 285) PLQPEQLQV (SEQ ID NO: 286) TLEEITGYL (SEQ ID NO: 287)	Nakatsuka *et al.* Mod. Pathol. 19(6):804-814 (2006). Pils *et al.* Br. J. Cancer 96(3):485-91 (2007). Scardino *et al.* Eur J Immunol. 31(11):3261-70 (2001). Scardino *et al.* J Immunol. 168(11):5900-6 (2002).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		ALIHHNTHL (SEQ ID NO: 288) PLTSIISAV (SEQ ID NO: 289) VLRENTSPK (SEQ ID NO: 290) TYLPTNASL (SEQ ID NO: 291)	Kawashima *et al.* Cancer Res. 59(2):431-5 (1999). Okugawa *et al.* Eur J Immunol. 30(11):3338-46 (2000).
23	*MUC1*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
24	*p53*	VVPCEPPEV (SEQ ID NO: 283)	Hung *et al.* Immunol. Rev. 222:43-69 (2008). http://cancerimmunity.org/peptide/mutations/
25	*p62*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)
26	*Survivin*		Reuschenbach *et al.* Cancer Immunol. Immunother. 58:1535-1544 (2009)

Table 11. Prostate cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*DKK1*	ALGGHPLLGV (SEQ ID NO: 368)	Qian *et al.* Blood. 110(5):1587-94 (2007).
2	*ENAH (hMena)*	TMNGSKSPV (SEQ ID NO: 337)	Di Modugno *et al.* Int. J. Cancer. 109(6):909-18 (2004).
3	*Kallikrein 4*	FLGYLILGV (SEQ ID NO: 410); SVSESDTIRSISIAS (SEQ ID NO: 199); LLANGRMPTVLQCVN (SEQ ID NO: 209); and RMPTVLQCVNVSVVS (SEQ ID NO: 220)	Wilkinson *et al.* Cancer Immunol Immunother. 61(2):169-79 (2012). Hural *et al.* J. Immunol. 169(1):557-65 (2002).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
4	*PSMA*	NYARTEDFF (SEQ ID NO: 391)	Horiguchi *et al.* Clin Cancer Res. 8(12):3885-92 (2002).
5	*STEAP1*	MIAVFLPIV (SEQ ID NO: 411) and HQQYFYKIPILVINK (SEQ ID NO: 412)	Rodeberg *et al.* Clin. Cancer Res. 11(12):4545-52 (2005). Kobayashi *et al.* Cancer Res. 67(11):5498-504 (2007).
6	*PAP*	FLFLLFFWL (SEQ ID NO: 413); TLMSAMTNL (SEQ ID NO: 414); and ALDVYNGLL (SEQ ID NO: 415)	Olson *et al.* Cancer Immunol Immunother. 59(6):943-53 (2010).
7	*PSA* **(prostate carcinoma)**	FLTPKKLQCV (SEQ ID NO: 416) and VISNDVCAQV (SEQ ID NO: 417)	Correale *et al.* J Natl. Cancer Inst. 89(4):293-300 (1997).
8	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAELARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRLTAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRLT (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRLTAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAELARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
			Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
9	*BAGE-1* (non-small cell lung carcinoma)	AARAVFLAL (SEQ ID NO: 340)	Boel *et al.* Immunity. 2(2):167-75 (1995).
10	*GAGE-1,2,8* (non-small cell lunch carcinoma)	YRPRPRRY (SEQ ID NO: 404)	Van den Eynde *et al.* J Exp Med. 182(3):689-98 (1995).
11	*GAGE-3,4,5,6,7* (lung squamous cell carcinoma and lung adenocarcinoma)	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).
12	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
13	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
14	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
15	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCPGMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
			Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
16	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).

Table 12. Kidney cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*FGF5*	NTYASPRFK (SEQ ID NO: 419)	Hanada *et al.* Nature. 427(6971):252-6 (2004).
2	*Hepsin*	SLLSGDWVL (SEQ ID NO: 383); GLQLGVQAV (SEQ ID NO: 384); and PLTEYIQPV (SEQ ID NO: 385)	Guo *et al.* Scand J Immunol. 78(3):248-57 (2013).
3	*Intestinal carboxyl esterase*	SPRWWPTCL (SEQ ID NO: 386)	Ronsin *et al.* J Immunol. 163(1):483-90 (1999).
4	*M-CSF*	LPAVVGLSPGEQEY (SEQ ID NO: 390)	Probst-Kepper *et al.* J Exp Med. 193(10):1189-98 (2001).
5	*RU2AS*	LPRWPPPQL (SEQ ID NO: 369)	Van Den Eynde *et al.* J. Exp. Med. 190(12):1793-800 (1999).
6	*hsp70-2* **(renal cell carcinoma)**	SLFEGIDIYT (SEQ ID NO: 420)	Gaudin *et al.* J. Immunol. 162(3):1730-8 (1999).
7	*Mannan-MUC-1* (renal cell carcinoma)	PDTRPAPGSTAPPAHGVTSA (SEQ ID NO: 312) STAPPVHNV (SEQ ID NO: 313) LLLLTVLTV (SEQ ID NO: 314) PGSTAPPAHGVT (SEQ ID NO: 315)	Loveland *et al.* Clin. Cancer Res. 12(3 Pt 1):869-77 (2006). Loveland *et al.* Clin. Cancer Res. 12(3 Pt 1):869-77 (2006). Godelaine *et al.* Cancer Immunol Immunother. 56(6):753-9 (2007). Ma *et al.* Int J Cancer. 129(10):2427-34 (2011).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
			Wen *et al.* Cancer Sci. 102(8):1455-61 (2011). Jerome *et al.* J Immunol. 151(3):1654-62 (1993). Brossart *et al.* Blood. 93(12):4309-17 (1999). Hiltbold *et al.* Cancer Res. 58(22):5066-70 (1998).
8	*MAGE-A9* (renal cell carcinoma)	ALSVMGVYV (SEQ ID NO: 421)	Oehlrich *et al.* Int J Cancer. 117(2):256-64 (2005).

Table 13. Melanoma

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*Hepsin*	SLLSGDWVL (SEQ ID NO: 383); GLQLGVQA (SEQ ID NO: 422); and PLTEYIQPV (SEQ ID NO: 385)	Guo *et al.* Scand J Immunol. 78(3):248-57 (2013).
2	*ARTC1*	YSVYFNLPADTIYTN (SEQ ID NO: 423)	Wang et al J Immunol. 174(5):2661-70 (2005).
3	*B-RAF*	EDLTVKIGDFGLATEKSR WSGSHQFEQLS (SEQ ID NO: 424)	Sharkey *et al.* Cancer Res. 64(5):1595-9 (2004).
4	*beta-catenin*	SYLDSGIHF (SEQ ID NO: 425)	Robbins *et al.* J. Exp. Med. 183(3):1185-92 (1996).
5	*Cdc27*	FSWAMDLDPKGA (SEQ ID NO: 426)	Wang *et al.* Science. 284(5418):1351-4 (1999).
6	*CDK4*	ACDPHSGHFV (SEQ ID NO: 427)	Wölfel *et al.* Science. 269(5228):1281-4 (1995).
7	*CDK12*	CILGKLFTK (SEQ ID NO: 428)	Robbins *et al.* Nat Med. 19(6):747-52. (2013).
8	*CDKN2A*	AVCPWTWLR (SEQ ID NO: 429)	Huang *et al.* J Immunol. 172(10):6057-64 (2004).
9	***CLPP***	ILDKVLVHL (SEQ ID NO: 430)	Corbière *et al.* Cancer Res. 71(4):1253-62 (2011).
10	***CSNK1A1***	GLFGDIYLA (SEQ ID NO: 431)	Robbins *et al.* Nat Med. 19(6):747-52 (2013).
11	*FN1*	MIFEKHGFRRTTPP (SEQ ID NO: 432)	Wang *et al.* J Exp Med. 195(11):1397-406 (2003).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
12	*GAS7*	SLADEAEVYL (SEQ ID NO: 433)	Robbins, *et al.* Nat Med. 19(6):747-52 (2013).
13	*GPNMB*	TLDWLLQTPK (SEQ ID NO: 434)	Lennerz *et al.* Proc. Natl. Acad. Sci. U.S.A. 102(44):16013-8 (2005).
14	*HAUS3*	ILNAMIAKI (SEQ ID NO: 435)	Robbins *et al.* Nat Med. 19(6):747-52 (2013).
15	*LDLR-fucosyltransferase*	WRRAPAPGA (SEQ ID NO: 436) and PVTWRRAPA (SEQ ID NO: 437)	Wang *et al.* J Exp Med. 189(10):1659-68 (1999).
16	*MART2*	FLEGNEVGKTY (SEQ ID NO: 438)	Kawakami *et al.* J Immunol. 166(4):2871-7 (2001).
17	*MATN*	KTLTSVFQK (SEQ ID NO: 439)	Robbins *et al.* Nat Med. 19(6):747-52 (2013).
18	*MUM-1*	EEKLIVVLF (SEQ ID NO: 440)	Coulie *et al.* Proc. Natl. Acad. Sci. U.S.A. 92(17):7976-80 (1995).
19	*MUM-2*	SELFRSGLDSY (SEQ ID NO: 441) and FRSGLDSYV (SEQ ID NO: 442)	Chiari *et al.* Cancer Res. 59(22):5785-92 (1999).
20	*MUM-3*	EAFIQPITR (SEQ ID NO: 443)	Baurain *et al.* J. Immunol. 164(11):6057-66 (2000).
21	*neo-PAP*	RVIKNSIRLTL (SEQ ID NO: 444)	Topalian *et al.* Cancer Res. 62(19):5505-9 (2002).
22	*Myosin class I*	KINKNPKYK (SEQ ID NO: 445)	Zorn, *et al.* Eur. J. Immunol. 29(2):592-601 (1999).
23	*PPP1R3B*	YTDFHCQYV (SEQ ID NO: 446)	Robbins *et al.* Nat Med. 19(6):747-52 (2013). Lu *et al.* J Immunol. 190(12):6034-42 (2013).
24	*PRDX5*	LLLDDLLVSI (SEQ ID NO: 447)	Sensi *et al.* Cancer Res. 65(2):632-40 (2005).
25	*PTPRK*	PYYFAAELPPRNLPEP (SEQ ID NO: 448)	Novellino *et al.* J. Immunol. 170(12):6363-70 (2003).
26	*N-ras*	ILDTAGREEY (SEQ ID NO: 449)	Linard *et al.* J. Immunol. 168(9):4802-8 (2002).
27	*RBAF600*	RPHVPESAF (SEQ ID NO: 450)	Lennerz *et al.* Proc. Natl. Acad. Sci. U.S.A. 102(44):16013-8 (2005).
28	*SIRT2*	KIFSEVTLK (SEQ ID NO: 451)	Lennerz *et al.* Proc. Natl. Acad. Sci. U.S.A. 102(44):16013-8 (2005).
29	*SNRPD1*	SHETVIIEL (SEQ ID NO: 452)	Lennerz *et al.* Proc. Natl. Acad. Sci. U.S.A. 102(44):16013-8 (2005).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
30	*Triosephosphate isomerase*	GELIGILNAAKVPAD (SEQ ID NO: 453)	Pieper *et al.* J Exp Med. 189(5):757-66 (1999).
31	*OA1*	LYSACFWWL (SEQ ID NO: 454)	Touloukian *et al.* J. Immunol. 170(3):1579-85 (2003).
32	*RAB38 / NY-MEL-1*	VLHWDPETV (SEQ ID NO: 455)	Walton *et al.* J Immunol. 177(11):8212-8 (2006).
33	*TRP-1 / gp75*	MSLQRQFLR (SEQ ID NO: 456); ISPNSVFSQWRVVCDSLEDY (SEQ ID NO: 457); SLPYWNFATG (SEQ ID NO: 458); and SQWRVVCDSLEDYDT (SEQ ID NO: 459)	Touloukian *et al.* Cancer Res. 62(18):5144-7 (2002). Robbins *et al.* J. Immunol. (10):6036-47 (2002). Osen *et al.* PLoS One. 5(11):e14137 (2010).
34	*TRP-2*	SVYDFFVWL (SEQ ID NO: 460); TLDSQVMSL (SEQ ID NO: 461); LLGPGRPYR (SEQ ID NO: 462); ANDPIFVVL (SEQ ID NO: 463); QCTEVRADTRPWSGP (SEQ ID NO: 464); and ALPYWNFATG (SEQ ID NO: 465)	Parkhurst *et al.* Cancer Res. 58(21):4895-901 (1998). Noppen *et al.* Int. J. Cancer. 87(2):241-6 (2000). Wang *et al.* J. Exp. Med. 1184(6):2207-16 (1996). Wang *et al.* J. Immunol. 160(2):890-7 (1998). Castelli *et al.* J. Immunol. 162(3):1739-48 (1999). Paschen *et al.* Clin. Cancer Res. (14):5241-7 (2005). Robbins *et al.* J. Immunol. 169(10):6036-47 (2002).
35	*tyrosinase*	KCDICTDEY (SEQ ID NO: 466); SSDYVIPIGTY (SEQ ID NO: 467); MLLAVLYCL (SEQ ID NO: 468); CLLWSFQTSA (SEQ ID NO: 469); YMDGTMSQV (SEQ ID NO: 470); AFLPWHRLF (SEQ ID NO: 236); IYMDGTADFSF (SEQ ID NO: 471);	Kittlesen *et al.* J. Immunol. 160(5):2099-106 (1998). Kawakami *et al.* J. Immunol. (12):6985-92 (1998). Wölfel *et al.* Eur. J. Immunol. 24(3):759-64 (1994). Riley *et al.* J. Immunother. 24(3):212-20 (2001). Skipper *et al.* J. Exp. Med. 183(2):527-34 (1996). Kang *et al.* J. Immunol. 155(3):1343-8 (1995). Dalet *et al.* Proc. Natl. Acad. Sci. U.S.A. 108(29):E323-31 (2011)

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		QCSGNFMGF (SEQ ID NO: 472); TPRLPSSADVEF (SEQ ID NO: 473); LPSSADVEF (SEQ ID NO: 474); LHHAFVDSIF (SEQ ID NO: 475); SEIWRDIDF (SEQ ID NO: 476); QNILLSNAPLGPQFP (SEQ ID NO: 477); SYLQDSDPDSFQD (SEQ ID NO: 478); and FLLHHAFVDSIFEQWLQR HRP (SEQ ID NO: 479)	Lennerz *et al.* Proc. Natl. Acad. Sci. U.S.A. 102(44):16013-8 (2005). Benlalam *et al.* J. Immunol. 171(11):6283-9 (2003). Morel *et al.* Int. J. Cancer. 83(6):755-9 (1999). Brichard *et al.* Eur. J. Immunol. 26(1):224-30 (1996). Topalian *et al.* J. Exp. Med. (5):1965-71 (1996). Kobayashi *et al.* Cancer Res. 58(2):296-301 (1998).
36	***Melan-A/MART-1***	YTTAEEAAGIGILTVILGV LLLIGCWYCRR (SEQ ID NO: 480)	Meng *et al.* J. Immunother. 23:525-534 (2011)
37	*gp100 / Pmel17*	ALNFPGSQK (SEQ ID NO: 481) ALNFPGSQK (SEQ ID NO: 481) VYFFLPDHL (SEQ ID NO: 482) RTKQLYPEW (SEQ ID NO: 483) HTMEVTVYHR (SEQ ID NO: 484) SSPGCQPPA (SEQ ID NO: 485) VPLDCVLYRY (SEQ ID NO: 486) LPHSSSHWL (SEQ ID NO: 487) SNDGPTLI (SEQ ID NO: 488) GRAMLGTHTMEVTVY (SEQ ID NO: 489) WNRQLYPEWTEAQRLD (SEQ ID NO: 490) TTEWVETTARELPIPEPE (SEQ ID NO: 491)	El Hage *et al.* Proc. Natl. Acad. Sci. U.S.A. 105(29):10119-24 (2008). Kawashima *et al.* Hum Immunol. 59(1):1-14 (1998). Robbins *et al.* J Immunol. 159(1):303-8 (1997). Sensi *et al.* Tissue Antigens. 59(4):273-9 (2002). Lennerz *et al.* Proc Natl Acad Sci U S A. 102(44):16013-8 (2005). Benlalam *et al.* J Immunol. 171(11):6283-9 (2003). Vigneron *et al.* Tissue Antigens. 65(2):156-62 (2005). Castelli *et al.* J Immunol. 162(3):1739-48 (1999). Touloukian *et al.* J Immunol. 164(7):3535-42 (2000). Parkhurst *et al.* J Immunother. 27(2):79-91 (2004). Lapointe *et al.* J Immunol. 167(8):4758-64 (2001). Kobayashi *et al.* Cancer Res. 61(12):4773-8 (2001).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		TGRAMLGTHTMEVTVY H (SEQ ID NO: 492) GRAMLGTHTMEVTVY (SEQ ID NO: 489)	
38	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRL T (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
39	*BAGE-1*	AARAVFLAL (SEQ ID NO: 340)	Boel *et al.* Immunity. 2(2):167-75 (1995).
40	*GAGE-1,2,8*	YRPRPRRY (SEQ ID NO: 404)	Van den Eynde *et al.* J Exp Med. 182(3):689-98 (1995).
41	*GAGE-3,4,5,6,7* (cutaneous melanoma)	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).
42	*GnTVf*	VLPDVFIRCV (SEQ ID NO: 493)	Guilloux *et al.* J Exp Med. 183(3):1173-83 (1996).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		VLPDVFIRC (SEQ ID NO: 628)	
43	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
44	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
45	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
46	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCP GMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
47	*LY6K*	RYCNLEGPPI (SEQ ID NO: 494) KWTEPYCVIAAVKIFPRF FMVAKQ (SEQ ID NO: 495) KCCKIRYCNLEGPPINSSV F (SEQ ID NO: 496)	Suda *et al.* Cancer Sci. 98(11):1803-8 (2007). Tomita *et al.* Oncoimmunology. 3:e28100 (2014).
48	*MAGE-A1*	EADPTGHSY (SEQ ID NO: 341)	Traversari *et al.* J Exp Med. 176(5):1453-7 (1992).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		KVLEYVIKV (SEQ ID NO: 342) SLFRAVITK (SEQ ID NO: 343) EVYDGREHSA (SEQ ID NO: 344) RVRFFFPSL (SEQ ID NO: 345) EADPTGHSY (SEQ ID NO: 341) REPVTKAEML (SEQ ID NO: 346) KEADPTGHSY (SEQ ID NO: 347) DPARYEFLW (SEQ ID NO: 348) ITKKVADLVGF (SEQ ID NO: 349) SAFPTTINF (SEQ ID NO: 350) SAYGEPRKL (SEQ ID NO: 351) RVRFFFPSL (SEQ ID NO: 345) TSCILESLFRAVITK (SEQ ID NO: 352) PRALAETSYVKVLEY (SEQ ID NO: 353) FLLLKYRAREPVTKAE (SEQ ID NO: 354) EYVIKVSARVRF (SEQ ID NO: 355)	Ottaviani *et al.* Cancer Immunol Immunother. 54(12):1214-20 (2005). Pascolo *et al.* Cancer Res. 61(10):4072-7 (2001). Chaux *et al.* J Immunol. 163(5):2928-36 (1999). Luiten *et al.* Tissue Antigens. 55(2):149-52 (2000). Luiten *et al.* Tissue Antigens. 56(1):77-81 (2000). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Stroobant *et al.* Eur J Immunol. 42(6):1417-28 (2012). Corbière *et al.* Tissue Antigens. 63(5):453-7 (2004). Goodyear *et al.* Cancer Immunol Immunother. 60(12):1751-61 (2011). van der Bruggen *et al.* Eur J Immunol. 24(9):2134-40 (1994). Wang *et al.* Cancer Immunol Immunother. 56(6):807-18 (2007). Chaux *et al.* J Exp Med. 189(5):767-78 (1999). Chaux *et al.* Eur J Immunol. 31(6):1910-6 (2001).
49	*MAGE-A6*	MVKISGGPR (SEQ ID NO: 529) EVDPIGHVY (SEQ ID NO: 530) REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358) ISGGPRISY (SEQ ID NO: 406)	Zorn *et al.* Eur J Immunol. 29(2):602-7 (1999). Benlalam *et al.* J Immunol. 171(11):6283-9 (2003). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Vantomme *et al.* Cancer Immun. 3:17 (2003).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LLKYRAREPVTKAE (SEQ ID NO: 359)	Chaux *et al.* J Exp Med. 189(5):767-78 (1999).
50	*MAGE-A10*	GLYDGMEHL (SEQ ID NO: 497) DPARYEFLW (SEQ ID NO: 348)	Huang *et al.* J Immunol. 162(11):6849-54 (1999). Chaux *et al.* J Immunol. 163(5):2928-36 (1999).
51	*MAGE-A12*	FLWGPRALV (SEQ ID NO: 498) VRIGHLYIL (SEQ ID NO: 499) EGDCAPEEK (SEQ ID NO: 358) REPFTKAEMLGSVIR (SEQ ID NO: 500) AELVHFLLLKYRAR (SEQ ID NO: 501)	van der Bruggen *et al.* Eur J Immunol. 24(12):3038-43 (1994). Heidecker *et al.* J Immunol. 164(11):6041-5 (2000). Panelli *et al.* J Immunol. 164(8):4382-92 (2000). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Wang *et al.* Cancer Immunol Immunother. 56(6):807-18 (2007). Chaux *et al.* J Exp Med. 189(5):767-78 (1999).
52	*MAGE-C2*	LLFGLALIEV (SEQ ID NO: 502) ALKDVEERV (SEQ ID NO: 405) SESIKKKVL (SEQ ID NO: 503) ASSTLYLVF (SEQ ID NO: 504) SSTLYLVFSPSSFST (SEQ ID NO: 505)	Ma *et al.* Int J Cancer. 109(5):698-702 (2004). Godelaine *et al.* Cancer Immunol Immunother. 56(6):753-9 (2007). Ma *et al.* Int J Cancer. 129(10):2427-34 (2011). Wen *et al.* Cancer Sci. 102(8):1455-61 (2011).
53	*NA88-A*	QGQHFLQKV (SEQ ID NO: 506)	Moreau-Aubry *et al.* J Exp Med. 191(9):1617-24 (2000).
54	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).
55	*SSX-2*	KASEKIFYV (SEQ ID NO: 360) EKIQKAFDDIAKYFSK (SEQ ID NO: 361) FGRLQGISPKI (SEQ ID NO: 362) WEKMKASEKIFYVYMKRK (SEQ ID NO: 363) KIFYVYMKRKYEAMT (SEQ ID NO: 364)	Ayyoub *et al.* J Immunol. 168(4):1717-22 (2002). Ayyoub *et al.* J Immunol. 172(11):7206-11 (2004). Neumann *et al.* Cancer Immunol Immunother. 60(9):1333-46 (2011). Ayyoub *et al.* Clin Immunol. 114(1):70-8 (2005). Neumann *et al.* Int J Cancer. 112(4):661-8 (2004).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		KIFYVYMKRKYEAM (SEQ ID NO: 365)	Ayyoub *et al.* J Clin Invest. 113(8):1225-33 (2004).
56	*SSX-4*	INKTSGPKRGKHAWTHR LRE (SEQ ID NO: 329) YFSKKEWEKMKSSEKIV YVY (SEQ ID NO: 330) MKLNYEVMTKLGFKVTL PPF (SEQ ID NO: 331) KHAWTHRLRERKQLVV YEEI (SEQ ID NO: 332) LGFKVTLPPFMRSKRAA DFH (SEQ ID NO: 333) KSSEKIVYVYMKLNYEV MTK (SEQ ID NO: 334) KHAWTHRLRERKQLVV YEEI (SEQ ID NO: 332)	Ayyoub *et al.* J Immunol. 174(8):5092-9 (2005). Valmori *et al.* Clin Cancer Res. 12(2):398-404 (2006).
57	*TRAG-3*	CEFHACWPAFTVLGE (SEQ ID NO: 366)	Janjic *et al.* J Immunol. 177(4):2717-27 (2006).
58	*TRP2-INT2g*	EVISCKLIKR (SEQ ID NO: 507)	Lupetti *et al.* J Exp Med. 188(6):1005-16 (1998).
59	*pgk*		Morgan *et al.*, J. Immunol. 171:3287-3295 (2003)

Table 14. Squamous cell carcinoma

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*CASP-8*	FPSDSWCYF (SEQ ID NO: 508)	Mandruzzato *et al.* J. Exp. Med. 186(5):785-93 (1997).
2	*p53*	VVPCEPPEV (SEQ ID NO: 283)	Ito *et al.* Int. J. Cancer. 120(12):2618-24 (2007).
3	*SAGE*	LYATVIHDI (SEQ ID NO: 509)	Miyahara *et al.* Clin Cancer Res. 11(15):5581-9 (2005).

Table 15. Chronic myeloid leukemia

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*BCR-ABL*	SSKALQRPV (SEQ ID NO: 510); GFKQSSKAL (SEQ ID NO: 511); ATGFKQSSKALQRPVAS (SEQ ID NO: 512); and ATGFKQSSKALQRPVAS (SEQ ID NO: 512)	Yotnda *et al.* J. Clin. Invest. 101(10):2290-6 (1998). Bosch *et al.* Blood. 88(9):3522-7 (1996). Makita *et al.* Leukemia. 16(12):2400-7 (2002).
2	*dek-can*	TMKQICKKEIRRLHQY (SEQ ID NO: 513)	Makita *et al.* Leukemia. 16(12):2400-7 (2002).
3	*EFTUD2*	KILDAVVAQK (SEQ ID NO: 514)	Lennerz *et al.* Proc. Natl. Acad. Sci. U.S.A. 102(44):16013-8 (2005).
4	*GAGE-3,4,5,6,7*	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).

Table 16. Acute lymphoblastic leukemia

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*ETV6-AML1*	RIAECILGM (SEQ ID NO: 515) and IGRIAECILGMNPSR (SEQ ID NO: 516)	Yotnda *et al.* J. Clin. Invest. (2):455-62 (1998). Yun *et al.* Tissue Antigens. 54(2):153-61 (1999).
2	*GAGE-3,4,5,6,7*	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).

Table 17. Acute myelogenous leukemia

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*FLT3-ITD*	YVDFREYEYY (SEQ ID NO: 517)	Graf *et al.* Blood. 109(7):2985-8 (2007).
2	*Cyclin-A1*	FLDRFLSCM and (SEQ ID NO: 518) SLIAAAAFCLA (SEQ ID NO: 519)	Ochsenreither *et al.* Blood. 119(23):5492-501 (2012).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
3	*GAGE-3,4,5,6,7*	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).

Table 18. Chronic lymphocytic leukemia

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*FNDC3B*	VVMSWAPPV (SEQ ID NO: 520)	Rajasagi *et al.* Blood. 124(3):453-62 (2014).
2	*GAGE-3,4,5,6,7*	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).

Table 19. Promyelocytic leukemia

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*pml-RARalpha*	NSNHVASGAGEAAIETQS SSSEEIV (SEQ ID NO: 521)	Gambacorti-Passerini *et al.* Blood. 81(5):1369-75 (1993).
2	*GAGE-3,4,5,6,7*	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).

Table 20. Multiple myeloma

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*MAGE-C1*	ILFGISLREV (SEQ ID NO: 522) KVVEFLAML (SEQ ID NO: 523) SSALLSIFQSSPE (SEQ ID NO: 524) SFSYTLLSL (SEQ ID NO: 525) VSSFFSYTL (SEQ ID NO: 526)	Anderson *et al.* Cancer Immunol Immunother. 60(7):985-97 (2011). Nuber *et al.* Proc Natl Acad Sci U S A. 107(34):15187-92 (2010).
2	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255)	Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRL T (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
3	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCP GMPHL (SEQ ID NO: 323)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
4	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
5	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
6	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
7	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).

Table 21. B-cell lymphoma

No.	Tumor-associated antigen	Reported immunogenic epitopes	Source
1	*D393-CD20*	KPLFRRMSSLELVIA (SEQ ID NO: 528)	Vauchy *et al.* Int J Cancer. 137(1):116-26 (2015).

Table 22. Bladder carcinoma

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*BAGE-1*	AARAVFLAL (SEQ ID NO: 340)	Boel *et al.* Immunity. 2(2):167-75 (1995).
2	*GAGE-1,2,8*	YRPRPRRY (SEQ ID NO: 404)	Van den Eynde *et al.* J Exp Med. 182(3):689-98 (1995).
3	*GAGE-3,4,5,6,7*	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).
4	*MAGE-A4* (transitional cell carcinoma of urinary bladder)	EVDPASNTY (SEQ ID NO: 325) GVYDGREHTV (SEQ ID NO: 326) NYKRCFPVI (SEQ ID NO: 327) SESLKMIF (SEQ ID NO: 328)	Kobayashi *et al.* Tissue Antigens. 62(5):426-32 (2003). Duffour *et al.* Eur J Immunol. 29(10):3329-37 (1999). Miyahara *et al.* Clin Cancer Res. 11(15):5581-9 (2005). Ottaviani *et al.* Cancer Immunol Immunother. 55(7):867-72 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
			Zhang *et al.* Tissue Antigens. 60(5):365-71 (2002).
5	*MAGE-A6*	MVKISGGPR (SEQ ID NO: 529) EVDPIGHVY (SEQ ID NO: 530) REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358) ISGGPRISY (SEQ ID NO: 406) LLKYRAREPVTKAE (SEQ ID NO: 359)	Zorn *et al.* Eur J Immunol. 29(2):602-7 (1999). Benlalam *et al.* J Immunol. 171(11):6283-9 (2003). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Vantomme *et al.* Cancer Immun. 3:17 (2003). Chaux *et al.* J Exp Med. 189(5):767-78 (1999).
6	*SAGE*	LYATVIHDI (SEQ ID NO: 509)	Miyahara *et al.* Clin Cancer Res. 11(15):5581-9 (2005).
7	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRL T (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262)	Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	
8	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCP GMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
9	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
10	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
11	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
12	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).

Table 23. Head and neck cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources

1	*BAGE-1* (head and neck squamous cell carcinoma)	AARAVFLAL (SEQ ID NO: 340)	Boel *et al.* Immunity. 2(2):167-75 (1995).
2	*GAGE-1,2,8*	YRPRPRRY (SEQ ID NO: 404)	Van den Eynde *et al.* J Exp Med. 182(3):689-98 (1995).
3	*GAGE-3,4,5,6,7*	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).
4	*LY6K*	RYCNLEGPPI (SEQ ID NO: 494) KWTEPYCVIAAVKIFPRF FMVAKQ (SEQ ID NO: 495) KCCKIRYCNLEGPPINSSV F (SEQ ID NO: 496)	Suda *et al.* Cancer Sci. 98(11):1803-8 (2007). Tomita *et al.* Oncoimmunology. 3:e28100 (2014).
5	*MAGE-A3* (head and neck squamous cell carcinoma)	EVDPIGHLY (SEQ ID NO: 532) FLWGPRALV (SEQ ID NO: 498) KVAELVHFL (SEQ ID NO: 533) TFPDLESEF (SEQ ID NO: 534) VAELVHFLL (SEQ ID NO: 535) MEVDPIGHLY (SEQ ID NO: 536) EVDPIGHLY (SEQ ID NO: 532) REPVTKAEML (SEQ ID NO: 346) AELVHFLLL (SEQ ID NO: 537) MEVDPIGHLY (SEQ ID NO: 536) WQYFFPVIF (SEQ ID NO: 538) EGDCAPEEK (SEQ ID NO: 358) KKLLTQHFVQENYLEY (SEQ ID NO: 539) RKVAELVHFLLLKYR (SEQ ID NO: 540) KKLLTQHFVQENYLEY (SEQ ID NO: 539)	Gaugler *et al.* J Exp Med. 179(3):921-30 (1994). van der Bruggen *et al.* Eur J Immunol. 24(12):3038-43 (1994). Kawashima *et al.* Hum Immunol. 59(1):1-14 (1998). Oiso *et al.* Int J Cancer. 81(3):387-94 (1999). Miyagawa *et al.* Oncology. 70(1):54-62 (2006). Bilsborough *et al.* Tissue Antigens. 60(1):16-24 (2002). Schultz *et al.* Tissue Antigens. 57(2):103-9 (2001). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Schultz *et al.* J Exp Med. 195(4):391-9 (2002). Herman *et al.* Immunogenetics. 43(6):377-83 (1996). Russo *et al.* Proc Natl Acad Sci U S A. 97(5):2185-90 (2000). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Schultz *et al.* Cancer Res. 60(22):6272-5 (2000). Cesson *et al.* Cancer Immunol Immunother. 60(1):23-35 (2011). Schultz *et al.* J Immunol. 172(2):1304-10 (2004).

		ACYEFLWGPRALVETS (SEQ ID NO: 541) RKVAELVHFLLLKYR (SEQ ID NO: 540) VIFSKASSSLQL (SEQ ID NO: 542) VFGIELMEVDPIGHL (SEQ ID NO: 543) GDNQIMPKAGLLIIV (SEQ ID NO: 544) TSYVKVLHHMVKISG (SEQ ID NO: 545) RKVAELVHFLLLKYRA (SEQ ID NO: 546) FLLLKYRAREPVTKAE (SEQ ID NO: 354)	Zhang *et al.* J Immunol. 171(1):219-25 (2003). Cesson *et al.* Cancer Immunol Immunother. 60(1):23-35 (2010). Kobayashi *et al.* Cancer Res. 61(12):4773-8 (2001). Cesson *et al.* Cancer Immunol Immunother. 60(1):23-35 (2011). Consogno *et al.* Blood. 101(3):1038-44 (2003). Manici *et al.* J Exp Med. 189(5):871-6 (1999). Chaux *et al.* J Exp Med. 189(5):767-78 (1999).
6	*MAGE-A6*	MVKISGGPR (SEQ ID NO: 529) EVDPIGHVY (SEQ ID NO: 530) REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358) ISGGPRISY (SEQ ID NO: 406) LLKYRAREPVTKAE (SEQ ID NO: 359)	Zorn *et al.* Eur J Immunol. 29(2):602-7 (1999). Benlalam *et al.* J Immunol. 171(11):6283-9 (2003). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Vantomme *et al.* Cancer Immun. 3:17 (2003). Chaux *et al.* J Exp Med. 189(5):767-78 (1999).
7	*SAGE*	LYATVIHDI (SEQ ID NO: 509)	Miyahara *et al.* Clin Cancer Res. 11(15):5581-9 (2005).

Table 24. Esophageal cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*GAGE-3,4,5,6,7* (Esophageal squamous cell carcinoma and esophageal adenocarcinoma)	YYWPRPRRY (SEQ ID NO: 418)	De Backer *et al.* Cancer Res. 59(13):3157-65 (1999).
2	*MAGE-A2*	YLQLVFGIEV (SEQ ID NO: 356) EYLQLVFGI (SEQ ID NO: 357)	Kawashima *et al.* Hum Immunol. 59(1):1-14 (1998). Tahara *et al.* Clin Cancer Res. 5(8):2236-41 (1999).

		REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358) LLKYRAREPVTKAE (SEQ ID NO: 359)	Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Chaux *et al.* J Exp Med. 189(5):767-78 (1999).
3	*MAGE-A6*	MVKISGGPR (SEQ ID NO: 529) EVDPIGHVY (SEQ ID NO: 530) REPVTKAEML (SEQ ID NO: 346) EGDCAPEEK (SEQ ID NO: 358) ISGGPRISY (SEQ ID NO: 406) LLKYRAREPVTKAE (SEQ ID NO: 359)	Zorn *et al.* Eur J Immunol. 29(2):602-7 (1999). Benlalam *et al.* J Immunol. 171(11):6283-9 (2003). Tanzarella *et al.* Cancer Res. 59(11):2668-74 (1999). Breckpot *et al.* J Immunol. 172(4):2232-7 (2004). Vantomme *et al.* Cancer Immun. 3:17 (2003). Chaux *et al.* J Exp Med. 189(5):767-78 (1999).
4	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002).

		MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRL T (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263)	Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).

		AGATGGRGPRGAGA (SEQ ID NO: 264)	
5	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCP GMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
6	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
7	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
8	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
9	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).

Table 25. Brain cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*TAG-1*	SLGWLFLLL (SEQ ID NO: 335) LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).

2	*TAG-2*	LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).

Table 26. Pharynx cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*TAG-1*	SLGWLFLLL (SEQ ID NO: 335) LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
2	*TAG-2*	LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).

Table 27. Tumors of the tongue

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*TAG-1*	SLGWLFLLL (SEQ ID NO: 335) LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).
2	*TAG-2*	LSRLSNRLL (SEQ ID NO: 336)	Adair *et al.* J Immunother. 31(1):7-17 (2008).

Table 28. Synovial cell sarcoma

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAEVPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		CLSRRPWKRSWSAGSCP GMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
2	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246) KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009). Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRL T (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
3	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
4	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
5	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	
6	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).

Table 29. Neuroblastoma

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237) LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCP GMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
2	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239))	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		SLLMWITQC (SEQ ID NO: 237)	Valmori *et al.* Cancer Res. 60(16):4499-506 (2000).
		MLMAQEALAFL (SEQ ID NO: 240)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999).
		YLAMPFATPME (SEQ ID NO: 241)	Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013).
		ASGPGGGAPR (SEQ ID NO: 242)	Wang *et al.* J Immunol. 161(7):3598-606 (1998).
		LAAQERRVPR (SEQ ID NO: 243)	Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008).
		TVSGNILTIR (SEQ ID NO: 244)	Ebert *et al.* Cancer Res. 69(3):1046-54 (2009).
		APRGPHGGAASGL (SEQ ID NO: 245)	Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013).
		MPFATPMEAEL (SEQ ID NO: 246)	Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009).
		KEFTVSGNILTI (SEQ ID NO: 247)	Jäger *et al.* Cancer Immun. 2:12 (2002).
		MPFATPMEA (SEQ ID NO: 248)	Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001).
		FATPMEAEL (SEQ ID NO: 249)	Mandic *et al.* J Immunol. 174(3):1751-9 (2005).
		FATPMEAELAR (SEQ ID NO: 250)	Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004).
		LAMPFATPM (SEQ ID NO: 238)	Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010).
		ARGPESRLL (SEQ ID NO: 239)	Slager *et al.* J Immunol. 172(8):5095-102 (2004).
		SLLMWITQCFLPVF (SEQ ID NO: 251)	Mizote *et al.* Vaccine. 28(32):5338-46 (2010).
		LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252)	Jager *et al.* J Exp Med. 191(4):625-30 (2000).
		EFYLAMPFATPM (SEQ ID NO: 253)	Zarour *et al.* Cancer Res. 60(17):4946-52 (2000).
		PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254)	Zeng *et al.* J Immunol. 165(2):1153-9 (2000).
		RLLEFYLAMPFA (SEQ ID NO: 255)	Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009).
		QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256)	Zarour *et al.* Cancer Res. 62(1):213-8 (2002).
			Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRLT (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRLTAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAELARRSLAQ (SEQ ID NO: 252) KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	
3	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
4	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
5	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
6	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).

Table 30. Uterine cancer

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
1	*LAGE-1*	MLMAQEALAFL (SEQ ID NO: 240) SLLMWITQC (SEQ ID NO: 237)	Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Rimoldi *et al.* J Immunol. 165(12):7253-61 (2000).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		LAAQERRVPR (SEQ ID NO: 243) ELVRRILSR (SEQ ID NO: 321) APRGVRMAV (SEQ ID NO: 322) SLLMWITQCFLPVF (SEQ ID NO: 251) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) CLSRRPWKRSWSAGSCP GMPHL (SEQ ID NO: 323) ILSRDAAPLPRPG (SEQ ID NO: 324) AGATGGRGPRGAGA (SEQ ID NO: 264)	Wang *et al.* J Immunol. 161(7):3598-606 (1998). Sun *et al.* Cancer Immunol Immunother. 55(6):644-52 (2006). Slager *et al.* Cancer Gene Ther. 11(3):227-36 (2004). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Slager *et al.* J Immunol. 170(3):1490-7 (2003). Wang *et al.* Immunity. 20(1):107-18 (2004). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).
2	*NY-ESO-1*	HLA-A2-restricted peptide p157–165 (SLLMWITQC (SEQ ID NO: 237)), HLA-Cw3-restricted p92–100 (LAMPFATPM (SEQ ID NO: 238)) and HLA-Cw6-restricted p80–88 (ARGPESRLL (SEQ ID NO: 239)) SLLMWITQC (SEQ ID NO: 237) MLMAQEALAFL (SEQ ID NO: 240) YLAMPFATPME (SEQ ID NO: 241) ASGPGGGAPR (SEQ ID NO: 242) LAAQERRVPR (SEQ ID NO: 243) TVSGNILTIR (SEQ ID NO: 244) APRGPHGGAASGL (SEQ ID NO: 245) MPFATPMEAEL (SEQ ID NO: 246)	Jager *et al.* Proc. Natl. Acad. Scie. U.S.A. 103(39):14453-8 (2006). Gnjatic *et al.* PNAS September 26, 2000 vol. 97 no. 20 p. 10919 Jager *et al.* J Exp Med. 187(2):265-70 (1998). Chen *et al.* J Immunol. 165(2):948-55 (2000). Valmori *et al.* Cancer Res. 60(16):4499-506 (2000). Aarnoudse *et al.* Int J Cancer. 82(3):442-8 (1999). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Wang *et al.* J Immunol. 161(7):3598-606 (1998). Matsuzaki *et al.* Cancer Immunol Immunother. 57(8)1185-95 (2008). Ebert *et al.* Cancer Res. 69(3):1046-54 (2009). Eikawa *et al.* Int J Cancer. 132(2):345-54 (2013). Knights *et al.* Cancer Immunol Immunother. 58(3):325-38 (2009).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		KEFTVSGNILTI (SEQ ID NO: 247) MPFATPMEA (SEQ ID NO: 248) FATPMEAEL (SEQ ID NO: 249) FATPMEAELAR (SEQ ID NO: 250) LAMPFATPM (SEQ ID NO: 238) ARGPESRLL (SEQ ID NO: 239) SLLMWITQCFLPVF (SEQ ID NO: 251) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252) EFYLAMPFATPM (SEQ ID NO: 253) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) RLLEFYLAMPFA (SEQ ID NO: 255) QGAMLAAQERRVPRAAE VPR (SEQ ID NO: 256) PFATPMEAELARR (SEQ ID NO: 257) PGVLLKEFTVSGNILTIRL T (SEQ ID NO: 258) VLLKEFTVSG (SEQ ID NO: 259) AADHRQLQLSISSCLQQL (SEQ ID NO: 260) LKEFTVSGNILTIRL (SEQ ID NO: 261) PGVLLKEFTVSGNILTIRL TAADHR (SEQ ID NO: 254) LLEFYLAMPFATPMEAEL ARRSLAQ (SEQ ID NO: 252)	Jäger *et al.* Cancer Immun. 2:12 (2002). Zeng *et al.* Proc Natl Acad Sci U S A. 98(7):3964-9 (2001). Mandic *et al.* J Immunol. 174(3):1751-9 (2005). Chen *et al.* Proc Natl Acad Sci U S A. 101(25):9363-8 (2004). Ayyoub *et al.* Clin Cancer Res. 16(18):4607-15 (2010). Slager *et al.* J Immunol. 172(8):5095-102 (2004). Mizote *et al.* Vaccine. 28(32):5338-46 (2010). Jager *et al.* J Exp Med. 191(4):625-30 (2000). Zarour *et al.* Cancer Res. 60(17):4946-52 (2000). Zeng *et al.* J Immunol. 165(2):1153-9 (2000). Bioley *et al.* Clin Cancer Res. 15(13):4467-74 (2009). Zarour *et al.* Cancer Res. 62(1):213-8 (2002). Hasegawa *et al.* Clin Cancer Res. 12(6):1921-7 (2006).

No.	Tumor-associated antigen	Reported immunogenic epitopes	Sources
		KEFTVSGNILT (SEQ ID NO: 262) LLEFYLAMPFATPM (SEQ ID NO: 263) AGATGGRGPRGAGA (SEQ ID NO: 264)	
3	*HERV-K-MEL*	MLAVISCAV (SEQ ID NO: 316)	Schiavetti *et al.* Cancer Res. 62(19):5510-6 (2002).
4	*KK-LC-1*	RQKRILVNL (SEQ ID NO: 317)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006).
5	*KM-HN-1*	NYNNFYRFL (SEQ ID NO: 318) EYSKECLKEF (SEQ ID NO: 319) EYLSLSDKI (SEQ ID NO: 320)	Fukuyama *et al.* Cancer Res. 66(9):4922-8 (2006). Monji *et al.* Clin Cancer Res. 10(18 Pt 1):6047-57 (2004).
6	*Sp17*	ILDSSEEDK (SEQ ID NO: 306)	Chiriva-Internati *et al.* Int J Cancer. 107(5):863-5 (2003).

Table 31. Examples of proteins encoded by Copenhagen Vaccinia genes deleted in CopMD5p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:219	C2L (26% 5')	AAA47999.1	MESVIFSINGEIIQVNKEIITASPYNF FKRIQDHHLKDEAIILNGINYHAFES LLDYIRWKKINITINNVEMILVAAIII DVPPVVDLCVKTMIHNINSTNCIRM FNFSKRYGIKKLYNASMSEIINNITA VTSDPEFGKLSKDELTTILSHENVN VNHEDVTAMILLKWIHKNPNDVDII NILHPKFMTNTMRNAISLLGLTISKS TKPVTRNGIKHNIVVIKNSDYISTIT HYSPRTEYWTIVGNTDRQFYNANV LHNCLYIIGGMINNRHVYSVSRVDL ETKKWKTVTNMSSLKSEVSTCVND GKLYVIGGLEFSISTGVAEYLKHGT SKWIRLPNLITPRYSGASVFVNDDI YVMGGVYTTYEKYVVLNDVECFT KNRWIKKSPMPRHHSIVYAVEYDG DIYVITGITHETRNYLYKYIVKEDK WIELYMYFNHVGKMFVCSCGDYIL IIADAKYEYYPKSNTWNLFDMSTR NIEYYDMFTKDETPKCNVTHKSLPS	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			FLSNCEKQFLQ	
SEQ ID NO:24	C1L	AAA48000.1	MVKNNKISNSCRMIMSTNPNNILM RHLKNLTDDEFKCIIHRSSDFLYLSD SDYTSITKETLVSEIVEEYPDDCNKI LAIIFLVLDKDIDVDIETKLKPKPAV RFAILDKMTEDIKLTDLVRHYFRYI EQDIPLGPLFKKIDSYRTRAINKYSK ELGLATEYFNKYGHLMFYTLPIPYN RFFCRNSIGFLAVLSPTIGHVKAFYK FIEYVSIDDRRKFKKELMSK	Inside Deletion
SEQ ID NO:25	N1L	AAA48001.1	MRTLLIRYILWRNDNDQTYYNDDF KKLMLLDELVDDGDVCTLIKNMR MTLSDGPLLDRLNQPVNNIEDAKR MIAISAKVARDIGERSEIRWEESFTI LFRMIETYFDDLMIDLYGEK	Inside Deletion
SEQ ID NO:26	N2L	AAA48002.1	MTSSAMDNNEPKVLEMVYDATILP EGSSMDPNIMDCINRHINMCIQRTY SSSIIAILNRFLTMNKDELNNTQCHII KEFMTYEQMAIDHYGEYVNAILYQ IRKRPNQHHTIDLFKKIKRTPYDTFK VDPVEFVKKVIGFVSILNKYKPVYS YVLYENVLYDEFKCFINYVETKYF	Inside Deletion
SEQ ID NO:27	M1L	AAA48003.1	MIFVIESKLLQIYRNRNRNINFYTTM DNIMSAEYYLSLYAKYNSKNLDVF RNMLQAIEPSGNNYHILHAYCGIKG LDERFVEELLHRGYSPNETDDDGN YPLHIASKINNNRIVAMLLTHGADP NACDKHNKTPLYYLSGTDDEVIERI NLLVQYGAKINNSVDEEGCGPLLA CTDPSERVFKKIMSIGFEARIVDKFG KNHIHRHLMSDNPKASTISWMMKL GISPSKPDHDGNTPLHIVCSKTVKN VDIIDLLLPSTDVNKQNKFGDSPLT LLIKTLSPAHLINKLLSTSNVITDQT VNICIFYDRDDVLEIINDKGKQYDS TDFKMAVEVGSIRCVKYLLDNDIIC EDAMYYAVLSEYETMVDYLLFNH FSVDSVVNGHTCMSECVRLNNPVI	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			LSKLMLHNPTSETMYLTMKAIEKD KLDKSIIIPFIAYFVLMHPDFCKNRR YFTSYKRFVTDYVHEGVSYEVFDD YF	
SEQ ID NO:28	M2L	AAA48004.1	MVYKLVLLFCIASLGYSVEYKNTIC PPRQDYRYWYFAAELTIGVNYDIN STIIGECHMSESYIDRNANIVLTGYG LEINMTIMDTDQRFVAAAEGVGKD NKLSVLLFTTQRLDKVHHNISVTIT CMEMNCGTTKYDSDLPESIHKSSSC DITINGSCVTCVNLETDPTKINPHYL HPKDKYLYHNSEYGMRGSYGVTFI DELNQCLLDIKELSYDICYRE	Inside Deletion
SEQ ID NO:29	HR/K1L	AAA48005.1	MDLSRINTWKSKQLKSFLSSKDTFK ADVHGHSALYYAIADNNVRLVCTL LNAGALKNLLENEFPLHQAATLED TKIVKILLFSGMDDSQFDDKGNTAL YYAVDSGNMQTVKLFVKKNWRL MFYGKTGWKTSFYHAVMLNDVSI VSYFLSEIPSTFDLAILLSCIHTTIKN GHVDMMILLLDYMTSTNTNNSLLF IPDIKLAIDNKDIEMLQALFKYDINI YSVNLENVLLDDAEITKMIIEKHVE YKSDSYTKDLDIVKNNKLDEIISKN KELRLMYVNCVKKN	Inside Deletion
SEQ ID NO:30	SPI-3/K2L	AAA48006.1	MIALLILSLTCSVSTYRLQGFTNAGI VAYKNIQDDNIVFSPFGYSFSMFMS LLPASGNTRIELLKTMDLRKRDLGP AFTELISGLAKLKTSKYTYTDLTYQ SFVDNTVCIKPLYYQQYHRFGLYR LNFRRDAVNKINSIVERRSGMSNVV DSNMLDNNTLWAIINTIYFKGTWQ YPFDITKTRNASFTNKYGTKTVPM MNVVTKLQGNTITIDDEEYDMVRL PYKDANISMYLAIGDNMTHFTDSIT AAKLDYWSFQLGNKVYNLKLPKFS IENKRDIKSIAEMMAPSMFNPDNAS FKHMTRDPLYIYKMFQNAKIDVDE QGTVAEASTIMVATARSSPEKLEFN TPFVFIIRHDITGFILFMGKVESP	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:31	K ORF A	AAA48007.1	MGHIITYCQVHTNISILIRKAHHIIFF VIDCDCISLQFSNYVHHGNRFRTVL ISKTSIACFSDIKRILPCTFKIYSINDC P	Inside Deletion
SEQ ID NO:32	K ORF B	AAA48008.1	MGTVFVPYLLVKLALRVLVISNGY CHVPLKYIVLMIAHRVLLSSILESTT LDIPDLRSTIELILLTASRLKFNLYRP NL	Inside Deletion
SEQ ID NO:33	K3L	AAA48009.1	MLAFCYSLPNAGDVIKGRVYEKDY ALYIYLFDYPHSEAILAESVKMHM DRYVEYRDKLVGKTVKVKVIRVD YTKGYIDVNYKRMCRHQ	Inside Deletion
SEQ ID NO:34	K4L	AAA48010.1	MNPDNTIAVITETIPIGMQFDKVYLS TFNMWREILSNTTKTLDISSFYWSL SDEVGTNFGTIILNEIVQLPKRGVRV RVAVNKSNKPLKDVERLQMAGVE VRYIDITNILGGVLHTKFWISDNTHI YLGSANMDWRSLTQVKELGIAIFN NRNLAADLTQIFEVYWYLGVNNLP YNWKNFYPSYYNTDHPLSINVSGV PHSVFIASAPQQLCTMERTNDLTAL LSCIRNASKFVYVSVMNFIPIIYSKA GKILFWPYIEDELRRSAIDRQVSVK LLISCWQRSSFIMRNFLRSIAMLKSK NIDIEVKLFIVPDADPPIPYSRVNHA KYMVTDKTAYIGTSNWTGNYFTDT CGASINITPDDGLGLRQQLEDIFMR DWNSKYSYELYDTSPTKRCKLLKN MKQCTNDIYCDEIQPEKEIPEYSLE	Inside Deletion
SEQ ID NO:35	K5L	AAA48011.1	MGATISILASYDNPNLFTAMILMSP LVNADAVSRLNLLAAKLMGTITPN APVGKLCPESVSRDMDKVYKYQY DPLINHEKIKAGFASQVLKATNKVR KIISKINTPRLSYSREQTMRLVMFQ VHIISCNMQIVIE	Inside Deletion
SEQ ID NO:36	K6L	AAA48012.1	MSANCMFNLDNDYIYWKPITYPKA LVFISHGAGKHSGRYDELAENISSL GILVFSHDHIGHGRSNGEKMMIDDF GTARGNY	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:37	K7R	AAA48013.1	MATKLDYEDAVFYFVDDDKICSRD SIIDLIDEYITWRNHVIVFNKDITSCG RLYKELMKFDDVAIRYYGIDKINEI VEAMSEGDHYINFTKVHDQESLFA TIGICAKITEHWGYKKISESRFQSLG NITDLMTDDNINILILFLEKKLN	Inside Deletion
SEQ ID NO:38	F1L	AAA48014.1	MLSMFMCNNIVDYVDDIDNGIVQD IEDEASNNVDHDYVYPLPENMVYR FDKSTNILDYLSTERDHVMMAVRY YMSKQRLDDLYRQLPTKTRSYIDII NIYCDKVSNDYNRDMNIMYDMAS TKSFTVYDINNEVNTILMDNKGLG VRLATISFITELGRRCMNPVKTIKM FTLLSHTICDDCFVDYITDISPPDNTI PNTSTREYLKLIGITAIMFATYKTLK YMIG	Inside Deletion
SEQ ID NO:39	DUT/F2L	AAA48015.1	MFNMNINSPVRFVKETNRAKSPTR QSPGAAGYDLYSAYDYTIPPGERQL IKTDISMSMPKICYGRIAPRSGLSLK GIDIGGGVIDEDYRGNIGVILINNGK CTFNVNTGDRIAQLIYQRIYYPELEE VQSLDSTNRGDQGFGSTGLR	Inside Deletion
SEQ ID NO:40	F3L (75% 3')	AAA48016.1	MPIFVNTVYCKNILALSMTKKFKTII DAIGGNIIVNSTILKKLSPYFRTHLR QKYTKNKDPVTRVCLDLDIHSLTSI VIYSYTGKVYIDSHNVVNLLRASIL TSVEFIIYTCINFILRDFRKEYCVECY MMGIEYGLSNLLCHTKNFIAKHFLE LEDDIIDNFDYLSMKLILESDELNVP DEDYVVDFVIKWYIKRRNKLGNLL LLIKNVIRSNYLSPRGINNVKWILDC TKIFHCDKQPRKSYKYPFIEYPMNM DQIIDIFHMCTSTHVGEVVYLIGGW MNNEIHNNAIAVNYISNNWIPIPPM NSPRLYATGIPANNKLYVVGGLPNP TSVERWFHGDAAWVNMPSLLKPR CNPAVASINNVIYVMGGHSETDTTT EYLLPNHDQWQFGPSTYYPHYKSC ALVFGRRLFLVGRNAEFYCESSNT WTLIDDPIYPRDNPELIIVDNKLLLI GGFYRGSYIDTIEVYNHHTYSWNI	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			WDGK	

Table 32. Examples of proteins encoded by Western Reserve Vaccinia genes equivalent to those deleted in CopMD5p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:41	VACWR026 (26% 5')	AAO89305.1	MESVIFSINGEIIQVNKEIITASPYNF FKRIQDHHLKDEAIILNGINYHAFES LLDYIRWKKINITINNVEMILVAAIII DVPPVVDLCVKTMIHNINSTNCIRM FNFSKRYGIKKLYNASMSEIINNITA VTSDPEFGKLSKDELTTILSHENVN VNHEDVTAMILLKWIHKNPNDVDII NILHPKFMTNTMRNAISLLGLTISKS TKPVTRNGIKHNIVVIKNSDYISTIT HYSPRTEYWTIVGNTDRQFYNANV LHNCLYIIGGMINNRHVYSVSRVDL ETKKWKTVTNMSSLKSEVSTCVND GKLYVIGGLEFSISTGVAEYLKHGT SKWIRLPNLITPRYSGASVFVNDDI YVMGGVYTTYEKYVVLNDVECFT KNRWIKKSPMPRHHSIVYAVEYDG DIYVITGITHETRNYLYKYIVKEDK WIELYMYFNHVGKMFVCSCGDYIL IIADAKYEYYPKSNTWNLFDMSTR NIEYYDMFTKDETPKCNVTHKSLPS FLSNCEKQFLQ	Inside Deletion
SEQ ID NO:42	VACWR027	AAO89306.1	MVKNNKIQKNKISNSCRMIMSTDP NNILMRHLKNLTDDEFKCIIHRSSD FLYLSDSDYTSITKETLVSEIVEEYP DDCNKILAIIFLVLDKDIDVDIKTKL KPKPAVRFAILDKMTEDIKLTDLVR HYFRYIEQDIPLGPLFKKIDSYRTRA INKYSKELGLATEYFNKYGHLMFY TLPIPYNRFFCRNSIGFLAVLSPTIGH VKAFYKFIEYVSIDDRRKFKKELMS K	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:43	VACWR028	AAO89307.1	MRTLLIRYILWRNDNDQTYYNDNF KKLMLLDELVDDGDVCTLIKNMR MTLSDGPLLDRLNQPVNNIEDAKR MIAISAKVARDIGERSEIRWEESFTI LFRMIETYFDDLMIDLYGEK	Inside Deletion
SEQ ID NO:44	VACWR029	AAO89308.1	MTSSAMDNNEPKVLEMVYDATILP EGSSMDPNIMDCINRHINMCIQRTY SSSIIAILDRFLMMNKDELNNTQCHI IKEFMTYEQMAIDHYGGYVNAILY QIRKRPNQHHTIDLFKRIKRTRYDT FKVDPVEFVKKVIGFVSILNKYKPV YSYVLYENVLYDEFKCFINYVETK YF	Inside Deletion
SEQ ID NO:45	VACWR030	AAO89309.1	MIFVIESKLLQIYRNRNRNINFYTTM DNIMSAEYYLSLYAKYNSKNLDVF RNMLQAIEPSGNNYHILHAYCGIKG LDERFVEELLHRGYSPNETDDDGN YPLHIASKINNNRIVAMLLTHGADP NACDKHNKTPLYYLSGTDDEVIERI NLLVQYGAKINNSVDEEGCGPLLA CTDPSERVFKKIMSIGFEARIVDKFG KNHIHRHLMSDNPKASTISWMMKL GISPSKPDHDGNTPLHIVCSKTVKN VDIIDLLLPSTDVNKQNKFGDSPLT LLIKTLSPAHLINKLLSTSNVITDQT VNICIFYDRDDVLEIINDKGKQYDS TDFKMAVEVGSIRCVKYLLDNDIIC EDAMYYAVLSEYETMVDYLLFNH FSVDFVVNGHTCMSECVRLNNPVI LSKLMLHNPTSETMYLTMKAIEKD RLDKSIIIPFIAYFVLMHPDFCKNRR YFTSYKRFVTDYVHEGVSYEVFDD YF	Inside Deletion
SEQ ID NO:46	VACWR031	AAO89310.1	MVYKLVLLFCIASLGYSVEYKNTIC PPRQDYRYWYFAAELTIGVNYDIN STIIGECHMSESYIDRNANIVLTGYG LEINMTIMDTDQRFVAAAEGVGKD NKLSVLLFTTQRLDKVHHNISVTIT CMEMNCGTTKYDSDLPESIHKSSSC DITINGSCVTCVNLETDPTKINPHYL	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			HPKDKYLYHNSEYSMRGSYGVTFI DELNQCLLDIKELSYDICYRE	
SEQ ID NO:47	VACWR032	AAO89311.1	MDLSRINTWKSKQLKSFLSSKDAF KADVHGHSALYYAIADNNVRLVCT LLNAGALKNLLENEFPLHQAATLE DTKIVKILLFSGLDDSQFDDKGNTA LYYAVDSGNMQTVKLFVKKNWRL MFYGKTGWKTSFYHAVMLNDVSI VSYFLSEIPSTFDLAILLSCIHITIKNG HVDMMILLLDYMTSTNTNNSLLFIP DIKLAIDNKDIEMLQALFKYDINIYS ANLENVLLDDAEIAKMIIEKHVEYK SDSYTKDLDIVKNNKLDEIISKNKE LRLMYVNCVKKN	Inside Deletion
SEQ ID NO:48	SPI-3	AAO89312.1	MIALLILSLTCSVSTYRLQGFTNAGI VAYKNIQDDNIVFSPFGYSFSMFMS LLPASGNTRIELLKTMDLRKRDLGP AFTELISGLAKLKTSKYTYTDLTYQ SFVDNTVCIKPSYYQQYHRFGLYRL NFRRDAVNKINSIVERRSGMSNVV DSNMLDNNTLWAIINTIYFKGIWQY PFDITKTRNASFTNKYGTKTVPMM NVVTKLQGNTITIDDEEYDMVRLP YKDANISMYLAIGDNMTHFTDSITA AKLDYWSFQLGNKVYNLKLPKFSI ENKRDIKSIAEMMAPSMFNPDNASF KHMTRDPLYIYKMFQNAKIDVDEQ GTVAEASTIMVATARSSPEKLEFNT PFVFIIRHDITGFILFMGKVESP	Inside Deletion
SEQ ID NO:49	VACWR034	AAO89313.1	MLAFCYSLPNAGDVIKGRVYEKDY ALYIYLFDYPHFEAILAESVKMHM DRYVEYRDKLVGKTVKVKVIRVD YTKGYIDVNYKRMCRHQ	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:50	VACWR035	AAO89314.1	MNPDNTIAVITETIPIGMQFDKVYLS TFNMWREILSNTTKTLDISSFYWSL SDEVGTNFGTIILNKIVQLPKRGVR VRVAVNKSNKPLKDVERLQMAGV EVRYIDITNILGGVLHTKFWISDNT HIYLGSANMDWRSLTQVKELGIAIF NNRNLAADLTQIFEVYWYLGVNNL PYNWKNFYPSYYNTDHPLSINVSG VPHSVFIASAPQQLCTMERTNDLTA LLSCIRNASKFVYVSVMNFIPIIYSK AGNILFWPYIEDELRRAAIDRQVSV KLLISCWQRSSFIMRNFLRSIAMLKS KNINIEVKLFIVPDADPPIPYSRVNH AKYMVTDKTAYIGTSNWTGNYFT DTCGASINITPDDGLGLRQQLEDIF MRDWNSKYSYELYDTSPTKRCRLL KNMKQCTNDIYCDEIQPEKEIPEYS LE	Inside Deletion
SEQ ID NO:51	VACWR036	AAO89315.1	MQHANCNREIKIYEGAKHHLHKET DEVKKSVMKEIETWIFNRVK	Outside Deletion
SEQ ID NO:52	VACWR037	AAO89316.1	MTLVQHVVTIKSTYWVIPWELASY DNPNLFTAMILMSPLVNADAVSKL NLLAAKLMGTITLNAPVGKLCPES VSRDMDKVYKYQYDPLINHEKIKA GFASQVLKATNKVRKIISKINTPRLS YSREQTIRLAMF	Inside Deletion
SEQ ID NO:53	VACWR038	AAO89317.1	MSANCMFNLDNDYIYWKPITYPKA LVFISHGAGKHSGRYDELAENISSL GILVFSHDHIGHGRSNGEKMMIDDF GTARGNY	Inside Deletion
SEQ ID NO:54	VACWR039	AAO89318.1	MATKLDYEDAVFYFVDDDKICSRD SIIDLIDEYITWRNHVIVFNKDITSCG RLYKELMKFDDVAIRYYGIDKINEI VEAMSEGDHYINFTKVHDQESLFA TIGICAKITEHWGYKKISESRFQSLG NITDLMTDDNINILILFLEKKLN	Inside Deletion
SEQ ID NO:55	VACWR040	AAO89319.1	MLSMFMCNNIVDYVDDIDNGIVQD IEDEASNNVDHDYVYPLPENMVYR FDKSTNILDYLSTERDHVMMAVRY YMSKQRLDDLYRQLPTKTRSYIDII NIYCDKVSNDYNRDMNIMYDMAS	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			TKSFTVYDINNEVNTILMDNKGLG VRLATISFITELGRRCMNPVETIKMF TLLSHTICDDYFVDYITDISPPDNTIP NTSTREYLKLIGITAIMFATYKTLK YMIG	
SEQ ID NO:56	DUT	AAO89320.1	MFNMNINSPVRFVKETNRAKSPTR QSPYAAGYDLYSAYDYTIPPGERQL IKTDISMSMPKFCYGRIAPRSGLSLK GIDIGGGVIDEDYRGNIGVILINNGK CTFNVNTGDRIAQLIYQRIYYPELEE VQSLDSTNRGDQGFGSTGLR	Inside Deletion
SEQ ID NO:57	VACWR042 (75% 3')	AAO89321.1	MPIFVNTVYCKNILALSMTKKFKTII DAIGGNIIVNSTILKKLSPYFRTHLR QKYTKNKDPVTWVCLDLDIHSLTSI VIYSYTGKVYIDSHNVVNLLRASIL TSVEFIIYTCINFILRDFRKEYCVECY MMGIEYGLSNLLCHTKNFIAKHFLE LEDDIIDNFDYLSMKLILESDELNVP DEDYVVDFVIKWYIKRRNKLGNLL LLIKNVIRSNYLSPRGINNVKWILDC TKIFHCDKQPRKSYKYPFIEYPMNM DQIIDIFHMCTSTHVGEVVYLIGGW MNNEIHNNAIAVNYISNNWIPIPPM NSPRLYASGIPANNKLYVVGGLPNP TSVERWFHGDAAWVNMPSLLKPR CNPAVASINNVIYVMGGHSETDTTT EYLLPNHDQWQFGPSTYYPHYKSC ALVFGRRLFLVGRNAEFYCESSNT WTLIDDPIYPRDNPELIIVDNKLLLI GGFYRESYIDTIEVYNHHTYSWNIW DGK	Inside Deletion

Table 33. Examples of proteins encoded by Tian Tan Vaccinia genes equivalent to those deleted in CopMD5p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:58	TC2L (26% 5')	AAF33878.1	MESVIFSINGEIIQVNKEIITASPYNF FKRIQDHHLKDEAIILNGINYHAFES LLDYIRWKKINITINNVEMILVAAIII DVPPVVDLCVKTMIHNINSTNCIRM FNFSKQYGIKKLYNASMSEIINNITA VTSDPEFGKLSKDELTTILSHEDVN VNHEDVTAMILLKWIHKNPNDVDII NILHPKFMTNTMRNAISLLGLTISKS TKPVTRNGIKHNIVVIKNSDYISTIT HYSPRTEYWTIVGNTDRQFYNANV LHNCLYIIGGMINNRHVYSVSRVDL ETKKWKTVTNMSSLKSEVSTCVNN GKLYVIGGLEFSISTGVAEYLKHGT SKWIRLPNLITPRYSGASVFVNDDI YVMGGVYTTYEKYVVLNDVECFT KNRWIKKSPMPRHHSIVYAVEYDG DIYVITGITHETRNYLYKYIVKEDK WIELYMYFNHVGKMFVCSCGDYIL IIADAKYEYYPKSNTWNLFDMSTR NIEYYDMFTKDETPKCNVTHKSLPS FLSNCEKQFLQ	Inside Deletion
SEQ ID NO:59	TC1L	AAF33879.1	MVKNNKISNSCRMIMSTDPNNILM RHLKNLTDDEFKCIIHRSSDFLYLSD SDYTSITKETLVSEIVEEYPDDCNKI LAIIFLVLDKDIDVDIKTKLKPKPAV RFAILDKMTEDIKLTDLVRHYFRYI EQDIPLGPLFKKIDSYRTRAINKYSK ELGLATEYFNKYGHLMFYTLPIPYN RFFCRNSIGFLAVLSPTIGHVKAFYK FIEYVSIDDRRKFKKELMSK	Inside Deletion
SEQ ID NO:60	TN1L	AAF33880.1	MRTLLIRYILWRNDNDQTYYNDDF KKLMLLDELVDDGDVCTLIKNMR MTLSDGPLLDRLNQPVNNIEDAKR MIAISAKVARDIGERSEIRWEESFTI LFRMIETYFDDLMIDLYGEK	Inside Deletion
SEQ ID NO:61	TN2L	AAF33881.1	MTSSAMDNNEPKVLEMVYDATILP EGSSMDPYIMDCINRHINMCIQRTY	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			SSSIIAILDRFLMMNKDELNNTQCHI IKNL	
SEQ ID NO:62	TM1L	AAF33882.1	MIFVIESKLLQIYRNRNRNINFYTTM DNIMSAEYYLSLYAKYNSKNLDVF RNMLQAIEPSGNNYHILHAYCGIKG LDERFVEELLHRGYSPNETDDDGN YPLHIASKINNNRIVAMLLTHGADP NACDKHNKTPLYYLSGTDDEVIERI NLLVQYGAKINNSVDEEGCGPLLA CTDPSERVFKKIMSIGFEARIVDKFG KNHIHRHLMSDNPKASTISWMMKL GISPSKPDHDGNTPLHIVCSKTVKN VDIIDLLLPSTDVNKQNKFGDSPLT LLIKTLSPAHLINKLLSTSNVITDQT VNICIFYDRDDVLEIINDKGKQYDS TDFKMAVEVGSIRCVKYLLDNDIIC EDAMYYAVLSEYETMVDYLLFNH FSVDFVVNGHTCMSECVRLNNPVI LSKLMLHNLTSETMYLTMKAIEKD RLDKSIIIPFIAYFVLMHPDFCKNRR YFTSYKRFVTDYVHEGVSYEVFDD YF	Inside Deletion
SEQ ID NO:63	TM2L	AAF33883.1	MSSSTRLPVLVLAAELTIGVNYDIN STIIGECHMSESYIDRNANIVLTGYG LEINMTIMDTDQRFVAAAEGVGKD NKLSVLLFTTQRLDKVHHNISVTIT CMEMNCGTTKYDSDLPESIHKSSSC DITINGSCVTCVNLETDPTKINPHYL HPKDKYLYHNSEYGMRGSYGVTFI DELNQCLLDIKELSYDICYRE	Inside Deletion
SEQ ID NO:64	TK1L	AAF33884.1	MLQALFKYDINIYSANLENVLLDD AEIAKMIIEKHVEYKSDSYTKDLDI VKNNKLDEIISKNKELRLMYVNCV KKN	Inside Deletion
SEQ ID NO:65	TK2L	AAF33885.1	MDLSRINTWKSKQLKSFLSSKDTFK ADVHGHSALYYAIADNNVRLVCTL LNSGALKNLLENEFPLHQAATLEDT KIVKILLFSGLDDSQFDDKGNTALY YAVDSGNMQTVKLFVKKNWRLMF YGKTGWKTSFYHAVMLNDVSIVSY	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			FLSEIPSTFDLAILLSCIHITIKNGHV DMMILLLDYMTVDKHQ	
SEQ ID NO:66	TK3L	AAF33886.1	MIALLILSLACSASAYRLQGFTNAGI VAYKNIQDDNIVFSPFGYSFSMFMS LLPASGNTRIELLKTMDLRKRDLGP AFTELISGLAKLKTSKYTYTDLTYQ SFVDNTVCIKPSYYQQYHRFGLYRL NFRRDAVNKINSIVERRSGMSNVV DSNMLDNNTLWAIINTIYFKGTWQ YPFDITKTRNASFTNKYGTKTVPM MNVVTKLQGNTITIDDEEYDMVRL PYKDANISMYLAIGDNMTHFTDSIT AAKDYWSFQLGNKVYNLKLPKFSI ENKRDIKSIAEMMAPSMFNPDNASF KHMTRDPLYIYKMFQNAKIDVDEQ GTVAEASTIMVATARSSPEELEFNT PFVFIIRHDITGFILFMGKVESP	Inside Deletion
SEQ ID NO:67	ORFR	AAF33887.1	MGHIITYCQVHTNISILIRKAYHIIFF VIDCDCISLQFSNYVHHGNRFRTVL ISKTSIACFSDIKRILPCTFKIYSINDC P	
SEQ ID NO:68	TK4L	AAF33888.1	MLAFCYSLPNAGDVIKGRVYEKDY ALYIYLFDYPHSEAILAESVKMHM DRYVEYRDKLVGKTVKVKVIRVD YTKGYIDVNYKRMCRHQ	Inside Deletion
SEQ ID NO:69	TK6L	AAF33889.1	MTLVQHVVTIKSTYWVIPWELASY DNPNLFTAMILMSPLVNADAVSKL NLLAAKLMGTITLNAPVGKLCPES VSRDMDKVYKYQYDPLINHEKIKA GFASQVLKATNKVRKIISKINTPRLS YSREQTIRLAMF	Inside Deletion
SEQ ID NO:70	TK8R	AAF33890.1	MATKLDYEDAVFYFVDDDKICSRD SIIDLIDEYITWRNHVIVFNKDITSCG RLYKELMKFDDVAIRYYGIDKINEI VEAMSEGDHYINFTKVHDQESLFA TIGICAKITEHWGYKKISESRFQSLG NITDLMTDDNINILILFLEKKLN	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:71	TF1L	AAF33891.1	MLSMFMCNNIVDYVDDIDNGIVQD IEDEASNNVDRDYVYPLPENMVYR FDKSTNILDYLSTERDHVMMAVRY YMSKQRLDDLYRQLPTKTRSYIDII NIYCDKVSNDYNRDMNIMYDMAS TKSFTVYDINNEVNTILMDNKGLG VRLATISFITELGRRCMNPVKTIKM FTLLSHTICDDCFVDYITDISPPDNTI PNTSTREYLKLIGITAIMFATYKTLK YMIG	Inside Deletion
SEQ ID NO:72	TF2L	AAF33892.1	MFNMNINSPVRFVKETNRAKSPTR QSPGAAGYDLYSAYDYTIPPGERQL IKTDISMSMPKICYGRIAPRSGLSLK GIDIGGGVIDEDYRGNIGVILINNGK CTFNVNTGDRIAQLIYQRIYYPELEE VQSLDSTDRGDQGFGSTGLR	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:73	TF3L (75% 3')	AAF33893.1	MPIFVNTVYCKNILALSMTKKFKTII DAIGGNIIVNSTILKKLSPYFRTHLR QKYTKNKDPVTRVCLDLDIHSLTSI VIYSYTGKVYIDSHNVVNLLRASIL TSVEFIIYTCINFILRDFRKEYCVECY MMGIEYGLSNLLCHTKNFIAKHFLE LEDDIIDNFDYLSMKLILESDELNVP DEDYVVDFVIKWYIKRRNKLGNLL LLIKNVIRSNYLSPRGINNVKWILDC TKIFHCDKQPRKSYKYPFIEYPMNM DQIIDIFHMCTSTHVGEVVYLIGGW MNNEIHNNAIAVNYISNNWIPIPPM NSPRLYASGIPANNKLYVVGGLPNP TSVERWFHGDAAWVNMPSLLKPR CNPAVASINNVIYVMGGHSETDTTT EYLLPNHDQWQFGPSTYYPHYKSC ALVFGRRLFLVGRNAEFYCESSNT WTLIDDPIYPRDNPELIIVDNKLLLI GGFYRESYIDTIEVYNHHTYSWNIW DGK	Inside Deletion
	TK5L			
	ORFR			
	TK7L			

Table 34. Examples of proteins encoded by Wyeth Vaccinia genes equivalent to those deleted in CopMD5p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:74	VAC_DPP20_035 (26% 5')	AEY74729.1	MESVTFSINGEIIQVNKEIITASPYNF FKRIQEHHINDEVIILNGINYHAFES LLDYMRWKKINITINNVEMILVAA VIIDVTPVVDLCVKTMIHNINSTNCI RMFNFSKRYGIKKLYNASMSEIINN ITAVTSDPEFGKLSKDELTTILSHED VNVNHEDVTAMILLKWIHKNPNDV DIINILHPKFMTNTMRNAISLLGLTI SKSTKPVTRNGIKHNIVVIKNSDYIS TITHYSPRTEYWTIVGNTDRQFYNA	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			NVLHNCLYIIGGMINNRHVYSVSRV DLETKKWKTVTNMSSLKSEVSTCV NNGKLYVIGGLEFSISTGVAEYLKH GTSKWIRLPNLITPRYSGASVFVND DIYVMGGVYTTYEKYVVLNDVECF TKNRWIKKSPMPRHHSIVYAVEYD GDIYAITGITHETRNYLYKYIVKED KWIELYMYFNHVGKMFVCSCGDYI LIIADAKYEYYPKSNTWNLFDMST RNIEYYDMFTKDETHKSLPSFLSNC EKQFLQ	
SEQ ID NO:75	VAC_DPP10_036	AEY74730.1	MVKNNKISNSCRMIMSTNPNNILM RHLKNLTDDEFKCIIHRSSDFLYLSD RDYTSITKETLVSEIVEEYPDDCNKI LAIIFLVLDKDIDVDIKTKLKPKPAV RFAILDKMTEDIKLTDLVRHYFRYI EQDIPLGPLFKKIDSYRTRAINKYSK ELGLATEYFNKYGHLMFYTLPIPYN RFFCRNSIGFLAVLSPTIGHVKAFYK FIEYVSIDDRRKFKKELMSK	Inside Deletion
SEQ ID NO:76	N1L	AEY74731.1	MRTLLIRYILWRNDNDQTYYNDDF KKLMLLDELVDDGDVCTLIKNMR MTLSDGPLLDRLNQPVNNIEDAKR MIAISAKVARDIGERSEIRWEESFTI LFRMIETYFDDLMIDLYGEK	Inside Deletion
SEQ ID NO:77	VAC_DPP11_038	AEY74732.1	MTSSAMDNNEPKVLEMVYDATILP EGSSMDPNIIDCINRHINMCIQRTYS SSIIAILDRFLTMNKDELNNTQCHII KEFMTYEQMAIDHYGGYVNAILYQ IRKRPNQHHTIDLFKKIKRTRYDTF KVDPVEFVKKVIGFVSILNKYKPVY SYVLYENVLYDEFKCFIDYVETKYF	Inside Deletion
SEQ ID NO:78	VAC_DPP11_039	AEY74733.1	MLHNPTSETMYLTMNAIKKDKLDK SIIIPFIAYFVLMHPDFCKNRRYFTS YKRFVTDYVHEGVSYEVFDDYF	Not Present
SEQ ID NO:79	VAC_DPP12_040	AEY74734.1	MSIGFEARIVDKFGKNHIHRHLMSD NPKASTISWMMKLGISPSKPDHDG NTPLHIVCSKTVKYVDIIDLLLPSTD VNKQNKFGDSPLTLLIKTLSLAHLI NKLLSTSNVITDQTVNICIFYDRDD VLEIINDKGKQYDFKMAVEVGSIKC	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			VKYLLDNDIICEDAMYYAVLSEYK TMVDYLLFNHFSVDSVVNGHTCMS ECVKLNNRHFIEADVT	
SEQ ID NO:80	VAC_DPP12 _041	AEY74735.1	MIFVIESKLLQIYRNRNRNINFYTTM DNIMSAEYYLSLYAKYNSKNLDVF RNMLQAIEPSGNNYHILHAYCGIKG LDERFVEELLHRGYSPNETDDDGN YPLHIASKINNNRIVAMLLTHGADP NACDKHNKTPLYYLSGTDDEVIERI NLLVQYGAKINN	Not Present
SEQ ID NO:81	VAC_DPP12 _042	AEY74736.1	MVYKLVLLFCIASLGYSVEYKNTIC PPRQDYRYWYFAAELTIGVNYDIN STIIGECHMSESYIDRNANIVLTGYG LEINMTIMDTDQRFVAAAEGVGKD NKLSVLLFTTQRLDKVHHNISVTIT CMEMNCGTTKYDSDLPESIHKSSSC DITINGSCVTCVNLETDPTKINPHYL HPKDKYLYHNSEYGMRGSYGVTFI DELNQCLLDIKELSYDICYRE	Inside Deletion
SEQ ID NO:82	VAC_DPP10 _043	AEY74737.1	MDLSRINTWKSKQLKSFLSSKDTFK ADVHGHSALYYAIADNNVRLVCTL LNAGALKNLLENEFPLHQAATLED TKIVKILLFSGLDDSQFDDKGNTAL YYAVDSGNMQTVKLFVKKNWRL MFYGKTGWKTSFYHAVMLNDVSI VSYFLSEIPSTFDLAILLSCIHITIKNG HVDMMILLLDYMTSTNTNNSLLFIP DIKLAIDNKDIEMLQALFKYDINIYS ANLENVLLDDAEIAKMIIEKHVEYK SDSYTKDLDIVKNNKLDEIISKNKE LRLMYVNCVKKN	Inside Deletion
SEQ ID NO:83	VAC_DPP20 _044	AEY74738.1	MIALLILSLTCSVSTYRLQGFTNAGI VAYKNIQDDNIVFSPFGYSFSMFMS LLPASGNTRIELLKTMDLRKRDLGP AFTELISGLAKLKTSKYTYTDLTYQ SFVDNTVCIKPSYYQQYHRLNFRR DAVNKINSIVERRSGMSNVVDSNM LDNNTLWAIINTIYFKGIWQYPFDIT KTRNASFTNKYGTKTVPMMNVVT KLQGNTITIDDKEYDMVRLPYKDA NISMYLAIGDNMTHFTDSITAAKLD	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			YWSFQLGNKVYNLKLPKFSIENKR DIKSIAEMMAPSMFNPDNASFKHM TRDPLYIYKMFQNAKIDVDEQGTV AEASTIMVATARSSPEKLEFNTPFV FIIRHDITGFILFMGKVESP	
SEQ ID NO:84	VAC_DPP10_045	AEY74739.1	MLAFCYSLPNAGDVIKGRVYENDY ALYIYLFDYPHFEAILAESVKMHM DRYVEYRDKLVGKTVKVKVIRVD YTKGYIDVNYKRMCRHQ	Inside Deletion
SEQ ID NO:85	K4L	AEY74740.1	MNPDNTIAVITETIPIGMQFDKVYLS TFNMWREILSNTTKTLDISSFYWSL SDEVGTNFGTIILNEIVQLPKRGVRV RVAVNKSNKPLKDVERLQMAGVE VRYIDITNILGGVLHTKFWISDNTHI YLGSANMDWRSLTQVKELGIAIFN NRNLAADLTQIFEVYWYLGVNNLP YNWKNFYPSYYNTDHPLSINVSGV PHSVFIASAPQQLCTMERTNDLTAL LSCIRNASKFVYVSVMNFIPIIYSKA GKILFWPYIEDELRRSAIDRQVSVK LLISCWQRSSFIMRNFLRSIAMLKSK NINIEVKLFIVPDADPPIPYSRVNHA KYMVTDKTAYIGTSNWTGNYFTDT CGASINITPDDGLGLRQQLEDIFMR DWNSKYSYELYDTSPTKRCKLLKN MKQCTNDIYCDEIQPEKEIPEYSLE	Inside Deletion
SEQ ID NO:86	VAC_DPP20_047	AEY74741.1	MGATISILASYDNPNLFTAMILMSP LVNADAVSKLNLLAAKLMGTITPN APVGKLCPESVSRDMDKVYKYQY DPLINHEKIKAGFASQVLKATNKVR KIISKINTPPTLILQGTNNEISDVLGA YYFMQHANCNREIKIYEGAKHHLH KETDEVKKSVMKEIETWIFNRVK	Inside Deletion
SEQ ID NO:87	List034/VAC_DPP20_048	AEY74742.1	MSANCMFNLDNDYIYWKPITYPKA LVFISHGAGKHSGRYDELAENISSL GILVFSHDHIGHGRSNGEKMMIDDF GTARGNY	Inside Deletion
SEQ ID NO:88	K7R/VAC_DPP20_49	AEY74743.1	MATKLDYEDAVFYFVDDDKICSRD SIIDLIDEYITWRNHVIVFNKDITSCG RLYKELMKFDDVAIRYYGIDKINEI VEAMSEGDHYINFTKVHDQESLFA	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			TIGICAKITEHWGYKKISESRFQSLG NITDLMTDDNINILILFLEKKLN	
SEQ ID NO:89	LIVPclone14_046/VAC_DPP20_047	AEY74744.1	MLSMFMCNNIVDYVDDIDNGIVQD IEDEASNNVDHDYVYPLPENMVYR FDKSTNILDYLSTERDHVMMAVRY YMSKQRLDDLYRQLPTKTRSYIDII NIYCDKVSNDYNRDMNIMYDMAS TKSFTVYDINNEVNTILMDNKGLG VRLATISFITKLGRRCMNPVKTIKM FTLLSHTICDDCFVDYITDISPPDNTI PNTSTREYLKLIGITAIMFATYKTLK YMIG	Inside Deletion
SEQ ID NO:90	F2L/VAC_DPP20_051	AEY74745.1	MFNMNINSPVRFVKETNRAKSPTR QSPGAAGYDLYSAYDYTIPPGERQL IKTDISMSMPKICYGRIAPRSGLSLK GIDIGGGVIDEDYRGNIGVILINNGK CTFNVNTGDRIAQLIYQRIYYPELEE VQSLDSTNRGDQGFGSTGLR	Inside Deletion
SEQ ID NO:91	F3L (75% 3')	AEY74746.1	MPIFVNTVYCKNILALSMTKKFKTII DAIGGNIIVNSTILKKLSPYFRTHLR QKYTKNKDPVTRVCLDLDIHSLTSI VIYSYTGKVYIDSHNVVNLLRASIL TSVEFIIYTCINFILRDFRKEYCVECY MMGIEYGLSNLLCHTKNFIAKHFLE LEDDIIDNFDYLSMKLILESDELNVP DEDYVVDFVIKWYIKRRNKLGNLL LLIKNVIRSNYLSPRGINNVKWILDC TKIFHCDKQPRKSYKYPFIEYPMNM DQIIDIFHMCTSTHVGEVVYLIGGW MNNEIHNNAIAVNYISNNWIPIPPM NSPRLYASGIPANNKLYVVGGLPNP TSVERWFHGDAAWVNMPSLLKPR CNPAVASINNVIYVMGGHSETDTTT EYLLPNHDQWQFGPSTYYPHYKSC ALVFGRRLFLVGRNAEFYCESSNT WTLIDDPIYPRDNPELIIVDNKLLLI GGFYRESYIDTIEVYNHHTYSWNIW DGK	Inside Deletion

Table 35. Examples of proteins encoded by Lister Vaccinia genes equivalent to those deleted in CopMD5p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:92	List023 (26% 5')	ABD52473.1	MESVIFSINGEIIQVNKEIITASPYNF FKRIQDHHLKDEAIILNGINYHAFES LLDYMRWKKINITINNVEMILVAAI IIDVPPVVDLCVKTMIHNINFTNCIR MFNFSKRYGIKKLYNASMSEIINNIT AVTSDPEFGKLSKDELTTILSHEDV NVNHEDVTAMILLKWIHKNPNDVD IINILHPKFMTNTMRNAISLLGLTIS KSTKPVTRNGIKHNIVVIKNSDYIST ITHYSPRTEYWTIVGNTDRQFYNAN VLHNCLYIIGGMINNRHVYSVSRVD LKTKKWKTVTNMSSLKSEVSTCVN DGKLYVIGGLEFSISTGVAEYLKHG TSKWIRLPNLITPRYSGASVFVNDDI YVMGGVYTTYEKYVVLNDVECFT KNRWIKKSPMPRHHSIVYAVEYDG DIYVITGITHETRNYLYKYIVKEDK WIELYMYFNHVGKMFVCSCGDYIL IIADAKYEYYPKSNTWNLFDMSTR NIEYYDMFTKDETPKCNVTHKSLPS FLSNCEKQFLQ	Inside Deletion
SEQ ID NO:93	C1L/List024	ABD52474.1	MVKNNKISNSCRMIMSTNPNNILM RHLKNLTDDEFKCIIHRSSDFLYLSD SDYTSITKETLVSEIVEEYPDDCNKI LAIIFLVLDKDIDVDIETKLKPKPAV RFAILDKMTADIKLTDLVRHYFRYI EQDIPLGPLFKKIDSYRTRAINKYSK ELGLATEYFNKYGHLMFYTLPIPYN RFFCRNSIGFLAVLSPTIGHVKAFYK FIEYVSIDDRRKFKKELMSK	Inside Deletion
SEQ ID NO:94	N1L/List025	ABD52475.1	MRTLLIRYILWRNDNDQTYYNDDF KKLMLLDELVDDGDVCTLIKNMR MTLSDGPLLDRLNQPVNNIEDAKR MIAISAKVARDIGERSEIRWEESFTI LFRMIETYFDDLMIDLYGEK	Inside Deletion
SEQ ID NO:95	List026	ABD52476.1	MTSSAMDNNEPKVLEMVYDATILP EGSSMDPNIMDCINRHINMCIQRTY SSSIIAILDRFLTMNKDELNNTQCHII	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			KEFMTYEQMAIDHYGEYVNAILYQ IRKRPNQHHTIDLFKKIKRTRYDTF KVDPVEFVKKVIGFVSILNKYKPVY SYVLYENVLYDEFKCFIDYVETKYF	
SEQ ID NO:96	List027	ABD52477.1	MIFVIESKLLQIYRNRNINFYTTMD NIMSAEYYLSLYAKYNSKNLDVFR NMLQAIEPSGNNYHILHAYCGIKGL DERFVEELLHRGYSPNETDDDGNY PLHIASKINNNRIVAMLLTHGADPN ACDKQHKTPLYYLSGTDDEVIERIN LLVQYGAKINNSVDEEGCGPLLAC TDPSERVFKKIMSIGFEARIVDKFGK NHIHRHLMSDNPKASTISWMMKLG ISPSKPDHDGNTPLHIVCSKTVKNV DIIDLLLPSTDVNKQNKFGDSPLTLL IKTLSPAHLINKLLSTSNVITDQTVN ICIFYDRDDVLEIINDKGKQYDSTDF KMAVEVGSIRCVKYLLDNDIICEDA MYYAVLSEYETMVDYLLFNHFSVD SVVNGHTCMSECVRLNNPVILSKL MLHNPTSETMYLTMKAIEKDRLDK SIIIPFIAYFVLMHPDFCKNRRYFTS YKRFVTDYVHEGVSYEVFDDYF	Inside Deletion
SEQ ID NO:97	List028	ABD52478.1	MVYKLVLLFCIASLGYSVEYKNTIC PPRQDYRYWYFAAELTIGVNYDIN STIIGECHMSESYIDRNANIVLTGYG LEINMTIMDTDQRFVAAAEGVGKD NKLSVLLFTTQRLDKVHHNISVTIT CMEMNCGTTKYDSDLPESIHKSSSC DITINGSCVTCVNLETDPTKINPHYL HPKDKYLYHNSEYGMRGSYGVTFI DELNQCLLDIKELSYDICYRE	Inside Deletion
SEQ ID NO:98	K1L/List029	ABD52479.1	MDLSRINTWKSKQLKSFLSSKDAF KADINGHSALYYAIADNNVRLVCT LLNAGALKNLLENEFPLHQAATLE DTKIVKILLFSGLDDSQFDDKGNTA LYYAVDSGNMQTVKLFVKKNWRL MFYGKTGWKTSFYHAVMLNDVSI VSYFLSEIPSTFDLAILLSCIHITIKNG HVDMMILLLDYMTSTNTNNSLLFIP DIKLAIDNKDIEMLQALFKYDINIYS ANLENVLLDDAEIAKMIIEKHVEYK	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			SDSYTKDLDIVKNNKLDEIISKNKE LKLMYVNCVKKN	
SEQ ID NO:99	List030	ABD52480.1	IELLKTMDLRKRDLGPAFTELISGL AKLKTSKYTYTDLTYQSFVDNTVCI KPSYYQQYHRFGLYRLNFRRDAVN KINSIVERRSGMSNVVDSNMLDNN TLWAIINTIYFKGIWQYPFDITKTRN ASFTNKYGTKTVPMMNVVTKLQG NTITIDDEEYDMVRLPYKDANISMY LAIGDNMTHFTDSITAAKLDYWSS QLGNKVYNLKLPKFSIENKRDIKSI AEMMAPSMFNPDNASFKHMTRDP LYIYKMFQNAKIDVDEQGTVAEAS TIMVATARSSPEKLEFNTPFVFIIRH DITGFILFMGKVESP	Inside Deletion
SEQ ID NO:100	K3L/List031	ABD52483.1	MLAFCYSLPNAGDVIKGRVYENDY ALYIYLFDYPHSEAILAESVKMHM DRYVEYRDKLVGKTVKVKVIRVD YTKGYIDVNYKRMCRHQ	Inside Deletion
SEQ ID NO:101	K4L/List032	ABD52484.1	MNPDNTIAVITETIPIGMQFDKVYLS TFNMWREILSNTTKTLDISSFYWSL SDEVGTNFGTIILNEIVQLPKRGVRV RVAVNKSNKPLKDVERLQMAGVE VRYIDITNILGGVLHTKFWISDNTHI YLGSANMDWRSLTQVKELGIAIFN NRNLAADLTQIFEVYWYLGVNNLP YNWKNFYPSYYNTDHPLSINVSGV PHSVFIASAPQQLCTMERTNDLTAL LSCIRNASKFVYVSVMNFIPIIYSKA GKILFWPYIEDELRRSAIDRQVSVK LLISCWQRSSFIMRNFLRSIAMLKSK NINIEVKLFIVPDADPPIPYSRVNHA KYMVTDKTAYIGTSNWTGNYFTDT CGASINITPDDGLGLRQQLEDIFMR DWNSKYSYELYDTSPTKRCKLLKN MKQCTNDIYCDEIQPEKEIPEYSLE	Inside Deletion
SEQ ID NO:102	List033	ABD52485.1	MGHSMGATISILASYDNPNLFTAMI LMSPLVNADAVSRLNLLAAKLMGT ITPNAPVGKLCPESVSRDMDKVYK YQYDPLINHEKIKAGFASQVLKATN KVRKIISKINTPPTLILQGTNNKISDV	Outside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			LGAYYFMQHANCNREIKIYEGAKH HLHKETDEVKKSVMKEIETWIFNR VK	
SEQ ID NO:103	List034	ABD52486.1	MSANCMFNLDNDYIYWKPITYPKA LVFISHGAGKHSGRYDELAENISSL GILVFSHDHIGHGRSNGEKMMIDDF GTARGNY	Inside Deletion
SEQ ID NO:104	K7R/List035	ABD52487.1	MATKLDYEDAVFYFVDDDKICSRD SIIDLIDEYITWRNHVIVFNKDITSCG RLYKELMKFDDVAIRYYGIDKINEI VEAMSEGDHYINFTKVHDQESLFA TIGICAKITEHWGYKKISESRFQSLG NITDLMTDDNINILILFLEKKLN	Inside Deletion
SEQ ID NO:105	F1L/List036	ABD52489.1	MLSMFMCNNIVDYVDDIDNGIVQD IEDEASNNVDHDYVYPLPENMVYR FDKSTNILDYLSTERDHVMMAVRY YMSKQRLDDLYRQLPTKTRSYIDII NIYCDKVSNDYNRDMNIMYDMAS TKSFTVYDINNEVNTILMDNKGLG VRLATISFITELGRRCMNPVKTIKM FTLLSHTICDDCFVDYITDISPPDNTI PNTSTREYLKLIGITAIMFATYKTLK YMIG	Inside Deletion
SEQ ID NO:106	List037	ABD52490.1	MFNMNINSPVRFVKETNRAKSPTR QSPGAAGYDLYSAYDYTIPPGERQL IKTDISMSMPKFCYGRIAPRSGLSLK GIDIGGGVIDEDYRGNIGVILINNGK CTFNVNTGDRIAQLIYQRIYYPELEE VQSLDSTNRGDQGFGSTGLR	Inside Deletion
SEQ ID NO:107	List038 (75% 3')	ABD52491.1	MPIFVNTVYCKNILALSMTKKFKTII DAIGGNIIVNSTILKKLSPYFRTHLR QKYTKNKDPVTRVCLDLDIHSLTSI VIYSYTGKVYIDSHNVVNLLRASIL TSVEFIIYTCINFILRDFRKEYCVECY MMGIEYGLSNLLCHTKNFIAKHFLE LEDDIIDNFDYLSIKLILESDELNVP DEDYVVDFVIKWYIKRRNKLGNLL LLIKNVIRSNYLSPRGINNVKWILDC TKIFHCDKQPRKSYKYPFIEYPMNM DQIIDIFHMCTSTHVGEVVYLIGGW MNNEIHNNAIAVNYISNNWIPIPPM	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			NSPRLYASGIPANNKLYVVGGLPNP TSVERWFHGDAAWVNMPSLLKPR CNPAVASINNVIYVMGGHSETDTTT EYLLPNHDQWQFGPSTYYPHYKSC ALVFGRRLFLVGRNAEFYCESSNT WTLIDDPIYPRDNPELIIVDNKLLLI GGFYRESYIDTIEVYNHHTYSWNIW DGK	

Table 36. Examples of proteins encoded by Copenhagen Vaccinia genes deleted in CopMD3p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:108	B14R (41% 3')	AAA48211.1	MNHCLLAISAVYFKAKWLTPFEKE FTSDYPFYVSPTEMVDVSMMSMYG ELFNHASVKESFGNFSIIELPYVGDT SMMVILPDKIDGLESIEQNLTDTNF KKWCNSLDAMFIDVHIPKFKVTGS YNLVDTLVKSGLTEVFGSTGDYSN MCNLDVSVDAMIHKTYIDVNEEYT EAAAATCALVSDCASTITNEFCVDH PFIYVIRHVDGKILFVGRYCSPTTNC	Inside Deletion
SEQ ID NO:109	B15R	AAA48212.1	MTANFSTHVFSPQHCGCDRLTSIDD VKQCLTEYIYWSSYAYRNRQCAGQ LYSTLLSFRDDAELVFIDIRELVKN MPWDDVKDCTEIIRCYIPDEQKTIR EISAIIGLCAYAATYWGGEDHPTSN SLNALFVMLEMLNYVDYNIIFRRM N	Inside Deletion
SEQ ID NO:110	B ORF E	AAA48213.1	MYNSSIHTPEYDVIIHVIEHLKHHK QCVQTVTSGMVFTSPVSSSICTKSD DGRNLSDGFLLIRYITTDDFCTIFDII PRHIFYQLANVDEH	Inside Deletion
SEQ ID NOS:111 and 625	B16R	AAA48214.1	MSILPVIFLPIFFYSSFVQTFNASECI DKGXYFASFMELENEPVILPCPQIN TLSSGYNILDILWEKRGADNDRIIPI DNGSNMLILNPTQSDSGIYICITTNE TYCDMMSLNLTIVSVSESNIDFISYP QIVNERSTGEMVCPNINAFIASNVN ADIIWSGHRRLRNKRLKQRTPGIITI	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			EDVRKNDAGYYTCVLEYIYGGKTY NVTRIVKLEVRDKIIHPTMQLPEGV VTSIGSNLTIACRVSLRPPTTDADVF WISNGMYYEEDDGDGDGRISVANK IYMTDKRRVITSRLNINPVKEEDAT TFTCMAFTIPSISKTVTVSIT[a] [a] SEQ ID NO: 111 represents the amino acid sequence prior to the "X" and SEQ ID NO: 625 represents the amino acid sequence after the "X."	
SEQ ID NO:112	B ORF F	AAA48215.1	MVIIPGVRCLSLLFLRRRCPLHIISAF TLLAINALILGHTISPVDLSFTICGYE IKSIFDSETDTIVKFNDIMSQ	Inside Deletion
SEQ ID NO:113	B17L	AAA48216.1	MSRKFMQVYEYDREQYLDEFIEDR YNDSFITSPEYYSAEKYMCRYTTLN HNCVNVRRCALDSKLLHDIITNCKI YNNIELVRATKFVYYLDLIKCNWV SKVGDSVLYPVIFITHTSTRNLDKV SVKTYKGVKVKKLNRCADHAIVIN PFVKFKLTLPNKTSHAKVLVTFCKL RTDITPVEAPLPGNVLVYTFPDINK RIPGYIHVNIEGCIDGMIYINSSKFA CVLKLHRSMYRIPPFPIDICSCCSQY TNDDIEIPIHDLIKDVAIFKNKETVY YLKLNNKTIARFTYFNNIDTAITQE HEYVKIALGIVCKLMINNMHSIVGV NHSNTFVNCLLEDNV	Inside Deletion
SEQ ID NO:114	B18R	AAA48217.1	MSRRLIYVLNINRKSTHKIQENEIYT YFSHCNIDHTSTELDFVVKNYDLNR RQHVTGYTALHCYLYNNYFTNDV LKILLNHDVNVTMKTSSGRMPVYI LLTRCCNISHDVVIDMIDKDKNHLS HRDYSNLLLEYIKSRYMLLKEEDID ENIVSTLLDKGIDPNFKQDGYTALH YYYLCLAHVYKPGECRKPITIKKAK RIISLFIQHGANLNALDNCGNTPFHL YLSIEMCNNIHMTKMLLTFNPNFKI CNNHGLTPILCYITSDYIQHDILVML IHHYETNVGEMPIDERRMIVFEFIKT YSTRPADSITYLMNRFKNINIYTRY EGKTLLHVACEYNNTQVIDYLIRIN GDINALTDNNKHATQLIIDNKENSP	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			YTINCLLYILRYIVDKNVIRSLVDQL PSLPIFDIKSFEKFISYCILLDDTFYD RHVKNRDSKTYRYAFSKYMSFDK YDGIITKCHDETMLLKLSTVLDTTL YAVLRCHNSRKLRRYLTELKKYNN DKSFKIYSNIMNERYLNVYYKDMY VSKVYDKLFPVFTDKNCLLTLLPSE IIYEILYMLTINDLYNISYPPTKV	
SEQ ID NO:115	B19R	AAA48218.1	MTMKMMVHIYFVSLSLLLLLFHSY AIDIENEITEFFNKMRDTLPAKDSK WLNPACMFGGTMNDMATLGEPFS AKCPPIEDSLLSHRYKDYVVKWER LEKNRRRQVSNKRVKHGDLWIAN YTSKFSNRRYLCTVTTKNGDCVQG IVRSHIKKPPSCIPKTYELGTHDKYG IDLYCGILYAKHYNNITWYKDNKEI NIDDIKYSQTGKELIIHNPELEDSGR YDCYVHYDDVRIKNDIVVSRCKILT VIPSQDHRFKLILDPKINVTIGEPANI TCTAVSTSLLIDDVLIEWENPSGWLI GFDFDVYSVLTSRGGITEATLYFEN VTEEYIGNTYKCRGHNYYFEKTLT TTVVLE	Inside Deletion
SEQ ID NO:116	B20R	AAA48219.1	MDEDTRLSRYLYLTDREHINVDSIK QLCKISDPNACYRCGCTALHEYFY NYRSVNGKYKYRYNGYYQYYSSS DYENYNEYYYDDYDRTGMNSESD SESDNISIKTEYENEYEFYDETQDQS TQHNDL	Inside Deletion
SEQ ID NO:117	B21R	AAA48220.1	MSLESFIITTFNNNSSTNIDNMCHLY VKVCPSSLLFRLFVECCDINKLVEG TTPLHCYLMNEGFESSVLKNLLKE YVMNTFNVHDIHYTNI	Inside Deletion
SEQ ID NO:118	B22R	AAA48221.1	MISLSFLIHNPLKKWKLKPSISINGY RSTFTMAFPCAQFRPCHCHATKDSL NTVADVRHCLTEYILWVSHRWTHR ESAGSLYRLLISFRTDATELFGGELK DSLPWDNIDNCVEIIKCFIRNDSMK TAEELRAIIGLCTQSAIVSGRVFNDK YIDILLMLRKILNENDYLTLLDHIRT AKY	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:119	B23R	AAA48222.1	MIAFIIFREIGIISTRIAMDYCGRECTI LCRLLDEDVTYKKIKLEIETCHNLS KHIDRRGNNALHCYVSNKCDTDIKI VRLLLSRGVERLCRNNEGLTPLGA YSKHRYVKSQIVHLLISSYSNSSNEL KSNINDFDLSSDNIDLRLLKYLIVDK RIRPSKNTNYAINGLGLVDIYVTTP NPRPEVLLWLLKSECYSTGYVFRTC MYNSDMCKNSLHYYISSHRESQSL SKDVIKCLINNNVSIHGRDEGGSLPI QYYWSFSTIDIEIVKLLLIKDVDTCR VYDVSPILEAYYLNKRFRVTPYNV DMEIVNLLIERRHTLVDVMRSITSY DSREYNHYIIDNILKRFRQQDESIVQ AMLINYLHYGDMVVRCMLDNGQQ LSSARLLC	Inside Deletion
SEQ ID NO:120	B24R	AAA48223.1	MYGLILSRFNNCGYHCYETILIDVF DILSKYMDDIDMIDNENKTLLYYA VDVNNIQFAKRLLEYGASVTTSRSII NTAIQKSSYQRENKTRIVDLLLSYH PTLETMIDAFNRDIRYLYPEPLFACI RYALILDDDFPSKVSMISPVIIRN	Inside Deletion
SEQ ID NO:121	B ORF G	AAA48224.1	MRRCIHIKERKIHMTNIVDRNVTFIL TVVHKYVRYVPHTVANDAHNLVH LAHLIHFIIYFFIIRDVRKKKKKKKK NRTIYFFSNVYARHIK	Inside Deletion
SEQ ID NO:122	B25R	AAA48225.1	MSRINITKKIYCSVFLFLFLFLSYISN YEKVNDEMYEMGEMDEIVSIVRDS MWYIPNVFMDDGKNEGHVSVNNV CHMYFTFFDVDTSSHLFKLVIKHCD LNKRGNSPLHCYTMNTRFNPSVLKI LLHHGMRNFDSKDEKGHHYLIHSL SIDNKIFDILTDTIDDFSKSSDLLLCY LRYKFNGSLNYYVLYKGSDPNCAD EDELTSLHYYCKHISTFYKSNYYKL SHTKMRAEKRFIYAIIDYGANINAV THLPSTVYQT	Inside Deletion
SEQ ID NO:123	B26R	AAA48226.1	MEQTLTRLHTYLQQYTKHSPRVVY ALLSRGYVIILIVHPSWNDCATGHIL IMLLNWHEQKEEGQHLLYLFIKHN QGYTLNILRYLLDRFDIQKDEYIYR	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			LSKL	
SEQ ID NO:124	B27R	AAA48227.1	MLPHTSDTTSTFRLKTVFDLVFENR NIIYKADVVNDIIHHRLKVSLPMIKS LFYKMSEFSPYDDYYVKKILAYCL LRDESFAELHSKFCLNEDYKSVFM KNISFDKIDSIIVT	Inside Deletion
SEQ ID NO:125	B28R	AAA48228.1	MKSVLYSYILFLSCIIINGRDIAPHAP SDGKCKDNEYKRHNLCPGTYASRL CDSKTNTQCTPCGSGTFTSRNNHLP ACLSCNGRRDRVTLLTIESVNALPD IIVFSKDHPDARHVFPKQNVE	Inside Deletion
SEQ ID NO:126	C23L/B29R (44% 5')	AAA48229.1	MHVPASLQQSSSSSSSCTEEENKHH MGIDVIIKVTKQDQTPTNDKICQSV TEITESESDPDPEVESEDDSTSVEDV DPPTTYYSIIGGGLRMNFGFTKCPQI KSISESADGNTVNARLSSVSPGQGK DSPAITREEALAMIKDCEVSIDIRCS EEEKDSDIKTHPVLGSNISHKKVSY EDIIGSTIVDTKCVKNLEFSVRIGDM CKESSELEVKDGFKYVDGSASEGA TDDTSLIDSTKLKACV	Inside Deletion

Table 37. Examples of proteins encoded by Western Reserve Vaccinia genes equivalent to those deleted in CopMD3p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:127	SPI-2/B13R/VACWR195 (26% 3')	AAO89474.1	MDIFREIASSMKGENVFISPASISSV LTILYYGANGSTAEQLSKYVEKEEN MDKVSAQNISFKSINKVYGRYSAV FKDSFLRKIGDKFQTVDFTDCRTID AINKCVDIFTEGKINPLLDEPLSPDT CLLAISAVYFKAKWLTPFEKEFTSD YPFYVSPTEMVDVSMMSMYGKAF NHASVKESFGNFSIIELPYVGDTSM MVILPDKIDGLESIEQNLTDTNFKK WCNSLEATFIDVHIPKFKVTGSYNL VDTLVKSGLTEVFGSTGDYSNMCN SDVSVDAMIHKTYIDVNEEYTEAA	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			AATCALVSDCASTITNEFCVDHPFI YVIRHVDGKILFVGRYCSPTTNC	
SEQ ID NO:128	VACWR196	AAO89475.1	MTANFSTHVFSPQHCGCDRLTSIDD VRQCLTEYIYWSSYAYRNRQCAGQ LYSTLLSFRDDAELVFIDIRELVKN MPWDDVKDCAEIIRCYIPDEQKTIR EISAIIGLCAYAATYWGGEDHPTSN SLNALFVMLEMLNYVDYNIIFRRM N	Inside Deletion
SEQ ID NO:129	VACWR197	AAO89476.1	MSILPVIFLSIFFYSSFVQTFNAPECI DKGQYFASFMELENEPVILPCPQIN TLSSGYNILDILWEKRGADNDRIIPI DNGSNMLILNPTQSDSGIYICITTNE TYCDMMSLNLTIVSVSESNIDLISYP QIVNERSTGEMVCPNINAFIASNVN ADIIWSGHRRLRNKRLKQRTPGIITI EDVRKNDAGYYTCVLEYIYGGKTY NVTRIVKLEVRDKIIPSTMQLPDGIV TSIGSNLTIACRVSLRPPTTDADVF WISNGMYYEEDDGDGNGRISVANK IYMTDKRRVITSRLNINPVKEEDAT TFTCMAFTIPSISKTVTVSIT	Inside Deletion
SEQ ID NO:130	VACWR198	AAO89477.1	MSRKFMQVYEYDREQYLDEFIEDR YNDSFITSPEYYSAEKYMCRYTTLN HNCINVRRCALDSKLLHDIITNCKIY NNIELVRATKFVYYLDLIKCNWVS KVGDSVLYPVIFITHTSTRNLDKVS VKTYKGVKVKKLNRCADHAIVINP FVKFKLTLPNKTSHAKVLVTFCKL KTDITPVEAPLPGNVLVYTFPDINK RIPGYIHLNIEGCIDGMIYINSSKFAC VLKLHRSMYRIPPFPIDICSCCSQYI NYDIEIPIHDLIKDVAIFKNKETVYY LKLNNKTIARFTYFNNIDTAITQEHE YVKIALGIVCKLMINNMHSIVGVN HSNTFVNCLLEDNV	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:131	VACWR199	AAO89478.1	MSRRLIYVLNINRESTHKIQENEIYT YFSHCNIDHTSTELDFVVKNYDLNR RQPVTGYTALHCYLYNNYFTNDVL KILLNHGVDVTMKTSSGRMPVYIL LTRCCNISHDVVIDMIDKDKNHLLH RDYSNLLLEYIKSRYMLLKEEDIDE NIVSTLLDKGIDPNFKQDGYTALHY YYLCLAHVYKPGECRKPITIKKAKR IISLFIQHGANLNALDNCGNTPFHLY LSIEMCNNIHMTKMLLTFNPNFEIC NNHGLTPILCYITSDYIQHDILVMLI HHYETNVGEMPIDERRIIVFEFIKTY STRPADSITYLMNRFKNIDIYTRYE GKTLLHVACEYNNTHVIDYLIRING DINALTDNNKHATQLIIDNKENSPY TINCLLYILRYIVDKNVIRSLVDQLP SLPIFDIKSFEKFISYCILLDDTFYNR HVRNRDSKTYRYAFSKYMSFDKY DGIITKCHKETILLKLSTVLDTTLYA VLRCHNSKKLRRYLTELKKYNNDK SFKIYSNIMNERYLNVYYKDMYVS KVYDKLFPVFTDKNCLLTLLPSEIIY EILYMLTINDLYNISYPPTKV	Inside Deletion
SEQ ID NO:132	B18R/VACWR200	AAO89479.1	MTMKMMVHIYFVSLLLLLFHSYAI DIENEITEFFNKMRDTLPAKDSKWL NPACMFGGTMNDIAALGEPFSAKC PPIEDSLLSHRYKDYVVKWERLEK NRRRQVSNKRVKHGDLWIANYTS KFSNRRYLCTVTTKNGDCVQGIVR SHIRKPPSCIPKTYELGTHDKYGIDL YCGILYAKHYNNITWYKDNKEINID DIKYSQTGKELIIHNPELEDSGRYDC YVHYDDVRIKNDIVVSRCKILTVIPS QDHRFKLILDPKINVTIGEPANITCT AVSTSLLIDDVLIEWENPSGWLIGF DFDVYSVLTSRGGITEATLYFENVT EEYIGNTYKCRGHNYYFEKTLTTT VVLE	Inside Deletion
SEQ ID NO:133	VACWR201	AAO89480.1	MHVIDVDVRLYMSTFIIIDQSTENTS IDTTVTINIIYLAIMKIIMNIIMMIMIE LV	Not Present

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:134	VACWR202	AAO89481.1	MNSESDNISIKTEYEFYDETQDQST QLVGYDIKLKTNEDDFMAMIDQW VSMII	Not Present
SEQ ID NO:135	VACWR203	AAO89482.1	MEMYPRHRYSKHSVFKGFSDKVR KNDLDMNVVKELLSNGASLTIKDS SNKDPITVYFRRTIMNLEMIDERKYI VHSYLKNYKNFDYPFFRKLVLTNK HCLNNYYNISDSKYGTPLHILASNK KLITPNYMKLLVYNGNDINARGED TQMRTPLHKYLCKFVYHNIEYGIR YYNEKIIDAFIELGADLTIPNDDGMI PVVYCIHSNAEYGYNNITNIKIIRKL LNLSRRASHNLFRDRVMHDYISNT YIDLECLDIIRSLDGFDINGYFEGRT PLHCAIQHNFTQIAKYLLDRGADIV VPNTLIIHQYIQ	Inside Deletion
SEQ ID NO: 136	VACWR204	AAO89483.1	MEEDTNISNKVIRYNTVNNIWETLP NFWTGTINPGVVSHKDDIYVVCDIK DEKNVKTCIFRYNTNTYNGWELVT TTESRLSALHTILYNNTIMMLHCYE SYMLQDTFNVYTREWNHMCHQHS NSYIMYNILPIY	Not Present
SEQ ID NO:629	VACWR204.5	AAO89483.1	MLNFSLCLYPVFILNKLVLRTQSIIL HTINNASIKNR	Not Present
SEQ ID NO:137	SPI-1/VACWR205	AAO89484.1	MDIFKELILKHTDENVLISPVSILSTL SILNHGAAGSTAEQLSKYIENMNEN TPDDNNDMDVDIPYCATLATANKI YGSDSIEFHASFLQKIKDDFQTVNF NNANQTKELINEWVKTMTNGKINS LLTSPLSINTRMTVVSAVHFKAMW KYPFSKHLTYTDKFYISKNIVTSVD MMVSTENNLQYVHINELFGGFSIIDI PYEGNSSMVIILPDDIEGIYNIEKNIT DEKFKKWCGMLSTKSIDLYMPKFK VEMTEPYNLVPILENLGLTNIFGYY ADFSKMCNETITVEKFLHTTFIDVN EEYTEASAVTGVFMTNFSMVYRTK VYINHPFMYMIKDNTGRILFIGKYC YPQ	Outside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:138	C13L/VACWR206	AAO89485.1	MMIYGLIACLIFVTSSIASPLYIPVIP PISEDKSFNSVEVLVSLFRDDQKDY TVTSQFNNYTIDTKDWTIGVLSTPD GLDIPLTNITYWSRFTIGRALFKSES EDIFQKKMSILGVSIECKKSSTLLTF LTVRKMTRVFNKFPDMAYYRGDC LKAVYVTMTYKNTKTGETDYTYLS NGGLPAYYRNGVDG	Outside Deletion
SEQ ID NO:139	VACWR207	AAO89486.1	MKLFTQNDRYFGLLDSCTHIFCITCI NIWHKTRRETGASDNCPICRTRFRN ITMSKFYKLVN	Outside Deletion
SEQ ID NO:140	p28/VACWR208	AAO89487.1	MEFDPAKINTSSIDHVTILQYIDEPN DIRLTVCIIRNINNITYYINITKINTHL ANQFRAWKKRIAGRDYMTNLSRD TGIQQSKLTETIRNCQKNRNIYGLYI HYNLVINVVIDWITDVIVQSILRGL VNWYIANNTYTPNTPNNTTTISELD IIKILDKYEDVYRVSKEKECGICYEV VYSKR	Outside Deletion
SEQ ID NO:141	C10L/VACWR209	AAO89488.1	MDIYDDKGLQTIKLFNNEFDCIRND IRELFKHVTDSDSIQLPMEDNSDIIE NIRKILYRRLKNVECVDIDSTITFMK YDPNDDNKRTCSNWVPLTNNYME YCLVIYLETPICGGKIKLYHPTGNIK SDKDIMFAKTLDFKSKKVLTGRKTI AVLDISVSYNRSMTTIHYNDDVDID IHTDKNGKELCYCYITIDDHYLVDV ETIGVIVNRSGKCLLVNNHLGIGIV KDKRISDSFGDVCMDTIFDFSEARE LFSLTNDDNRNIAWDTDKLDDDTD IWTPVTEDDYKFLSRLVLYAKSQSD TVFDYYVLTGDTEPPTVFIFKVTRF YFNMPK	Outside Deletion
SEQ ID NO:142	VGF-1/VACWR210	AAO89489.1	MSMKYLMLLFAAMIIRSFADSGNAI ETTSPEITNATTDIPAIRLCGPEGDG YCLHGDCIHARDIDGMYCRCSHGY TGIRCQHVVLVDYQRSENPNTTTSY IPSPGIMLVLVGIIIITCCLLSVYRFTR RTKLPIQDMVVP	Outside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:143	VACWR211	AAO89490.1	MDEIVRIVRDSMWYIPNVFMDDGK NEGHVSVNNVCHMYFTFFDVDTSS HLFKLVIKHCDLNKRGNSPLHCYT MNTRFNPSVLKILLHHGMRNFDSK DEKGHHYQSITRSLIY	Inside Deletion
SEQ ID NO:144	C20L/VAC WR212	AAO89491.1	MLFYLEEPIRGYVIILIVHPSWNDCA TGHILIMLLNWHEQKEEGQHLLYL FIKHNQGYTLNILRYLLDRFDIQKD EYYNTAFQNCNNNVASYIGYDINL PTKDGIRLGV	Inside Deletion
SEQ ID NO:145	VACWR213	AAO89492.1	MLPHTSDTTSTFRLKTVFDLVFENR NIIYKADVVNDIIHHRLKVSLPMIKS LFYKMSLPTTITT	Inside Deletion
SEQ ID NO:146	VACWR214	AAO89493.1	MYDDLIEQCHLSMERKSKLVDKAL NKLESTIGQSRLSYLPPEIMRNII	Outside Deletion
SEQ ID NO:147	B28R/VAC WR215	AAO89494.1	MKSVLYSYILFLSCIIINGRDIAPHAP SDGKCKDNEYKRHNLCPGTYASRL CDSKTNTQCTPCGSGTFTSRNNHLP ACLSCNGRRDRVTRLTIESVNALPD IIVFSKDHPDARHVFPKQNVE	Inside Deletion
SEQ ID NO:148	VACWR216	AAO89495.1	MDSLRPVVVVNWIQINFHIDIVKGI TGYGFAFICGRDGVRICSETTRRTD DVSGYSVSYSTFCLGNTCLASG	Outside Deletion
SEQ ID NO:149	VACWR217	AAO89496.1	MWKLICIQLTTTTGLSESISTSELTIT MNHKDCNPVFREEYFSVLNKVATS GFFTGERCAL	Outside Deletion
SEQ ID NO:150	B29R/VAC WR218 (44% 5')	AAO89497.1	MHVPASLQQSSSSSSSCTEEENKHH MGIDVIIKVTKQDQTPTNDKICQSV TEITESESDPDPEVESEDDSTSVEDV DPPTTYYSIIGGGLRMNFGFTKCPQI KSISESADGNTVNARLSSVSPGQGK DSPAITHEEALAMIKDCEVSIDIRCS EEEKDSDIKTHPVLGSNISHKKVSY EDIIGSTIVDTKCVKNLEFSVRIGDM CKESSELEVKDGFKYVDGSASEGA TDDTSLIDSTKLKACV	Inside Deletion

Table 38. Examples of proteins encoded by Tian Tan Vaccinia genes equivalent to those deleted in CopMD3p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:151	TF3L (41% 3')	AAF34083.1	MNHCLLAISAVYFKAKWLTPFEKE FTSDYPFYVSPTEMVDVSMMSMYG KAFNHASVKESFGNFSIIELPYVGD TSMMVILPDKIDGLESIEQNLTDTN FKKWCDFMDAMFIDVHIPKFKVTG SYNLVDTLVKSGLTEVFGSTGDYS NMCNLDVSVDAMIHKTYIDVNEEY TEAAAATCALVSDCASTITNEFCVD HPFIYVIRHVDGKILFVGRYCSPTTN C	Inside Deletion
SEQ ID NO:152	TB15R	AAF34084.1	MTANFSTHVFSPQHCGCDRLTSIDD VKQCLTEYIYWSSYAYRNRQCAGQ LYSTLLSFRDDAELVFIDIRELVKN MPWDDVKDCTEIIRCYIPDEQKTIR EISAIIGLCAYAATYWGGEDHPTSN SLNALFVMLEMLNYVDYNIIFRRM N	Inside Deletion
SEQ ID NO:153	ORFL	AAF34085.1	MYNSSIHTPEYDVIIHVIEHLKHHK QCVQTVTSGMVFTSPVSSSICTKSD DGRNLSDGFLLIRYITTDDFCTIFDII PRHIFYQLANVDEH	
SEQ ID NO:154	TB16R	AAF34086.1	MELENEPVILPCPQINTLSSGYNILDI LWEKRGADNDRIIPIDNGSNMLILN PTQSDSGIYICITTNETYCDMMSLN LTIVSVLESNIDLISYPQIVNERSTGE MVCPNINAFIASNVNADIIWSGHRR LRNKRLKQRTPGIITIEDVRKNDAG YYTCVLEYIYRGKTYNVTRIVKLEV RDKIIPSTMQLPDGIVTSIGSNLTIAC RVSLRPPTTDADVFWISNGMYYEE DDGDGNGRISVANKIYMTDKRRVI TSRLNINPVKEEDATTFTCMAFTIPS ISKTVTVSIT	Inside Deletion
SEQ ID NO:155	ORFL	AAF34087.1	MVIIPGVRCLSLLFLRRRCPLHIISAF TLLAINALILGHTISPVDLSFTICGYE IRSIFDSKTDTIVKFNDIMSQ	

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:156	TB17L	AAF34088.1	MSRKFMQVYEYDREQYLDEFIEDR YNDSFITSPEYYSAEKYMCRYTTLN HNCVNVRRCALDSKLLHDIITNCKI YNNIELVRATKFVYYLDLIKCNWV SKVGDSVLYPVIFITHTSTRNLDKV SVKTYKGVKVKKLNRCADHAIVIN PFVKFKLTLPNKTSHAKVLVTFCKL RTDITQIEAPLSGNVLVYTFPNINKR IPGYIHVNIEGCIDGMIYINSSKFAC VLKLHRSMYRIPPFPIDICSCCSQYT NGDIEIPIHDLIKDVAIFKNKETVYY LKLNNKTIARFTYFNNIDTAITQEHE YVKIALGIVCKLMINNMHSIVGVN HSNTFVNCLLEDNV	Inside Deletion
SEQ ID NO:157	TB18R	AAF34089.1	MSRRLIYVLNINRESTHKIQENEIYT YFSHCNIDHTSTELDFVVKNYDLNR RHPVTGYTALHCYLYNNYFTNDVL KILLNHGVDVTMKTSSGRMPVYIL LTRCCNISHDVVIDMIDKDKNHLLH RDYSNLLLEYIKSRYMLLKEEDIDE NIVSTLLDKGIDPNFKQDGYTALHY YYLCLAHVYKPGECRKPITIKKAKR IISLFIQHGANLNALDNCGNTPFHLY LSIEMCNNIHMTKMLLTFNPNFKIC NNHGLTPILCYITSDYIQHDILVMLI HHYETNVGEMPIDERRIIVFEFIKTY STRPADSITYLMNRFKNINIYTRYE GKTLLHVACEYNNTQVIDYLIRING DINALTDNNKHATQLIIDNKENSPY TINCLLYILRYIVDKNVIRSLVDQLP SLPIFDIKSFEKFISYCILLDDTFYDR HVKNRNSKTYRYAFSKYMSFDKY DGIITKCHDETMLLKLSTVLDTTLY AVLRCHNSRKLRRYLTELKKYNND KSFKIYSNIMNERYLNVYYKDMYV SKVYDKLFPVFTDKNCLLTLLPSEII YEILYMLTINDLYNISYPPTKV	Inside Deletion
SEQ ID NO:158	TB19R	AAF34090.1	MTMKMMVHIYFVSLSLLLLLFHSY AIDIENEITEFFNKMRDTLPAKDSK WLNPACMFGGTMNDIAALGEPFSA KCPPIEDSLLSHRYKDYVVKWERL EKNRRRQVSNKRVKHGDLWIANY	Inside Deletion

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
			TSKFSNRRYLCTVTTKNGDCVQGI VRSHIKKPPSCIPKTYELGTHDKYGI DLYCGILYAKHYNNITWYKDNKEI NIDDIKYSQTGKELIIHNPELEDSGR YDCYVHYDDVRIKNDIVVSRCKILT VIPSQDHRFKLILDPKINVTIGEPANI TCTAVSTSLLIDDVLIEWENPSGWLI GFDFDVYSVLTSRGGITEATLYFEN VTEEYIGNTYKCRGHNYYFEKTLT TTVVLE	
SEQ ID NO:159	ORFR	AAF34091.1	MHVIDVDVRLYMSTFIIIDQSTENTS IDTTVTINIIYLAIMKIIMNIIMMIMIE LV	
SEQ ID NO:160	TB21R	AAF34092.1	LKNVECVDIDSTITFMKYDPNDDN KRTCSNWVPLTNNYMEYCLVIYLE TPICGGKIKLYHPTGNIKSDKDIMFA KTLDFKSTKVLTGRKTIAVLDISVS YNRSMTTIHYNDDVDIDIHTDKNG KELCYCYITIDDHYLVDVETIGVIV NRSGKCLLVNNHLGIGIVKDKRISD SFGDVCMDTIFDFSEARELFSLTND DNRNIAWDTDKLDDDTDIWTPVTE NDYKFLSRLVLYAKSQSDTVFDYY VLTGDTEPPTVFIFKVTRFYFNMPK	
SEQ ID NO:161	TB22L	AAF34093.1	MYCRCSHGYTGIRCQHVVLVDYQ RSEKPNTTTSYIPSPGIMLVLVGIIIIT CCLLSVYRFTRRTKLPLQDMVVP	
SEQ ID NO:162	TB23R (44% 5')	AAF34094.1	MHVPASLQQSSSSSSSCTEEENKHH MGIDVIIKVTKQDQTPTNDKICQSV TEITESESDPDPEVESEDDSTSVEDV DPPTTYYSIIGGGLRMNFGFTKCPQI KSISESADGNTVNARLSSVSPGQGK DSPAITHEEALAMIKDCEVSIDIRCS EEEKDSDIKTHPVLGSNISHKKVSY EDIIGSTIVDTKCVKNLEFSVRIGDM CKESSELEVKDGFKYVDGSASEGA TDDTSLIDSTKLKACV	Inside Deletion
	TB20R			
	ORFL			

Table 39. Examples of proteins encoded by Wyeth Vaccinia genes equivalent to those deleted in CopMD3p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:163	VAC_DPP20_207	AEY74905.1	MNHCLLAISAVYFKAKWLTPFEKE FTSDYPFYVSPTEMVDVSMMSMYG KAFNHASVKESFGNFSIIELPYVGD TSMMVILPDKIDGLESIEQNLTDTN FKKWCDFMDAMFIDVHIPKFKVTG SYNLVDTLVKSGLTEVFGSTGDYS NMCNLDVSVDAMIHKTYIDVNEEY TEAAAATCALVSDCASTVTNEFCA DHPFIYVIRHVDGKILFVGRYCSPTT NC	Inside Deletion
SEQ ID NO:164	VAC_DPP10_208	AEY74906.1	MTANFSTHVFSPQHCGCDRLTSIDD VKQCLTEYIYWSSYAYRNRQCAGQ LYSTLLSFRDDAELVFIDIRELVKH MPWDDVKDCAEIIRCYIPDEQKTIR EISAIIGLCAYAATYWGGEDHPTSN SLNALFVMLEMLNYVDYNIIFRRM N	Inside Deletion
SEQ ID NO:165	VAC_DPP12_209	AEY74907.1	MSILPVIFLSIFFYSSFVQTFNASECI DKGQYFASFMELENEPVILPCPQIN TLSSGYNILDILWEKRGADNDRIIPI DNGSNMLILNPTQSDSGIYICITTNE TYCDMMSLNLTIVSVSESNIDLISYP QIVNERSTGEMVCPNINAFIASNVN ADIIWSGHRRLRNKRLKQRTPGIITI EDVRKNDAGYYTCVLEYIYGGKTY NVTRIVKLEVRDKIIPSTMQLPDGIV TSIGSNLTIACRVSLRPPTTDTDVFW ISNGMYYEEDDGDGDGRISVANKI YMTDKRRVITSRLNINPVKEEDATT FTCMAFTIPSISKTVTVSIT	Inside Deletion
SEQ ID NO:166	VAC_DPP20_210	AEY74908.1	MSRKFMQVYEYDREQYLDEFIEDR YNDSFITSPEYYSAEKYMCRYTTLN HNCVNVRRCALDSKLLHDIITNCKI YNNIELVRATKFVYYLDLIKCNWV SKVGDSVLYPVIFITHTSTRNLDKV SVKTYKGVKVKKLNRCADHAIVIN PFVKFKLTLPNKTSHAKVLVTFCKL RTDITQIEAPLSGNVLVYTFPDINKR IPGYIHVNIEGCIDGMIYINSSKFAC	Inside Deletion

			VLKLHRSMYRIPPFPIDICSCCSQYT NDDIEIPIHDLIKDVAIFKNKETVYY LKLNNKTIARFTYFNNIDTAITQEHE YVKIALGIVCKLMINNMHSIVGVN HSNTFVNCLLEDNV	
SEQ ID NO:167	VAC_DPP20_211	AEY74909.1	MSRRLIYVLNINRESTHKIQENEIYT YFSHCNIDHTSTELDFVVKNYDLNR RQPVTGYTALHCYLYNNYFTNDVL KILLNHGVDVTMKTSSGRMPVYIL LTRCCNISHDVVIDMIDKDKNHLSH RDYSNLLLEYIKSRYMLLKEEDIDE NIVSTLLDKGIDPNFKQDGYTALHY YYLCLAHVYKPGECRKPITIKKAKR IISLFIQHGANLNALDNCGNTPFHLY LSIEMCNNIHMTKMLLTFNPNFKIC NNHGLTPILCYITSDYIQHDILVMLI HHYETNVGEMPIDERRIIVFEFIKTY STRPADSITYLMNRFKNINIYTRYE GKTLLHVACEYNNTHVIDYLIRING DINALTDNNKHAIQLIIDNKENSPYT IDCLLYILRYIVDKNVIRSLVDQLPS LPIFDIKSFEKFISYCILLDDTFYNRH VRNRNSKTYRYAFSKYMSFDKYD GIITKCHDETMLLKLSTVLDTTLYA VLRCHNSKKLRRYLNELKKYNND KSFKIYSNIMNERYLNVYYKDMYV SKVYDKLFPVFTDKNCLLTLLPSEII YEILYMLTINDLYNISYPPTKV	Inside Deletion
SEQ ID NO:168	VAC_DPP20_212	AEY74910.1	MTMKMMVHIYFVSLSLLLLLFHSY AIDIENEITEFFNKMRDTLPAKDSK WLNPACMFGGTMNDIATLGEPFSA KCPPIEDSLLSHRYKDYVVKWERL EKNRRRQVSNKRVKHGDLWIANY TSKFSNRRYLCTVTTKNGDCVQGI VRSHIRKPPSCIPKTYELGTHDKYGI DLYCGILYAKHYNNITWYKDNKEI NIDDIKYSQTGKKLIIHNPELEDSGR YDCYVHYDDVRIKNDIVVSRCKILT VIPSQDHRFKLKRNCGYASN	Inside Deletion
SEQ ID NO:169	VAC_DPP10_217	AEY74911.1	MRQIKINGTDMLTVMYMLNKPTK KRYVNNPIFTDWANKQYKFYNQII YNANKLIEQSKKIDDMIEEVSIDDN RLSTLPLEIRHLIFSYAFL	Not Present

SEQ ID NO:170	VAC_DPP10_218	AEY74912.1	MSSKGGSGGMWSVFIHGHDGSNKGSKTYTSGGGGMWGGGSSSGVNGGVKSGTGKI	Outside Deletion
SEQ ID NO:171	VAC_DPP10_219	AEY74913.1	MFDYLENEEVALDELKQMLRDRDPNDTRNQFKNNALHAYLFNEHCNNVEVVKLLLDSGTNPLRKNWRQLPH	Outside Deletion
SEQ ID NO:172	VAC_DPP10_220	AEY74914.1	MLKLKDIAMALLEATGFSNINDFNIFSYMKSKNVDVDLIKVLVEHGFDLSVKCENHRSVIENYVMTMILFIENGCSVLYEDEY	Outside Deletion
SEQ ID NO:173	VAC_DPP10_221	AEY74915.1	MKGIDNTAYSYIDDLTCCTRGIMADYLNSDYRYNKDVDLVKLFLENGKPHGIMCSIVPLWRNDKETIFLILKTMNSDVLQHILIEYMTFGDIPLVEYGTVVNKEAIHGYFRNINIDSYTMKYLLKKEGRCHQLSRLDTYVNPTMDVIISTLIHTKRVFVTCLMLAQFLVL	Outside Deletion
SEQ ID NO:174	VAC_DPP10_222	AEY74916.1	MPSIISIGHLCKSNYGCYNFYTYTYKKGLCDMSYACPILSTINICLPYLKDINMIDKRGETLLHKAVRYNKQSLVSLLLESGSDVNIRSNNGYTCIAIAINESKNIELLKMLLCHKPTLDYVIDSLREISNIVDNDYAIKQCIKYAMIIDDCTSSKIPEFISQRYNDYIDLCN	Outside Deletion
SEQ ID NO:175	VAC_DPP10_223	AEY74917.1	MKKIMVGGNTMFSLIFTDHGAKIIHRYANNPELREYYELKQNKIYVEAYDIISNAIVKHDRIHKTIESVDDNTYISNLPYTIKYKIFEQQ	Outside Deletion
SEQ ID NO:176	VAC_DPP10_224	AEY74918.1	MRILFLIAFMYGCVHSYVNAVETKCSNLDIVTSSGEFHCSGCVEHMPNFSYMYWLAKDMRSDEDAKFIEHLGEGIKEDETVRTIDGRIVTLQKVLHVTDTNKFAHYRFTCVLTTIDGVSKKNIWLK	Outside Deletion
SEQ ID NO:177	VAC_DPP10_225	AEY74919.1	MKLFTQNDRYFGLLDSCNHIFCITCINIWHKTRRETGASDNCPICRTRFRNITMSKFYKLVN	Outside Deletion
SEQ ID NO:178	VAC_DPP10_226	AEY74920.1	MHYPKYYINITKINPHLANQFRAWKKRIAGRDYMTNLSKDTGIQQSKL	Outside Deletion

			YVTVKKIETYMVYIYTTI	
SEQ ID NO:179	VAC_DPP20_227	AEY74921.1	MDIYDDKGLQTIKLFNNEFDCIRND IRELFKHVTDSDSIQLPMEDNSDIIE NIRKILYRRLKNVECVDIDNTITFM KYDPNDDNKRTCSNWVPLTNNYM EYCLVIYLETPICGGKIKLYHPTGNI KSDKDIMFAKTLDFKSKKVLTGRK TIAVLDISVSYNRSITTIHYNDDVDI DIHTDKNGKELCYCYITIDDHYLVD VETIGVIVNRSGKCLLVNNHLGIGI VKDKRISDSFGDVCMDTIFDFSEAR ELFSLTNDDNRNIAWDTDKLDDDT DIWTPVTENDYKFLSRLVLYAKSQS DTVFDYYVLTGDTEPPTVFIFKVTR FYFNMPK	Outside Deletion
SEQ ID NO:180	VAC_DPP20_228	AEY74922.1	MLINYLMLLFAAMIIRSFADSGNAI ETTLPEITNATTDIPAIRLCGPEGDG YCLHGDCIHARDIDGMYCRCSHGY TGIRCQHVVLVDYQRSEKPNTTTSY IPSPGIMLVLVGIIIITCCLLSVYRFTR RTNKLPLQDMVVP	Outside Deletion
SEQ ID NO:181	VAC_DPP20_229	AEY74923.1	MDIFKELIVKHPDENVLISPVSILSTL SILNHGAAGSTAEQLSKYIENMNEN TPDDKKDDNNDMDVDIPYCATLAT ANKIYGSDSIEFHASFLQKIKDDFQT VNFNNANQTKELINEWVKTMTNG KINSLLTSPLSINTRMTVVSAVHFK AMWKYPFSKHLTYTDKFYISKNIV TSVDMMVGTENNLQYVHINELFGG FSIIDIPYEGNSSMVIILPDDIEGIYNI EKNITDEKFKKWCGMLSTKSIDLY MPKFKVEMTEPYNLVPILENLGLTN IFGYYADFSKMCNETITVEKFLHTT FIDVNEEYTEASAVTGVFMTNFAM VYRTKVYINHPFMYMIKDTTGRILF IGKYCYPQ	Outside Deletion
SEQ ID NO:182	C13L/VAC_DPP20_230	AEY74924.1	MMIYGLIACLIFVTSSIASPLYIPVIP PITEDKSFNSVEVLVSLFRDDQKDY TVTSQFNNYTIDTKDWTIGVLSTPD GLDIPLTNITYWSRFTIGRALFKSES EDIFQKKMSILGVSIECKKSSTLLTF LTVRKMTRVFNKFPDMAYYRGDC LKAVYVTMTYKNTKTGETDYTYLS	Outside Deletion

			NGGLPAYYRNGVDG	
SEQ ID NO:183	VAC_DPP20_231	AEY74925.1	MNLQKLSLAIYLTATCSWCYETCIRKTALYHDIQLEHVEDNKDSVASLPYK	Outside Deletion
SEQ ID NO:184	VAC_DPP20_232	AEY74926.1	MSLESFIITTFNNNSSTNIDNMCHLYVKVCPSSLLFRLFVECCDINKLVEGTTPLHCYLMNEGFESSVLKNLLKEYVMTSITQIFNS	Inside Deletion
SEQ ID NO:185	VAC_DPP20_233	AEY74927.1	MISLSFLIHNPLKKWKLKPSISINGYRSTFTMAFPCAQFRPCHCHATKDSLNTVADVRHCLTEYILWVSHRWTHRETAGPLYRLLISFRTDATELFGGELKDSLPWDNIDNCVEIIKCFIRNDSMKTAEELRAIIGLCTQSAIVSGRVFNDKYIDILLMLRKILNENDYLTLLDHIRTAKY	Inside Deletion
SEQ ID NO:186	VAC_DPP20_234	AEY74928.1	MIAFIIFREIGIISTRIAMDCTCILCRLLDEDVTYKKIKLEIETCHNLSKHIDRRGNNALHCYVFNKCDTDIKIVRLLLSRGVERLCRNNEGLTPLGVYSKHRYVKSQIVHLLISSYSNSSNELKSNINDFDLSSDNIDLRLLKYLIVDKRIRPSKNTNYAINSLGLVDIYVTTPNPRPEVLLWLLKSECYSTGYVFRTCMYNSDMCKNSLHYYISSHRESQSLSKDVIKCLINNNVSIHGRDEGGSLPIQYYWSFSTIDIEIVKLLLIKDVDTCRVYDVSPILEAYYLNKRFRVTPYNVDMEIVNLLIERRHTLVDVMRSITSYDSREYNHYIIDNILKRFRQQDESIVQAMLINYLHYGDMVVRCMLDNGQQLSSARLLC	Inside Deletion
SEQ ID NO:187	VAC_DPP20_235	AEY74929.1	MYGLILSRFNNCGYHCYETILIDVFDILSKYMDNIDMIDNENKTLLYYAVDVNNIQFAKRLLEYGASVTTSRSIINTAIQKSSYRRENKTKLVDLLLSYHPTLETMIDAFNRDIRYLYPEPLFACIRYALILDDDFPSKVKYDISGRHKELKRYRVDINRMKNAYISGVSMFDILFKRSKRHRLRYAKNPTSNGTKKN	Inside Deletion

SEQ ID NO:188	VAC_DPP20_236	AEY74930.1	MSRINITKKIYCSVFLFLFLSYISNYEKVNDEMYEMGEMDEIVSIVRDSMWYIPNVFMDDGKNEGHVSVNNVCHMYFTFFDVDTSSHLFKLVIKHCDLNKRGNSPLHCYTMNTRFNPSVLKILLHHGMRNFDSKDDHYQSITRSLIY	Inside Deletion
SEQ ID NO:189	VAC_DPP20_237	AEY74931.1	MEQTLTRLHTYLQQYTKHSPRVVYALLSRGYVIILIVHPSWNDCATGHILIMLLNWHEQKEEGQHLLYLFIKHNQGYTLNILRYLLDRFDIQKDEYYNTAFQNCNNNVASYIGYDINLPTKDGIRLGV	Inside Deletion
SEQ ID NO:190	VAC_DPP20_238	AEY74932.1	MLPHTSDTTSTFRLKTVFDLVFENRNIIYKADVVNDIIHHRLKVPMIKSLFYKMSEFSPYDDYYVKKILAYCLLRDESFAELHSKFCLNEDYKSVFMKNISFDKIDSIIVT	Inside Deletion
SEQ ID NO:191	VAC_DPP20_239	AEY74933.1	MHHPMESVKTTNTNAIICVREHTLPDYANTQCTPCGSGTFTSRNNHLPACLSCNGRRDRVTLLTIESVNALPDIIVFSKDHPDARHVFPKQNVE	Inside Deletion
SEQ ID NO:192	VAC_DPP20_241 (43% 5')	AEY74934.1	MHVPASLQQSSSSCTEEENKHHMGIDVIIKVTKQDQTPTNDKICQSVTEITESESDPDPEVESEDDSTSVEDVDLPTTYYSIIGGGLRMNFGFTKCPQIKSISESADGNTVNARLSSVSPGQGKDSPAITHEEALAMIKDCEVSIDIRCSEEEKDSDIKTHPVLGSNISHKKVSYEDIIGSTIVDTKCVKNLEFSVRIGDMCKESSELEVKDGFKYVDGSASEGATDDTSLIDSTKLKACV	Inside Deletion
SEQ ID NO:193	VAC_DPP10_225	AEY74919.1	MKLFTQNDRYFGLLDSCNHIFCITCINIWHKTRRETGASDNCPICRTRFRNITMSKFYKLVN	Outside Deletion
SEQ ID NO:194	VAC_DPP10_226	AEY74920.1	MHYPKYYINITKINPHLANQFRAWKKRIAGRDYMTNLSKDTGIQQSKLYVTVKKIETYMVYIYTTI	Outside Deletion
SEQ ID NO:195	VAC_DPP20_227	AEY74921.1	MDIYDDKGLQTIKLFNNEFDCIRNDIRELFKHVTDSDSIQLPMEDNSDIIENIRKILYRRLKNVECVDIDNTITFMKYDPNDDNKRTCSNWVPLTNNYM	Outside Deletion

			EYCLVIYLETPICGGKIKLYHPTGNI KSDKDIMFAKTLDFKSKKVLTGRK TIAVLDISVSYNRSITTIHYNDDVDI DIHTDKNGKELCYCYITIDDHYLVD VETIGVIVNRSGKCLLVNNHLGIGI VKDKRISDSFGDVCMDTIFDFSEAR ELFSLTNDDNRNIAWDTDKLDDDT DIWTPVTENDYKFLSRLVLYAKSQS DTVFDYYVLTGDTEPPTVFIFKVTR FYFNMPK	
SEQ ID NO:196	VAC_DPP20_228	AEY74922.1	MLINYLMLLFAAMIIRSFADSGNAI ETTLPEITNATTDIPAIRLCGPEGDG YCLHGDCIHARDIDGMYCRCSHGY TGIRCQHVVLVDYQRSEKPNTTTSY IPSPGIMLVLVGIIIITCCLLSVYRFTR RTNKLPLQDMVVP	Outside Deletion
SEQ ID NO:197	VAC_DPP20_239	AEY74933.1	MHHPMESVKTTNTNAIICVREHTLP DYANTQCTPCGSGTFTSRNNHLPA CLSCNGRRDRVTLLTIESVNALPDII VFSKDHPDARHVFPKQNVE	Inside Deletion
SEQ ID NO:198	VAC_DPP20_241 (43% 5')	AEY74934.1	MHVPASLQQSSSSCTEEENKHHMG IDVIIKVTKQDQTPTNDKICQSVTEI TESESDPDPEVESEDDSTSVEDVDL PTTYYSIIGGGLRMNFGFTKCPQIKS ISESADGNTVNARLSSVSPGQGKDS PAITHEEALAMIKDCEVSIDIRCSEE EKDSDIKTHPVLGSNISHKKVSYEDI IGSTIVDTKCVKNLEFSVRIGDMCK ESSELEVKDGFKYVDGSASEGATD DTSLIDSTKLKACV	Inside Deletion

Table 40. Examples of proteins encoded by Lister Vaccinia genes equivalent to those deleted in CopMD3p vector

SEQ ID NO.	Gene	Protein Accession ID	Amino Acid Sequence	Location
SEQ ID NO:200	B15R/List191	ABD52695.1	MTANFSTHVFSPQHCGCDRLTSIDD VKQCLTEYIYWSSYAYRNRQCAGQ LYSTLLSFRDDAELVFIDIRELVKN MPWDDVKDCTEIIRCYIPDEQKTIR EISAIIGLCAYAATYWGGEDHPTSN SLNALFVMLEMLNYVDYNIIFRRM	Inside Deletion

			N	
SEQ ID NO:201	List192	ABD52696.1	MSILPVIFLPIFFYSSFVQTFNAPECI DKGQYFASFMELENEPVILPCPQIN TLSSGYNILDILWEKRGADNDRIIPI DNGSNMLILNPTQSDSGIYICITTNE TYCDMMSLNLTIVSVSESNIDLISYP QIVNERSTGEMVCPNINAFIASNVN ADIIWSGHRRLRNKRLKQRTPGIITI EDVRKNDAGYYTCVLEYIYRGKTY NVTRIVKLEVRDKIIPSTMQLPDGIV TSIGSNLTIACRVSLRPPTTDADVF WISNGMYYEEDDGDGNGRISVANK IYMTDKRRVITSRLNINPVKEEDAT TFTCMAFTIPSISKTVTVSIT	Inside Deletion
SEQ ID NO:202	B17L/List193	ABD52698.1	MSRKFMQVYEYDREQYLDEFIEDR YNDSFITSPEYYSAEKYMCRYTTLN HNCINVRRCALDSKLLHDIITNCKIY NNIELVRATKFVYYLDLIKCNWVS KVGDSVLYPVIFITHTSTRNLDKVS VKTYKGVKVKKLNRCADHAIVINP FVKFKLTLPNKTSHAKVLVTFCKLR TDITQIEAPLSGNVLVYTFPDINKRI PGYIHVNIEGCIDGMIYINSSKFACV LKLHRSMYRIPPFPIDICSCCSQYTN DDIEIPIHDLIKDVAIFKNKETVYYL KLNNKTIARFTYFNNIDTAITQEHE YVKIALGIVCKLMINNMHSIVGVN HSNTFVNCLLEDNV	Inside Deletion
SEQ ID NO:203	crmE/List195	ABD52700.1	MTKVIIILGFLIINTNSLSMKCEQGV SYYNSQELKCCKLCKPGTYSDHRC DKYSDTICGHCPSDTFTSIYNRSPW CHSCRGPCGTNRVEVTPCTPTTNRI CHCDSNSYCLLKASDGNCVTCAPK TKCGRGYGKKGEDEMGNTICKKC RKGTYSDIVSDSDQCKPMTR	Not Present
SEQ ID NO:204	L6/List196	ABD52701.1	MAMPSLSACSSIEDDFNYGSSVASA SVHIRMAFLRKVYGILCLQFLLTTA TTAVFLYFDCMRTFIQGSPVLILAS MFGSIGLIFALTLHRHKHPLNLYLL CGFTLSESLTLASVVTFYDVHVVM QAFMLTTAAFLALTTYTLQSKRDFS KLGAGLFAALWILILSGLLGIFVQN	Not Present

			ETVKLVLSAFGALVFCGFIIYDTHSL IHKLSPEEYVLASINLYLDIINLFLHL LQLLEVSNKK	
SEQ ID NO:205	List197	ABD52704.1	MASPCAKFRPCHCHATKDSLNTVA DVRHCLTEYILWVSHRWTHRESAG SLYRLLISFRTDATELFGGELKDSLP WDNCVEIIKCFIRNDSMKTAEELRA IIGLCTQSAIVSGRVFNDKYIDILLM LRKILNENDYLTLLDHIRTAKY	Inside Deletion
SEQ ID NO:206	List199C	ABD52706.1	MEQTLTRLHTYLQQYTKHSPRVVY ALLSRGYVIILIVHPSWNDCATGHIL IMLLNWHEQKEEGQHLLYLFIKHN QGYTLNILRYLLDRFDIQKDEYYNT AFQNCNNNVASYIGYDINLPTKDGI RLGV	Inside Deletion
SEQ ID NO:207	List199D	ABL63830.1	MLPHTSDTTSTFRLKTVFDLVFENR NIIYKADVVNDIIHHRLKVSLPMIKS LFYKMSLPTTITT	Inside Deletion
SEQ ID NO:208	C23L/List201 (47% 5')	ABL63827.1	MKQYIVLACMCLAAAAMPASLQQ SSSSSSSCTEEENKHHMGIDVIIKVT KQDQTPTNDKICQSVTEITESESDPD PEVESEDDSTSVEDVDPPTTYYSIIG GGLRMNFGFTKCPQIKSISESADGN TVNARLSSVSPGQGKDSPAITHEEA LAMIKDCEVSIDIRCSEEEKDSDIKT HPVLGSNISHKKVSYEDIIGSTIVDT KCVKNLEFSVRIGDMCKESSELEVK DGFKYVDGSASEGATDDTSLIDSTK LKACV	Inside Deletion
	List198A			
	List198B			
	List199A			
	List199B			
	List200			

	List194			

Table 41. Gene Alignment

[00686] An exemplary alignment of select orthopoxvirus genes is shown below. Various genes of 5 vaccinia virus strains, Copenhagen ("cop"), Western Reserver ("WR"), Tian Tan ("Tian"), Wyeth, and Lister, align as follows:

C2L

CLUSTAL O(1.2.4) multiple sequence alignment

```
cop     MESVIFSINGEIIQVNKEIITASPYNFFKRIQDHHLKDEAIILNGINYHAFESLLDYIRW 60
WR      MESVIFSINGEIIQVNKEIITASPYNFFKRIQDHHLKDEAIILNGINYHAFESLLDYIRW 60
Tian    MESVIFSINGEIIQVNKEIITASPYNFFKRIQDHHLKDEAIILNGINYHAFESLLDYIRW 60
Wyeth   MESVTFSINGEIIQVNKEIITASPYNFFKRIQEHHINDEVIILNGINYHAFESLLDYMRW 60
Lister  MESVIFSINGEIIQVNKEIITASPYNFFKRIQDHHLKDEAIILNGINYHAFESLLDYMRW 60
        **** ***************************:**::**.*****************:**

cop     KKINITINNVEMILVAAIIIDVPPVVDLCVKTMIHNINSTNCIRMFNFSKRYGIKKLYNA 120
WR      KKINITINNVEMILVAAIIIDVPPVVDLCVKTMIHNINSTNCIRMFNFSKRYGIKKLYNA 120
Tian    KKINITINNVEMILVAAIIIDVPPVVDLCVKTMIHNINSTNCIRMFNFSKQYGIKKLYNA 120
Wyeth   KKINITINNVEMILVAAVIIDVTPVVDLCVKTMIHNINSTNCIRMFNFSKRYGIKKLYNA 120
Lister  KKINITINNVEMILVAAIIIDVPPVVDLCVKTMIHNINFTNCIRMFNFSKRYGIKKLYNA 120
        *****************:**** ************** **********:*********

cop     SMSEIINNITAVTSDPEFGKLSKDELTTILSHENVNVNHEDVTAMILLKWIHKNPNDVDI 180
WR      SMSEIINNITAVTSDPEFGKLSKDELTTILSHENVNVNHEDVTAMILLKWIHKNPNDVDI 180
Tian    SMSEIINNITAVTSDPEFGKLSKDELTTILSHEDVNVNHEDVTAMILLKWIHKNPNDVDI 180
Wyeth   SMSEIINNITAVTSDPEFGKLSKDELTTILSHEDVNVNHEDVTAMILLKWIHKNPNDVDI 180
Lister  SMSEIINNITAVTSDPEFGKLSKDELTTILSHEDVNVNHEDVTAMILLKWIHKNPNDVDI 180
        ********************************:************************

cop     INILHPKFMTNTMRNAISLLGLTISKSTKPVTRNGIKHNIVVIKNSDYISTITHYSPRTE 240
WR      INILHPKFMTNTMRNAISLLGLTISKSTKPVTRNGIKHNIVVIKNSDYISTITHYSPRTE 240
Tian    INILHPKFMTNTMRNAISLLGLTISKSTKPVTRNGIKHNIVVIKNSDYISTITHYSPRTE 240
Wyeth   INILHPKFMTNTMRNAISLLGLTISKSTKPVTRNGIKHNIVVIKNSDYISTITHYSPRTE 240
Lister  INILHPKFMTNTMRNAISLLGLTISKSTKPVTRNGIKHNIVVIKNSDYISTITHYSPRTE 240
        ************************************************************

cop     YWTIVGNTDRQFYNANVLHNCLYIIGGMINNRHVYSVSRVDLETKKWKTVTNMSSLKSEV 300
WR      YWTIVGNTDRQFYNANVLHNCLYIIGGMINNRHVYSVSRVDLETKKWKTVTNMSSLKSEV 300
Tian    YWTIVGNTDRQFYNANVLHNCLYIIGGMINNRHVYSVSRVDLETKKWKTVTNMSSLKSEV 300
Wyeth   YWTIVGNTDRQFYNANVLHNCLYIIGGMINNRHVYSVSRVDLETKKWKTVTNMSSLKSEV 300
Lister  YWTIVGNTDRQFYNANVLHNCLYIIGGMINNRHVYSVSRVDLKTKKWKTVTNMSSLKSEV 300
        ****************************************:*****************
```

```
cop     STCVNDGKLYVIGGLEFSISTGVAEYLKHGTSKWIRLPNLITPRYSGASVFVNDDIYVMG 360
WR      STCVNDGKLYVIGGLEFSISTGVAEYLKHGTSKWIRLPNLITPRYSGASVFVNDDIYVMG 360
Tian    STCVNNGKLYVIGGLEFSISTGVAEYLKHGTSKWIRLPNLITPRYSGASVFVNDDIYVMG 360
Wyeth   STCVNNGKLYVIGGLEFSISTGVAEYLKHGTSKWIRLPNLITPRYSGASVFVNDDIYVMG 360
Lister  STCVNDGKLYVIGGLEFSISTGVAEYLKHGTSKWIRLPNLITPRYSGASVFVNDDIYVMG 360
        *****:**************************************************

cop     GVYTTYEKYVVLNDVECFTKNRWIKKSPMPRHHSIVYAVEYDGDIYVITGITHETRNYLY 420
WR      GVYTTYEKYVVLNDVECFTKNRWIKKSPMPRHHSIVYAVEYDGDIYVITGITHETRNYLY 420
Tian    GVYTTYEKYVVLNDVECFTKNRWIKKSPMPRHHSIVYAVEYDGDIYVITGITHETRNYLY 420
Wyeth   GVYTTYEKYVVLNDVECFTKNRWIKKSPMPRHHSIVYAVEYDGDIYAITGITHETRNYLY 420
Lister  GVYTTYEKYVVLNDVECFTKNRWIKKSPMPRHHSIVYAVEYDGDIYVITGITHETRNYLY 420
        ********************************************.*************

cop     KYIVKEDKWIELYMYFNHVGKMFVCSCGDYILIIADAKYEYYPKSNTWNLFDMSTRNIEY 480
WR      KYIVKEDKWIELYMYFNHVGKMFVCSCGDYILIIADAKYEYYPKSNTWNLFDMSTRNIEY 480
Tian    KYIVKEDKWIELYMYFNHVGKMFVCSCGDYILIIADAKYEYYPKSNTWNLFDMSTRNIEY 480
Wyeth   KYIVKEDKWIELYMYFNHVGKMFVCSCGDYILIIADAKYEYYPKSNTWNLFDMSTRNIEY 480
Lister  KYIVKEDKWIELYMYFNHVGKMFVCSCGDYILIIADAKYEYYPKSNTWNLFDMSTRNIEY 480
        ************************************************************

cop     YDMFTKDETPKCNVTHKSLPSFLSNCEKQFLQ 512 (SEQ ID NO: 219)
WR      YDMFTKDETPKCNVTHKSLPSFLSNCEKQFLQ 512 (SEQ ID NO: 41)
Tian    YDMFTKDETPKCNVTHKSLPSFLSNCEKQFLQ 512 (SEQ ID NO: 58)
Wyeth   YDMFTKDET------HKSLPSFLSNCEKQFLQ 506 (SEQ ID NO: 74)
Lister  YDMFTKDETPKCNVTHKSLPSFLSNCEKQFLQ 512 (SEQ ID NO: 92)
        *********      *****************
```

C1L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop     MVKNNKI-----SNSCRMIMSTNPNNILMRHLKNLTDDEFKCIIHRSSDFLYLSDSDYTS 55
WR      MVKNNKIQKNKISNSCRMIMSTDPNNILMRHLKNLTDDEFKCIIHRSSDFLYLSDSDYTS 60
Tian    MVKNNKI-----SNSCRMIMSTDPNNILMRHLKNLTDDEFKCIIHRSSDFLYLSDSDYTS 55
Wyeth   MVKNNKI-----SNSCRMIMSTNPNNILMRHLKNLTDDEFKCIIHRSSDFLYLSDRDYTS 55
Lister  MVKNNKI-----SNSCRMIMSTNPNNILMRHLKNLTDDEFKCIIHRSSDFLYLSDSDYTS 55
        *******     **********:****************************** ****

Cop     ITKETLVSEIVEEYPDDCNKILAIIFLVLDKDIDVDIETKLKPKPAVRFAILDKMTEDIK 115
WR      ITKETLVSEIVEEYPDDCNKILAIIFLVLDKDIDVDIKTKLKPKPAVRFAILDKMTEDIK 120
Tian    ITKETLVSEIVEEYPDDCNKILAIIFLVLDKDIDVDIKTKLKPKPAVRFAILDKMTEDIK 115
Wyeth   ITKETLVSEIVEEYPDDCNKILAIIFLVLDKDIDVDIKTKLKPKPAVRFAILDKMTEDIK 115
Lister  ITKETLVSEIVEEYPDDCNKILAIIFLVLDKDIDVDIETKLKPKPAVRFAILDKMTADIK 115
        ************************************:***************** ***

Cop     LTDLVRHYFRYIEQDIPLGPLFKKIDSYRTRAINKYSKELGLATEYFNKYGHLMFYTLPI 175
WR      LTDLVRHYFRYIEQDIPLGPLFKKIDSYRTRAINKYSKELGLATEYFNKYGHLMFYTLPI 180
Tian    LTDLVRHYFRYIEQDIPLGPLFKKIDSYRTRAINKYSKELGLATEYFNKYGHLMFYTLPI 175
Wyeth   LTDLVRHYFRYIEQDIPLGPLFKKIDSYRTRAINKYSKELGLATEYFNKYGHLMFYTLPI 175
Lister  LTDLVRHYFRYIEQDIPLGPLFKKIDSYRTRAINKYSKELGLATEYFNKYGHLMFYTLPI 175
        ************************************************************

Cop     PYNRFFCRNSIGFLAVLSPTIGHVKAFYKFIEYVSIDDRRKFKKELMSK 224 (SEQ ID
NO: 24)
```

```
WR     PYNRFFCRNSIGFLAVLSPTIGHVKAFYKFIEYVSIDDRRKFKKELMSK 229 (SEQ ID
NO: 42)
Tian   PYNRFFCRNSIGFLAVLSPTIGHVKAFYKFIEYVSIDDRRKFKKELMSK 224 (SEQ ID
NO: 59)
Wyeth  PYNRFFCRNSIGFLAVLSPTIGHVKAFYKFIEYVSIDDRRKFKKELMSK 224 (SEQ ID
NO: 75)
Lister PYNRFFCRNSIGFLAVLSPTIGHVKAFYKFIEYVSIDDRRKFKKELMSK 224 (SEQ ID
NO: 93)
       ************************************************
```

N1L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MRTLLIRYILWRNDNDQTYYNDDFKKLMLLDELVDDGDVCTLIKNMRMTLSDGPLLDRLN 60
WR     MRTLLIRYILWRNDNDQTYYNDNFKKLMLLDELVDDGDVCTLIKNMRMTLSDGPLLDRLN 60
Tian   MRTLLIRYILWRNDNDQTYYNDDFKKLMLLDELVDDGDVCTLIKNMRMTLSDGPLLDRLN 60
Wyeth  MRTLLIRYILWRNDNDQTYYNDDFKKLMLLDELVDDGDVCTLIKNMRMTLSDGPLLDRLN 60
Lister MRTLLIRYILWRNDNDQTYYNDDFKKLMLLDELVDDGDVCTLIKNMRMTLSDGPLLDRLN 60
       ********************:***********************************

Cop    QPVNNIEDAKRMIAISAKVARDIGERSEIRWEESFTILFRMIETYFDDLMIDLYGEK 117
WR     QPVNNIEDAKRMIAISAKVARDIGERSEIRWEESFTILFRMIETYFDDLMIDLYGEK 117
Tian   QPVNNIEDAKRMIAISAKVARDIGERSEIRWEESFTILFRMIETYFDDLMIDLYGEK 117
Wyeth  QPVNNIEDAKRMIAISAKVARDIGERSEIRWEESFTILFRMIETYFDDLMIDLYGEK 117
Lister QPVNNIEDAKRMIAISAKVARDIGERSEIRWEESFTILFRMIETYFDDLMIDLYGEK 117
       ************************************************************
```

Cop (SEQ ID NO: 25)
WR (SEQ ID NO: 43)
Tian (SEQ ID NO: 60)
Wyeth (SEQ ID NO: 76)
Lister (SEQ ID NO: 94)

N2L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MTSSAMDNNEPKVLEMVYDATILPEGSSMDPNIMDCINRHINMCIQRTYSSSIIAILNRF 60
WR     MTSSAMDNNEPKVLEMVYDATILPEGSSMDPNIMDCINRHINMCIQRTYSSSIIAILDRF 60
Tian   MTSSAMDNNEPKVLEMVYDATILPEGSSMDPYIMDCINRHINMCIQRTYSSSIIAILDRF 60
Wyeth  MTSSAMDNNEPKVLEMVYDATILPEGSSMDPNIIDCINRHINMCIQRTYSSSIIAILDRF 60
Lister MTSSAMDNNEPKVLEMVYDATILPEGSSMDPNIMDCINRHINMCIQRTYSSSIIAILDRF 60
       ***************************** *:**********************:**

Cop    LTMNKDELNNTQCHIIKEFMTYEQMAIDHYGEYVNAILYQIRKRPNQHHTIDLFKKIKRT 120
WR     LMMNKDELNNTQCHIIKEFMTYEQMAIDHYGGYVNAILYQIRKRPNQHHTIDLFKRIKRT 120
Tian   LMMNKDELNNTQCHIIKNL---------------------------------------- 79
Wyeth  LTMNKDELNNTQCHIIKEFMTYEQMAIDHYGGYVNAILYQIRKRPNQHHTIDLFKKIKRT 120
Lister LTMNKDELNNTQCHIIKEFMTYEQMAIDHYGEYVNAILYQIRKRPNQHHTIDLFKKIKRT 120
       * ***************::

Cop    PYDTFKVDPVEFVKKVIGFVSILNKYKPVYSYVLYENVLYDEFKCFINYVETKYF 175
```

```
WR     RYDTFKVDPVEFVKKVIGFVSILNKYKPVYSYVLYENVLYDEFKCFINYVETKYF 175
Tian   ---------------------------------------------------- 
Wyeth  RYDTFKVDPVEFVKKVIGFVSILNKYKPVYSYVLYENVLYDEFKCFIDYVETKYF 175
Lister RYDTFKVDPVEFVKKVIGFVSILNKYKPVYSYVLYENVLYDEFKCFIDYVETKYF 175
```

Cop (SEQ ID NO: 26)
WR (SEQ ID NO: 44)
Tian (SEQ ID NO: 61)
Wyeth (SEQ ID NO: 77)
Lister (SEQ ID NO: 95)

M1L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MIFVIESKLLQIYRNRNRNINFYTTMDNIMSAEYYLSLYAKYNSKNLDVFRNMLQAIEPS 60
WR     MIFVIESKLLQIYRNRNRNINFYTTMDNIMSAEYYLSLYAKYNSKNLDVFRNMLQAIEPS 60
Tian   MIFVIESKLLQIYRNRNRNINFYTTMDNIMSAEYYLSLYAKYNSKNLDVFRNMLQAIEPS 60
Wyeth  MIFVIESKLLQIYRNRNRNINFYTTMDNIMSAEYYLSLYAKYNSKNLDVFRNMLQAIEPS 60
Lister MIFVIESKLLQIYRN--RNINFYTTMDNIMSAEYYLSLYAKYNSKNLDVFRNMLQAIEPS 58
       ***************  ****************************************

Cop    GNNYHILHAYCGIKGLDERFVEELLHRGYSPNETDDDGNYPLHIASKINNNRIVAMLLTH 120
WR     GNNYHILHAYCGIKGLDERFVEELLHRGYSPNETDDDGNYPLHIASKINNNRIVAMLLTH 120
Tian   GNNYHILHAYCGIKGLDERFVEELLHRGYSPNETDDDGNYPLHIASKINNNRIVAMLLTH 120
Wyeth  GNNYHILHAYCGIKGLDERFVEELLHRGYSPNETDDDGNYPLHIASKINNNRIVAMLLTH 120
Lister GNNYHILHAYCGIKGLDERFVEELLHRGYSPNETDDDGNYPLHIASKINNNRIVAMLLTH 118
       ************************************************************

Cop    GADPNACDKHNKTPLYYLSGTDDEVIERINLLVQYGAKINNSVDEEGCGPLLACTDPSER 180
WR     GADPNACDKHNKTPLYYLSGTDDEVIERINLLVQYGAKINNSVDEEGCGPLLACTDPSER 180
Tian   GADPNACDKHNKTPLYYLSGTDDEVIERINLLVQYGAKINNSVDEEGCGPLLACTDPSER 180
Wyeth  GADPNACDKHNKTPLYYLSGTDDEVIERINLLVQYGAKINN------------------- 161
Lister GADPNACDKQHKTPLYYLSGTDDEVIERINLLVQYGAKINNSVDEEGCGPLLACTDPSER 178
       *********::****************************

Cop    VFKKIMSIGFEARIVDKFGKNHIHRHLMSDNPKASTISWMMKLGISPSKPDHDGNTPLHI 240
WR     VFKKIMSIGFEARIVDKFGKNHIHRHLMSDNPKASTISWMMKLGISPSKPDHDGNTPLHI 240
Tian   VFKKIMSIGFEARIVDKFGKNHIHRHLMSDNPKASTISWMMKLGISPSKPDHDGNTPLHI 240
Wyeth  ------------------------------------------------------------
Lister VFKKIMSIGFEARIVDKFGKNHIHRHLMSDNPKASTISWMMKLGISPSKPDHDGNTPLHI 238


Cop    VCSKTVKNVDIIDLLLPSTDVNKQNKFGDSPLTLLIKTLSPAHLINKLLSTSNVITDQTV 300
WR     VCSKTVKNVDIIDLLLPSTDVNKQNKFGDSPLTLLIKTLSPAHLINKLLSTSNVITDQTV 300
Tian   VCSKTVKNVDIIDLLLPSTDVNKQNKFGDSPLTLLIKTLSPAHLINKLLSTSNVITDQTV 300
Wyeth  ------------------------------------------------------------
Lister VCSKTVKNVDIIDLLLPSTDVNKQNKFGDSPLTLLIKTLSPAHLINKLLSTSNVITDQTV 298


Cop    NICIFYDRDDVLEIINDKGKQYDSTDFKMAVEVGSIRCVKYLLDNDIICEDAMYYAVLSE 360
WR     NICIFYDRDDVLEIINDKGKQYDSTDFKMAVEVGSIRCVKYLLDNDIICEDAMYYAVLSE 360
Tian   NICIFYDRDDVLEIINDKGKQYDSTDFKMAVEVGSIRCVKYLLDNDIICEDAMYYAVLSE 360
Wyeth  ------------------------------------------------------------
```

```
Lister NICIFYDRDDVLEIINDKGKQYDSTDFKMAVEVGSIRCVKYLLDNDIICEDAMYYAVLSE 358


Cop    YETMVDYLLFNHFSVDSVVNGHTCMSECVRLNNPVILSKLMLHNPTSETMYLTMKAIEKD 420
WR     YETMVDYLLFNHFSVDFVVNGHTCMSECVRLNNPVILSKLMLHNPTSETMYLTMKAIEKD 420
Tian   YETMVDYLLFNHFSVDFVVNGHTCMSECVRLNNPVILSKLMLHNLTSETMYLTMKAIEKD 420
Wyeth  ------------------------------------------------------------
Lister YETMVDYLLFNHFSVDSVVNGHTCMSECVRLNNPVILSKLMLHNPTSETMYLTMKAIEKD 418


Cop    KLDKSIIIPFIAYFVLMHPDFCKNRRYFTSYKRFVTDYVHEGVSYEVFDDYF 472
WR     RLDKSIIIPFIAYFVLMHPDFCKNRRYFTSYKRFVTDYVHEGVSYEVFDDYF 472
Tian   RLDKSIIIPFIAYFVLMHPDFCKNRRYFTSYKRFVTDYVHEGVSYEVFDDYF 472
Wyeth  ----------------------------------------------------
Lister RLDKSIIIPFIAYFVLMHPDFCKNRRYFTSYKRFVTDYVHEGVSYEVFDDYF 470

Cop  (SEQ ID NO: 27)
WR  (SEQ ID NO: 45)
Tian  (SEQ ID NO: 62)
Wyeth  (SEQ ID NO: 80)
Lister  (SEQ ID NO: 96)
```

M2L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MVYKLVLLFCIASLGYSVEYKNTICPPRQDYRYWYFAAELTIGVNYDINSTIIGECHMSE 60
WR     MVYKLVLLFCIASLGYSVEYKNTICPPRQDYRYWYFAAELTIGVNYDINSTIIGECHMSE 60
Tian   ----------------------MSSSTRLPVLVLAAELTIGVNYDINSTIIGECHMSE 36
Wyeth  MVYKLVLLFCIASLGYSVEYKNTICPPRQDYRYWYFAAELTIGVNYDINSTIIGECHMSE 60
Lister MVYKLVLLFCIASLGYSVEYKNTICPPRQDYRYWYFAAELTIGVNYDINSTIIGECHMSE 60
                                          :************************

Cop    SYIDRNANIVLTGYGLEINMTIMDTDQRFVAAAEGVGKDNKLSVLLFTTQRLDKVHHNIS 120
WR     SYIDRNANIVLTGYGLEINMTIMDTDQRFVAAAEGVGKDNKLSVLLFTTQRLDKVHHNIS 120
Tian   SYIDRNANIVLTGYGLEINMTIMDTDQRFVAAAEGVGKDNKLSVLLFTTQRLDKVHHNIS 96
Wyeth  SYIDRNANIVLTGYGLEINMTIMDTDQRFVAAAEGVGKDNKLSVLLFTTQRLDKVHHNIS 120
Lister SYIDRNANIVLTGYGLEINMTIMDTDQRFVAAAEGVGKDNKLSVLLFTTQRLDKVHHNIS 120
       ************************************************************

Cop    VTITCMEMNCGTTKYDSDLPESIHKSSSCDITINGSCVTCVNLETDPTKINPHYLHPKDK 180
WR     VTITCMEMNCGTTKYDSDLPESIHKSSSCDITINGSCVTCVNLETDPTKINPHYLHPKDK 180
Tian   VTITCMEMNCGTTKYDSDLPESIHKSSSCDITINGSCVTCVNLETDPTKINPHYLHPKDK 156
Wyeth  VTITCMEMNCGTTKYDSDLPESIHKSSSCDITINGSCVTCVNLETDPTKINPHYLHPKDK 180
Lister VTITCMEMNCGTTKYDSDLPESIHKSSSCDITINGSCVTCVNLETDPTKINPHYLHPKDK 180
       ************************************************************

Cop    YLYHNSEYGMRGSYGVTFIDELNQCLLDIKELSYDICYRE 220 (SEQ ID NO: 28)
WR     YLYHNSEYSMRGSYGVTFIDELNQCLLDIKELSYDICYRE 220 (SEQ ID NO: 46)
Tian   YLYHNSEYGMRGSYGVTFIDELNQCLLDIKELSYDICYRE 196 (SEQ ID NO: 63)
Wyeth  YLYHNSEYGMRGSYGVTFIDELNQCLLDIKELSYDICYRE 220 (SEQ ID NO: 81)
Lister YLYHNSEYGMRGSYGVTFIDELNQCLLDIKELSYDICYRE 220 (SEQ ID NO: 97)
       ********.*******************************
```

K1L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop     MDLSRINTWKSKQLKSFLSSKDTFKADVHGHSALYYAIADNNVRLVCTLLNAGALKNLLE 60
WR      MDLSRINTWKSKQLKSFLSSKDAFKADVHGHSALYYAIADNNVRLVCTLLNAGALKNLLE 60
Tian    MDLSRINTWKSKQLKSFLSSKDTFKADVHGHSALYYAIADNNVRLVCTLLNSGALKNLLE 60
Wyeth   MDLSRINTWKSKQLKSFLSSKDTFKADVHGHSALYYAIADNNVRLVCTLLNAGALKNLLE 60
Lister  MDLSRINTWKSKQLKSFLSSKDAFKADINGHSALYYAIADNNVRLVCTLLNAGALKNLLE 60
        **********************:****::**********************:********

Cop     NEFPLHQAATLEDTKIVKILLFSGMDDSQFDDKGNTALYYAVDSGNMQTVKLFVKKNWRL 120
WR      NEFPLHQAATLEDTKIVKILLFSGLDDSQFDDKGNTALYYAVDSGNMQTVKLFVKKNWRL 120
Tian    NEFPLHQAATLEDTKIVKILLFSGLDDSQFDDKGNTALYYAVDSGNMQTVKLFVKKNWRL 120
Wyeth   NEFPLHQAATLEDTKIVKILLFSGLDDSQFDDKGNTALYYAVDSGNMQTVKLFVKKNWRL 120
Lister  NEFPLHQAATLEDTKIVKILLFSGLDDSQFDDKGNTALYYAVDSGNMQTVKLFVKKNWRL 120
        ************************:**********************************

Cop     MFYGKTGWKTSFYHAVMLNDVSIVSYFLSEIPSTFDLAILLSCIHTTIKNGHVDMMILLL 180
WR      MFYGKTGWKTSFYHAVMLNDVSIVSYFLSEIPSTFDLAILLSCIHITIKNGHVDMMILLL 180
Tian    MFYGKTGWKTSFYHAVMLNDVSIVSYFLSEIPSTFDLAILLSCIHITIKNGHVDMMILLL 180
Wyeth   MFYGKTGWKTSFYHAVMLNDVSIVSYFLSEIPSTFDLAILLSCIHITIKNGHVDMMILLL 180
Lister  MFYGKTGWKTSFYHAVMLNDVSIVSYFLSEIPSTFDLAILLSCIHITIKNGHVDMMILLL 180
        ******************************************** **************

Cop     DYMTSTNTNNSLLFIPDIKLAIDNKDIEMLQALFKYDINIYSVNLENVLLDDAEITKMII 240
WR      DYMTSTNTNNSLLFIPDIKLAIDNKDIEMLQALFKYDINIYSANLENVLLDDAEIAKMII 240
Tian    DYMTVDKHQ-------------------------------------------------- 189
Wyeth   DYMTSTNTNNSLLFIPDIKLAIDNKDIEMLQALFKYDINIYSANLENVLLDDAEIAKMII 240
Lister  DYMTSTNTNNSLLFIPDIKLAIDNKDIEMLQALFKYDINIYSANLENVLLDDAEIAKMII 240
        ****  : :

Cop     EKHVEYKSDSYTKDLDIVKNNKLDEIISKNKELRLMYVNCVKKN 284 (SEQ ID NO: 29)
WR      EKHVEYKSDSYTKDLDIVKNNKLDEIISKNKELRLMYVNCVKKN 284 (SEQ ID NO: 47)
Tian    ------------------------------------------- (SEQ ID NO: 65)
Wyeth   EKHVEYKSDSYTKDLDIVKNNKLDEIISKNKELRLMYVNCVKKN 284 (SEQ ID NO: 82)
Lister  EKHVEYKSDSYTKDLDIVKNNKLDEIISKNKELKLMYVNCVKKN 284 (SEQ ID NO: 98)
```

K2L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop     MIALLILSLTCSVSTYRLQGFTNAGIVAYKNIQDDNIVFSPFGYSFSMFMSLLPASGNTR 60
WR      MIALLILSLTCSVSTYRLQGFTNAGIVAYKNIQDDNIVFSPFGYSFSMFMSLLPASGNTR 60
Tian    MIALLILSLACSASAYRLQGFTNAGIVAYKNIQDDNIVFSPFGYSFSMFMSLLPASGNTR 60
Wyeth   MIALLILSLTCSVSTYRLQGFTNAGIVAYKNIQDDNIVFSPFGYSFSMFMSLLPASGNTR 60
Lister  ------------------------------------------------------------

Cop     IELLKTMDLRKRDLGPAFTELISGLAKLKTSKYTYTDLTYQSFVDNTVCIKPLYYQQYHR 120
WR      IELLKTMDLRKRDLGPAFTELISGLAKLKTSKYTYTDLTYQSFVDNTVCIKPSYYQQYHR 120
Tian    IELLKTMDLRKRDLGPAFTELISGLAKLKTSKYTYTDLTYQSFVDNTVCIKPSYYQQYHR 120
```

```
Wyeth  IELLKTMDLRKRDLGPAFTELISGLAKLKTSKYTYTDLTYQSFVDNTVCIKPSYYQQYHR 120
Lister IELLKTMDLRKRDLGPAFTELISGLAKLKTSKYTYTDLTYQSFVDNTVCIKPSYYQQYHR 60
       ************************************************** *******

Cop    FGLYRLNFRRDAVNKINSIVERRSGMSNVVDSNMLDNNTLWAIINTIYFKGTWQYPFDIT 180
WR     FGLYRLNFRRDAVNKINSIVERRSGMSNVVDSNMLDNNTLWAIINTIYFKGIWQYPFDIT 180
Tian   FGLYRLNFRRDAVNKINSIVERRSGMSNVVDSNMLDNNTLWAIINTIYFKGTWQYPFDIT 180
Wyeth  -----LNFRRDAVNKINSIVERRSGMSNVVDSNMLDNNTLWAIINTIYFKGIWQYPFDIT 175
Lister FGLYRLNFRRDAVNKINSIVERRSGMSNVVDSNMLDNNTLWAIINTIYFKGIWQYPFDIT 120
            ****************************************** ********

Cop    KTRNASFTNKYGTKTVPMMNVVTKLQGNTITIDDEEYDMVRLPYKDANISMYLAIGDNMT 240
WR     KTRNASFTNKYGTKTVPMMNVVTKLQGNTITIDDEEYDMVRLPYKDANISMYLAIGDNMT 240
Tian   KTRNASFTNKYGTKTVPMMNVVTKLQGNTITIDDEEYDMVRLPYKDANISMYLAIGDNMT 240
Wyeth  KTRNASFTNKYGTKTVPMMNVVTKLQGNTITIDDKEYDMVRLPYKDANISMYLAIGDNMT 235
Lister KTRNASFTNKYGTKTVPMMNVVTKLQGNTITIDDEEYDMVRLPYKDANISMYLAIGDNMT 180
       **********************************:************************

Cop    HFTDSITAAKLDYWSFQLGNKVYNLKLPKFSIENKRDIKSIAEMMAPSMFNPDNASFKHM 300
WR     HFTDSITAAKLDYWSFQLGNKVYNLKLPKFSIENKRDIKSIAEMMAPSMFNPDNASFKHM 300
Tian   HFTDSITAA-KDYWSFQLGNKVYNLKLPKFSIENKRDIKSIAEMMAPSMFNPDNASFKHM 299
Wyeth  HFTDSITAAKLDYWSFQLGNKVYNLKLPKFSIENKRDIKSIAEMMAPSMFNPDNASFKHM 295
Lister HFTDSITAAKLDYWSSQLGNKVYNLKLPKFSIENKRDIKSIAEMMAPSMFNPDNASFKHM 240
       *********  **** ****************************************

Cop    TRDPLYIYKMFQNAKIDVDEQGTVAEASTIMVATARSSPEKLEFNTPFVFIIRHDITGFI 360
WR     TRDPLYIYKMFQNAKIDVDEQGTVAEASTIMVATARSSPEKLEFNTPFVFIIRHDITGFI 360
Tian   TRDPLYIYKMFQNAKIDVDEQGTVAEASTIMVATARSSPEELEFNTPFVFIIRHDITGFI 359
Wyeth  TRDPLYIYKMFQNAKIDVDEQGTVAEASTIMVATARSSPEKLEFNTPFVFIIRHDITGFI 355
Lister TRDPLYIYKMFQNAKIDVDEQGTVAEASTIMVATARSSPEKLEFNTPFVFIIRHDITGFI 300
       **************************************:*******************

Cop    LFMGKVESP 369 (SEQ ID NO: 30)
WR     LFMGKVESP 369 (SEQ ID NO: 48)
Tian   LFMGKVESP 368 (SEQ ID NO: 66)
Wyeth  LFMGKVESP 364 (SEQ ID NO: 83)
Lister LFMGKVESP 309 (SEQ ID NO: 547)
       *********
```

K ORF A

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop  MGHIITYCQVHTNISILIRKAHHIIFFVIDCDCISLQFSNYVHHGNRFRTVLISKTSIAC 60
Tian MGHIITYCQVHTNISILIRKAYHIIFFVIDCDCISLQFSNYVHHGNRFRTVLISKTSIAC 60
     ********************:************************************

Cop  FSDIKRILPCTFKIYSINDCP 81 (SEQ ID NO: 31)
Tian FSDIKRILPCTFKIYSINDCP 81 (SEQ ID NO: 67)
     *********************
```

K3L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop     MLAFCYSLPNAGDVIKGRVYEKDYALYIYLFDYPHSEAILAESVKMHMDRYVEYRDKLVG 60
WR      MLAFCYSLPNAGDVIKGRVYEKDYALYIYLFDYPHFEAILAESVKMHMDRYVEYRDKLVG 60
Tian    MLAFCYSLPNAGDVIKGRVYEKDYALYIYLFDYPHSEAILAESVKMHMDRYVEYRDKLVG 60
Wyeth   MLAFCYSLPNAGDVIKGRVYENDYALYIYLFDYPHFEAILAESVKMHMDRYVEYRDKLVG 60
Lister MLAFCYSLPNAGDVIKGRVYENDYALYIYLFDYPHSEAILAESVKMHMDRYVEYRDKLVG 60
       ********************:************* ************************

Cop     KTVKVKVIRVDYTKGYIDVNYKRMCRHQ 88 (SEQ ID NO: 33)
WR      KTVKVKVIRVDYTKGYIDVNYKRMCRHQ 88 (SEQ ID NO: 49)
Tian    KTVKVKVIRVDYTKGYIDVNYKRMCRHQ 88 (SEQ ID NO: 68)
Wyeth   KTVKVKVIRVDYTKGYIDVNYKRMCRHQ 88 (SEQ ID NO: 84)
Lister KTVKVKVIRVDYTKGYIDVNYKRMCRHQ 88 (SEQ ID NO: 100)
       ****************************
```

K4L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop     MNPDNTIAVITETIPIGMQFDKVYLSTFNMWREILSNTTKTLDISSFYWSLSDEVGTNFG 60
WR      MNPDNTIAVITETIPIGMQFDKVYLSTFNMWREILSNTTKTLDISSFYWSLSDEVGTNFG 60
Wyeth   MNPDNTIAVITETIPIGMQFDKVYLSTFNMWREILSNTTKTLDISSFYWSLSDEVGTNFG 60
Lister MNPDNTIAVITETIPIGMQFDKVYLSTFNMWREILSNTTKTLDISSFYWSLSDEVGTNFG 60
       ************************************************************

Cop     TIILNEIVQLPKRGVRVRVAVNKSNKPLKDVERLQMAGVEVRYIDITNILGGVLHTKFWI 120
WR      TIILNKIVQLPKRGVRVRVAVNKSNKPLKDVERLQMAGVEVRYIDITNILGGVLHTKFWI 120
Wyeth   TIILNEIVQLPKRGVRVRVAVNKSNKPLKDVERLQMAGVEVRYIDITNILGGVLHTKFWI 120
Lister TIILNEIVQLPKRGVRVRVAVNKSNKPLKDVERLQMAGVEVRYIDITNILGGVLHTKFWI 120
       *****:******************************************************

Cop     SDNTHIYLGSANMDWRSLTQVKELGIAIFNNRNLAADLTQIFEVYWYLGVNNLPYNWKNF 180
WR      SDNTHIYLGSANMDWRSLTQVKELGIAIFNNRNLAADLTQIFEVYWYLGVNNLPYNWKNF 180
Wyeth   SDNTHIYLGSANMDWRSLTQVKELGIAIFNNRNLAADLTQIFEVYWYLGVNNLPYNWKNF 180
Lister SDNTHIYLGSANMDWRSLTQVKELGIAIFNNRNLAADLTQIFEVYWYLGVNNLPYNWKNF 180
       ************************************************************

Cop     YPSYYNTDHPLSINVSGVPHSVFIASAPQQLCTMERTNDLTALLSCIRNASKFVYVSVMN 240
WR      YPSYYNTDHPLSINVSGVPHSVFIASAPQQLCTMERTNDLTALLSCIRNASKFVYVSVMN 240
Wyeth   YPSYYNTDHPLSINVSGVPHSVFIASAPQQLCTMERTNDLTALLSCIRNASKFVYVSVMN 240
Lister YPSYYNTDHPLSINVSGVPHSVFIASAPQQLCTMERTNDLTALLSCIRNASKFVYVSVMN 240
       ************************************************************

Cop     FIPIIYSKAGKILFWPYIEDELRRSAIDRQVSVKLLISCWQRSSFIMRNFLRSIAMLKSK 300
WR      FIPIIYSKAGNILFWPYIEDELRRAAIDRQVSVKLLISCWQRSSFIMRNFLRSIAMLKSK 300
Wyeth   FIPIIYSKAGKILFWPYIEDELRRSAIDRQVSVKLLISCWQRSSFIMRNFLRSIAMLKSK 300
Lister FIPIIYSKAGKILFWPYIEDELRRSAIDRQVSVKLLISCWQRSSFIMRNFLRSIAMLKSK 300
       **********:*************:**********************************

Cop     NIDIEVKLFIVPDADPPIPYSRVNHAKYMVTDKTAYIGTSNWTGNYFTDTCGASINITPD 360
WR      NINIEVKLFIVPDADPPIPYSRVNHAKYMVTDKTAYIGTSNWTGNYFTDTCGASINITPD 360
Wyeth   NINIEVKLFIVPDADPPIPYSRVNHAKYMVTDKTAYIGTSNWTGNYFTDTCGASINITPD 360
Lister NINIEVKLFIVPDADPPIPYSRVNHAKYMVTDKTAYIGTSNWTGNYFTDTCGASINITPD 360
       **:********************************************************
```

```
Cop     DGLGLRQQLEDIFMRDWNSKYSYELYDTSPTKRCKLLKNMKQCTNDIYCDEIQPEKEIPE 420
WR      DGLGLRQQLEDIFMRDWNSKYSYELYDTSPTKRCRLLKNMKQCTNDIYCDEIQPEKEIPE 420
Wyeth   DGLGLRQQLEDIFMRDWNSKYSYELYDTSPTKRCKLLKNMKQCTNDIYCDEIQPEKEIPE 420
Lister  DGLGLRQQLEDIFMRDWNSKYSYELYDTSPTKRCKLLKNMKQCTNDIYCDEIQPEKEIPE 420
        ********************************:************************

Cop     YSLE 424 (SEQ ID NO: 34)
WR      YSLE 424 (SEQ ID NO: 50)
Wyeth   YSLE 424 (SEQ ID NO: 85)
Lister  YSLE 424 (SEQ ID NO: 101)
        ****
```

K5L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop     -------------MGATISILASYDNPNLFTAMILMSPLVNADAVSRLNLLAAKLMGTIT 47
WR      MTLVQHVVTIKSTYWVIPWELASYDNPNLFTAMILMSPLVNADAVSKLNLLAAKLMGTIT 60
Tian    MTLVQHVVTIKSTYWVIPWELASYDNPNLFTAMILMSPLVNADAVSKLNLLAAKLMGTIT 60
Wyeth   -------------MGATISILASYDNPNLFTAMILMSPLVNADAVSKLNLLAAKLMGTIT 47
Lister  ---------MGHSMGATISILASYDNPNLFTAMILMSPLVNADAVSRLNLLAAKLMGTIT 51
                      .    *************************:*************

Cop     PNAPVGKLCPESVSRDMDKVYKYQYDPLINHEKIKAGFASQVLKATNKVRKIISKINTPR 107
WR      LNAPVGKLCPESVSRDMDKVYKYQYDPLINHEKIKAGFASQVLKATNKVRKIISKINTPR 120
Tian    LNAPVGKLCPESVSRDMDKVYKYQYDPLINHEKIKAGFASQVLKATNKVRKIISKINTPR 120
Wyeth   PNAPVGKLCPESVSRDMDKVYKYQYDPLINHEKIKAGFASQVLKATNKVRKIISKINTPP 107
Lister  PNAPVGKLCPESVSRDMDKVYKYQYDPLINHEKIKAGFASQVLKATNKVRKIISKINTPP 111
         ******************************************************

Cop     LSYSREQTMRL-----VMFQVHIISCNMQIVIE--------------------------- 135
WR      LSYSREQTIRL-----AMF---------------------------------------- 134
Tian    LSYSREQTIRL-----AMF---------------------------------------- 134
Wyeth   TLILQGTNNEISDVLGAYYFMQHANCNREIKIYEGAKHHLHKETDEVKKSVMKEIETWIF 167
Lister  TLILQGTNNKISDVLGAYYFMQHANCNREIKIYEGAKHHLHKETDEVKKSVMKEIETWIF 171
            :  . .:     . :

Cop     ---- (SEQ ID NO: 35)
WR      ---- (SEQ ID NO: 52)
Tian    ---- (SEQ ID NO: 69)
Wyeth   NRVK 171 (SEQ ID NO: 86)
Lister  NRVK 175 (SEQ ID NO: 102)
```

K6L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop     MSANCMFNLDNDYIYWKPITYPKALVFISHGAGKHSGRYDELAENISSLGILVFSHDHIG 60
WR      MSANCMFNLDNDYIYWKPITYPKALVFISHGAGKHSGRYDELAENISSLGILVFSHDHIG 60
Wyeth   MSANCMFNLDNDYIYWKPITYPKALVFISHGAGKHSGRYDELAENISSLGILVFSHDHIG 60
```

```
Lister MSANCMFNLDNDYIYWKPITYPKALVFISHGAGKHSGRYDELAENISSLGILVFSHDHIG 60
       ************************************************************

Cop    HGRSNGEKMMIDDFGTARGNY 81 (SEQ ID NO: 36)
WR     HGRSNGEKMMIDDFGTARGNY 81 (SEQ ID NO: 53)
Wyeth  HGRSNGEKMMIDDFGTARGNY 81 (SEQ ID NO: 87)
Lister HGRSNGEKMMIDDFGTARGNY 81 (SEQ ID NO: 103)
       *********************
```

K7R

```
CLUSTAL O(1.2.4) multiple sequence alignment

Cop     MATKLDYEDAVFYFVDDDKICSRDSIIDLIDEYITWRNHVIVFNKDITSCGRLYKELMKF 60
WR      MATKLDYEDAVFYFVDDDKICSRDSIIDLIDEYITWRNHVIVFNKDITSCGRLYKELMKF 60
Tian    MATKLDYEDAVFYFVDDDKICSRDSIIDLIDEYITWRNHVIVFNKDITSCGRLYKELMKF 60
Wyeth   MATKLDYEDAVFYFVDDDKICSRDSIIDLIDEYITWRNHVIVFNKDITSCGRLYKELMKF 60
Lister MATKLDYEDAVFYFVDDDKICSRDSIIDLIDEYITWRNHVIVFNKDITSCGRLYKELMKF 60
       ************************************************************

Cop     DDVAIRYYGIDKINEIVEAMSEGDHYINFTKVHDQESLFATIGICAKITEHWGYKKISES 120
WR      DDVAIRYYGIDKINEIVEAMSEGDHYINFTKVHDQESLFATIGICAKITEHWGYKKISES 120
Tian    DDVAIRYYGIDKINEIVEAMSEGDHYINFTKVHDQESLFATIGICAKITEHWGYKKISES 120
Wyeth   DDVAIRYYGIDKINEIVEAMSEGDHYINFTKVHDQESLFATIGICAKITEHWGYKKISES 120
Lister DDVAIRYYGIDKINEIVEAMSEGDHYINFTKVHDQESLFATIGICAKITEHWGYKKISES 120
       ************************************************************

Cop     RFQSLGNITDLMTDDNINILILFLEKKLN 149 (SEQ ID NO: 37)
WR      RFQSLGNITDLMTDDNINILILFLEKKLN 149 (SEQ ID NO: 54)
Tian    RFQSLGNITDLMTDDNINILILFLEKKLN 149 (SEQ ID NO: 70)
Wyeth   RFQSLGNITDLMTDDNINILILFLEKKLN 149 (SEQ ID NO: 88)
Lister RFQSLGNITDLMTDDNINILILFLEKKLN 149 (SEQ ID NO: 104)
       *****************************
```

F1L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop     MLSMFMCNNIVDYVDDIDNGIVQDIEDEASNNVDHDYVYPLPENMVYRFDKSTNILDYLS 60
WR      MLSMFMCNNIVDYVDDIDNGIVQDIEDEASNNVDHDYVYPLPENMVYRFDKSTNILDYLS 60
Tian    MLSMFMCNNIVDYVDDIDNGIVQDIEDEASNNVDRDYVYPLPENMVYRFDKSTNILDYLS 60
Wyeth   MLSMFMCNNIVDYVDDIDNGIVQDIEDEASNNVDHDYVYPLPENMVYRFDKSTNILDYLS 60
Lister MLSMFMCNNIVDYVDDIDNGIVQDIEDEASNNVDHDYVYPLPENMVYRFDKSTNILDYLS 60
       *********************************:**************************

Cop     TERDHVMMAVRYYMSKQRLDDLYRQLPTKTRSYIDIINIYCDKVSNDYNRDMNIMYDMAS 120
WR      TERDHVMMAVRYYMSKQRLDDLYRQLPTKTRSYIDIINIYCDKVSNDYNRDMNIMYDMAS 120
Tian    TERDHVMMAVRYYMSKQRLDDLYRQLPTKTRSYIDIINIYCDKVSNDYNRDMNIMYDMAS 120
Wyeth   TERDHVMMAVRYYMSKQRLDDLYRQLPTKTRSYIDIINIYCDKVSNDYNRDMNIMYDMAS 120
Lister TERDHVMMAVRYYMSKQRLDDLYRQLPTKTRSYIDIINIYCDKVSNDYNRDMNIMYDMAS 120
       ************************************************************

Cop     TKSFTVYDINNEVNTILMDNKGLGVRLATISFITELGRRCMNPVKTIKMFTLLSHTICDD 180
WR      TKSFTVYDINNEVNTILMDNKGLGVRLATISFITELGRRCMNPVETIKMFTLLSHTICDD 180
Tian    TKSFTVYDINNEVNTILMDNKGLGVRLATISFITELGRRCMNPVKTIKMFTLLSHTICDD 180
Wyeth   TKSFTVYDINNEVNTILMDNKGLGVRLATISFITKLGRRCMNPVKTIKMFTLLSHTICDD 180
Lister TKSFTVYDINNEVNTILMDNKGLGVRLATISFITELGRRCMNPVKTIKMFTLLSHTICDD 180
       *********************************:*********:***************

Cop     CFVDYITDISPPDNTIPNTSTREYLKLIGITAIMFATYKTLKYMIG 226 (SEQ ID NO:
38)
```

```
WR     YFVDYITDISPPDNTIPNTSTREYLKLIGITAIMFATYKTLKYMIG 226 (SEQ ID NO:
55)
Tian   CFVDYITDISPPDNTIPNTSTREYLKLIGITAIMFATYKTLKYMIG 226 (SEQ ID NO:
71)
Wyeth  CFVDYITDISPPDNTIPNTSTREYLKLIGITAIMFATYKTLKYMIG 226 (SEQ ID NO:
89)
Lister CFVDYITDISPPDNTIPNTSTREYLKLIGITAIMFATYKTLKYMIG 226 (SEQ ID NO:
105)
       *******************************************
```

F2L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MFNMNINSPVRFVKETNRAKSPTRQSPGAAGYDLYSAYDYTIPPGERQLIKTDISMSMPK 60
WR     MFNMNINSPVRFVKETNRAKSPTRQSPYAAGYDLYSAYDYTIPPGERQLIKTDISMSMPK 60
Tian   MFNMNINSPVRFVKETNRAKSPTRQSPGAAGYDLYSAYDYTIPPGERQLIKTDISMSMPK 60
Wyeth  MFNMNINSPVRFVKETNRAKSPTRQSPGAAGYDLYSAYDYTIPPGERQLIKTDISMSMPK 60
Lister MFNMNINSPVRFVKETNRAKSPTRQSPGAAGYDLYSAYDYTIPPGERQLIKTDISMSMPK 60
       ************************* ******************************

Cop    ICYGRIAPRSGLSLKGIDIGGGVIDEDYRGNIGVILINNGKCTFNVNTGDRIAQLIYQRI 120
WR     FCYGRIAPRSGLSLKGIDIGGGVIDEDYRGNIGVILINNGKCTFNVNTGDRIAQLIYQRI 120
Tian   ICYGRIAPRSGLSLKGIDIGGGVIDEDYRGNIGVILINNGKCTFNVNTGDRIAQLIYQRI 120
Wyeth  ICYGRIAPRSGLSLKGIDIGGGVIDEDYRGNIGVILINNGKCTFNVNTGDRIAQLIYQRI 120
Lister FCYGRIAPRSGLSLKGIDIGGGVIDEDYRGNIGVILINNGKCTFNVNTGDRIAQLIYQRI 120
       :************************************************************

Cop    YYPELEEVQSLDSTNRGDQGFGSTGLR 147 (SEQ ID NO: 39)
WR     YYPELEEVQSLDSTNRGDQGFGSTGLR 147 (SEQ ID NO: 56)
Tian   YYPELEEVQSLDSTDRGDQGFGSTGLR 147 (SEQ ID NO: 72)
Wyeth  YYPELEEVQSLDSTNRGDQGFGSTGLR 147 (SEQ ID NO: 90)
Lister YYPELEEVQSLDSTNRGDQGFGSTGLR 147 (SEQ ID NO: 106)
       **************:************
```

F3L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MPIFVNTVYCKNILALSMTKKFKTIIDAIGGNIIVNSTILKKLSPYFRTHLRQKYTKNKD 60
WR     MPIFVNTVYCKNILALSMTKKFKTIIDAIGGNIIVNSTILKKLSPYFRTHLRQKYTKNKD 60
Tian   MPIFVNTVYCKNILALSMTKKFKTIIDAIGGNIIVNSTILKKLSPYFRTHLRQKYTKNKD 60
Wyeth  MPIFVNTVYCKNILALSMTKKFKTIIDAIGGNIIVNSTILKKLSPYFRTHLRQKYTKNKD 60
Lister MPIFVNTVYCKNILALSMTKKFKTIIDAIGGNIIVNSTILKKLSPYFRTHLRQKYTKNKD 60
       ************************************************************

Cop    PVTRVCLDLDIHSLTSIVIYSYTGKVYIDSHNVVNLLRASILTSVEFIIYTCINFILRDF 120
WR     PVTWVCLDLDIHSLTSIVIYSYTGKVYIDSHNVVNLLRASILTSVEFIIYTCINFILRDF 120
Tian   PVTRVCLDLDIHSLTSIVIYSYTGKVYIDSHNVVNLLRASILTSVEFIIYTCINFILRDF 120
Wyeth  PVTRVCLDLDIHSLTSIVIYSYTGKVYIDSHNVVNLLRASILTSVEFIIYTCINFILRDF 120
Lister PVTRVCLDLDIHSLTSIVIYSYTGKVYIDSHNVVNLLRASILTSVEFIIYTCINFILRDF 120
       *** ********************************************************
```

```
Cop     RKEYCVECYMMGIEYGLSNLLCHTKNFIAKHFLELEDDIIDNFDYLSMKLILESDELNVP 180
WR      RKEYCVECYMMGIEYGLSNLLCHTKNFIAKHFLELEDDIIDNFDYLSMKLILESDELNVP 180
Tian    RKEYCVECYMMGIEYGLSNLLCHTKNFIAKHFLELEDDIIDNFDYLSMKLILESDELNVP 180
Wyeth   RKEYCVECYMMGIEYGLSNLLCHTKNFIAKHFLELEDDIIDNFDYLSMKLILESDELNVP 180
Lister  RKEYCVECYMMGIEYGLSNLLCHTKNFIAKHFLELEDDIIDNFDYLSIKLILESDELNVP 180
        ********************************************:***********

Cop     DEDYVVDFVIKWYIKRRNKLGNLLLLIKNVIRSNYLSPRGINNVKWILDCTKIFHCDKQP 240
WR      DEDYVVDFVIKWYIKRRNKLGNLLLLIKNVIRSNYLSPRGINNVKWILDCTKIFHCDKQP 240
Tian    DEDYVVDFVIKWYIKRRNKLGNLLLLIKNVIRSNYLSPRGINNVKWILDCTKIFHCDKQP 240
Wyeth   DEDYVVDFVIKWYIKRRNKLGNLLLLIKNVIRSNYLSPRGINNVKWILDCTKIFHCDKQP 240
Lister  DEDYVVDFVIKWYIKRRNKLGNLLLLIKNVIRSNYLSPRGINNVKWILDCTKIFHCDKQP 240
        ************************************************************

Cop     RKSYKYPFIEYPMNMDQIIDIFHMCTSTHVGEVVYLIGGWMNNEIHNNAIAVNYISNNWI 300
WR      RKSYKYPFIEYPMNMDQIIDIFHMCTSTHVGEVVYLIGGWMNNEIHNNAIAVNYISNNWI 300
Tian    RKSYKYPFIEYPMNMDQIIDIFHMCTSTHVGEVVYLIGGWMNNEIHNNAIAVNYISNNWI 300
Wyeth   RKSYKYPFIEYPMNMDQIIDIFHMCTSTHVGEVVYLIGGWMNNEIHNNAIAVNYISNNWI 300
Lister  RKSYKYPFIEYPMNMDQIIDIFHMCTSTHVGEVVYLIGGWMNNEIHNNAIAVNYISNNWI 300
        ************************************************************

Cop     PIPPMNSPRLYATGIPANNKLYVVGGLPNPTSVERWFHGDAAWVNMPSLLKPRCNPAVAS 360
WR      PIPPMNSPRLYASGIPANNKLYVVGGLPNPTSVERWFHGDAAWVNMPSLLKPRCNPAVAS 360
Tian    PIPPMNSPRLYASGIPANNKLYVVGGLPNPTSVERWFHGDAAWVNMPSLLKPRCNPAVAS 360
Wyeth   PIPPMNSPRLYASGIPANNKLYVVGGLPNPTSVERWFHGDAAWVNMPSLLKPRCNPAVAS 360
Lister  PIPPMNSPRLYASGIPANNKLYVVGGLPNPTSVERWFHGDAAWVNMPSLLKPRCNPAVAS 360
        ************:***********************************************

Cop     INNVIYVMGGHSETDTTTEYLLPNHDQWQFGPSTYYPHYKSCALVFGRRLFLVGRNAEFY 420
WR      INNVIYVMGGHSETDTTTEYLLPNHDQWQFGPSTYYPHYKSCALVFGRRLFLVGRNAEFY 420
Tian    INNVIYVMGGHSETDTTTEYLLPNHDQWQFGPSTYYPHYKSCALVFGRRLFLVGRNAEFY 420
Wyeth   INNVIYVMGGHSETDTTTEYLLPNHDQWQFGPSTYYPHYKSCALVFGRRLFLVGRNAEFY 420
Lister  INNVIYVMGGHSETDTTTEYLLPNHDQWQFGPSTYYPHYKSCALVFGRRLFLVGRNAEFY 420
        ************************************************************

Cop     CESSNTWTLIDDPIYPRDNPELIIVDNKLLLIGGFYRGSYIDTIEVYNHHTYSWNIWDGK 480
WR      CESSNTWTLIDDPIYPRDNPELIIVDNKLLLIGGFYRESYIDTIEVYNHHTYSWNIWDGK 480
Tian    CESSNTWTLIDDPIYPRDNPELIIVDNKLLLIGGFYRESYIDTIEVYNHHTYSWNIWDGK 480
Wyeth   CESSNTWTLIDDPIYPRDNPELIIVDNKLLLIGGFYRESYIDTIEVYNHHTYSWNIWDGK 480
Lister  CESSNTWTLIDDPIYPRDNPELIIVDNKLLLIGGFYRESYIDTIEVYNHHTYSWNIWDGK 480
        ********************************** **********************
```

Cop (SEQ ID NO: 40)
WR (SEQ ID NO: 57)
Tian (SEQ ID NO: 73)
Wyeth (SEQ ID NO: 91)
Lister (SEQ ID NO: 107)

B14R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop   ------------------------------------------------------------
WR    MDIFREIASSMKGENVFISPASISSVLTILYYGANGSTAEQLSKYVEKEENMDKVSAQNI 60
Tian  ------------------------------------------------------------
Wyeth ------------------------------------------------------------


Cop   ------------------------------------------------------------
WR    SFKSINKVYGRYSAVFKDSFLRKIGDKFQTVDFTDCRTIDAINKCVDIFTEGKINPLLDE 120
Tian  ------------------------------------------------------------
Wyeth ------------------------------------------------------------


Cop   ---MNHCLLAISAVYFKAKWLTPFEKEFTSDYPFYVSPTEMVDVSMMSMYGELFNHASVK 57
WR    PLSPDTCLLAISAVYFKAKWLTPFEKEFTSDYPFYVSPTEMVDVSMMSMYGKAFNHASVK 180
Tian  ---MNHCLLAISAVYFKAKWLTPFEKEFTSDYPFYVSPTEMVDVSMMSMYGKAFNHASVK 57
Wyeth ---MNHCLLAISAVYFKAKWLTPFEKEFTSDYPFYVSPTEMVDVSMMSMYGKAFNHASVK 57
          : ****************************************: *******

Cop   ESFGNFSIIELPYVGDTSMMVILPDKIDGLESIEQNLTDTNFKKWCNSLDAMFIDVHIPK 117
WR    ESFGNFSIIELPYVGDTSMMVILPDKIDGLESIEQNLTDTNFKKWCNSLEATFIDVHIPK 240
Tian  ESFGNFSIIELPYVGDTSMMVILPDKIDGLESIEQNLTDTNFKKWCDFMDAMFIDVHIPK 117
Wyeth ESFGNFSIIELPYVGDTSMMVILPDKIDGLESIEQNLTDTNFKKWCDFMDAMFIDVHIPK 117
      ********************************************: ::* ********

Cop   FKVTGSYNLVDTLVKSGLTEVFGSTGDYSNMCNLDVSVDAMIHKTYIDVNEEYTEAAAAT 177
WR    FKVTGSYNLVDTLVKSGLTEVFGSTGDYSNMCNSDVSVDAMIHKTYIDVNEEYTEAAAAT 300
Tian  FKVTGSYNLVDTLVKSGLTEVFGSTGDYSNMCNLDVSVDAMIHKTYIDVNEEYTEAAAAT 177
Wyeth FKVTGSYNLVDTLVKSGLTEVFGSTGDYSNMCNLDVSVDAMIHKTYIDVNEEYTEAAAAT 177
      ******************************** ************************

Cop   CALVSDCASTITNEFCVDHPFIYVIRHVDGKILFVGRYCSPTTNC 222 (SEQ ID NO:
108)
WR    CALVSDCASTITNEFCVDHPFIYVIRHVDGKILFVGRYCSPTTNC 345 (SEQ ID NO:
127)
Tian  CALVSDCASTITNEFCVDHPFIYVIRHVDGKILFVGRYCSPTTNC 222 (SEQ ID NO:
151)
Wyeth CALVSDCASTVTNEFCADHPFIYVIRHVDGKILFVGRYCSPTTNC 222 (SEQ ID NO:
548)
      **********:*****.****************************
```

B15R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MTANFSTHVFSPQHCGCDRLTSIDDVKQCLTEYIYWSSYAYRNRQCAGQLYSTLLSFRDD 60
WR     MTANFSTHVFSPQHCGCDRLTSIDDVRQCLTEYIYWSSYAYRNRQCAGQLYSTLLSFRDD 60
Tian   MTANFSTHVFSPQHCGCDRLTSIDDVKQCLTEYIYWSSYAYRNRQCAGQLYSTLLSFRDD 60
Wyeth  MTANFSTHVFSPQHCGCDRLTSIDDVKQCLTEYIYWSSYAYRNRQCAGQLYSTLLSFRDD 60
Lister MTANFSTHVFSPQHCGCDRLTSIDDVKQCLTEYIYWSSYAYRNRQCAGQLYSTLLSFRDD 60
       *************************:********************************

Cop    AELVFIDIRELVKNMPWDDVKDCTEIIRCYIPDEQKTIREISAIIGLCAYAATYWGGEDH 120
WR     AELVFIDIRELVKNMPWDDVKDCAEIIRCYIPDEQKTIREISAIIGLCAYAATYWGGEDH 120
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```
Tian   AELVFIDIRELVKNMPWDDVKDCTEIIRCYIPDEQKTIREISAIIGLCAYAATYWGGEDH 120
Wyeth  AELVFIDIRELVKHMPWDDVKDCAEIIRCYIPDEQKTIREISAIIGLCAYAATYWGGEDH 120
Lister AELVFIDIRELVKNMPWDDVKDCTEIIRCYIPDEQKTIREISAIIGLCAYAATYWGGEDH 120
       *************:*********:**********************************

Cop    PTSNSLNALFVMLEMLNYVDYNIIFRRMN 149 (SEQ ID NO: 109)
WR     PTSNSLNALFVMLEMLNYVDYNIIFRRMN 149 (SEQ ID NO: 128)
Tian   PTSNSLNALFVMLEMLNYVDYNIIFRRMN 149 (SEQ ID NO: 152)
Wyeth  PTSNSLNALFVMLEMLNYVDYNIIFRRMN 149 (SEQ ID NO: 164)
Lister PTSNSLNALFVMLEMLNYVDYNIIFRRMN 149 (SEQ ID NO: 200)
       ****************************
```

B ORF E

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop  MYNSSIHTPEYDVIIHVIEHLKHHKQCVQTVTSGMVFTSPVSSSICTKSDDGRNLSDGFL 60
Tian MYNSSIHTPEYDVIIHVIEHLKHHKQCVQTVTSGMVFTSPVSSSICTKSDDGRNLSDGFL 60
     ************************************************************

Cop  LIRYITTDDFCTIFDIIPRHIFYQLANVDEH 91 (SEQ ID NO: 110)
Tian LIRYITTDDFCTIFDIIPRHIFYQLANVDEH 91 (SEQ ID NO: 153)
     ******************************
```

B16R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MSILPVIFLPIFFYSSFVQTFNASECIDKGXYFASFMELENEPVILPCPQINTLSSGYNI 60
WR     MSILPVIFLSIFFYSSFVQTFNAPECIDKGQYFASFMELENEPVILPCPQINTLSSGYNI 60
Tian   ----------------------------------MELENEPVILPCPQINTLSSGYNI 24
Wyeth  MSILPVIFLSIFFYSSFVQTFNASECIDKGQYFASFMELENEPVILPCPQINTLSSGYNI 60
Lister MSILPVIFLPIFFYSSFVQTFNAPECIDKGQYFASFMELENEPVILPCPQINTLSSGYNI 60
                                         ************************

Cop    LDILWEKRGADNDRIIPIDNGSNMLILNPTQSDSGIYICITTNETYCDMMSLNLTIVSVS 120
WR     LDILWEKRGADNDRIIPIDNGSNMLILNPTQSDSGIYICITTNETYCDMMSLNLTIVSVS 120
Tian   LDILWEKRGADNDRIIPIDNGSNMLILNPTQSDSGIYICITTNETYCDMMSLNLTIVSVL 84
Wyeth  LDILWEKRGADNDRIIPIDNGSNMLILNPTQSDSGIYICITTNETYCDMMSLNLTIVSVS 120
Lister LDILWEKRGADNDRIIPIDNGSNMLILNPTQSDSGIYICITTNETYCDMMSLNLTIVSVS 120
       ************************************************************

Cop    ESNIDFISYPQIVNERSTGEMVCPNINAFIASNVNADIIWSGHRRLRNKRLKQRTPGIIT 180
WR     ESNIDLISYPQIVNERSTGEMVCPNINAFIASNVNADIIWSGHRRLRNKRLKQRTPGIIT 180
Tian   ESNIDLISYPQIVNERSTGEMVCPNINAFIASNVNADIIWSGHRRLRNKRLKQRTPGIIT 144
Wyeth  ESNIDLISYPQIVNERSTGEMVCPNINAFIASNVNADIIWSGHRRLRNKRLKQRTPGIIT 180
Lister ESNIDLISYPQIVNERSTGEMVCPNINAFIASNVNADIIWSGHRRLRNKRLKQRTPGIIT 180
       *****:******************************************************
Cop    IEDVRKNDAGYYTCVLEYIYGGKTYNVTRIVKLEVRDKIIHPTMQLPEGVVTSIGSNLTI 240
WR     IEDVRKNDAGYYTCVLEYIYGGKTYNVTRIVKLEVRDKIIPSTMQLPDGIVTSIGSNLTI 240
Tian   IEDVRKNDAGYYTCVLEYIYRGKTYNVTRIVKLEVRDKIIPSTMQLPDGIVTSIGSNLTI 204
Wyeth  IEDVRKNDAGYYTCVLEYIYGGKTYNVTRIVKLEVRDKIIPSTMQLPDGIVTSIGSNLTI 240
Lister IEDVRKNDAGYYTCVLEYIYRGKTYNVTRIVKLEVRDKIIPSTMQLPDGIVTSIGSNLTI 240
```

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       ******************** ******************  *****:*:**********

Cop    ACRVSLRPPTTDADVFWISNGMYYEEDDGDGDGRISVANKIYMTDKRRVITSRLNINPVK 300
WR     ACRVSLRPPTTDADVFWISNGMYYEEDDGDGNGRISVANKIYMTDKRRVITSRLNINPVK 300
Tian   ACRVSLRPPTTDADVFWISNGMYYEEDDGDGNGRISVANKIYMTDKRRVITSRLNINPVK 264
Wyeth  ACRVSLRPPTTDTDVFWISNGMYYEEDDGDGDGRISVANKIYMTDKRRVITSRLNINPVK 300
Lister ACRVSLRPPTTDADVFWISNGMYYEEDDGDGNGRISVANKIYMTDKRRVITSRLNINPVK 300
       ************:*****************:****************************

Cop    EEDATTFTCMAFTIPSISKTVTVSIT 326 (SEQ ID NOS: 111 and 625)[a]
WR     EEDATTFTCMAFTIPSISKTVTVSIT 326 (SEQ ID NO: 129)
Tian   EEDATTFTCMAFTIPSISKTVTVSI- 289 (SEQ ID NO: 549)
Wyeth  EEDATTFTCMAFTIPSISKTVTVSIT 326 (SEQ ID NO: 165)
Lister EEDATTFTCMAFTIPSISKTVTVSIT 326 (SEQ ID NO: 201)
       *************************
```

[a] SEQ ID NO: 111 represents the amino acid sequence prior to the "X" and SEQ ID NO: 625 represents the amino acid sequence after the "X."

B ORF F

```
CLUSTAL O(1.2.4) multiple sequence alignment

Cop  MVIIPGVRCLSLLFLRRRCPLHIISAFTLLAINALILGHTISPVDLSFTICGYEIKSIFD 60
Tian MVIIPGVRCLSLLFLRRRCPLHIISAFTLLAINALILGHTISPVDLSFTICGYEIRSIFD 60
     ********************************************************:****

Cop  SETDTIVKFNDIMSQ 75 (SEQ ID NO: 112)
Tian SKTDTIVKFNDIMSQ 75 (SEQ ID NO: 155)
     *:*************
```

B17L

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MSRKFMQVYEYDREQYLDEFIEDRYNDSFITSPEYYSAEKYMCRYTTLNHNCVNVRRCAL 60
WR     MSRKFMQVYEYDREQYLDEFIEDRYNDSFITSPEYYSAEKYMCRYTTLNHNCINVRRCAL 60
Tian   MSRKFMQVYEYDREQYLDEFIEDRYNDSFITSPEYYSAEKYMCRYTTLNHNCVNVRRCAL 60
Wyeth  MSRKFMQVYEYDREQYLDEFIEDRYNDSFITSPEYYSAEKYMCRYTTLNHNCVNVRRCAL 60
Lister MSRKFMQVYEYDREQYLDEFIEDRYNDSFITSPEYYSAEKYMCRYTTLNHNCINVRRCAL 60
       ************************************************:*******

Cop    DSKLLHDIITNCKIYNNIELVRATKFVYYLDLIKCNWVSKVGDSVLYPVIFITHTSTRNL 120
WR     DSKLLHDIITNCKIYNNIELVRATKFVYYLDLIKCNWVSKVGDSVLYPVIFITHTSTRNL 120
Tian   DSKLLHDIITNCKIYNNIELVRATKFVYYLDLIKCNWVSKVGDSVLYPVIFITHTSTRNL 120
Wyeth  DSKLLHDIITNCKIYNNIELVRATKFVYYLDLIKCNWVSKVGDSVLYPVIFITHTSTRNL 120
Lister DSKLLHDIITNCKIYNNIELVRATKFVYYLDLIKCNWVSKVGDSVLYPVIFITHTSTRNL 120
       ************************************************************

Cop    DKVSVKTYKGVKVKKLNRCADHAIVINPFVKFKLTLPNKTSHAKVLVTFCKLRTDITPVE 180
WR     DKVSVKTYKGVKVKKLNRCADHAIVINPFVKFKLTLPNKTSHAKVLVTFCKLKTDITPVE 180
Tian   DKVSVKTYKGVKVKKLNRCADHAIVINPFVKFKLTLPNKTSHAKVLVTFCKLRTDITQIE 180
Wyeth  DKVSVKTYKGVKVKKLNRCADHAIVINPFVKFKLTLPNKTSHAKVLVTFCKLRTDITQIE 180
Lister DKVSVKTYKGVKVKKLNRCADHAIVINPFVKFKLTLPNKTSHAKVLVTFCKLRTDITQIE 180
```

```
       **************************************************:**** :*

Cop    APLPGNVLVYTFPDINKRIPGYIHVNIEGCIDGMIYINSSKFACVLKLHRSMYRIPPFPI 240
WR     APLPGNVLVYTFPDINKRIPGYIHLNIEGCIDGMIYINSSKFACVLKLHRSMYRIPPFPI 240
Tian   APLSGNVLVYTFPNINKRIPGYIHVNIEGCIDGMIYINSSKFACVLKLHRSMYRIPPFPI 240
Wyeth  APLSGNVLVYTFPDINKRIPGYIHVNIEGCIDGMIYINSSKFACVLKLHRSMYRIPPFPI 240
Lister APLSGNVLVYTFPDINKRIPGYIHVNIEGCIDGMIYINSSKFACVLKLHRSMYRIPPFPI 240
       *** *********:**********:**********************************

Cop    DICSCCSQYTNDDIEIPIHDLIKDVAIFKNKETVYYLKLNNKTIARFTYFNNIDTAITQE 300
WR     DICSCCSQYINYDIEIPIHDLIKDVAIFKNKETVYYLKLNNKTIARFTYFNNIDTAITQE 300
Tian   DICSCCSQYTNGDIEIPIHDLIKDVAIFKNKETVYYLKLNNKTIARFTYFNNIDTAITQE 300
Wyeth  DICSCCSQYTNDDIEIPIHDLIKDVAIFKNKETVYYLKLNNKTIARFTYFNNIDTAITQE 300
Lister DICSCCSQYTNDDIEIPIHDLIKDVAIFKNKETVYYLKLNNKTIARFTYFNNIDTAITQE 300
       ********* * ************************************************

Cop    HEYVKIALGIVCKLMINNMHSIVGVNHSNTFVNCLLEDNV 340 (SEQ ID NO: 113)
WR     HEYVKIALGIVCKLMINNMHSIVGVNHSNTFVNCLLEDNV 340 (SEQ ID NO: 130)
Tian   HEYVKIALGIVCKLMINNMHSIVGVNHSNTFVNCLLEDNV 340 (SEQ ID NO: 156)
Wyeth  HEYVKIALGIVCKLMINNMHSIVGVNHSNTFVNCLLEDNV 340 (SEQ ID NO: 166)
Lister HEYVKIALGIVCKLMINNMHSIVGVNHSNTFVNCLLEDNV 340 (SEQ ID NO: 202)
       ************************************
```

B18R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MSRRLIYVLNINRKSTHKIQENEIYTYFSHCNIDHTSTELDFVVKNYDLNRRQHVTGYTA 60
WR     MSRRLIYVLNINRESTHKIQENEIYTYFSHCNIDHTSTELDFVVKNYDLNRRQPVTGYTA 60
Tian   MSRRLIYVLNINRESTHKIQENEIYTYFSHCNIDHTSTELDFVVKNYDLNRRHPVTGYTA 60
Wyeth  MSRRLIYVLNINRESTHKIQENEIYTYFSHCNIDHTSTELDFVVKNYDLNRRQPVTGYTA 60
       *************:************************************: ******

Cop    LHCYLYNNYFTNDVLKILLNHDVNVTMKTSSGRMPVYILLTRCCNISHDVVIDMIDKDKN 120
WR     LHCYLYNNYFTNDVLKILLNHGVDVTMKTSSGRMPVYILLTRCCNISHDVVIDMIDKDKN 120
Tian   LHCYLYNNYFTNDVLKILLNHGVDVTMKTSSGRMPVYILLTRCCNISHDVVIDMIDKDKN 120
Wyeth  LHCYLYNNYFTNDVLKILLNHGVDVTMKTSSGRMPVYILLTRCCNISHDVVIDMIDKDKN 120
       *********************.*:**********************************

Cop    HLSHRDYSNLLLEYIKSRYMLLKEEDIDENIVSTLLDKGIDPNFKQDGYTALHYYYLCLA 180
WR     HLLHRDYSNLLLEYIKSRYMLLKEEDIDENIVSTLLDKGIDPNFKQDGYTALHYYYLCLA 180
Tian   HLLHRDYSNLLLEYIKSRYMLLKEEDIDENIVSTLLDKGIDPNFKQDGYTALHYYYLCLA 180
Wyeth  HLSHRDYSNLLLEYIKSRYMLLKEEDIDENIVSTLLDKGIDPNFKQDGYTALHYYYLCLA 180
       ** ************************************************************

Cop    HVYKPGECRKPITIKKAKRIISLFIQHGANLNALDNCGNTPFHLYLSIEMCNNIHMTKML 240
WR     HVYKPGECRKPITIKKAKRIISLFIQHGANLNALDNCGNTPFHLYLSIEMCNNIHMTKML 240
Tian   HVYKPGECRKPITIKKAKRIISLFIQHGANLNALDNCGNTPFHLYLSIEMCNNIHMTKML 240
Wyeth  HVYKPGECRKPITIKKAKRIISLFIQHGANLNALDNCGNTPFHLYLSIEMCNNIHMTKML 240
       ************************************************************

Cop    LTFNPNFKICNNHGLTPILCYITSDYIQHDILVMLIHHYETNVGEMPIDERRMIVFEFIK 300
WR     LTFNPNFEICNNHGLTPILCYITSDYIQHDILVMLIHHYETNVGEMPIDERRIIVFEFIK 300
```

```
Tian  LTFNPNFKICNNHGLTPILCYITSDYIQHDILVMLIHHYETNVGEMPIDERRIIVFEFIK 300
Wyeth LTFNPNFKICNNHGLTPILCYITSDYIQHDILVMLIHHYETNVGEMPIDERRIIVFEFIK 300
      *******:****************************************:*******

Cop   TYSTRPADSITYLMNRFKNINIYTRYEGKTLLHVACEYNNTQVIDYLIRINGDINALTDN 360
WR    TYSTRPADSITYLMNRFKNIDIYTRYEGKTLLHVACEYNNTHVIDYLIRINGDINALTDN 360
Tian  TYSTRPADSITYLMNRFKNINIYTRYEGKTLLHVACEYNNTQVIDYLIRINGDINALTDN 360
Wyeth TYSTRPADSITYLMNRFKNINIYTRYEGKTLLHVACEYNNTHVIDYLIRINGDINALTDN 360
      ********************:********************:*****************

Cop   NKHATQLIIDNKENSPYTINCLLYILRYIVDKNVIRSLVDQLPSLPIFDIKSFEKFISYC 420
WR    NKHATQLIIDNKENSPYTINCLLYILRYIVDKNVIRSLVDQLPSLPIFDIKSFEKFISYC 420
Tian  NKHATQLIIDNKENSPYTINCLLYILRYIVDKNVIRSLVDQLPSLPIFDIKSFEKFISYC 420
Wyeth NKHAIQLIIDNKENSPYTIDCLLYILRYIVDKNVIRSLVDQLPSLPIFDIKSFEKFISYC 420
      **** **************:****************************************

Cop   ILLDDTFYDRHVKNRDSKTYRYAFSKYMSFDKYDGIITKCHDETMLLKLSTVLDTTLYAV 480
WR    ILLDDTFYNRHVRNRDSKTYRYAFSKYMSFDKYDGIITKCHKETILLKLSTVLDTTLYAV 480
Tian  ILLDDTFYDRHVKNRNSKTYRYAFSKYMSFDKYDGIITKCHDETMLLKLSTVLDTTLYAV 480
Wyeth ILLDDTFYNRHVRNRNSKTYRYAFSKYMSFDKYDGIITKCHDETMLLKLSTVLDTTLYAV 480
      ********:***:**:************************.**:***************

Cop   LRCHNSRKLRRYLTELKKYNNDKSFKIYSNIMNERYLNVYYKDMYVSKVYDKLFPVFTDK 540
WR    LRCHNSKKLRRYLTELKKYNNDKSFKIYSNIMNERYLNVYYKDMYVSKVYDKLFPVFTDK 540
Tian  LRCHNSRKLRRYLTELKKYNNDKSFKIYSNIMNERYLNVYYKDMYVSKVYDKLFPVFTDK 540
Wyeth LRCHNSKKLRRYLNELKKYNNDKSFKIYSNIMNERYLNVYYKDMYVSKVYDKLFPVFTDK 540
      ******:******.*********************************************

Cop   NCLLTLLPSEIIYEILYMLTINDLYNISYPPTKV 574 (SEQ ID NO: 114)
WR    NCLLTLLPSEIIYEILYMLTINDLYNISYPPTKV 574 (SEQ ID NO: 131)
Tian  NCLLTLLPSEIIYEILYMLTINDLYNISYPPTKV 574 (SEQ ID NO: 157)
Wyeth NCLLTLLPSEIIYEILYMLTINDLYNISYPPTKV 574 (SEQ ID NO: 167)
      **********************************
```

B19R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop   MTMKMMVHIYFVSLSLLLLLFHSYAIDIENEITEFFNKMRDTLPAKDSKWLNPACMFGGT 60
WR    MTMKMMVHIYFVSL--LLLLFHSYAIDIENEITEFFNKMRDTLPAKDSKWLNPACMFGGT 58
Tian  MTMKMMVHIYFVSLSLLLLLFHSYAIDIENEITEFFNKMRDTLPAKDSKWLNPACMFGGT 60
Wyeth MTMKMMVHIYFVSLSLLLLLFHSYAIDIENEITEFFNKMRDTLPAKDSKWLNPACMFGGT 60
      **************  ****************************************

Cop   MNDMATLGEPFSAKCPPIEDSLLSHRYKDYVVKWERLEKNRRRQVSNKRVKHGDLWIANY 120
WR    MNDIAALGEPFSAKCPPIEDSLLSHRYKDYVVKWERLEKNRRRQVSNKRVKHGDLWIANY 118
Tian  MNDIAALGEPFSAKCPPIEDSLLSHRYKDYVVKWERLEKNRRRQVSNKRVKHGDLWIANY 120
Wyeth MNDIATLGEPFSAKCPPIEDSLLSHRYKDYVVKWERLEKNRRRQVSNKRVKHGDLWIANY 120
      ***:*:**************************************************

Cop   TSKFSNRRYLCTVTTKNGDCVQGIVRSHIKKPPSCIPKTYELGTHDKYGIDLYCGILYAK 180
WR    TSKFSNRRYLCTVTTKNGDCVQGIVRSHIRKPPSCIPKTYELGTHDKYGIDLYCGILYAK 178
Tian  TSKFSNRRYLCTVTTKNGDCVQGIVRSHIKKPPSCIPKTYELGTHDKYGIDLYCGILYAK 180
Wyeth TSKFSNRRYLCTVTTKNGDCVQGIVRSHIRKPPSCIPKTYELGTHDKYGIDLYCGILYAK 180
      ****************************:****************************
```

```
Cop   HYNNITWYKDNKEINIDDIKYSQTGKELIIHNPELEDSGRYDCYVHYDDVRIKNDIVVSR 240
WR    HYNNITWYKDNKEINIDDIKYSQTGKELIIHNPELEDSGRYDCYVHYDDVRIKNDIVVSR 238
Tian  HYNNITWYKDNKEINIDDIKYSQTGKELIIHNPELEDSGRYDCYVHYDDVRIKNDIVVSR 240
Wyeth HYNNITWYKDNKEINIDDIKYSQTGKKLIIHNPELEDSGRYDCYVHYDDVRIKNDIVVSR 240
      *************************:********************************

Cop   CKILTVIPSQDHRFKLILDPKINVTIGEPANITCTAVSTSLLIDDVLIEWENPSGWLIGF 300
WR    CKILTVIPSQDHRFKLILDPKINVTIGEPANITCTAVSTSLLIDDVLIEWENPSGWLIGF 298
Tian  CKILTVIPSQDHRFKLILDPKINVTIGEPANITCTAVSTSLLIDDVLIEWENPSGWLIGF 300
Wyeth CKILTVIPSQDHRFKLKRNCGYASN---------------------------------- 265
      ***************  :     .

Cop   DFDVYSVLTSRGGITEATLYFENVTEEYIGNTYKCRGHNYYFEKTLTTTVVLE 353
WR    DFDVYSVLTSRGGITEATLYFENVTEEYIGNTYKCRGHNYYFEKTLTTTVVLE 351
Tian  DFDVYSVLTSRGGITEATLYFENVTEEYIGNTYKCRGHNYYFEKTLTTTVVLE 353
Wyeth ---------------------------------------------------
```

Cop (SEQ ID NO: 115)
WR (SEQ ID NO: 132)
Tian (SEQ ID NO: 158)
Wyeth (SEQ ID NO: 168)

B21R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop   MSLESFIITTFNNNSSTNIDNMCHLYVKVCPSSLLFRLFVECCDINKLVEGTTPLHCYLM 60
Wyeth MSLESFIITTFNNNSSTNIDNMCHLYVKVCPSSLLFRLFVECCDINKLVEGTTPLHCYLM 60
      ************************************************************

Cop   NEGFESSVLKNLLKEYVMNTFNVHDIHYTNI 91 (SEQ ID NO: 117)
Wyeth NEGFESSVLKNLLKEYVMTSITQIFNS---- 87 (SEQ ID NO: 184)
      ******************.:::.
```

B22R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MISLSFLIHNPLKKWKLKPSISINGYRSTFTMAFPCAQFRPCHCHATKDSLNTVADVRHC 60
Wyeth  MISLSFLIHNPLKKWKLKPSISINGYRSTFTMAFPCAQFRPCHCHATKDSLNTVADVRHC 60
Lister ------------------------------MASPCAKFRPCHCHATKDSLNTVADVRHC 29
                                     ** ***:**********************

Cop    LTEYILWVSHRWTHRESAGSLYRLLISFRTDATELFGGELKDSLPWDNIDNCVEIIKCFI 120
Wyeth  LTEYILWVSHRWTHRETAGPLYRLLISFRTDATELFGGELKDSLPWDNIDNCVEIIKCFI 120
Lister LTEYILWVSHRWTHRESAGSLYRLLISFRTDATELFGGELKDSLPWD---NCVEIIKCFI 86
       ****************:** **************************   **********

Cop    RNDSMKTAEELRAIIGLCTQSAIVSGRVFNDKYIDILLMLRKILNENDYLTLLDHIRTAK 180
Wyeth  RNDSMKTAEELRAIIGLCTQSAIVSGRVFNDKYIDILLMLRKILNENDYLTLLDHIRTAK 180
Lister RNDSMKTAEELRAIIGLCTQSAIVSGRVFNDKYIDILLMLRKILNENDYLTLLDHIRTAK 146
       ************************************************************
```

```
Cop     Y 181 (SEQ ID NO: 118)
Wyeth   Y 181 (SEQ ID NO: 185)
Lister Y 147 (SEQ ID NO: 205)
        *
```

B23R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MIAFIIFREIGIISTRIAMDYCGRECTILCRLLDEDVTYKKIKLEIETCHNLSKHIDRRG 60
Wyeth MIAFIIFREIGIISTRIAMDCT----CILCRLLDEDVTYKKIKLEIETCHNLSKHIDRRG 56
      ********************       ********************************

Cop    NNALHCYVSNKCDTDIKIVRLLLSRGVERLCRNNEGLTPLGAYSKHRYVKSQIVHLLISS 120
Wyeth NNALHCYVFNKCDTDIKIVRLLLSRGVERLCRNNEGLTPLGVYSKHRYVKSQIVHLLISS 116
      ******** ******************************.******************

Cop    YSNSSNELKSNINDFDLSSDNIDLRLLKYLIVDKRIRPSKNTNYAINGLGLVDIYVTTPN 180
Wyeth YSNSSNELKSNINDFDLSSDNIDLRLLKYLIVDKRIRPSKNTNYAINSLGLVDIYVTTPN 176
      ***********************************************.************

Cop    PRPEVLLWLLKSECYSTGYVFRTCMYNSDMCKNSLHYYISSHRESQSLSKDVIKCLINNN 240
Wyeth PRPEVLLWLLKSECYSTGYVFRTCMYNSDMCKNSLHYYISSHRESQSLSKDVIKCLINNN 236
      ************************************************************

Cop    VSIHGRDEGGSLPIQYYWSFSTIDIEIVKLLLIKDVDTCRVYDVSPILEAYYLNKRFRVT 300
Wyeth VSIHGRDEGGSLPIQYYWSFSTIDIEIVKLLLIKDVDTCRVYDVSPILEAYYLNKRFRVT 296
      ************************************************************

Cop    PYNVDMEIVNLLIERRHTLVDVMRSITSYDSREYNHYIIDNILKRFRQQDESIVQAMLIN 360
Wyeth PYNVDMEIVNLLIERRHTLVDVMRSITSYDSREYNHYIIDNILKRFRQQDESIVQAMLIN 356
      ************************************************************

Cop    YLHYGDMVVRCMLDNGQQLSSARLLC 386 (SEQ ID NO: 119)
Wyeth YLHYGDMVVRCMLDNGQQLSSARLLC 382 (SEQ ID NO: 186)
      *************************
```

B24R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MYGLILSRFNNCGYHCYETILIDVFDILSKYMDDIDMIDNENKTLLYYAVDVNNIQFAKR 60
Wyeth MYGLILSRFNNCGYHCYETILIDVFDILSKYMDNIDMIDNENKTLLYYAVDVNNIQFAKR 60
      ********************************:*************************

Cop    LLEYGASVTTSRSIINTAIQKSSYQRENKTRIVDLLLSYHPTLETMIDAFNRDIRYLYPE 120
Wyeth LLEYGASVTTSRSIINTAIQKSSYRRENKTKLVDLLLSYHPTLETMIDAFNRDIRYLYPE 120
      ************************:*****::****************************

Cop    PLFACIRYALILDDDFPSKVSMISPVIIRN------------------------------ 150
Wyeth PLFACIRYALILDDDFPSKVKYDISGRHKELKRYRVDINRMKNAYISGVSMFDILFKRSK 180
      ********************.       ::
```

```
Cop   ------------------ (SEQ ID NO: 120)
Wyeth RHRLRYAKNPTSNGTKKN 198 (SEQ ID NO: 187)
```

B25R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop   MSRINITKKIYCSVFLFLFLFLSYISNYEKVNDEMYEMGEMDEIVSIVRDSMWYIPNVFM 60
WR    ------------------------------------MDEIVRIVRDSMWYIPNVFM 20
Wyeth MSRINITKKIYCSVFLF--LFLSYISNYEKVNDEMYEMGEMDEIVSIVRDSMWYIPNVFM 58
                                           ***** **************

Cop   DDGKNEGHVSVNNVCHMYFTFFDVDTSSHLFKLVIKHCDLNKRGNSPLHCYTMNTRFNPS 120
WR    DDGKNEGHVSVNNVCHMYFTFFDVDTSSHLFKLVIKHCDLNKRGNSPLHCYTMNTRFNPS 80
Wyeth DDGKNEGHVSVNNVCHMYFTFFDVDTSSHLFKLVIKHCDLNKRGNSPLHCYTMNTRFNPS 118
      ************************************************************

Cop   VLKILLHHGMRNFDSKDEKGHHYLIHSLSIDNKIFDILTDTIDDFSKSSDLLLCYLRYKF 180
WR    VLKILLHHGMRNFDSKDEKGHHYQSITRSLIY---------------------------- 112
Wyeth VLKILLHHGMRNFDSKD---DHYQSITRSLIY---------------------------- 147
      *****************   .**   : *:

Cop   NGSLNYYVLYKGSDPNCADEDELTSLHYYCKHISTFYKSNYYKLSHTKMRAEKRFIYAII 240
WR    ------------------------------------------------------------
Wyeth ------------------------------------------------------------


Cop   DYGANINAVTHLPSTVYQT 259 (SEQ ID NO: 122)
WR    ------------------- (SEQ ID NO: 143)
Wyeth ------------------- (SEQ ID NO: 188)
```

B26R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MEQTLTRLHTYLQQYTKHSPRVVYALLSRGYVIILIVHPSWNDCATGHILIMLLNWHEQK 60
WR     -------------------MLFYLEEPIRGYVIILIVHPSWNDCATGHILIMLLNWHEQK 41
Wyeth  MEQTLTRLHTYLQQYTKHSPRVVYALLSRGYVIILIVHPSWNDCATGHILIMLLNWHEQK 60
Lister MEQTLTRLHTYLQQYTKHSPRVVYALLSRGYVIILIVHPSWNDCATGHILIMLLNWHEQK 60
                           .      ******************************

Cop    EEGQHLLYLFIKHNQGYTLNILRYLLDRFDIQKDEYIYRLSKL----------------- 103
WR     EEGQHLLYLFIKHNQGYTLNILRYLLDRFDIQKDEYYNTAFQNCNNNVASYIGYDINLPT 101
Wyeth  EEGQHLLYLFIKHNQGYTLNILRYLLDRFDIQKDEYYNTAFQNCNNNVASYIGYDINLPT 120
Lister EEGQHLLYLFIKHNQGYTLNILRYLLDRFDIQKDEYYNTAFQNCNNNVASYIGYDINLPT 120
       ********************************     :

Cop    -------- (SEQ ID NO: 123)
WR     KDGIRLGV 109 (SEQ ID NO: 144)
Wyeth  KDGIRLGV 128 (SEQ ID NO: 189)
Lister KDGIRLGV 128 (SEQ ID NO: 206)
```

B27R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    MLPHTSDTTSTFRLKTVFDLVFENRNIIYKADVVNDIIHHRLKVSLPMIKSLFYKMSEFS 60
WR     MLPHTSDTTSTFRLKTVFDLVFENRNIIYKADVVNDIIHHRLKVSLPMIKSLFYKMSLPT 60
Wyeth  MLPHTSDTTSTFRLKTVFDLVFENRNIIYKADVVNDIIHHRLK--VPMIKSLFYKMSEFS 58
Lister MLPHTSDTTSTFRLKTVFDLVFENRNIIYKADVVNDIIHHRLKVSLPMIKSLFYKMSLPT 60
       ****************************************  :***********  :

Cop    PYDDYYVKKILAYCLLRDESFAELHSKFCLNEDYKSVFMKNISFDKIDSIIVT 113
WR     TITT---------------------------------------------------- 64
Wyeth  PYDDYYVKKILAYCLLRDESFAELHSKFCLNEDYKSVFMKNISFDKIDSIIVT 111
Lister TITT---------------------------------------------------- 64

Cop  (SEQ ID NO: 124)
WR  (SEQ ID NO: 207)
Wyeth  (SEQ ID NO: 190)
Lister  (SEQ ID NO: 145)
```

B28R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop   MKSVLYSYILFLSCIIINGRDIAPHAPSDGKCKDNEYKRHNLCPGTYASRLCDSKTNTQC 60
WR    MKSVLYSYILFLSCIIINGRDIAPHAPSDGKCKDNEYKRHNLCPGTYASRLCDSKTNTQC 60
Wyeth ----------------------MHHPMESVKTTN--TNAIICV---REHTLPDYANTQC 32
                           * * :.  . *  ..  :*     .:   . :****

Cop   TPCGSGTFTSRNNHLPACLSCNGRRDRVTLLTIESVNALPDIIVFSKDHPDARHVFPKQN 120
WR    TPCGSGTFTSRNNHLPACLSCNGRRDRVTRLTIESVNALPDIIVFSKDHPDARHVFPKQN 120
Wyeth TPCGSGTFTSRNNHLPACLSCNGRRDRVTLLTIESVNALPDIIVFSKDHPDARHVFPKQN 92
      **************************** ******************************

Cop   VE 122 (SEQ ID NO: 125)
WR    VE 122 (SEQ ID NO: 147)
Wyeth V- 93 (SEQ ID NO: 527)
      *
```

C23L/B29R

CLUSTAL O(1.2.4) multiple sequence alignment

```
Cop    --------------MHVPASLQQSSSSSSSCTEEENKHHMGIDVIIKVTKQDQTPTNDKI 46
WR     --------------MHVPASLQQSSSSSSSCTEEENKHHMGIDVIIKVTKQDQTPTNDKI 46
Tian   --------------MHVPASLQQSSSSSSSCTEEENKHHMGIDVIIKVTKQDQTPTNDKI 46
Wyeth  --------------MHVPASLQQ---SSSSCTEEENKHHMGIDVIIKVTKQDQTPTNDKI 43
Lister MKQYIVLACMCLAAAAMPASLQQSSSSSSSCTEEENKHHMGIDVIIKVTKQDQTPTNDKI 60
                     :******   **********************************

Cop    CQSVTEITESESDPDPEVESEDDSTSVEDVDPPTTYYSIIGGGLRMNFGFTKCPQIKSIS 106
WR     CQSVTEITESESDPDPEVESEDDSTSVEDVDPPTTYYSIIGGGLRMNFGFTKCPQIKSIS 106
Tian   CQSVTEITESESDPDPEVESEDDSTSVEDVDPPTTYYSIIGGGLRMNFGFTKCPQIKSIS 106
```

```
Wyeth   CQSVTEITESESDPDPEVESEDDSTSVEDVDLPTTYYSIIGGGLRMNFGFTKCPQIKSIS 103
Lister  CQSVTEITESESDPDPEVESEDDSTSVEDVDPPTTYYSIIGGGLRMNFGFTKCPQIKSIS 120
        ****************************** **************************

Cop     ESADGNTVNARLSSVSPGQGKDSPAITREEALAMIKDCEVSIDIRCSEEEKDSDIKTHPV 166
WR      ESADGNTVNARLSSVSPGQGKDSPAITHEEALAMIKDCEVSIDIRCSEEEKDSDIKTHPV 166
Tian    ESADGNTVNARLSSVSPGQGKDSPAITHEEALAMIKDCEVSIDIRCSEEEKDSDIKTHPV 166
Wyeth   ESADGNTVNARLSSVSPGQGKDSPAITHEEALAMIKDCEVSIDIRCSEEEKDSDIKTHPV 163
Lister  ESADGNTVNARLSSVSPGQGKDSPAITHEEALAMIKDCEVSIDIRCSEEEKDSDIKTHPV 180
        **************************:*******************************

Cop     LGSNISHKKVSYEDIIGSTIVDTKCVKNLEFSVRIGDMCKESSELEVKDGFKYVDGSASE 226
WR      LGSNISHKKVSYEDIIGSTIVDTKCVKNLEFSVRIGDMCKESSELEVKDGFKYVDGSASE 226
Tian    LGSNISHKKVSYEDIIGSTIVDTKCVKNLEFSVRIGDMCKESSELEVKDGFKYVDGSASE 226
Wyeth   LGSNISHKKVSYEDIIGSTIVDTKCVKNLEFSVRIGDMCKESSELEVKDGFKYVDGSASE 223
Lister  LGSNISHKKVSYEDIIGSTIVDTKCVKNLEFSVRIGDMCKESSELEVKDGFKYVDGSASE 240
        ************************************************************

Cop     GATDDTSLIDSTKLKACV 244 (SEQ ID NO: 126)
WR      GATDDTSLIDSTKLKACV 244 (SEQ ID NO: 531)
Tian    GATDDTSLIDSTKLKACV 244 (SEQ ID NO: 162)
Wyeth   GATDDTSLIDSTKLKACV 241 (SEQ ID NO: 192)
Lister  GATDDTSLIDSTKLKACV 258 (SEQ ID NO: 208)
        ******************
```

Table 42. Nucleotide sequences of wild-type Copenhagen strain vaccinia virus genome and the coding sequences (CDSs) of representative genes

Description and SEQ ID NO	Nucleotide sequence
Vaccinia virus Copenhagen, complete genome (GenBank Accession No. M35027.1) (SEQ ID NO: 590)	GTAAAATTAAATTAATTATAAAATTATGTATATGATTTACTAACTTTAGTTAGATAAGTTAGTAATACAT AAATTTTAGTATATTAATATTATATTTTAAATATTTATTTAGTGTCTAGAAAAAAATGTGTGACCAACGA CCGTAGGAAACTCTAGAGGGTAAGAAAAATCAATCGCTTTATAGAGACCATCAGAAAGAGGTTTAATATT TTTGTGAGACCATCGAAGGAGAAAGAGATAAAACTTTTTTACGACTCCATCAGAAAGAGGTTTAATATTT TTGTGAGACCATCGAAGGAGAAAGAGATAAAACTTTTTTACGACTCCATCAGAAAGAGGTTTAATATTTT TGTGAGACCATCGAAGGAGAAAGAGATAAAACTTTTTTACGACTCCATCAGAAAGAGGTTTAATATTTTT GTGAGAAAGGAGAAAGAGATAAAACTTTTTTACGACTCCATCAGAAAGAGGTTTAATATTTTTGTGAGAC CATCGAAGGAGAAAGAGATAAAACTTTTTTACGACTCCATCAGAAAGAGGTTTAATATTTTTGTGAGACC ATCGAAGGAGAAAGAGATAAAACTTTTTTACGACTCCATCAGAAAGAGGTTTAATATTTTTGTGAGACCA TCGAAGGAGAAAGAGATAAAACTTTTTTACGACTCCATCAGAAAGAGGTTTAATATTTTTGTGAGACCAT CGAAGGAGACTCCATCAGAAAGAGGTTTAATATTTTTGTGAGAAAGGAGAAAGAGATAAAACTTTTTTAC GACTCCATCAGAAAGAGGTTTAATATTTTTGTGAGAAAGGAGAAAGAGATAAAACTTTTTTACGACTCCA TCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGGAGAAAGAGATAAAACTTTTTTACGACTCCAT CAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGGAGAAAGAGATAAAACTTTTTTACGACTCCATC AGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCCATC AGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCCATC AGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCCATC AGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC

	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC
	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC
	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC
	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC
	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC
	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC
	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC
	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCC
	ATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGATAAAACTTTTTTACGACTCCAT
	CAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCCAT
	CAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGATAAAACTTTTTTACGACTCCAT
	CAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGAAAGAGATAGTTAGTCTAGATAT
	TTTTCTTAGTACAAAAGTCAATGTTTTAAAATATATGGACAAGAATTTGTCTGTATAAAAACTTGTGTGA
	AATTTTGTACCAAAGAAAAAATGTGAGCAGTATCCCCTACATGGATTTTACTAGATCATTTATATACCAA
	AAAATATTATACGATCTACGTTTTATTATATGATTTTAACGTGTAAATTATAAACATTATTTTATGATAT
	ACAATTGTCTGGTAACCTAGATGGGCATAGGGGATGTTGATAAGCTCGACGAGTATATGTTGTTGGACGT
	TATTGTTTAAGAAATAGTTGATGCATCAGAAAGAGAATAAAAAATATTTTAGTGAGACCATCGAAGAGAG
	AAAGAGATAAAACTTTTTTACGACTCCATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAG
	AAAGAGAATAAAAATATTTTATGACTCCATTGAAGAGAGAAAGAGAAAATGAGAATGAGAATAAAAATAT
	TTTAGTGACACCATCAGAAAGAGGTTTAATATTTTTGTGAGACCATCGAAGAGAGAAAGAGAATAAAAAT
	ATTTTATGACTCCATTGAAGAGAGAAAGAGAAAATGAGAATGAGAATAAAAATATTTTAGTGACACCATC
	AGAAAGAGGTTTAATATTTTTTATGAGACCATCAAAGAGAGAAAGAGAATAAAAATATTTTTGTAAAACT
	TTTTTTATGAGACCATCAAAGAGAGAAAGAGAATAAAAATATTTTTGTAAAACTTTTTTTGTGAGACCAT
	CGAAGAGAGAAAGAGAATAAAAATATTTTTGTAAAACTTTTTTTATGAGACCATCAAAGAGAGAAAGAGA
	ATAAAAATATTTTTGTAAAACTTTTTTTATGAGACCATCAAAGAGAGAAAGAGAATAAAAATATTTTTGT
	AAAACTTTTTTTATGAGACCATCAAAGAGAGAAAGAGAATAAAAATATTTTTGTAAAACTTTTTTTATGA
	GACCATCAAAGAGAGAAAGAGAATAAAAATATTTTTGTAAAACTTTTTTTATGAGACCATCAAAGAGAGA
	AAGAGAATAAAAATATTTTTGTAAAACTTTTTTTATGAGACCATCAAAGAGAGAAAGAGAATAAAAATAT
	TTTTGTAAAACTTTTTTTATGAGACCATCAGAAAGAGGTTTAATATTTTTGTGATACCCTGAAAGGAAAT
	AGGAATAGGAATAGGAATAGTGTCATAATCGTATCACACTATTGAGACAGAAAAAGAAGAAGTAACGAGA
	GGTAACTTTTTGTGAATGTAGTTAAGAACATTTTTGTTTTGCAAACCGGAATATAGTGTCCGGTACACTT
	TTTTAATTCGTGGTGTGCCTGAATCGTTCGATTAACCCTACTCATCCAATTTCAGATGAATAGAGTTATC
	GATTCAGACACACGCTTTGAGTTTTGTTGAATCGATGAGTGAAGTATCATCGGTTGCACCTTCAGATGCC
	GATCCGTCGACATACTTGAATCCATCCTTGACCTCAAGTTCAGATGATTCCTTGCACATGTCTCCGATAC
	GAACGCTAAACTCTAGATTCTTGACACATTTTGTATCGACGATCGTTGAACCGATGATATCTTCGTAACT
	CACTTTCTTATGAGAGATGTTAGACCCGAGTACTGGATGGGTCTTGATGTCGCTGTCTTTCTCTTCTTCG
	CTACATCTGATGTCGATAGACACCTCACAGTCTTTGATCATAGCCAGAGCTTCTTCACGAGTGATCGCGG
	GAGAGTCCTTACCTTGTCCTGGGGACACGCTGGACAATCTAGCATTCACTGTGTTTCCATCAGCGGATTC
	TGAGATGGATTTAATCTGAGGACATTTGGTGAATCCAAAGTTCATTCTCAGACCTCCACCGATGATGGAG
	TAATAAGTGGTAGGAGGATCTACATCCTCGACTGATGTGGAATCATCTTCTGATTCCACCTCGGGATCTG
	GATCTGACTCGGACTCTGTAATTTCCGTTACGGATTGGCAAATCTTATCATTGGTCGGTGTTTGGTCTTG
	CTTTGTGACTTTGATAATAACATCGATTCCCATATGATGTTTGTTTTCTTCTTCCGTACACGAGGAGGAG
	GATGAGGATGATTGCTGAAGACTGGCAGGCACATGCATGCCAGGACGATATATTGTTTCATAATTGCTAT
	TGATTGAGTACTGTTCTTTATGATTCTACTTCCTTACCATGCAATAAATTAGAATATATTTTCTACTTTT
	ACGAGAAATTAATTATTGTATTTATTATTTATGGGTGAAAAACTTACTATAAAAAGCGGGTGGGTTTGGA
	ATTAGTGATCAGTTTATGTATATCGCAACTACCGGGCATATGGCTATCGACATCGAGAACATTACCCACA
	TGATAAGAGATTGTATCAGTTTCGTAGTCTTGAGTATTGGTATTACTATATAGTATATAGATGTCGACGC
	TAGATATACAGTCTCCGAATGCGGCATGATACCGTCATCATTCTTTGCTTTCGTTAACTGTTTGGAGGAA
	GAATCTTTGTTATTGCATTTAATCTCGAAATTCAGAGTGCACACCTTTCTCCTGTAAAGAATCCTGAAGT
	CGCTACCTTATTAAGAACGGAGAAGTATCCATCACGAAATACGGGATTACAGTCTTTATGATTCATAGTA
	ATAGTTAGTTCCGACGTTGAGATGGATTCACTGAGACCGGTAGTGGTCGTCCGAGTACACGACGTGTCGT
	TGACGGGATACAGATTAATTTCCACATCGATATAGTTAAAGGTATTTCTGGGTACGGGTTCGCATTTATC
	TGCGGAAGAGACGGTGTGAGAATATGTTCCGAGACCACACGGAGAACAGATGACGTCTCCGGATACTCCG
	TATCCTATTCCACATTTTGTTTGGGAAACACATGCCTTGCATCCGGATGATCCTTTGAGAAGACAATAAT
	ATCCGGGAGAGCATTCACAGATTCTATTGTGAGTAGTGTTACACGATCGCGTCTTCCGTTACAACTTAGA
	CAAGCGGGTAAATGATTATTGCGAGATGTGAAGGTACCCGAACCACACGGCGTACATTGTGTGTTAGTCT
	TGCTATCGCATAATCTGGAAGCGTATGTTCCCGGACACAAATTATGGCGTTTGTATTCGTTGTCTTTACA
	CTTTCCATCGGATGGTGCATGCGGTGCTATATCTCTTCCGTTTATTATTATACATGAGAGAAACAATATA
	TACGAGTATAATACGGACTTCATAATTTAATAATGTAGTAATCGTTGTCGTGTTCCTGTTTCCTACTTCT
	CCAATCATATAGATATTTTCTTTCTATCATGGATAATATTTGTAATGGTTCTTTCCGTACAACATACTGT
	TTAGATGATATTGCGCATAATTTCCGGAGGCAAATACGATAGTCTAGATTGACCGATGGTAGACTCTAAT
	TTATTGAGTGCTTTGTCGACGAGTTTACTTTTACGCTCCATCGATAGATGGCACTGTTCTATGAGATCGT
	CGTACATGGGAAATGAAATGTGTCTGTCCGAATGTATGGCTTCAAGATAGCTGTGATACCGTATACAGGT
	CGGTGTCGGAGATTCGAATCTCTTTGAGGCGACTTATGTCACGATGATGGAATCTATCTTATCGAATGAT
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B8R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 169594.. 170412) (SEQ ID NO: 591)	ATGAGATATATTATAATTCTCGCAGTTTTGTTCATTAATAGTATACACGC TAAAATAACTAGTTATAAGTTTGAATCCGTCAATTTTGATTCCAAAATTG AATGGACTGGGGATGGTCTATACAATATATCCCTTAAAAATTATGGCATC AAGACGTGGCAAACAATGTATACAAATGTACCAGAAGGAACATACGACAT ATCCGCATTTCCAAAGAATGATTTCGTATCTTTCTGGGTTAAATTTGAAC AAGGCGATTATAAAGTGGAAGAGTATTGTACGGGACTATGCGTCGAAGTA AAAATTGGACCACCGACTGTAACATTGACTGAATACGACGACCATATCAA TTTGTACATCGAGCATCCGTATGCTACTAGAGGTAGCAAAAAGATTCCTA TTTACAAACGCGGTGACATGTGTGATATCTACTTGTTGTATACGGCTAAC TTCACATTCGGAGATTCTGAAGAACCAGTAACATATGATATCGATGACTA CGATTGCACGTCTACAGGTTGCAGCATAGACTTTGCCACAACAGAAAAAG TGTGCGTGACAGCACAGGGAGCCACAGAAGGGTTTCTCGAAAAAATTACT CCATGGAGTTCGGAAGTATGTCTGACACCTAAAAAGAATGTATATACATG TGCAATTAGATCCAAAGAAGATGTTCCCAATTTCAAGGACAAAATGGCCA GAGTTATCAAGAGAAAATTTAATAAACAGTCTCAATCTTATTTAACTAAA TTTCTCGGTAGCACATCAAATGATGTTACCACTTTTCTTAGCATGCTTAA CTTGACTAAATATTCATAA
B14R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 172887.. 173555) (SEQ ID NO: 592)	ATGAACCATTGTCTCCTAGCAATTAGTGCCGTATACTTTAAAGCAAAATG GTTGACGCCATTCGAAAAGGAATTTACCAGTGATTATCCCTTTTACGTAT CACCAACGGAAATGGTAGATGTAAGTATGATGTCTATGTACGGCGAGCTA TTTAATCACGCATCTGTAAAGGAATCATTCGGCAACTTTTCAATCATAGA ACTGCCATATGTTGGAGATACTAGTATGATGGTCATTCTTCCAGACAAGA TTGATGGATTAGAATCCATAGAACAAAATCTAACAGATACAAATTTTAAG AAATGGTGTAACTCTCTGGATGCTATGTTTATAGATGTTCACATTCCCAA GTTTAAGGTAACAGGCTCGTATAATCTGGTGGATACTCTAGTAAAGTCAG GACTGACAGAGGTGTTCGGTTCAACTGGAGATTATAGCAATATGTGTAAT TTAGATGTGAGTGTCGACGCTATGATCCACAAAACGTATATAGATGTCAA TGAAGAGTATACAGAAGCAGCTGCAGCAACTTGTGCACTGGTGTCAGACT GTGCATCAACAATTACAAATGAGTTCTGTGTAGATCATCCGTTCATCTAT GTGATTAGGCATGTTGATGGAAAAATTCTTTTCGTTGGTAGATATTGCTC TCCAACAACTAATTGTTAA
B15R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 173632.. 174081) (SEQ ID NO: 593)	ATGACAGCCAACTTTAGTACCCACGTCTTTTCACCACAGCACTGTGGATG TGACAGACTGACCAGTATTGATGACGTCAAACAATGTTTGACTGAATATA TTTATTGGTCGTCCTATGCATACCGCAACAGGCAATGCGCTGGACAGTTG TATTCCACACTCCTCTCTTTTAGAGATGATGCGGAATTAGTGTTCATCGA CATTCGCGAGCTGGTAAAAAATATGCCGTGGGATGATGTCAAAGATTGTA CAGAAATCATCCGTTGTTATATACCGGATGAGCAAAAAACCATCAGAGAG ATTTCGGCCATCATCGGACTTTGTGCATATGCTGCTACTTACTGGGGAGG TGAAGACCATCCCACTAGTAACAGTCTGAACGCATTGTTTGTGATGCTTG AGATGCTCAATTACGTGGATTATAACATCATATTCCGGCGTATGAATTGA
B16R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 174164.. 175144) (SEQ ID NO: 594)	ATGAGTATACTACCTGTTATATTTCTTCCTATATTTTTTTATTCTTCATT CGTTCAGACTTTTAACGCGTCTGAATGTATCGACAAA GGGTAATATTTT GCATCATTCATGGAGTTAGAAAACGAGCCAGTAATCTTACCATGTCCTCA AATAAATACGCTATCATCCGGATATAATATATTAGATATTTTATGGGAAA AACGAGGAGCGGATAATGATAGAATTATACCGATAGATAATGGTAGCAAT ATGCTAATTCTGAACCCGACACAATCAGACTCTGGTATTTATATATGCAT TACCACGAACGAAACCTACTGTGACATGATGTCGTTAAATTTGACAATCG TGTCTGTCTCAGAATCAAATATAGATTTTATCTCGTATCCACAAATAGTA AATGAGAGATCTACTGGCGAAATGGTATGTCCCAATATTAATGCATTTAT TGCTAGTAACGTAAACGCAGATATTATATGGAGCGGACATCGACGCCTTA GAAATAAGAGACTTAAACAACGGACACCTGGAATTATTACCATAGAAGAT GTTAGAAAAAATGATGCTGGTTATTATACATGTGTTTTAGAATATATATA CGGTGGCAAAACATATAACGTAACCAGAATTGTAAAATTAGAGGTACGGG ATAAAATAATACATCCTACTATGCAATTACCAGAAGGTGTTGTAACTTCA ATAGGTAGTAATTTGACTATTGCGTGTAGAGTATCGTTGAGACCTCCCAC AACGGATGCAGACGTCTTTTGGATAAGTAATGGTATGTATTACGAAGAAG ATGATGGGGACGGAGACGGTAGAATAAGTGTAGCAAATAAAATCTATATG

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B17L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 175190.. 176212) (SEQ ID NO: 595)	ATGTCTAGAAAGTTTATGCAGGTGTATGAATATGACAGAGAGCAATATCT CGATGAGTTCATTGAAGACAGATATAACGATAGTTTTATCACTAGTCCAG AATACTATAGCGCGGAAAAATACATGTGTAGATATACTACACTAAATCAC AATTGTGTAAACGTACGACGATGTGCGTTAGATTCCAAGTTATTACATGA TATCATAACCAATTGTAAAATATATAACAATATAGAATTAGTTAGGGCGA CAAAATTTGTTTATTATCTGGATCTGATAAAATGTAATTGGGTATCTAAG GTAGGTGATTCGGTTCTATATCCCGTTATATTTATAACACATACAAGTAC TAGAAATTTAGATAAAGTCTCTGTAAAAACATACAAGGGCGTTAAAGTAA AAAAACTTAATAGATGCGCGGATCATGCTATTGTAATTAATCCATTCGTC AAGTTTAAACTAACGTTGCCGAACAAAACAAGTCATGCAAAGGTATTGGT TACATTTTGTAAGTTAAGAACGGATATAACTCCGGTAGAAGCTCCGCTTC CGGGCAATGTTTTAGTTTATACATTTCCTGACATTAATAAAAGAATTCCT GGATATATACATGTCAACATAGAAGGATGTATCGATGGAATGATTTATAT AAATTCTTCAAAGTTTGCGTGTGTTTTAAAACTACATAGATCAATGTATC GCATTCCACCCTTTCCTATAGATATCTGCTCTTGTTGTTCACAATATACT AACGATGACATAGAAATTCCCATTCATGATTTAATAAAGGATGTGGCAAT TTTTAAAAATAAGGAGACGGTATATTATCTAAAATTAAATAATAAAACTA TAGCTAGATTTACGTACTTTAATAATATAGATACTGCAATTACACAAGAA CACGAGTATGTCAAAATAGCTCTAGGTATAGTCTGCAAGTTAATGATTAA TAATATGCATAGTATCGTGGGAGTTAATCATAGCAATACGTTCGTCAATT GCTTGTTGGAAGATAATGTATAA
B18R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 176349.. 178073) (SEQ ID NO: 596)	ATGAGTCGTCGTCTGATTTATGTTTTAAATATCAACCGCAAATCAACTCA TAAAATACAAGAGAATGAAATATATACATATTTTAGTCATTGCAATATAG ACCATACTTCTACAGAACTTGATTTTGTAGTTAAAAACTATGATCTAAAC AGACGACAACATGTAACTGGGTATACTGCACTACACTGCTATTTGTATAA TAATTACTTTACAAACGATGTACTGAAGATATTATTAAATCATGACGTAA ATGTAACGATGAAAACCAGTAGCGGACGTATGCCTGTTTATATATTGCTT ACTAGATGTTGTAATATTTCACATGATGTAGTGATAGATATGATAGACAA AGATAAAAACCACTTATCGCATAGAGACTATTCCAACCTACTACTAGAGT ATATAAAATCTCGTTACATGTTATTGAAGGAAGAGGATATCGATGAGAAC ATAGTATCAACTTTATTAGATAAGGGAATCGATCCTAACTTTAAACAAGA CGGATATACAGCGTTACATTATTATTATTTGTGTCTCGCACACGTTTATA AACCAGGTGAGTGTAGAAAACCGATAACGATAAAAAAGGCCAAGCGAATT ATTTCTTTGTTTATACAACATGGAGCTAATCTAAACGCGTTAGATAATTG TGGTAATACACCATTCCATTTGTATCTTAGTATTGAAATGTGTAATAATA TTCATATGACTAAAATGCTGTTGACTTTTAATCCGAATTTCAAAATATGT AATAATCATGGATTAACGCCTATACTATGTTATATAACTTCCGACTACAT ACAACACGATATTCTTGTTATGTTAATACATCACTATGAAACAAATGTTG GAGAAATGCCGATAGATGAGCGTCGTATGATCGTATTCGAGTTTATCAAA ACATATTCTACACGTCCTGCAGATTCGATAACTTATTTGATGAATAGGTT TAAAAATATAAATATTTATACCCGCTATGAAGGAAAGACATTATTACACG TAGCATGTGAATATAATAATACACAAGTAATAGATTATCTTATACGTATC AACGGAGATATAAATGCGTTAACCGACAATAACAAACACGCTACACAACT CATTATAGATAACAAAGAAAATTCCCCATATACCATTAATTGTTTACTGT ATATACTTAGATATATTGTAGATAAGAATGTGATAAGATCGTTGGTGGAT CAACTTCCATCTCTACCTATCTTCGATATAAAATCATTTGAGAAATTCAT ATCCTACTGTATACTTTTAGATGACACATTTTACGATAGGCACGTTAAGA ATCGCGATTCTAAAACGTATCGATACGCATTTTCAAAATACATGTCGTTC GATAAATACGATGGTATAATAACTAAATGTCACGACGAAACAATGTTACT CAAACTGTCCACTGTTCTAGACACTACACTATATGCAGTTTTAAGATGTC ATAATTCGAGAAAGTTAAGAAGATACCTCACCGAGTTAAAAAAATATAAT AACGATAAGTCCTTTAAAATATATTCTAATATTATGAATGAGAGATACCT TAATGTATATTATAAAGATATGTACGTGTCAAAGGTATATGATAAACTAT TTCCTGTTTTCACAGATAAAAATTGTCTACTAACATTACTACCTTCAGAA ATTATATACGAAATATTATACATGCTGACAATTAACGATCTTTATAATAT ATCGTATCCACCTACCAAAGTATAG
B19R CDS, Vaccinia virus Copenhagen (GenBank Accession	ATGACGATGAAAATGATGGTACATATATATTTCGTATCATTATCATTATT GTTATTGCTATTCCACAGTTACGCCATAGACATCGAAAATGAAATCACAG AATTCTTCAATAAAATGAGAGATACTCTACCAGCTAAAGACTCTAAATGG TTGAATCCAGCATGTATGTTCGGAGGCACAATGAATGATATGGCCACTCT AGGAGAGCCATTCAGTGCAAAGTGTCCTCCTATTGAAGACAGTCTTTTAT CGCACAGATATAAAGACTATGTGGTTAAATGGGAGAGGCTAGAAAAGAAT AGACGGCGACAGGTTTCTAATAAACGTGTTAAACATGGTGATTTATGGAT

No. M35027.1: 178145.. 179206) (SEQ ID NO: 597)	AGCCAACTATACATCTAAATTCAGTAACCGTAGGTATTTGTGCACCGTAA CTACAAAGAATGGTGACTGTGTTCAGGGTATAGTTAGATCTCATATTAAA AAACCTCCTTCATGCATTCCAAAAACATATGAACTAGGTACTCATGATAA GTATGGCATAGACTTATACTGTGGAATTCTTTACGCAAAACATTATAATA ATATAACTTGGTATAAAGATAATAAGGAAATTAATATCGACGACATTAAG TATTCACAAACGGGAAAGGAATTAATTATTCATAATCCAGAGTTAGAAGA TAGCGGAAGATACGACTGTTACGTTCATTACGACGACGTTAGAATCAAGA ATGATATCGTAGTATCAAGATGTAAAATACTTACGGTTATACCGTCACAA GACCACAGGTTTAAACTAATACTAGATCCGAAAATCAACGTAACGATAGG AGAACCTGCCAATATAACATGCACTGCTGTGTCAACGTCATTATTGATTG ACGATGTACTGATTGAATGGGAAAATCCATCCGGATGGCTTATAGGATTC GATTTTGATGTATACTCTGTTTTAACTAGTAGAGGCGGTATCACCGAGGC GACCTTGTACTTTGAAAATGTTACTGAAGAATATATAGGTAATACATATA AATGTCGTGGACACAACTATTATTTTGAAAAAACCCTTACAACTACAGTA GTATTGGAGTAA
B20R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 179300.. 179683) (SEQ ID NO: 598)	ATGGATGAAGATACGCGACTATCTAGGTATTTGTATCTCACCGATAGAGA ACATATAAATGTAGACTCTATTAAACAGTTGTGTAAAATATCAGATCCTA ATGCATGTTATAGATGTGGATGTACGGCTTTACATGAGTACTTTTATAAT TATAGATCAGTCAACGGAAAATACAAGTATAGATACAACGGTTACTATCA ATATTATTCATCTAGCGATTATGAAAATTATAATGAATATTATTATGATG ATTATGATAGAACTGGTATGAACAGCGAGAGCGATAGTGAGAGTGATAAT ATATCAATCAAAACAGAATATGAGAATGAATATGAATTCTATGATGAAAC ACAAGATCAAAGTACACAACACAATGACTTATAA
B21R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 180585.. 180860) (SEQ ID NO: 599)	ATGTCGTTAGAATCATTTATCATAACTACGTTTAATAATAATTCATCAAC GAATATCGATAACATGTGTCATTTATACGTTAAAGTCTGTCCGTCTTCTC TATTGTTTAGACTGTTTGTAGAATGCTGTGATATAAACAAACTAGTAGAA GGTACGACTCCGTTACACTGTTATCTAATGAATGAAGGATTTGAATCATC TGTTTTAAAAAACCTATTAAAGGAGTATGTCATGAATACGTTTAATGTTC ATGACATCCATTACACAAATATTTAA
B22R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 181199.. 181744) (SEQ ID NO: 600)	ATGATATCACTCTCATTCCTCATCCACAACCCATTAAAAAAATGGAAATT AAAGCCCTCTATTAGCATAAACGGCTACAGGTCTACCTTTACAATGGCCT TTCCTTGTGCCCAGTTCAGACCCTGTCATTGCCACGCTACTAAGGACTCC CTGAATACCGTGGCCGACGTCAGACATTGTCTGACTGAATACATCCTGTG GGTTTCTCATAGATGGACCCATAGAGAAAGCGCAGGGTCTCTCTACAGGC TTCTCATCTCTTTCAGAACTGATGCAACGGAGCTCTTTGGTGGTGAGTTG AAGGATTCACTTCCGTGGGACAATATCGACAATTGCGTGGAGATCATTAA ATGTTTCATCAGAAATGACTCCATGAAAACCGCCGAAGAACTTCGTGCAA TCATTGGACTTTGTACTCAATCAGCTATCGTCTCTGGAAGAGTCTTCAAC GATAAGTATATCGACATACTACTTATGCTGCGAAAGATTCTGAACGAGAA CGACTATCTCACCCTCTTGGATCATATCCGCACTGCTAAATACTAA
B23R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 181791.. 182951) (SEQ ID NO: 601)	ATGATTGCCTTCATCATTTTTCGTGAAATAGGAATAATTAGCACCAGAAT AGCTATGGATTATTGTGGTAGAGAGTGCACTATTCTATGTCGTCTACTGG ATGAAGATGTGACGTACAAAAAAATAAAACTAGAGATTGAAACGTGTCAC AACTTATCAAAACATATAGATAGACGAGGAAACAATGCGCTACATTGTTA CGTCTCCAATAAATGCGATACAGACATTAAGATTGTTCGACTGTTACTCT CTCGCGGAGTCGAGAGACTTTGTAGAAACAACGAAGGATTAACTCCGCTA GGAGCATACAGTAAGCATAGATACGTAAAATCTCAGATTGTGCATCTACT GATATCCAGCTATTCGAATTCCTCTAACGAACTCAAGTCGAATATAAATG ATTTCGATCTGTCTTCGGATAATATCGACTTACGTCTGCTAAAATACCTA ATTGTGGATAAACGGATACGTCCGTCCAAGAATACGAATTATGCAATCAA TGGTCTCGGATTGGTGGATATATACGTAACGACGCCTAATCCGAGACCAG AAGTATTGCTATGGCTTCTTAAATCAGAATGTTACAGCACCGGTTACGTA TTTCGTACCTGTATGTACAACAGTGATATGTGTAAGAACTCTCTTCATTA CTATATATCGTCTCATAGAGAATCTCAATCTCTATCCAAGGATGTAATTA

	AATGTTTGATCAATAACAATGTTTCCATCCATGGCAGAGACGAAGGAGGA TCTTTACCCATCCAATACTACTGGTCTTTCTCAACCATAGATATAGAGAT TGTTAAATTATTATTAATAAAGGATGTGGACACGTGTAGAGTATACGACG TCAGCCCTATATTAGAGGCGTATTATCTAAACAAGCGATTTAGAGTAACC CCATATAATGTAGACATGGAAATCGTTAATCTTCTTATTGAGAGACGTCA TACTCTTGTCGACGTAATGCGTAGTATTACTTCGTACGATTCCAGAGAAT ATAACCACTACATCATCGATAACATTCTAAAGAGATTTAGACAACAGGAT GAATCCATCGTACAAGCCATGTTGATAAACTACTTACATTACGGCGATAT GGTCGTTCGATGCATGTTAGATAACGGACAACAACTATCCTCTGCACGAC TACTTTGTTAA
B24R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 183045.. 183497) (SEQ ID NO: 602)	ATGTACGGTCTGATATTATCGAGATTTAATAATTGCGGGTATCACTGTTA TGAAACCATACTAATAGATGTATTTGATATACTAAGCAAGTACATGGATG ATATAGATATGATCGATAATGAGAATAAAACTCTACTATATTACGCGGTC GATGTCAATAATATACAATTTGCAAAGCGGTTATTGGAATATGGAGCGAG TGTTACAACATCACGCTCGATAATCAATACGGCCATCCAGAAAAGCAGTT ACCAAAGAGAAAACAAAACGAGGATAGTTGATTTATTACTTAGCTACCAT CCCACTCTAGAGACTATGATTGACGCATTTAATAGAGATATACGCTATCT ATATCCTGAACCATTATTCGCCTGTATCAGATACGCCTTAATCCTAGATG ATGATTTTCCTTCTAAAGTAAGTATGATATCGCCGGTCATCATAAGGAAC TAA
B25R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 183882.. 184661) (SEQ ID NO: 603)	ATGTCTCGCATAAACATTACTAAAAAAATATATTGTTCTGTTTTTCTTTT TCTTTTTCTTTTTCTTTCGTACATCTCTAATTATGAAAAAGTAAATGATG AAATGTATGAGATGGGCGAGATGGACGAGATTGTGAGCATCGTTCGCGAC AGTATGTGGTACATACCTAACGTATTTATGGACGACGGTAAGAATGAAGG TCACGTTTCTGTCAACAATGTTTGTCATATGTATTTTACGTTCTTTGATG TGGATACATCGTCTCATCTGTTTAAGCTAGTTATTAAACACTGCGATCTG AATAAACGAGGTAACTCTCCATTACATTGCTATACGATGAATACACGATT TAATCCATCTGTATTAAAGATATTGTTACACCACGGCATGCGTAACTTTG ATAGCAAGGATGAAAAAGGACACCACTATCTGATTCATTCACTATCAATC GATAACAAGATCTTTGATATACTAACGGACACCATTGATGACTTTAGTAA ATCATCCGATCTATTGCTGTGTTATCTTAGATATAAATTCAATGGGAGCT TAAACTACTACGTTCTGTACAAAGGATCCGACCCTAATTGCGCCGACGAG GATGAACTCACTTCTCTTCATTACTACTGTAAACACATATCCACGTTCTA CAAAAGCAATTATTACAAGTTAAGTCACACTAAGATGCGAGCCGAGAAGC GATTCATCTACGCGATAATAGATTATGGAGCAAACATTAACGCGGTTACA CACTTACCTTCAACAGTATACCAAACATAG
B26R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 184606.. 184917) (SEQ ID NO: 604)	ATGGAGCAAACATTAACGCGGTTACACACTTACCTTCAACAGTATACCAA ACATAGTCCTCGTGTGGTGTATGCTCTTTTATCTCGAGGATACGTAATAA TCTTGATTGTACACCCATCATGGAACGATTGTGCAACAGGTCATATTCTC ATAATGTTACTCAATTGGCACGAACAAAAGGAAGAAGGACAACATCTACT TTATCTATTCATAAAACATAATCAAGGATACACTCTCAATATACTACGGT ATCTACTAGATAGGTTCGACATTCAGAAAGACGAATACATATACCGCCTT TCAAAATTGTAA
B27R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 184923.. 185264) (SEQ ID NO: 605)	ATGTTGCCTCATACATCGGATACGACATCAACCTTCCGACTAAAGACGGT ATTCGACTTGGTGTTTGAAAACAGAAACATCATATACAAGGCGGATGTTG TGAATGACATCATCCACCACAGACTGAAAGTATCTCTACCTATGATTAAA TCGTTGTTCTACAAGATGTCAGAATTCTCTCCCTACGACGATTACTACGT AAAAAAGATACTAGCCTACTGCCTATTAAGGGACGAGTCATTCGCGGAAC TACATAGTAAATTCTGTTTAAACGAGGACTATAAAAGTGTATTTATGAAA AATATATCATTCGATAAGATAGATTCCATCATCGTGACATAA
B28R CDS, Vaccinia	ATGAAGTCCGTATTATACTCGTATATATTGTTTCTCTCATGTATAATAAT AAACGGAAGAGATATAGCACCGCATGCACCATCCGATGGAAAGTGTAAAG ACAACGAATACAAACGCCATAATTTGTGTCCGGGAACATACGCTTCCAGA

virus Copenhagen (GenBank Accession No. M35027.1: 185625.. 185993) (SEQ ID NO: 606)	TTATGCGATAGCAAGACTAACACACAATGTACGCCGTGTGGTTCGGGTAC CTTCACATCTCGCAATAATCATTTACCCGCTTGTCTAAGTTGTAACGGAA GACGCGATCGTGTAACACTACTCACAATAGAATCTGTGAATGCTCTCCCG GATATTATTGTCTTCTCAAAGGATCATCCGGATGCAAGGCATGTGTTTCC CAAACAAAATGTGGAATAG
B29R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 186730.. 187464) (SEQ ID NO: 607)	ATGCATGTGCCTGCCAGTCTTCAGCAATCATCCTCATCCTCCTCCTCGTG TACGGAAGAAGAAAACAAACATCATATGGGAATCGATGTTATTATCAAAG TCACAAAGCAAGACCAAACACCGACCAATGATAAGATTTGCCAATCCGTA ACGGAAATTACAGAGTCCGAGTCAGATCCAGATCCCGAGGTGGAATCAGA AGATGATTCCACATCAGTCGAGGATGTAGATCCTCCTACCACTTATTACT CCATCATCGGTGGAGGTCTGAGAATGAACTTTGGATTCACCAAATGTCCT CAGATTAAATCCATCTCAGAATCCGCTGATGGAAACACAGTGAATGCTAG ATTGTCCAGCGTGTCCCCAGGACAAGGTAAGGACTCTCCCGCGATCACTC GTGAAGAAGCTCTGGCTATGATCAAAGACTGTGAGGTGTCTATCGACATC AGATGTAGCGAAGAAGAGAAAGACAGCGACATCAAGACCCATCCAGTACT CGGGTCTAACATCTCTCATAAGAAAGTGAGTTACGAAGATATCATCGGTT CAACGATCGTCGATACAAAATGTGTCAAGAATCTAGAGTTTAGCGTTCGT ATCGGAGACATGTGCAAGGAATCATCTGAACTTGAGGTCAAGGATGGATT CAAGTATGTCGACGGATCGGCATCTGAAGGTGCAACCGATGATACTTCAC TCATCGATTCAACAAAACTCAAAGCGTGTGTCTGA
C1L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 24226.. 24900) (SEQ ID NO: 608)	ATGGTGAAAAATAATAAAATAAGTAATAGCTGCCGAATGATAATGAGTAC TAACCCTAATAATATTCTAATGAGACATCTCAAAAATCTTACAGATGATG AATTTAAATGTATTATTCATCGATCATCTGATTTTCTTTATTTGTCCGAT AGTGACTATACTAGTATAACCAAAGAAACATTAGTTAGTGAGATCGTAGA AGAATATCCGGATGATTGTAATAAAATATTAGCTATTATATTTTTGGTGT TAGATAAAGACATAGATGTAGATATAGAAACTAAACTAAAGCCTAAACCC GCAGTTAGATTTGCCATTCTAGACAAGATGACTGAGGATATTAAACTAAC GGATCTAGTCAGACATTATTTTAGATACATAGAACAAGATATACCACTAG GTCCGTTGTTCAAAAAAATAGATTCGTACAGAACAAGAGCCATTAATAAG TATTCGAAAGAGTTAGGATTGGCTACTGAATACTTTAATAAGTACGGACA TTTAATGTTTTATACTCTCCCTATACCATATAACAGATTCTTTTGTAGAA ATTCGATAGGCTTTTTAGCGGTTCTATCGCCTACGATAGGACACGTAAAA GCATTTTATAAATTCATAGAATATGTTTCTATAGATGATAGACGCAAATT TAAAAAGGAATTAATGTCGAAATGA
C2L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 22618.. 24156) (SEQ ID NO: 609)	ATGGAAAGCGTGATATTTTCTATCAATGGGGAAATTATACAAGTGAATAA GGAAATTATTACGGCGTCTCCGTATAATTTTTTTAAACGCATTCAGGATC ACCATCTAAAGGATGAAGCGATTATATTGAATGGTATAAACTATCACGCG TTTGAATCGCTATTAGACTATATGCGCTGGAAGAAGATAAACATCACCAT AAACAATGTAGAAATGATACTAGTTGCTGCCGTAATAATTGATGTTCCGC CTGTAGTAGATCTATGTGTAAAAACTATGATTCATAATATTAATTCCACA AATTGTATAAGGATGTTTAACTTTTCTAAAAGATATGGAATTAAAAAACT ATATAATGCGTCGATGTCAGAAATAATCAACAATATTACTGCGGTGACAT CCGATCCAGAATTTGGAAAATTATCAAAGGATGAACTGACAACTATCTTA TCCCACGAAGACGTTAACGTAAATCATGAGGATGTTACAGCTATGATATT ATTAAAGTGGATACATAAAAATCCAAACGATGTAGATATCATCAACATTT TACATCCCAAGTTTATGACTAATACTATGCGCAATGCTATATCATTGTTG GGATTAACTATATCCAAATCTACAAAGCCAGTGACACGAAATGGTATAAA ACATAATATAGTAGTCATTAAAAACTCTGATTATATATCCACAATAACCC ATTACTCTCCTAGGACAGAATATTGGACGATAGTCGGTAATACAGATAGA CAATTCTATAATGCAAATGTTTTACATAATTGTCTATACATTATTGGCGG CATGATTAACAATAGACATGTTTATTCCGTATCGCGGGTAGATCTTGAAA CGAAAAAATGGAAAACGGTTACTAATATGTCGTCGTTAAAATCAGAAGTT AGTACTTGTGTTAACGATGGAAAGTTATATGTAATAGGAGGATTAGAATT TTCTATTTCAACGGGTGTGGCAGAATATTTGAAACACGGCACTTCGAAAT GGATAAGACTTCCAAACTTAATTACTCCTAGATATTCAGGCGCGTCGGTA TTCGTAAACGATGATATATATGTAATGGGTGGAGTTTATACCACGTATGA AAAATATGTAGTATTAAACGATGTGGAATGTTTCACTAAAAATCGTTGGA TAAAAAAGTCTCCCATGCCTAGACATCATAGTATAGTTTATGCTGTAGAG TACGACGGCGACATCTATGTAATTACTGGAATTACTCACGAGACTCGTAA TTATCTATACAAATATATAGTTAAGGAAGACAAATGGATAGAATTGTACA TGTACTTTAACCATGTAGGAAAGATGTTCGTGTGTTCTTGCGGTGATTAT

	ATCTTAATTATAGCAGATGCAAAATACGAATATTATCCAAAATCAAATAC TTGGAATTTGTTCGATATGTCAACTCGTAATATCGAATATTATGATATGT TTACTAAAGATGAGACTCCAAAGTGTAACGTAACTCATAAGTCACTGCCA TCGTTTTTGAGCAACTGTGAAAAACAATTTCTACAATAG
F1L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 33417.. 34097) (SEQ ID NO: 610)	ATGTTGTCGATGTTTATGTGTAATAATATCGTAGATTATGTAGATGATAT AGATAATGGTATAGTACAGGATATAGAAGATGAGGCTAGCAATAATGTTG ATCACGACTATGTATATCCACTTCCAGAAAATATGGTATATAGATTTGAC AAGTCCACTAACATACTCGATTATCTATCAACGGAACGGGACCATGTAAT GATGGCTGTTCGATACTATATGAGTAAACAACGTTTAGACGACTTGTATA GACAGTTGCCCACAAAGACTAGATCATATATAGATATTATCAACATATAT TGTGATAAAGTTAGTAATGATTATAATAGGGACATGAATATCATGTATGA TATGGCATCTACAAAATCATTTACAGTTTATGACATAAATAACGAAGTTA ATACTATACTAATGGATAACAAGGGGTTGGGTGTAAGATTGGCGACAATT TCATTTATAACCGAATTGGGTAGACGATGTATGAATCCAGTAAAAACTAT AAAAATGTTTACTCTACTATCGCATACTATATGCGATGATTGTTTTGTAG ATTATATAACGGACATTTCACCACCAGATAATACCATCCCTAACACTAGC ACGCGTGAATATCTAAAGCTTATTGGCATCACAGCTATCATGTTTGCTAC ATATAAAACTCTCAAATACATGATAGGATAA
F2L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 34109.. 34552) (SEQ ID NO: 611)	ATGTTCAACATGAATATTAACTCACCAGTTAGATTTGTTAAGGAAACTAA CAGAGCTAAATCTCCTACTAGGCAATCGCCGGGTGCTGCCGGATATGATT TGTATAGCGCTTACGATTATACTATCCCTCCAGGAGAAAGACAGTTAATT AAGACAGATATTAGTATGTCCATGCCTAAGATTTGCTATGGTAGAATAGC TCCTAGGTCTGGTCTGTCACTAAAAGGCATTGATATAGGAGGTGGTGTAA TAGACGAAGATTATAGGGGAAACATAGGAGTCATTCTTATTAATAATGGA AAATGTACGTTTAATGTAAATACTGGAGATAGAATAGCTCAGCTAATCTA TCAACGTATATATTATCCAGAACTGGAAGAAGTACAATCTCTAGATAGTA CAAATAGAGGAGATCAAGGGTTTGGATCAACAGGACTTAGATAA
F3L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 34576.. 36018) (SEQ ID NO: 612)	ATGCCGATATTTGTCAATACTGTGTACTGTAAGAATATATTAGCATTGTC TATGACTAAGAAATTCAAAACAATTATTGATGCTATAGGTGGCAATATAA TAGTCAATTCTACGATATTGAAAAAGTTATCTCCTTACTTTCGCACACAT TTACGTCAAAAATACACGAAAAATAAAGATCCAGTTACAAGGGTTTGTCT AGACCTTGACATTCACAGTTTAACTTCTATAGTTATTTACTCGTATACTG GAAAGGTATATATAGATAGTCATAACGTCGTCAATTTATTACGTGCTTCT ATATTAACCTCTGTAGAATTTATCATCTACACTTGTATAAACTTTATCTT ACGAGATTTTAGAAAGGAATATTGTGTCGAGTGTTACATGATGGGTATAG AATACGGACTATCCAATCTCTTATGTCATACTAAAAACTTTATTGCCAAA CACTTTTTGGAACTGGAAGATGACATCATAGACAATTTTGATTATCTATC TATGAAACTTATTCTAGAAAGCGATGAACTAAATGTTCCAGATGAGGATT ATGTAGTTGATTTTGTCATTAAGTGGTATATAAAGCGAAGAAATAAATTA GGAAATCTGCTACTCCTTATCAAAAATGTAATCAGGTCAAATTATCTTTC TCCCAGAGGTATAAATAATGTAAAATGGATACTAGACTGTACCAAAATAT TTCATTGTGATAAACAACCACGCAAATCATACAAGTATCCATTCATAGAG TATCCTATGAACATGGATCAAATTATAGATATATTCCATATGTGTACAAG TACTCATGTTGGAGAAGTAGTATATCTCATCGGTGGATGGATGAACAATG AAATACATAACAATGCTATAGCTGTAAATTATATATCAAACAATTGGATT CCAATTCCTCCGATGAATAGCCCCAGACTGTATGCTACGGGGATACCCGC TAACAATAAATTATACGTAGTAGGAGGTCTACCAAATCCCACATCTGTTG AGCGTTGGTTCCACGGGGATGCTGCTTGGGTTAATATGCCGAGTCTTCTG AAACCTAGATGTAATCCAGCAGTGGCATCCATAAACAATGTTATATACGT AATGGGAGGACATTCTGAAACTGATACAACTACAGAATATTTGCTACCCA ATCATGATCAGTGGCAGTTTGGACCATCCACTTATTATCCTCATTATAAA TCATGCGCGTTAGTGTTCGGTAGAAGGTTATTCTTGGTTGGTAGAAATGC GGAATTTTATTGTGAATCCAGCAATACATGGACTCTGATAGATGATCCTA TTTATCCGAGGGATAATCCAGAATTGATCATAGTGGATAATAAACTGCTA TTGATAGGAGGATTTTATCGTGGATCGTATATAGATACTATAGAAGTGTA CAATCATCACACTTATTCATGGAATATATGGGATGGTAAATAA
K1L CDS, Vaccinia virus Copenhagen (GenBank Accession	ATGGATCTGTCACGAATTAATACTTGGAAGTCTAAGCAGCTGAAAAGCTT TCTCTCTAGTAAAGATACATTTAAGGCGGATGTCCATGGACATAGTGCCT TGTATTATGCAATAGCTGATAATAACGTGCGTCTAGTATGTACGTTGTTG AACGCTGGAGCATTGAAAAATCTTCTAGAGAATGAATTTCCATTACATCA GGCAGCCACATTAGAAGATACCAAAATAGTAAAGATTTTGCTATTCAGTG GAATGGATGATTCACAATTTGATGACAAAGGAAACACCGCATTGTATTAT

No. M35027.1: 28121.. 28975) (SEQ ID NO: 613)	GCGGTTGATAGTGGTAACATGCAAACGGTGAAACTGTTTGTTAAGAAAAA TTGGAGACTGATGTTCTATGGGAAAACTGGATGGAAAACTTCATTTTATC ATGCCGTCATGCTTAATGATGTAAGTATTGTATCATACTTTCTTTCAGAA ATACCATCTACTTTTGATCTGGCTATTCTCCTTAGTTGTATTCACACCAC TATAAAAAATGGACACGTGGATATGATGATTCTCTTGCTCGACTATATGA CGTCGACAAACACCAATAATTCCCTTCTCTTCATTCCGGACATTAAATTG GCTATAGATAATAAAGACATTGAGATGTTACAGGCTCTGTTCAAATACGA CATTAATATCTACTCTGTTAATCTGGAAAATGTACTATTGGATGATGCCG AAATAACTAAGATGATTATAGAAAAGCATGTTGAATACAAGTCTGACTCC TATACAAAAGATCTCGATATCGTCAAGAATAATAAATTGGATGAAATAAT TAGCAAAAACAAGGAACTCAGACTCATGTACGTCAATTGTGTAAAGAAAA ACTAA
K2L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 29204.. 30313) (SEQ ID NO: 614)	ATGATTGCGTTATTGATACTATCGTTAACGTGTTCAGTGTCTACCTATCG TCTGCAAGGATTTACCAATGCCGGTATAGTAGCGTATAAAAATATTCAAG ATGATAATATTGTCTTCTCACCGTTTGGTTATTCGTTTTCTATGTTTATG TCGCTATTGCCTGCATCAGGTAATACTAGAATAGAATTATTGAAGACTAT GGATTTGAGAAAAAGAGATCTGGGTCCAGCATTTACAGAATTAATATCAG GATTAGCTAAGCTGAAAACATCTAAATATACGTACACTGATCTAACTTAT CAAAGTTTCGTAGATAATACTGTGTGCATTAAACCGTTGTATTATCAACA ATATCATAGATTCGGCCTATATAGATTAAACTTTAGACGAGATGCGGTTA ATAAAATTAATTCTATAGTAGAACGTAGATCCGGTATGTCTAATGTAGTA GATTCTAATATGCTCGACAATAATACTCTATGGGCAATCATTAATACTAT ATATTTTAAAGGTACATGGCAATATCCGTTTGATATCACTAAAACACGCA ATGCTAGTTTTACTAATAAGTACGGTACGAAAACGGTTCCCATGATGAAC GTAGTTACTAAATTGCAAGGAAATACAATCACAATCGATGACGAAGAATA TGATATGGTGCGCCTTCCGTATAAGGATGCTAATATTAGTATGTACCTGG CAATAGGTGATAATATGACCCATTTCACAGATTCTATTACGGCTGCAAAA TTAGACTATTGGTCGTTTCAATTAGGGAATAAAGTGTACAATCTTAAACT CCCTAAATTTTCTATCGAAAATAAGAGGGATATTAAGTCGATAGCCGAAA TGATGGCTCCTAGTATGTTTAATCCAGATAATGCGTCGTTTAAACATATG ACTAGGGACCCATTATATATTTATAAAATGTTTCAGAATGCAAAGATAGA TGTCGACGAACAAGGAACTGTAGCAGAGGCATCTACTATCATGGTAGCTA CGGCGAGATCATCTCCTGAAAAACTGGAATTTAATACACCATTTGTGTTC ATCATTAGACATGATATTACTGGATTTATATTGTTTATGGGTAAGGTAGA ATCTCCTTAA
K3L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 30363.. 30629) (SEQ ID NO: 615)	ATGCTTGCATTTTGTTATTCGTTGCCCAATGCGGGCGATGTAATAAAGGG CAGAGTATACGAGAAGGATTATGCTCTATACATTTATCTTTTTGACTATC CTCACTCTGAAGCTATCTTGGCAGAGAGTGTTAAGATGCATATGGATAGA TATGTTGAATATAGGGATAAACTGGTAGGGAAAACTGTAAAAGTTAAAGT GATTAGAGTTGATTATACAAAAGGATATATAGATGTCAATTACAAAAGGA TGTGTAGACATCAATAA
K4L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 30681.. 31955) (SEQ ID NO: 616)	ATGAATCCGGATAATACAATCGCAGTGATTACAGAGACTATTCCTATAGG TATGCAATTTGATAAAGTATATTTGTCTACATTTAACATGTGGAGGGAAA TTCTATCCAATACCACAAAAACACTAGATATATCATCTTTTTATTGGAGT TTATCGGATGAAGTGGGTACGAATTTCGGCACGATAATATTAAACGAGAT TGTACAATTACCCAAAAGAGGAGTACGAGTTAGAGTAGCCGTCAATAAAT CTAACAAACCATTAAAGGATGTTGAAAGACTACAAATGGCCGGAGTTGAA GTACGATACATAGATATTACAAATATCCTAGGAGGAGTTCTTCATACAAA ATTTTGGATATCTGATAATACACATATTTATTTAGGAAGCGCTAACATGG ATTGGAGATCACTAACTCAGGTCAAAGAATTGGGTATTGCGATCTTCAAT AATAGGAACTTGGCAGCGGATCTCACTCAAATTTTTGAGGTATACTGGTA TCTTGGAGTTAACAATCTACCATATAATTGGAAAAACTTTTATCCGTCGT ATTATAATACAGATCATCCTCTTAGTATTAACGTAAGTGGTGTTCCACAC TCTGTATTTATTGCTTCTGCACCGCAACAACTATGTACTATGGAAAGAAC CAATGATTTAACCGCTTTATTGTCATGTATTAGAAATGCGAGTAAATTCG TTTATGTATCTGTTATGAACTTTATCCCTATTATTTATTCGAAGGCGGGT AAAATTTTGTTTTGGCCTTATATAGAAGATGAATTAAGAAGATCCGCTAT AGACAGACAAGTATCCGTTAAGCTATTGATTAGTTGCTGGCAACGATCTT CGTTTATCATGAGAAACTTTTTAAGATCTATCGCTATGCTAAAATCTAAA AACATAGATATAGAAGTAAAGCTATTTATTGTACCAGATGCTGATCCTCC

	CATTCCGTATTCTAGGGTAAACCATGCCAAATATATGGTAACCGATAAAA CGGCCTATATAGGTACCTCAAATTGGACAGGAAATTACTTTACGGATACA TGTGGAGCATCTATTAATATTACACCGGATGATGGATTAGGTCTTCGTCA ACAATTGGAAGATATTTTTATGCGTGATTGGAATTCAAAATACAGCTATG AATTGTACGATACTAGTCCTACTAAAAGGTGTAAACTATTAAAAAATATG AAACAATGTACAAATGATATATACTGCGATGAGATACAACCGGAAAAAGA AATTCCTGAATATTCTCTTGAATAA
K5L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 32087.. 32497) (SEQ ID NO: 617)	ATGGGAGCAACAATTTCTATACTAGCCTCTTACGATAATCCAAACTTGTT TACAGCAATGATTCTAATGTCTCCTCTAGTTAATGCAGATGCTGTTTCAA GACTGAATCTGCTAGCTGCCAAACTTATGGGAACCATCACACCAAATGCG CCAGTCGGAAAGCTATGTCCAGAATCAGTATCTAGAGATATGGATAAAGT TTATAAATACCAATACGACCCATTAATCAATCATGAAAAAATTAAGGCTG GATTTGCTAGTCAGGTCTTGAAGGCTACCAACAAGGTTAGAAAAATAATT TCCAAGATTAACACCCCCCGACTCTCATACTCCAGGGAACAAACAATGAG ATTAGTGATGTTTCAGGTGCATATTATTTCATGCAACATGCAAATTGTAA TAGAGAAATAA
K6L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 32519.. 32764) (SEQ ID NO: 618)	ATGAGTGCAAACTGTATGTTCAATCTGGACAATGATTACATATATTGGAA ACCTATTACATATCCTAAGGCATTAGTATTCATAAGTCATGGAGCTGGTA AACATTCTGGACGTTATGACGAACTAGCTGAAAACATATCATCGTTAGGA ATTTTAGTATTCTCACATGATCATATTGGACATGGAAGAAGTAATGGTGA AAAAATGATGATTGATGACTTTGGTACAGCACGTGGTAACTATTAA
K7R CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 32903.. 33352) (SEQ ID NO: 619)	ATGGCGACTAAATTAGATTATGAGGATGCTGTTTTTTACTTTGTGGATGA TGATAAAATATGTAGTCGCGACTCCATCATCGATCTAATAGATGAATATA TTACGTGGAGAAATCATGTTATAGTGTTTAACAAAGATATTACCAGTTGT GGAAGACTGTACAAGGAATTGATGAAGTTCGATGATGTCGCTATACGGTA CTATGGTATTGATAAAATTAATGAGATTGTCGAAGCTATGAGCGAAGGAG ACCACTACATCAATTTTACAAAAGTCCATGATCAGGAAAGTTTATTCGCT ACCATAGGAATATGTGCTAAAATCACTGAACATTGGGGATACAAAAAGAT TTCAGAATCTAGATTCCAATCATTGGGAAACATTACAGATCTGATGACCG ACGATAATATAAACATCTTGATACTTTTTCTAGAAAAAAAATTGAATTGA
M1L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 25928.. 27346) (SEQ ID NO: 620)	ATGATATTTGTTATAGAGAGTAAATTGTTGCAAATATACAGAAATAGAAA TAGAAATATTAATTTTTATACTACAATGGACAACATTATGTCGGCCGAGT ATTATCTATCTCTTTATGCCAAATATAATAGTAAAAATTTAGATGTATTT AGGAATATGCTACAAGCTATCGAACCTTCTGGAAATAATTATCACATTCT ACATGCGTATTGTGGAATTAAAGGACTAGATGAACGATTTGTCGAAGAAC TTCTTCATAGAGGATACTCTCCAAATGAGACGGATGATGATGGAAATTAT CCATTGCATATAGCTTCTAAAATTAATAATAATAGAATAGTCGCGATGCT GCTGACGCACGGCGCAGATCCAAACGCGTGTGATAAACATAATAAAACAC CTCTATATTATCTCTCGGGAACAGATGATGAAGTCATAGAGAGAATAAAT TTATTGGTACAGTATGGAGCCAAGATTAACAACTCGGTTGATGAAGAAGG ATGTGGTCCGTTGTTGGCGTGTACAGATCCTTCAGAAAGAGTGTTTAAAA AAATAATGTCCATCGGATTCGAAGCCAGGATAGTGGATAAATTTGGCAAA AATCATATTCATAGACATCTTATGTCAGACAATCCAAAAGCTTCTACAAT CTCATGGATGATGAAACTAGGAATTAGTCCCTCAAAACCAGATCATGATG GAAATACACCTCTCCATATTGTATGCTCTAAAACAGTCAAGAATGTAGAC ATTATAGATCTTTTACTTCCATCAACGGATGTTAATAAACAAAACAAATT CGGAGATAGTCCTCTTACACTTCTTATTAAGACATTGAGCCCAGCGCATC TTATTAACAAATTGCTATCGACTAGCAATGTTATTACGGATCAAACAGTT AATATTTGTATCTTTTATGATAGAGATGATGTTCTAGAAATTATTAATGA TAAAGGAAAGCAATATGATTCTACCGATTTTAAGATGGCTGTTGAAGTGG GATCCATAAGATGCGTCAAATATCTATTAGACAATGATATAATTTGTGAA GATGCTATGTACTACGCTGTACTATCTGAATACGAAACAATGGTAGACTA

	TCTATTGTTCAATCATTTTAGTGTAGACTCTGTAGTTAACGGTCATACAT GTATGAGCGAATGTGTAAGACTAAATAACCCAGTCATTTTATCGAAGCTG ATGTTACATAATCCTACTTCTGAGACCATGTATCTAACTATGAAAGCTAT AGAAAAAGATAAACTAGATAAATCTATTATTATTCCGTTTATCGCGTACT TTGTACTTATGCATCCGGACTTTTGTAAAAATCGTAGATACTTTACTTCA TATAAACGTTTTGTAACTGATTATGTTCATGAAGGAGTATCTTACGAAGT ATTCGATGATTATTTTTAA
M2L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 27324.. 27986) (SEQ ID NO: 621)	ATGGTTTACAAATTAGTCTTGCTCTTTTGTATCGCATCTCTCGGGTATTC GGTAGAATACAAGAATACTATATGTCCTCCTCGACAAGATTACCGGTATT GGTACTTTGCCGCCGAACTCACTATTGGTGTAAATTACGACATTAATTCT ACTATTATTGGTGAGTGTCATATGAGTGAAAGCTATATCGACAGAAATGC TAACATAGTGTTGACTGGATACGGACTAGAAATAAACATGACCATCATGG ATACGGATCAGAGATTTGTGGCAGCGGCTGAGGGTGTTGGTAAAGATAAT AAACTATCTGTTCTGTTGTTTACCACTCAGCGGCTAGATAAAGTTCATCA TAATATTAGTGTGACAATAACATGTATGGAAATGAATTGTGGAACCACAA AATACGATAGCGATCTTCCGGAATCAATTCATAAATCATCATCGTGTGAT ATAACTATAAATGGATCATGTGTGACATGTGTTAACTTAGAGACTGATCC AACAAAGATTAATCCCCATTACCTACACCCCAAGGATAAATATCTTTATC ATAATTCTGAGTATGGCATGCGTGGTAGTTATGGCGTGACATTTATAGAT GAACTAAACCAGTGCCTTCTTGACATAAAAGAACTAAGTTATGATATTTG TTATAGAGAGTAA
N1L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 24887.. 25240) (SEQ ID NO: 622)	ATGAGGACTCTACTTATTAGATATATTCTTTGGAGAAATGACAACGATCA AACCTATTATAATGATGATTTTAAAAAGCTTATGTTGTTGGATGAATTGG TAGATGACGGCGATGTATGTACATTGATTAAGAACATGAGAATGACGCTG TCCGACGGTCCATTGCTAGATAGATTGAATCAACCAGTTAATAATATAGA AGACGCTAAGCGAATGATCGCTATTAGTGCCAAAGTGGCTAGAGACATTG GTGAACGTTCAGAAATTAGATGGGAAGAGTCATTCACCATACTCTTTAGG ATGATTGAAACATATTTTGATGATCTAATGATTGATCTATATGGTGAAAA ATAA
N2L CDS, Vaccinia virus Copenhagen (GenBank Accession No. M35027.1: 25359.. 25886) (SEQ ID NO: 623)	ATGACGTCCTCTGCAATGGATAACAATGAACCTAAAGTACTAGAAATGGT ATATGATGCTACAATTTTACCCGAAGGTAGTAGCATGGATCCAAATATCA TGGATTGTATAAACAGACACATCAATATGTGTATACAACGCACCTATAGT TCTAGTATAATTGCCATTTTGAATAGATTCCTAACAATGAACAAGGATGA ACTAAACAATACACAGTGTCATATAATTAAAGAATTTATGACATACGAAC AAATGGCGATTGACCATTATGGAGAATATGTAAACGCTATTCTATATCAA ATTCGTAAAAGACCTAATCAACATCACACCATTGATCTGTTTAAAAAAAT AAAAAGAACCCCGTATGACACTTTTAAAGTGGATCCCGTAGAATTCGTAA AAAAAGTTATCGGATTTGTATCTATCTTGAACAAATATAAACCGGTTTAT AGTTACGTCCTGTACGAGAACGTCCTGTACGATGAGTTCAAATGTTTCAT TAACTACGTGGAAACTAAGTATTTCTAA

Table 43. Nucleotide sequences of recombinant vaccinia virus genomes

SKV genome comprising a deletion in the B8R gene and a loxP site: SEQ ID NO: 210
TCAGACACACGCTTTGAGTTTTGTTGAATCGATGAGTGAAGTATCATCGGTTGCACCTTCAGATGCCGATCCGTCGACAT ACTTGAATCCATCCTTGACCTCAAGTTCAGATGATTCCTTGCACATGTCTCCGATACGAACGCTAAACTCTAGATTCTTG ACACATTTTGTATCGACGATCGTTGAACCGATGATATCTTCGTAACTCACTTTCTTATGAGAGATGTTAGACCCGAGTAC TGGATGGGTCTTGATGTCGCTGTCTTTCTCTTCTTCGCTACATCTGATGTCGATAGACACCTCACAGTCTTTGATCATAG CCAGAGCTTCTTCACGAGTGATCGCGGGAGAGTCCTTACCTTGTCCTGGGGACACGCTGGACAATCTAGCATTCACTGTG TTTCCATCAGCGGATTCTGAGATGGATTTAATCTGAGGACATTTGGTGAATCCAAAGTTCATTCTCAGACCTCCACCGAT GATGGAGTAATAAGTGGTAGGAGGATCTACATCCTCGACTGATGTGGAATCATCTTCTGATTCCACCTCGGGATCTGGAT CTGACTCGGACTCTGTAATTTCCGTTACGGATTGGCAAATCTTATCATTGGTCGGTGTTTGGTCTTGCTTTGTGACTTTG ATAATAACATCGATTCCCATATGATGTTTGTTTTCTTCTTCCGTACACGAGGAGGAGGATGAGGATGATTGCTGAAGACT GGCAGGCACATGCATGCCAGGACGATATATTGTTTCATAATTGCTATTGATTGAGTACTGTTCTTTATGATTCTACTTCC TTACCATGCAATAAATTAGAATATATTTTCTACTTTTACGAGAAATTAATTATTGTATTTATTATTTATGGGTGAAAAAC TTACTATAAAAAGCGGGTGGGTTTGGAATTAGTGATCAGTTTATGTATATCGCAACTACCGGGCATATGGCTATCGACAT CGAGAACATTACCCACATGATAAGAGATTGTATCAGTTTCGTAGTCTTGAGTATTGGTATTACTATATAGTATATAGATG TCGACGCTAGATATACAGTCTCCGAATGCGGCATGATACCGTCATCATTCTTTGCTTTCGTTAACTGTTTGGAGGAAGAA TCTTTGTTATTGCATTTAATCTCGAAATTCAGAGTGCACACCTTTCTCCTGTAAAGAATCCTGAAGTCGCTACCTTATTA

AGAACGGAGAAGTATCCATCACGAAATACGGGATTACAGTCTTTATGATTCATAGTAATAGTTAGTTCCGACGTTGAGAT
GGATTCACTGAGACCGGTAGTGGTCGTCCGAGTACACGACGTGTCGTTGACGGGATACAGATTAATTTCCACATCGATAT
AGTTAAAGGTATTTCTGGGTACGGGTTCGCATTTATCTGCGGAAGAGACGGTGTGAGAAATATGTTCCGAGACCACACGGA
GAACAGATGACGTCTCCGGATACTCCGTATCCTATTCCACATTTTGTTTGGGAAACACATGCCTTGCATCCGGATGATCC
TTTGAGAAGACAATAATATCCGGGAGAGCATTCACAGATTCTATTGTGAGTAGTGTTACACGATCGCGTCTTCCGTTACA
ACTTAGACAAGCGGGTAAATGATTATTGCGAGATGTGAAGGTACCCGAACCACACGGCGTACATTGTGTGTTAGTCTTGC
TATCGCATAATCTGGAAGCGTATGTTCCCGGACACAAATTATGGCGTTTGTATTCGTTGTCTTTACACTTTCCATCGGAT
GGTGCATGCGGTGCTATATCTCTTCCGTTTATTATTATACATGAGAGAAACAATATATACGAGTATAATACGGACTTCAT
AATTTAATAATGTAGTAATCGTTGTCGTGTTCCTGTTTCCTACTTCTCCAATCATATAGATATTTTCTTTCTATCATGGA
TAATATTTGTAATGGTTCTTTCCGTACAACATACTGTTTAGATGATATTGCGCATAATTTCCGGAGGCAAATACGATAGT
CTAGATTGACCGATGGTAGACTCTAATTTATTGAGTGCTTTGTCGACGAGTTTACTTTTACGCTCCATCGATAGATGGCA
CTGTTCTATGAGATCGTCGTACATGGGAAATGAAATGTGTCTGTCCGAATGTATGGCTTCAAGATAGCTGTGATACCGTA
TACAGGTCGGTGTCGGAGATTCGAATCTCTTTGAGGCGACTTATGTCACGATGATGGAATCTATCTTATCGAATGATATA
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ACCAAGTCGAATACCGTCTTTAGTCGGAAGGTTGATGTCGTATCCGATGTATGAGGCAACATTGTTGTTACAATTTTGAA
AGGCGGTATTATAGTATTCGTCTTTCTGAATGTCGAACCTATCTAGTAGATACCGTAGTATATTGAGAGTGTATCCTTGA
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GAGGACTATGTTTGGTATACTGTTGAAGGTAAGTGTGTAACCGCGTTAATGTTTGCTCCATAATCTATTATCGCGTAGAT
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CTTACTTTAGAAGGAAAATCATCATCTAGGATTAAGGCGTATCTGATACAGGCGAATAATGGTTCAGGATATAGATAGCG
TATATCTCTATTAAATGCGTCAATCATAGTCTCTAGAGTGGGATGGTAGCTAAGTAATAAATCAACTATCCTCGTTTTGT
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AACCGCTTTGCAAATTGTATATTATTGACATCGACCGCGTAATATAGTAGAGTTTTATTCTCATTATCGATCATATCTAT
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TTCTTAGAAATATAAAACTTGTCTGTATATGTAAGATGTTTAGAAAATGGATATTTCCACATTGCTTTAAAATGGACGGC
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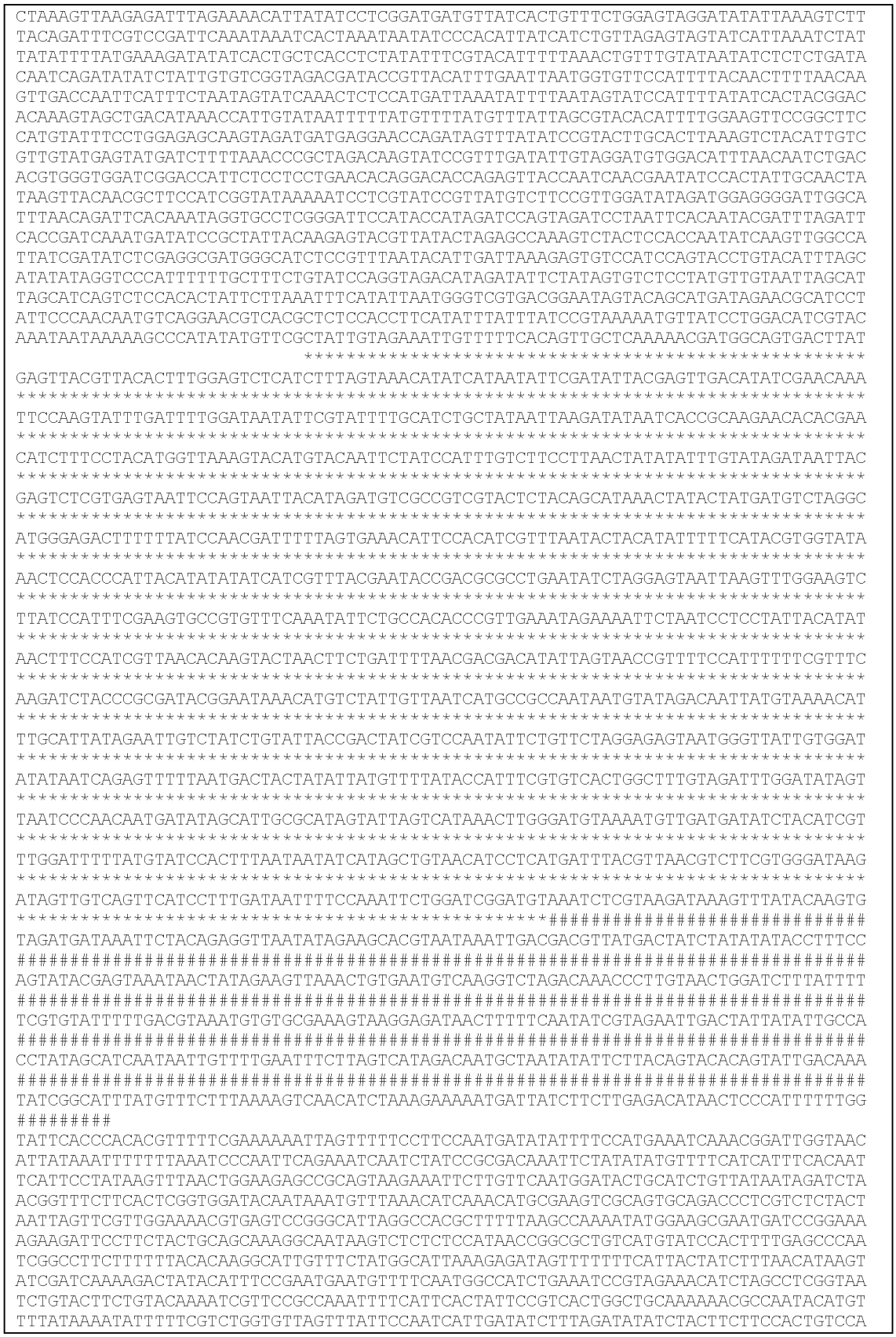

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TAGAAGCGCTTTTAACGACGATGGTATATACATCCGTAGAAATATGATTAACAAGTTGTACGGATACGCATCTCTAACTA

ACAAAACTCAAAGCGTGTGTCTGA
++++++++++++++++++++++++

(sequence having * beneath the letters: remaining portion of the C2L gene (*i.e.*, the partial C2L gene);
sequence having # beneath the letters: remaining portion of the F3L gene (*i.e.*, the partial F3L gene);
sequence having - beneath the letters: remaining portion of the B14R gene (*i.e.*, the partial B14R gene);
sequence having + beneath the letters: remaining portion of the B29R (ITR) gene (*i.e.*, the partial B29R(ITR) gene);
underlined: sequence that replaces a portion of the B8R gene sequence;
italicized and bold: remaining portion of the B8R gene (*i.e.*, the partial B8R gene);
sequence having ^ beneath the letters: loxP site;
sequences having x beneath the letters: potential transcription regulatory sequences of the B9R gene.)

SKV^{B8R+} genome comprising an intact B8R gene: SEQ ID NO: 624

TCAGACACACGCTTTGAGTTTTGTTGAATCGATGAGTGAAGTATCATCGGTTGCACCTTCAGATGCCGAT
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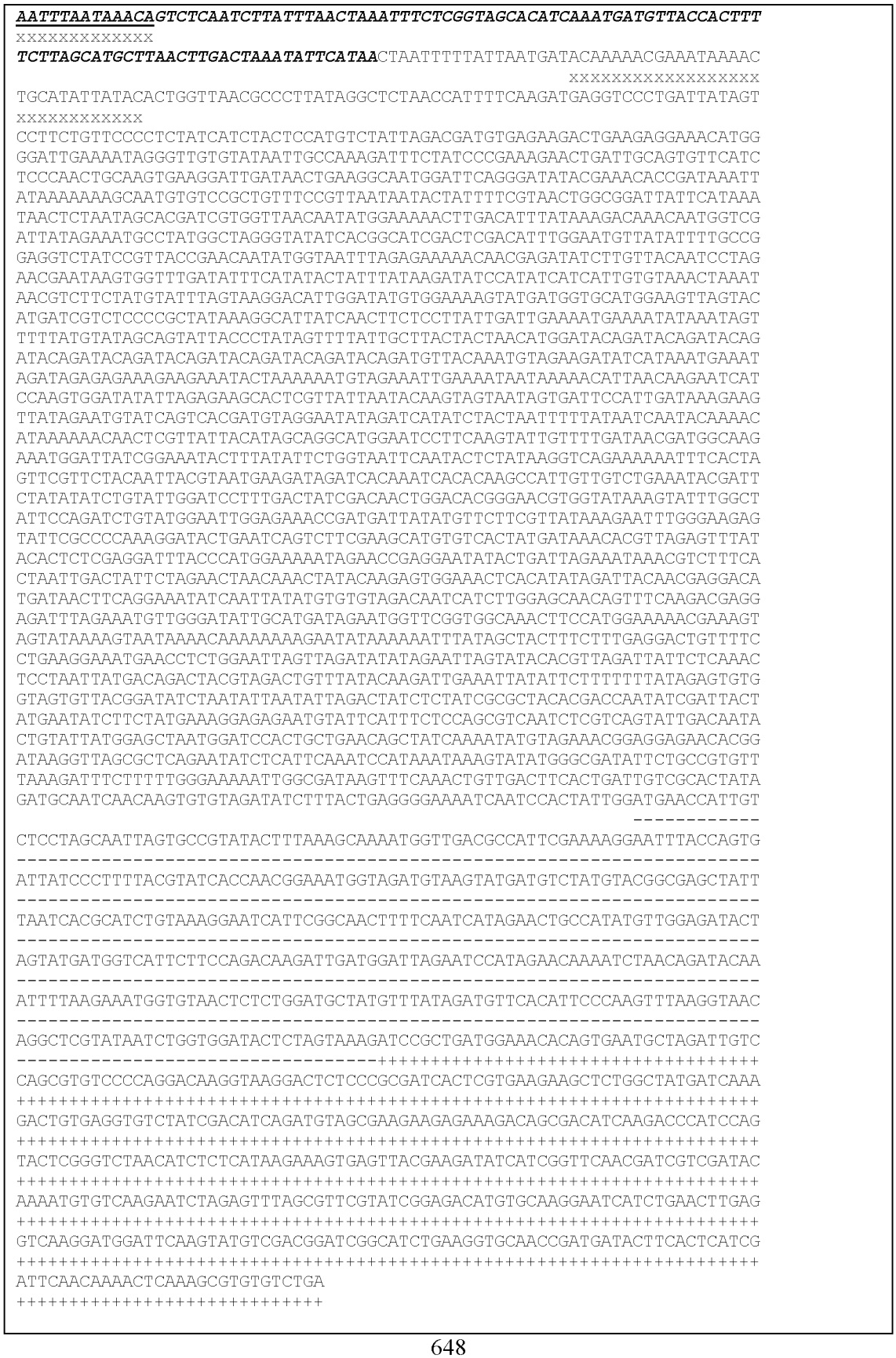
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(sequence having * beneath the letters: remaining portion of the C2L gene (*i.e.*, the partial C2L gene);
sequence having # beneath the letters: remaining portion of the F3L gene (*i.e.*, the partial F3L gene);
sequence having - beneath the letters: remaining portion of the B14R gene (*i.e.*, the partial B14R gene);
sequence having + beneath the letters: remaining portion of the B29R (ITR) gene (*i.e.*, the partial B29R (ITR) gene);
underlined: sequence that is deleted and replaced in SEQ ID NO: 210;
italicized and bold: portion of the B8R gene that remains in SEQ ID NO: 210;
sequences having x beneath the letters: potential transcription regulatory sequences of the B9R gene.)

Table 44. Nomenclature for certain abbreviations used in Tables 43 and 45

Nomenclature	Description
SKV^{B8R+}	CopMD5p3p
SKV	CopMD5p3p with a B8R gene deletion
1	Full-length anti-human CTLA-4 antibody (comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains)
1sc	Single chain variable fragment anti-human CTLA-4
m1sc	Single chain variable fragment anti-mouse CTLA-4 (9D9)
2	FLT3L (Human FLT3L that is cross reactive in both human and mouse)
3	Human IL12p35-TM
m3	Mouse IL12p35-TM
SKV-123-v2	SKV-123 with B8R and B19R promoter driving FLT3LG
3F	Human IL12p70-TM (p40-p35-TM)
m3F	Mouse IL12p70-TM (p40-p35-TM)
HeLa	Human cervical cancer cell line
U2OS	Human bone osteosarcoma epithelial cell line
HT-29	Human colorectal cancer cell line
CT26.WT	Murine colorectal cancer cell line
COLO-205	Human colorectal cancer cell line
MiaPaca-2	Human pancreatic cancer cell line

Table 45. Vector Table

Vector Name	**Transgene and Promoter/insertion locus/Comments**	**Replication competent**	**Cancer Cell Line cytotoxicity***	**Transgene expression**	**Cancer cell line tested**

SKV anti-CTLA-4 Vectors					
SKV-1sc-eGFP	Single chain variable fragment anti-human CTLA-4 driven by the B8R promoter; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-m1sc-eGFP	Single chain variable fragment anti-mouse CTLA-4 (9D9) driven by the B8R promoter; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
CopMD5p3p-1-eGFP	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter; eGFP driven by the E3L promoter. Inserted within the boundaries of the 5p deletion.	Yes	Yes	Yes	HeLa U2OS
CopMD5p3p-1	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter.	Yes	Yes	Yes	HeLa U2OS

	Inserted within the boundaries of the 5p deletion.				
SKV-1-eGFP	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter; eGFP driven by the E3L promoter. Inserted within the boundaries of the 5p deletion. Contains a B8R gene deletion.	Yes	Yes	Yes	HeLa U2OS
SKV-1	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter. Inserted within the boundaries of the 5p deletion. Contains a B8R gene deletion.	Yes	Yes	Yes	HeLa U2OS
SKV FLT3LVectors					
SKV-2-eGFP	FLT3L driven by the B8R promoter and the B19R promoter; eGFP driven by the p7.5 promoter.	Yes	Yes	Yes	HeLa U2OS

	Inserted into the B8R locus resulting in deletion of the B8R gene.				
SKV IL12 Vectors					
SKV-3-eGFP	Human IL12p35-TM driven by the B8R promoter and a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-m3-eGFP	Mouse IL12p35-TM driven by the B8R promoter and a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-m3F -eGFP	Mouse IL12p70-TM (p40-p35-TM) driven by the B8R promoter and a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-3F-eGFP	Human IL12p70-TM (p40-p35-TM) driven by the B8R promoter and a late promoter having the	Yes	Yes	Yes	HeLa U2OS

	nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.				
SKV anti-CTLA-4 and FLT3L Vectors					
SKV-1sc2-eGFP	Single chain variable fragment anti-CTLA-4 driven by the B8R promoter; FLT3L driven by the B19R promoter; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV anti-CTLA-4 and IL12 Vectors					
SKV-1sc3-eGFP	Single chain variable fragment anti-human CTLA-4 driven by the B8R promoter; human IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV FLT3L and IL12 Vectors					
SKV-23-eGFP	FLT3L driven by the B8R promoter; human IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP	Yes	Yes	Yes	HeLa U2OS

	driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.				
SKV-2m3-eGFP	FLT3L driven by the B8R promoter; mouse IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-2m3-v2-eGFP	FLT3L driven by the B8R promoter and the B19R promoter; mouse IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-2m3-v2	FLT3L driven by the B8R promoter and the B19R promoter; mouse IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV anti-CTLA-4, FLT3L and IL12 Vectors					

SKV-1sc23-eGFP	Single chain variable fragment anti-human CTLA-4 driven by the B8R promoter; FLT3L driven by the B19R promoter; human IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-1sc23	Single chain variable fragment anti-human CTLA-4 driven by the B8R promoter; FLT3L driven by the B19R promoter; human IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-123-eGFP	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter; FLT3L driven by the B8R promoter; human IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the	Yes	Yes	Yes	HeLa U2OS

	E3L promoter and downstream of anti-human CTLA-4. Anti-human CTLA-4 and eGFP are inserted within the boundaries of the 5p deletion and in the antisense orientation. Human IL12p35-TM and FLT3L are inserted into the B8R locus resulting in deletion of the B8R gene.				
SKV-123	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter; FLT3L driven by the B8R promoter; human IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561. Anti-human CTLA-4 is inserted within the boundaries of the 5p deletion and in the antisense orientation. Human IL12p35-TM and FLT3L are inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-123-v2-eGFP	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab	Yes	Yes	Yes	HeLa U2OS

	heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter; FLT3L driven by the B8R promoter and the B19R promoter; human IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter and downstream of anti-human CTLA-4. Anti-human CTLA-4 and eGFP are inserted within the boundaries of the 5p deletion and with the antisense orientation. Human IL12p35-TM and FLT3L are inserted into the B8R locus resulting in deletion of the B8R gene.				
SKV-123-v2	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter; FLT3L driven by the B8R promoter and the B19R promoter; human IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561. Anti-human CTLA-4 is inserted within the	Yes	Yes	Yes	HeLa U2OS HT-29 CT26.WT COLO-205 MiaPaca-2

	boundaries of the 5p deletion and in the antisense orientation. Human IL12p35-TM and FLT3L are inserted into the B8R locus resulting in deletion of the B8R gene.				
SKV-m1sc2m3-eGFP	Single chain variable fragment anti-mouse CTLA-4 (9D9) driven by the B8R promoter; FLT3L driven by the B19R promoter; mouse IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-12m3-v2-eGFP	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter; FLT3L driven by the B8R promoter and the B19R promoter; mouse IL12p35-TM driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Anti-human CTLA-4 and eGFP are inserted within	Yes	Yes	Yes	HeLa U2OS

	the boundaries of the 5p deletion. Mouse IL12p35-TM and FLT3L are inserted into the B8R locus resulting in deletion of the B8R gene.				
SKV-123F-v2-eGFP	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R promoter; FLT3L driven by the B8R promoter and the B19R promoter; human IL12p70-TM (p40-p35) driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Anti-human CTLA-4 and eGFP are inserted within the boundaries of the 5p deletion. Human IL12p70-TM (p40-p35-TM) and FLT3L are inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS
SKV-123F-v2	Full-length anti-human CTLA-4 antibody (full-length antibody comprising ipilimumab heavy and light chains with T2A intervening the heavy and light chains) driven by the H5R	Yes	Yes	Yes	HeLa U2OS

	promoter; FLT3L driven by the B8R promoter and the B19R promoter; human IL12p70-TM (p40-p35-TM) driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561. Anti-human CTLA-4 is inserted within the boundaries of the 5p deletion. Human IL12p70-TM (p40-p35-TM) and FLT3L are inserted into the B8R locus resulting in deletion of the B8R gene.				
SKV-m1sc2m3F-eGFP	Single chain variable fragment anti-mouse CTLA-4 (9D9) driven by the B8R promoter; FLT3L driven by the B19R promoter; mouse IL12p70-TM (p40-p30-TM) driven by a late promoter having the nucleotide sequence of SEQ ID NO: 561; eGFP driven by the p7.5 promoter. Inserted into the B8R locus resulting in deletion of the B8R gene.	Yes	Yes	Yes	HeLa U2OS

* Cancer cells infected by virus at MOI of 0.01.

Table 46. Nucleotide polymorphisms in Copenhagen virus genome

GenBank Reference	Position	Reference sequence	Polymorphism	Gene	Change	AA change
M35027	34	G	A		Not protein coding	
M35027	58	GTTAG	ATTAA		Not protein coding	
M35027	12006	ACCCCCA	ACCCCCCA,CCCCCCA	C14L	Frameshift	p.Cys70fs

M35027	16033	A	G		Not protein coding	
M35027	23443	C	T	C2L	Synonymous variant	p.Arg238Arg
M35027	24256	G	C	C1L	Synonymous variant	p.Arg215Arg
M35027	25525	G	C	N2L	Amino Acid Change	p.Pro121Arg
M35027	35080	CG	GC	F3L	Amino Acid Change	p.Thr313Ser
M35027	44312	A	G	F13L	Synonymous variant	p.Asp256Asp
M35027	46742	CG	GC	F16L	Amino Acid Change	p.Arg10Ala
M35027	77258	A	T	G7L	Amino Acid Change	p.Val348Glu
M35027	81834	G	A	L3L	Amino Acid Change	p.Leu138Phe
M35027	85139	T	C	J3R	Amino Acid Change	p.Val229Ala
M35027	104656	C	T	D6R	Amino Acid Change	p.Thr280Met
M35027	145840	T	A		Not protein coding	
M35027	148905	A	T	A41L	Synonymous variant	p.Thr84Thr
M35027	152700	GCG	GCCG	A46R	Frameshift	p.Asn186fs
M35027	179727	TGGGGGT	TGGGGGGT,TGGGGGG		Not protein coding	
M35027	191671	G	A		Not protein coding	
M35027	191695	GTTAG	ATTAA		Not protein coding	

6. Examples

[00687] The following examples are put forth so as to provide those of ordinary skill in the art with a description of how the compositions and methods claimed herein are performed, made, and evaluated, and are intended to be purely exemplary of the invention and are not intended to limit the scope of what the inventor regards as her invention.

6.1. Example 1 – Discovery of OncoVac

[00688] The open reading frames (ORFs) from 59 poxvirus strains were clustered into orthologs and aligned at the amino acid level (see FIG. 1 for phylogenetic analysis). Bayesian analysis was performed to determine relatedness of all strains. Poxviruses are very diverse in gene content and host range. There are several naturally occurring Vaccinia wild-type strains which are different from one another.

[00689] FIG. 33 shows the percentage of genes deleted in CopMD5p3p (Table 2) in various poxvirus genomes. Each dot on the graph represents one poxvirus genome. Homology searches were used to query poxviruses from other clades with amino acid sequences of Table 2 genes from the Copenhagen genome. The amount of deleted genes present in other pox viruses decreases with their increasing divergence.

[00690] Vaccinia wild type strains were mixed at equal plaque forming unit counts and sequenced with NGS (Input pool). The resulting mixture was passaged three times in different cancer cell lines. The final population was sequenced with Illumina NGS sequencing. Reads (short DNA fragments) were assigned to various strains based on sequence identity and used to calculate the percent of each strain in the final population. The abundance of different viral strains after passaging 5 Vaccinia viruses in different tumor types is shown in FIG. 2. The Copenhagen strain is able to outgrow other strains and therefore replicates faster.

[00691] Different Vaccinia wild type strains were also used to infect at low PFU (1×10^4) various patient tumor cores. Each strain infected on average 4 replicates each containing three 2 x 2 mm tumor cores. Replication was assessed through virus titering and is expressed as plaque forming units (PFU) as shown in FIG. 3. The Copenhagen strain grows to higher titres than other strains and therefore replicates faster in patient ex-vivo samples. Patient ex-vivo cores are a good mimic of a patient's 3D tumor.

[00692] Vaccinia wild-type strains were then subjected to a plaque assay on U2-OS cells with a 3% CMC overlay. Two days past infection, 20-30 plaques for each strain were measured for their size. Plaque size measurements for Copenhagen, Western Reserve, Wyeth, Lister, and Tian Tan are shown in FIG. 4. Plaque formation is affected by the ability of the virus to replicate, spread, and kill. The larger plaque sizes observed for the Copenhagen strain suggest that this strain is superior in these abilities which are important for the development of an oncolytic virus.

[00693] Finally, all 59 poxvirus genomes from FIG. 1 were used to find ORFs and clustered into orthologous groups. Groups containing Copenhagen genes were plotted based on location of the gene in the Copenhagen genome (x-axis) and size of the group (y-axis). When all 59 species share the same gene the conservation is considered to be 100%. Genes that are part of the major deletions CopMD5p and CopMD3p were found to be less important for viral replication as their deletion does not impact fitness.

[00694] A novel phenotype has been discovered by deleting the previously uncharacterized A47L gene. Deleting A47L induces the Copenhagen virus to create larger plaques

[00695] Illumina NGS deep sequencing revealed presence of major deletions during the plaque purification process. CopMD5p and CopMD3p represent clones which were plaque purified and found to harbor major genomic deletions. These 2 clones were used to co-infect a monolayer of HeLa cells at a high MOI (MOI 10) to induce recombination. Random plaque picking and PCR revealed presence of a double deleted CopMD5p3p which contained both genome deletions (see FIG. 5). Thus, two naturally occurring deletions in the wild-type Copenhagen population were discovered. These 2 deletions were combined and purified to give a replicating virus, referred to herein as "CopMD5p3p", that exhibits deletions in the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, F3L, B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes, as well as deletions in each of the B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R copies of ITRs. As used herein, "CopWT" refers to wild-type Copenhagen vaccinia virus, "CopMD5p" refers to a Copenhagen vaccinia virus harboring deletions in representative 5' genes (C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L), and "CopMD3p" refers to a Copenhagen vaccinia virus harboring deletions in representative 3' genes (B14R, B15R, B16R, B17L, B18R, B19R, and B20R) as well as deletions in each of the B21R, B22R, B23R, B24R, B25R, B26R, B27R, B28R, and B29R copies of ITRs.

6.2. Example 2 – Cancer cell death

[00696] Cancer cells were infected with CopMD5p3p at a range of MOIs (1 to 0.01) in 24-well plates in 4 replicates. Two days post infection with virus, plates were stained with crystal violet. Crystal violet stain was dissolved into SDS and read by spectrophotometry. Data is represented as percent absorbance of non-infected cells (see FIG. 6). This data shows that the majority of cancer cell lines die faster when exposed to the CopMD5p3p virus.

[00697] The ability of wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions to induce an anti-tumor immune response and to propagate in various cancer cell lines is also shown in FIGS. 23, 24 and 26-32.

6.3. Example 3 – Growth in cancer cells

[00698] Four cancer cell lines were infected with CopMD5p3p at a low MOI (0.001) in 24-well plates in triplicates, and at different time points, the virus was collected and tittered. Time 0h represents input. The growth curves of HeLa, 786-O, HT-29, and MCF7 are shown

in FIG. 7. This data shows that the modified CopMD5p3p virus is not impaired in its ability to grow in vitro. This means that the virus is replication competent, even in presence of interferon response. The ability to replicate in mammalian cell lines provides another important advantage. As such viruses may be manufactured with enhanced speed and efficiency.

6.4. Example 4 – Growth in patient tumor samples

[00699] Patient tumor samples were obtained immediately after surgery and cut into 2mm x 2mm cores. Three cores were infected with a small amount of virus (1×10^4 PFU), either wild-type Copenhagen or CopMD5p3p. After 72h virus output was assessed by plaque assay and final Viral Titer expressed as PFU (*see* FIG. 8). This data shows that the modified CopMD5p3p virus can replicate in fresh patient tumor samples. Replication in patient tumor samples is a good model of replication in a patient 3D tumor.

6.5. Example 5 – Syncytia in U2-OS cells

[00700] Monolayers of U2-OS cells were infected with either Copenhagen wild-type or CopMD5p3p virus. After 2h, the media was changed for overlay media as done for a plaque assay. At 48h post infection, pictures were taken with EVOS to assess plaque phenotype (see FIG. 9). Cell fusion, also known as syncytia, is thought to help the virus spread, since uninfected cells merge with infected cells. Additionally, it has been shown that fused cells are immunogenic and in the case of cancer cells can help initiate an anti-tumor immune response.

6.6. Example 6 – Syncytia in 786-O cells

[00701] Monolayers of 786-O cells were infected with either Copenhagen wild-type or CopMD5p3p virus. After 24h pictures were taken with EVOS at 10X magnification (see FIG. 10). This is additional evidence for the occurrence of syncytia. In FIG. 9, the phenotype of a plaque is shown. In the current experiment, monolayers of cells were infected without overlay. Most cells infected by the CopMD5p3p virus have fused.

6.7. Example 7 – Tumor control and weight loss in mouse model

[00702] Nude CD-1 mice were seeded with HT-29 human colon cancer xenograft. Once subcutaneous tumors have established an approximate 5mm x 5mm size, mice were treated

three times (dashed lines) 24h apart with 1 x 10^7 PFU of either vaccinia virus intravenously. Mice were measured approximately every other day for tumor size and weight loss (see FIG. 11). This experiment shows that CopMD5p3p is a much safer virus because it does not cause any weight loss or other signs of sickness in immunocompromised nude mice. This experiment also shows CopMD5p3p is able to control tumor growth similarly to the parental Copenhagen wild-type virus.

6.8. Example 8 – Pox lesion formation

[00703] Nude CD-1 mice were treated once with 1 x 10^7 PFU of either vaccinia virus intravenously, six mice per group. Two weeks post treatment, mice were sacrificed and pictures of tails were taken. Pox lesions on tails were counted manually on every mouse tail. Representative pictures shown in FIG. 12. This experiment shows that CopMD5p3p is a much safer virus because it does not cause any pox lesions in immunocompromised nude mice. This is important since prior Oncolytic Vaccinia clinical data has shown patients developing pox lesions upon treatment. Knockout of thymidine kinase (TK) is a popular way of increasing the safety of an OV (oncolytic virus), currently present in a Phase III Oncolytic Vaccinia and in FDA approved Oncolytic T-Vec. The data shows that deleting TK does not play a crucial role in this assay, where mice develop pox lesions when challenged with TK deleted viruses, but do not develop pox lesions with CopMD5p3p which has an intact TK.

6.9. Example 9 – IVIS Bio-distribution of Vaccinia after systemic administration

[00704] Vaccinia viruses wild-type Wyeth, wild-type Copenhagen, and CopMD5p3p were engineered to express Firefly Luciferase (Fluc) through transfection of infected cells with a pSEM1 plasmid replacing TK with Fluc. Viruses were plaque purified and expanded. All viruses are TK knockouts and encode functional Fluc in their TK locus.

[00705] Nude CD-1 mice were then seeded with HT-29 human colon cancer xenograft. Once subcutaneous tumors have established an approximate 5mm x 5mm size, mice were treated once with 1e7 PFU of either vaccinia Fluc encoding virus intravenously, four mice per group. Four days post treatment, mice were injected i.p. (intraperitoneal) with luciferin and imaged with IVIS for presence of virus (*see* FIG. 13). This experiment shows that CopMD5p3p is a much safer virus because it is more specific to the tumor. Other viruses show off target replication in the tail, muscle, paws and intra-nasal cavity. CopMD5p3p is only localized in the tumor. As shown in previous FIGS. 12 and 13, there is less detectable

CopMD5p3p in the tail compared to the other strains. FIG. 14 shows that CopMD5p3p also has lower titers in other organs when compared to other oncolytic Vaccinia. Since the CopMD5p3p replicates at the same level as the other viruses in the tumor but less in off-target tissues, CopMD5p3p fits the profile of an oncolytic virus better.

[00706] An additional example of the biodistribution of various vaccinia viral vectors, including the wild-type Copenhagen vaccinia virus and several modified Copenhagen vaccinia virions, is shown in FIG. 25.

6.10. Example 10 – Immunogenicity of Vaccinia in human PBMCs

[00707] PBMCs were isolated from blood of healthy human donors (n = 2). PBMCs were incubated with either Vaccinia for 24h and checked for early activation markers using Flow Cytometry (*see* FIG. 15). This experiment shows that CopMD5p3p is more immunogenic and more readily detectable by immune cells. We believe that this is a desirable trait, since OVs replicating in tumor tissue need to activate immune cells for a successful anti-tumor immune response.

6.11. Example 11 – Immunogenicity of Vaccinia in mouse splenocytes

[00708] Immune competent Balb/C mice were injected with 1e7 Vaccinia PFU Vaccinia virus intravenously. After one or two days, mice were sacrificed, spleens were harvested and analyzed for immune activation using Flow Cytometry (*see* FIG. 16). This experiment shows that CopMD5p3p is more immunogenic and more readily detectable by mouse immune cells. This data complements nicely the previous FIG. 15, since most of the in vivo experiments are done in mice.

6.12. Example 12 – Immunogenicity of Vaccinia in human cells

[00709] Human cancer cells 786-O were infected at an MOI of 0.01 with either virus. The next day, cells were harvested and nuclei and cytoplasm were separated by cell fractionation. Protein was extracted from each fraction and blotted for NF-kB subunits p65 and p50 (*see* FIG. 17). NF-kB immune transcription factor initiated an immune response once its subunit p65 and p50 are translocated to the nucleus. Some viruses are immunosuppressive and block this translocation, preventing an immune response. Suppressing NF-kB function is counter-intuitive to the goal of using oncolytic viruses in combination with immunotherapeutic

approaches. Thus, CopMD5p3p is a more advantageous virus as it behaves similarly to MG-1.

6.13. Example 13 – Synergy with immune checkpoint inhibitor Anti-CTLA-4 antibody in aggressive melanoma model

[00710] Immune competent C57BL/6 mice were seeded ($5x10^5$ cells) subcutaneously with B16-F10 melanoma tumors. Treatment began once subcutaneous tumors have established an approximate 5mm x 5mm size. Mice treated with CopMD5p3p virus received three 1e7 PFU doses into the tumor (intra-tumor) one day apart. Mice treated with Anti-CTLA-4 received five 100 ug doses of antibody i.p. one day apart. Survival were recorded every other day once treatment started (*see* FIG. 18). In this experiment we tested if the oncolytic effect of our CopMD5p3p virus can synergize with a well-known checkpoint inhibitor CTLA-4 in a very aggressive melanoma murine model. The median survival of mice treated with virus and checkpoint was higher than any other group. This suggests that CopMD5p3p has some stimulating properties that synergize with checkpoint blockade immunotherapy.

6.14. Example 14 – Synergy with immune checkpoint inhibitor Anti-CTLA-4 antibody

[00711] Immune competent Balb/C mice were seeded (5×10^5 cells) subcutaneously with CT26-LacZ tumors. Treatment began once subcutaneous tumors have established an approximate 5mm x 5mm size. Mice treated with Vaccinia virus received three (24h apart, first three dashed lines) 1e7 PFU doses into the tumour (intra-tumor). Mice treated with Anti-CTLA-4 received five (24h apart, dashed lines) 100 ug doses of antibody i.p. Tumor size and survival were recorded every other day once treatment started (*see* FIG. 19). The data shows that a TK knockout Vaccinia virus does not work as well with Anti-CTLA-4 as does CopMD5p3p. This suggests CopMD5p3p is more immunogenic and more capable of generating an anti-tumour immune response.

6.15. Example 15 – Synergy with immune checkpoint inhibitor Anti-PD1 antibody

[00712] Immune competent Balb/C mice were seeded (5×10^5 cells) subcutaneously with CT26-LacZ tumors. Treatment began once subcutaneous tumors have established an approximate 5mm x 5mm size. Mice treated with Vaccinia virus received three (24h apart, first three dashed lines) 1e7 PFU doses into the tumor (intra-tumor). Mice treated with Anti-PD1 received five (24h apart, last five dashed lines) 100 ug doses of antibody i.p. 24h after

the last dose of Vaccinia virus. Tumor size and survival were recorded every other day once treatment started (*see* FIG. 20). The data shows that a TK knockout Vaccinia virus does not work as well with Anti-PD1 as does CopMD5p3p. This suggests CopMD5p3p is more immunogenic and more capable of generating an anti-tumor immune response.

6.16. Example 16 - Synergy with immune checkpoint inhibitor Anti-PD1 antibody and Anti-CTLA-4 antibody

[00713] Immune competent Balb/C mice were seeded (5 x 10^5 cells) subcutaneously with CT26-LacZ tumors. Treatment began once subcutaneous tumors have established an approximate 5mm x 5mm size. Mice treated with Vaccinia virus received three (24h apart, first three dashed lines) 1e7 PFU doses into the tumor (intra-tumor). Mice treated with Anti-CTLA-4 received five (24h apart, first five dashed lines) 100 ug doses of antibody i.p. Mice treated with Anti-PD1 received five (24h apart, last five dashed lines) 100 µg doses of antibody i.p. 24h after the last dose of Vaccinia virus. Tumor size and survival were recorded every other day once treatment started (*see* FIG. 21). In this experiment we tested whether a lower dose (25 µg instead of 100 µg) of checkpoint inhibitor antibody could work if we blocked both checkpoints simultaneously. The CopMD5p3p still managed to achieve cures in this murine model with a lower dose (50 µg total) of checkpoints. Since checkpoint inhibitors have dose dependent toxicity, it is advantageous that very small doses of checkpoint blockers can still achieve an observable phenotype. As in other experiments, the CopMD5p3p virus manages to cure established tumors, and this effect is not observed with wild-type virus lacking the corresponding deletions of CopMD5p3p.

6.17. Example 17 – Administration for the treatment of a subject

[00714] Using the methods described herein, a clinician of skill in the art can administer to a subject (*e.g.*, a patient) a pharmaceutical composition containing a recombinant orthopoxvirus vector described herein to treat cancer or tumor cells. The cancer may be, for example, leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, or throat cancer, among others.

[00715] For instance, a clinician of skill in the art may assess that a patient is suffering from cancer or tumors and may administer to the patient a therapeutically effective amount (e.g., an amount sufficient to decrease the size of the tumor) of a pharmaceutical composition containing the recombinant orthopoxvirus vector disclosed herein. The pharmaceutical composition may be administered to the subject in one or more doses (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, or more) per a specified time interval (*e.g.*, weekly, daily, or hourly). The patient may be evaluated between doses to monitor the effectiveness of the therapy and to increase or decrease the dosage based on the patient's response. The pharmaceutical composition may be administered to the patient orally, parenterally (*e.g.*, topically), intravenously, intramuscularly, subcutaneously, or intranasally. The treatment may involve a single dosing of the pharmaceutical composition. The treatment may involve continued dosing of the pharmaceutical composition (*e.g.*, days, weeks, months, or years). The treatment may further involve the use of another therapeutic agent (*e.g.*, an immune checkpoint inhibitor, such as an anti-PD-1 or anti-CTLA-4 antibody or antigen-binding fragment thereof, IL-12, or Flt3 ligand, among other agents).

6.18. Example 18 – Targeted deletions of CopMD5p and CopMD3p in several Vaccinia strains

[00716] The following protocol for producing modified vaccinia viral vectors utilizes techniques described, *e.g.*, in Rintoul *et al.* PLoS One. 6(9): e24643 (2011), the disclosure of which is incorporated herein by reference.

[00717] Briefly, CopMD5p (Copenhagen vaccinia virus harboring deletions in 5' genes: (the C2L, C1L, N1L, N2L, M1L, M2L, K1L, K2L, K3L, K4L, K5L, K6L, K7R, F1L, F2L, and F3L genes) and CopMd3p (Copenhagen vaccinia virus harboring deletions in 3' genes: the B14R, B15R, B16R, B17L, B18R, B19R, and B20R genes) targeting recombinant constructs were synthesized by g-Block technology (IDT, Coralville Iowa). U2OS cells were infected with wildtype vaccinia virus (Wyeth, Western Reserve, Tian Tan, Lister) at an MOI of 0.01 in serum free DMEM for 1.5 hours. Viral supernatant was aspirated and U2OS cells were transfected with PCR amplified CopMD5p or CopMD3p targeting g-Blocks by Lipofectamine 2000 (Invitrogen) in OptiMEM (Gibco). DMEM supplemented with 10% FBS was added to cells 30 minutes after transfection and left overnight. The following day, transfection media was aspirated and fresh DMEM 10% FBS media was added to cells. 48 hours after infection transfection, U2OS cells were harvested and lysed by a single freeze

thaw cycle. Serially diluted lysates were plated onto a confluent monolayer of U2OS cells and eGFP positive (CopMD5p targeted) or mCherry positive (CopMD3p targeted) plaques were isolated and purified through 5 rounds of plaque purifications.

[00718] Double major deleted vaccinia viruses were generated by co-infection of CopMD5p and CopMD3p deleted vaccinia viruses at an MOI of 5 for each virus in U2OS cells. Cells were harvested the next day and lysed by one round of freeze thaw. Lysates were serially diluted and plated onto a confluent monolayer of U2OS cells and selected for double positive plaques (eGFP + mCherry). Plaques were purified by 5 rounds of plaque purification.

[00719] An exemplary scheme for the production of modified orthopoxvirus vectors (*e.g.*, modified vaccinia viral vectors, such as modified Copenhagen vaccinia viral vectors) of the disclosure is shown in FIG. 22.

6.19. Example 19 – SKV (CopMD5p3p-B8R-) has similar efficacy in tumour control compared to SKV-B8R+

[00720] The vaccinia virus (VV) B8R gene encodes a secreted protein with homology to gamma interferon receptor (IFN-γ). In vitro, the B8R protein binds to and neutralizes the antiviral activity of several species of gamma interferon including human and rat gamma interferon; it does not, however, bind significantly to murine IFN-γ. Here we describe the construction and characterization of recombinant VVs lacking the B8R gene. Homologous recombination between the targeting construct and the B8R locus resulted in the replacement of 75% of the B8R gene with the eGFP transgenes flanked by two loxP sites (SKV-GFP).

[00721] B8R- viruses showed similar efficacy to B8R+ viruses. FIG. 37. Survival of mice treated with either SKV or SKV-GFP was assessed. 5 x 10^5 CT26-LacZ cells were seeded subcutaneously on day 0. On day 14, 16 and 18 tumors were treated at a dose of 10^7 pfu with an intratumoural injection of either SKV or SKV-GFP. No significant decrease in efficacy was seen when the viruses injected had a deletion of the B8R locus.

6.20. Example 20 – Infection of normal versus cancer cell lines of SKV-B8R+ virus

[00722] Primary health cell viability was compared to that of cancer cells. Confluent normal or cancer cells were infected at a range of MOI (pfu/cell) for 48 hrs, after which viability was quantified. As indicated in FIG. 34, SKV-B8R+ virus preferentially infects cancer cells.

6.21. Example 21-SKV-B8R+ does not impair interferon signaling.

[00723] Interferon signaling was assessed by determining the number of genes in the interferon pathway that are upregulated (induced expression) or downregulated (repressed expression) in a variety of normal cell lines and one cancer cell line (786-O). FIG. 35 Confluent monolayers of 1 million cells were infected at an MOI of 3 (3e6 PFU) for 18h with either SKV-B8R+ (CopMD5p3p) or the parental Copenhagen virus having the TK gene disabled. RNA was sequenced using RNA-seq and gene expression of interferon genes was determined after read mapping and expression normalization. While the SKV-B8R+ (CopMD5p3p) virus mostly induces genes in the interferon pathway the parental Copenhagen represses genes. This suggests SKV-B8R+ (CopMD5p3p) is able to induce Type I Interferon signaling which is critical in viral clearance of normal cells.

6.22. Example 22 – B8R Negative vaccinia virus engineered to express Flt3L, IL-12 TM and anti-hCTLA-4

[00724] Modified vaccinia viruses containing both the CopMD5p3p and B8R deletions, as described above, were further engineered to express the immunotherapeutic transgenes, Flt3L and IL-12-TM, as well as an antibody to hCTLA-4, as shown in FIG. 38. The Flt3L, IL-12 TM and eGFP transgenes were inserted into the B8R locus on the Copenhagen vaccinia virus genome. See FIG. 36. Homologous recombination between the targeting construct and the B8R locus resulted in the replacement of 75% of the B8R gene with the Flt3-LG, IL-12-TM and eGFP transgenes (SKV-23). This strategy allowed the creation of a B8R knockout virus while inserting transgenes in lieu of B8R. The anti-CTLA-4 IgG was inserted into the SKV-23 backbone by targeting the boundaries of the 5p deletions to insert a heavy and light chain of a human anti-CTLA-4 antibody separated by a T2A proteomic motif (SKV-123v2; *see* FIG. 38).

[00725] Ability of these engineered viruses to express the membrane bound IL-12 transgene was assessed. Cells were infected with SKV-1sc23, SKV-3 or SKV-GFP engineered vaccinia genes. As depicted in FIG. 42, Vero cells were stained with an IL-12p35 specific antibody. Vero cells were co-labelled with wheat germ agglutinin (WGA) conjugated flouorophore as a counterstain to visualize the cell membrane specific staining patterns. hIL-12 production was further quantified for various SKV viruses expressing transgenes through western blot quantification. See FIG. 41. Monolayers of 1 $x10^6$ HeLa

cells were infected at MOI 0.1 ($1x10^5$ pfu) with various Vaccinia SKV expressing different combinations of the three transgenes (anti-hCTLA-4, FTL3L, IL—12). After 48 h post infection, supernatant and lysate were collected and probed for expression of IL-12 p35 subunit. SKV-123 and SKV-3, both viruses engineered to express IL-12 p35 subunit with a transmembrane domain only express the protein on lysate fractions, suggesting the IL-12 does not get secreted into the supernatant.

[00726] Expression levels of anti-hCTLA-4 and hFLT3L were measured using an ELISA protocol. Monolayers of 1e6 HeLa cells were infected at MOI 0.1 (1×10^5 pfu) with SKV-123 expressing all three transgenes. 48 hours post infection, the supernatant was collected and assayed via ELISA for expression of the human anti CTLA-4 antibody and the Flt3 ligand. As depicted in FIG. 40, the SKV-123 virus was capable of producing more antibody against CTLA-4 than Flt3 ligand soluble protein.

[00727] The SKV-123 virus expressing all three transgenes was evaluated in terms of transgene expression kinetics overtime (FIG. 39). Confluent monolayers of 786-O human adenocarcinoma cell lines were infected with SKV-123 virus at an MOI of 3 (3×10^6 pfu). RNA was sequenced using RNA-seq and gene expression of inserted transgenes were determined after read mapping and expression normalization. The data suggest that transgene expression peaks at 3-4 hr. after cell infection occurs.

[00728] In a separate experiment, expression of the three transgenes from the SKV-123v2 virus was further evaluated in three other cancer cell lines: HeLa human cervical cancer cells (American Type Culture Collection (ATCC) Cat. #: CCL-2), HT-29 human colorectal cancer cells (ATCC Cat. #: HTB-38), and CT26.WT murine colorectal cancer cells (ATCC Cat. #: CRL-2638). SKV-123 virus infection at MOIs of 0.1 or 1.0 resulted in CTLA-4 antibody, FLT3L, and IL-12 transgene product production in each of the HeLa, HT-29, and CT26.WT cancer cells (FIGS. 56-59).

6.23. Example 23 SKV expressing murine IL-12 p35 membrane bound has greater efficacy in controlling murine tumors.

[00729] The survival of mice treated with either SKV or SKV-3 virus (expressing murine membrane bound p35 IL-12) was assessed. 5e6 CT26-LacZ cells were seeded subcutaneously on day 0. On days 14, 16 and 18, tumors were treated at a dose of 1e7 pfu with an intratumoural injection of either SKV or SKV-3. Although SKV virus extended

survival of mice bearing CT26 colon tumors, SKV-3 expression of IL-12 is able to induce remissions that lead to durable cures. *See* FIG. 43.

6.24. Example 24 – Major double deletions in engineered in various vaccinia strains enhance cancer cell killing in vitro

[00730] Hela cells were infected at an MOI of 0.1 with the following strains of engineered vaccinia viruses: (1) parental wildtype virus (wt); (2) 5 prime major deleted (5p), (3) 3 prime major deleted (3p), and (4) recombined 5 prime and 3 prime major double deleted (5p3p). Cell viability was quantified by alamar blue assay 72 hours post infection. Both 5p and 5p3p major double deleted vaccinia strains are more cytotoxic in HeLa cells when compared to their parental wildtype and 3p major deleted strains. *See* FIGS. 44-47.

6.25. Example 25 – Efficacy of SKV on tumor volume and survival benefit in 8 different xenograft mouse models

[00731] The objective of these efficacy studies was to determine the anticancer activity of the modified vaccinia viruses comprising both the CopMD5p3p and B8R deletions (SKV) injected intravenously (IV) and/or intratumorally (IT) in athymic nude mice implanted subcutaneously (SC) with either Mia PaCa-2 human pancreatic tumor cells, PC-3 human prostate tumor cells, U87MG human glioma cells, UACC-62 human melanoma cells, UM-UC-3 human bladder tumor cells, COLO-205 human colon tumor cells, NCI-H460 human lung tumor cells or HT29 human colon adenocarcinoma cells.

[00732] Cells were cultured and when the required number of cells were obtained, a total of 45 female, 6-8 week old athymic nude mice were inoculated with tumor cells (Day 0). Each mouse was injected SC in the right flank with ten million cells (1×10^7 cells) in 0.2 mL of 1:1 Matrigel™. When 25 mice had tumors of approximately 100 to 200 mg (target group mean tumor weight of approximately 200 mg), treatment with Vaccinia virus was started.

[00733] The mice were administered 0.05 ml SKV (dose 1e7 pfu) either IT (10 mice) and/or IV (10 mice). Controls (5 mice) were administered 0.05 ml PBS. For IT injections, a 31G ½" needle attached to a sterile syringe was used to inject each tumor. If the tumor was large or irregularly shaped, the tumor was injected in a different area on each day of injection. Mice were observed twice daily for mortality and moribundity. Tumors were measured twice a week starting on first day of treatment. Tumor volumes (mm^3) were calculated using the

equation for an ellipsoid sphere (l x w^2)/2 = mm^3, where l and w refer to the larger and smaller dimensions collected at each measurement.

[00734] On Day 60 after tumor implantation or earlier, any moribund animal, any animal with excessive body weight loss (>30% of the body weight from first day of treatment) or any animal whose total tumor burden reached 4,000 mg, was ulcerated, or was sloughed off was removed from the study.

[00735] These efficacy studies showed a measurable reduction in tumor volume in the Mia PaCa-2, PC-3, U87MG, UACC-62 and UM-UC-3 xenograft models when a dose of 1e7 pfu SKV was administered IV or IT, as shown in FIGs. 48A-48E as well as in COLO-205, H460 and HT29 xenograft models when a dose of 1e7 pfu SKV was administered IT, as shown in FIGs. 48F-48H. These efficacy studies also showed a significant increase in percent survival ($p < 0.0001$) in the all 8 xenograft models when administered with SKV IV and/or IT compared to control mice treated with PBS alone, as shown in FIGS. 48A-48H.

6.26. Example 26 – Efficacy of various SKV vectors on tumor volume and survival benefit in a syngeneic mouse model

[00736] A number of SKV vectors were generated (see Tables 44 and 45 above). The purpose of this study was to compare the efficacy of SKV-12m3v2-eGFP, ipilimumab and SKV in a syngeneic mouse model where all encoded transgenes were active. MC38 colorectal cancer cells (5 x 10^5) were re-suspended in 100 µl of 1:1 mixture of Matrigel and serum free DMEM media were injected SC into the right flank of transgenic C57BL/6 mouse expressing human CTLA-4. Animals were then randomized into 5 treatment groups and then treated with PBS, PBS plus ipilimumab, SKV, anti-PD-1 antibody, SKV-12m3v2-eGFP or SKV-12m3v2-eGFP plus anti-PD-1 antibody. SKV-12m3v2-eGFP is SKV expressing the human anti-CTLA-4 antibody, human Flt3 ligand and mouse IL-12 TM p35. Virus was diluted in PBS to deliver 1 x 10^8 PFU/mouse in 50µl and then total volume injected into the center of the tumor creating a single needle track. Antibodies (ipilimumab 20µg in 100µl and anti-PD-1 antibody 250µg in 100µl) were diluted in sterile PBS to appropriate dose and delivered by ip injection. Mice bearing SC MC38 tumors were treated with 3 doses of either a) ipilimumab at 1 mg/kg, b) SKV at 1 x 10^8 PFU or c) SKV-12m3v2-eGFP at 1 x 10^8 PFU. Tumors were measured, volumes recorded and basic wellness assessed prior to treatment and then over the course of the study (21 days duration). Results from the study are shown in

FIGS. 49 (average tumor volume and survival curves) and FIG. 50 (individual tumor volumes). Ipilimumab alone resulted in delayed tumor growth and 1 cure (10%); SKV alone showed efficacy and 2 cures (20%); SKV expressing the three transgenes significantly improved tumor control, increased survival, and resulted in 3 cures (30%); addition of PD-1 antibody doubled the cure rate (30-60%); and PD-1 antibody alone had no effect (data not shown).

[00737] Tumor control, as compared to the PBS-treated group at the time of the first humane endpoint on study, was observed in response to treatment with ipilimumab ($P< 0.05$), SKV ($P< 0.05$), SKV-12m3v2-eGFP ($P< 0.05$), and SKV-12m3v2-eGFP + anti-PD-1 antibody ($P<0.05$). There was no statistically significant difference in tumor control between the different viruses or with the addition of anti-PD-1 antibody. All statistical tests were performed using multiple t-tests with GraphPad Prism 8.2.

[00738] Increased survival time compared to the PBS-treated group (median survival 19 days) was observed with treatment with SKV ($P< 0.005$, median survival 20=5 days, Ipilimumab ($P< 0.001$, median survival 30 days), SKV-12m3v2-eGFP ($P< 0.001$, median survival 33 days), and SKV-12m3v2-eGFP + anti-PD-1 antibody ($P< 0.001$). Complete tumor regression was observed in the following treatment groups: Ipilimumab (n=1), SKV (n=2), SKV-12m3v2-eGFP (n=3) and SKV-12m3v2-eGFP (n=6). Treatment with SKV-12m3v2-eGFP + anti-PD-1 antibody showed increased survival benefit compared to treatment with SKV alone ($P<0.05$); however, there was no statistically significant difference in survival when comparing SKV-12m3v2-eGFP + anti-PD-1 antibody to SKV-12m3v2-eGFP alone. All statistical tests were performed using the log-rank (Mantel-Cox) test with GraphPad Prism 8.2.

[00739] When the six mice with complete regression of initial tumors in the SKV-12m3v2-eGFP + anti-PD-1 antibody group were rechallenged with 5×10^5 MC38 cells on the opposite flank, 2 mice displayed tumor growth and 4 mice remained resistant to tumor growth.

6.27. Example 27 – Comparison of efficacy of SKV expressing membrane bound IL-12p35-TM subunit versus IL12p70-TM subunit on tumor volume MC-38 mouse models

[00740] The purpose of this study was to compare the efficacy of SKV-mIL12p35 to SKV-mIL12p70 and SKV in the MC38 tumor model to assess whether there are difference in tumor control and survival related to the immune stimulatory potential of the 2 IL12 subunits. MC38 colorectal cancer cells (5×10^5) were re-suspended in 100 µl of 1:1 mixture of

Matrigel and serum free DMEM media were injected SC into the right flank of C57BL/6 mice. Tumors were allowed to grow for 7 days until they were approximately 3x3 mm. Animals were then randomized into 4 treatment groups and then treated with PBS, SKV, SKV-mIL12p35 or SKV-mIL12p70. Virus was diluted in PBS to deliver 1 x 10^7 PFU/mouse in 100µl and then total volume was injected into the center of the tumor creating a single needle track. Results are shown in FIG. 51. SKV, SKV-mIL12p35 and SKV-mIL12p70 treated mice all showed a reduction in tumor volume in comparison to control PBS treated mice. SKV-mIL12p35 and SKV-mIL12p70 treatment were both more effective than SKV treatment alone. SKV-mIL12p35 and SKV-mIL12p70 treated mice showed comparable reductions in tumor volume.

6.28. Example 28 – SKV in a heterologous Prime-boost Oncolytic Vaccine Regimen

[00741] Preliminary results showed that SKV can be used to either prime or boost an immune response in a heterologous vaccine. Ovalbumin (OVA) was used as a foreign antigen in a heterologous prime-boost combination. Animals were primed on day 1, assessed on day 8-10 and then boosted on day 14 and assessed again after the boost at day 21-24. Healthy C57 black mice were treated with PBS (control), Adenovirus expressing OVA, wild-type Copenhagen strain vaccinia virus expressing OVA or CopMD5p3p (SKV backbone) expressing OVA as a prime or a boost. Tetramer analysis was performed evaluating OVA specific responses on Day 21. The mice were assessed at 10 days, showing that CopMD5p3p or SKV backbone but not Copenhagen virus induced immune responses both in prime and boost setting in C57BL/6 mice that were dosed with prime on day 1 and then immune boosted on Day 14 as shown in FIG. 52. CopMD5p3p (SKV backbone) can prime, and the prime response can be boosted by Maraba MG1 oncolytic rhabdovirus. CopMD5p3p (SKV backbone) can boost an Adenovirus prime response. CopMD5p3p (SKV backbone) outperformed parental Copenhagen virus in both priming and boosting an immune response to the foreign antigen.

6.29. Example 29 – BioDistribution of SKV-123 transgenes with IT vs IV administration

[00742] The effect of different routes of administration (IV vs IT) on the biodistribution of the transgenes (Anti-CTLA-4 antibody, FLT3L and IL-12-TM) expressed as a result of treatment with SKV-123 was studied. Female BALB/c mice were engrafted with CT26-LacZ

tumor cells (3 x 10^5 cells) and subsequently given SKV-123 two weeks later (dose 1 x 10^8 PFU) by either IV injection on Study Days 1, 3 and 5, or IT injection on Study Days 1 and 3. Blood and tissues were harvested on Days 2, 4, 6, 8 and 22 for tumor-bearing groups. Spleens were harvested on Days 28 and 43 for non-tumor-bearing groups. Serum was isolated from blood samples (collected from cardiac punctures) and tissues were homogenized for ELISA of FLT3L and anti-CTLA-4 antibody expression. ELISA was performed only on samples that tested positive for viral genomes by PCR. For IL-12-TM biodistribution, tissues were harvested on Days 2, 4, 8, 22, 28, and 43. Tissues were homogenized for Western Blot analysis of IL-12-TM transgene expression. Western Blotting was performed only on samples that tested positive for viral genomes by PCR. Anti-Tubulin was used as a loading control. Tubulin could not be detected in spleen and tail samples, however the presence of protein was confirmed with Ponceau staining of the blot after transfer. SKV-123 given by IV injection on Days 1 and 3 resulted in detectable levels of anti-CTLA-4 antibody and FLT3L in the serum (FIGs. 53A, 53B) and at lower concentrations in the tumors of mice on day 2 (FIGs. 53C, 53D). FLT3L could also be detected on Day 2 in the spleen and tail, and still at Day 4 after IV treatment (FIGs. 53C, 53D). Anti-CTLA-4 antibody remained detectable in the serum on Day 4 regardless of IV or IT treatment (FIG. 53A). IT treatment of SKV-123 resulted in FLT3L concentrations in the tumor on Day 4 (FIG. 53F), while anti-CTLA-4 antibody concentrations were low but detectable (FIG. 53E). Tumor-selective transgene expression has been demonstrated in murine tumor models in which therapeutic payload concentrations were achieved within the tumor (e.g., >7.5ng/ml FLT3L) without any detectable transgene product detected in the systemic circulation.

[00743] Western blotting for IL-12-TM showed only non-specific bands in liver (FIG. 54A), while no IL-12-TM was detected in the tumor, spleen, lungs or tail of animals (FIGs. 54A-54D). The biodistribution of SKV-123 in immunocompetent tumor-bearing mice was restricted to the tumor in IT treated animals and to the tumor and a limited number of other tissues at very low levels in the first few days following IV treatment.

[00744] Viral genomes were not detected in the brain, heart, kidney, ovary, inguinal lymph node, bone marrow, or serum at any of the time points assessed. Viral genomes were only detectable in tumor samples at the Day 4 time point, with the exception of one sample at the Day 9 time point. Genomes were detectable in some tail, lung, spleen, and liver samples,

primarily at the Day 2 and 4 time points. No genomes were detected in any samples from the Day 23 harvest group.

[00745] Viral titers for SKV-123 virus were highest in the tail at Day 2 post-treatment by IV injection, with detectable low levels in the spleen, lung and liver. At Day 4, titers were only detected in the tail for IV injection groups. Viral titers were detected in the tumor for both administration routes, with higher titers found after IT injection compared to IV injection. Virus was also detected in the lung at comparable levels for both routes of administration.

[00746] None of the environmental shedding samples (serum, urine, saliva) examined in this study contained any detectable viral genomes or replicating virus.

6.30. Example 30 – Efficacy of SKV-123v2 on tumor volume in a humanized mouse model

[00747] The efficacy of SKV-123v2 on the growth of tumours in a humanized mouse model was studied. NOD scid gamma (NSG) mice are a brand of immunodeficient laboratory mice that can be treated with human PBMCs and as a result develop a human-like immune system. Female NSG mice were implanted with human PBMCs and then 2 weeks later engrafted subcutaneously with 1 x 10^7 UM-UC-3 xenograft human bladder tumor cells. Tumor volumes (mm^3) were calculated using the equation for an ellipsoid sphere $(l \times w^2)/2 =$ mm^3, where l and w refer to the larger and smaller dimensions collected at each measurement. When tumors were a minimum of 100 mm^3, the mice were treated with SKV-123v2 at 1×10^8 PFU or saline control by IV injection every two days for three weeks. Basic mouse wellness was assessed and tumor volume measured over the course of the study. Tumors were measured twice a week starting on Day 4 of implantation and then from the first day of treatment. On Day 21 the SKV-123v2 treated animals had a mean tumor volume of 164 mm^3 corresponding to a difference of -8.4% relative to the vehicle-treated control with the maximum effect being observed on Day 32 with a difference of -53.2% relative to the control (FIG. 55).

6.31. Example 31 – *In vitro* infectivity comparison of SKV-123v2 in tumor and normal cells

[00748] Viral replication, cytotoxicity, transgene expression and cytokine production following SKV-123v2 virus infection of human normal (PBMC, PrEC) and cancer (786-O,

HeLa) cells were characterized *in vitro*. Human peripheral blood mononuclear cells (PBMCs) were purchased from Lonza (Cat#: CC-2702). Human prostate epithelial cells (PrEC) were purchased from Lonza (Cat. #: CC-2555). 786-O human renal adenocarcinoma cells were purchased from ATCC (Cat. #:CRL-1932). HeLa human cervical cancer cells were purchased from ATCC (Cat. #: CCL-2).

[00749] Cells were seeded on 24-well plates. Cell viability and cytokine expression were assessed at four time points: 6 hr, 24 hr, 48 hr and 72 hrs post infection. To determine the number of viable cells/mL and percent viability of each cell suspension, cell suspensions were placed in a ViCell cup at 0.6 mL each and samples were logged into the instrument. Dilutions were prepared. Cells were infected when monolayers were > 80% confluent (24 hrs following cell seeding). On the day of infection, virus was diluted to the appropriate doses as outlined in Table 47 below. Infection was conducted in 24-well plates.

Table 47. Infection Calculations for 24-Well Plates

MOI	SKV-123v2			
	# cells /well	# wells to make	Volume virus	Volume SFM (µL)
MOI 0.01	2×10^5	55	1.64 µL of 1:10×	2750
MOI 0.1	2×10^5	55	1.64 µL stock	2750
MOI 1	2×10^5	55	16.4 µL stock	2733.6

[00750] Cytokine profiling was conducted at the indicated time points. Infected cell supernatants were aliquoted, stored at -20°C and sent to Eve Technologies for analysis using the Human Cytokine Array/Chemokine Array 42-Plex with IL-18 (HD42). FLT3L and ipilimumab expression were assessed using ELISA assays. Cell Viability was conducted at each harvest timepoint using Alamar Blue, read out on Fluoroskan to determine % viability of treatment wells relative to untreated control wells. Viral titer was determined to assess replication kinetics between different cell lines.

[00751] Normal cells were cultured in the presence of serum growth factors and in a lack of contact inhibition in order to maximize cell viability at the time of infection. Under the tested conditions and at the equivalent cell density used for SKV-123v2 infection experiments, PrECs (prostate epithelial cells) demonstrated a proliferative rate almost as high as HeLa

cancer cells. To better define the phenotype of the tested normal cell lines when cultured under these conditions, a proliferation assay measuring BrdU incorporation was conducted on PrEC cells and PBMCs in a companion study. The intermediate replication of SKV-123v2 in PrECs as compared to the cancer cell lines and PBMCs correlated with the relative proliferation rate of this normal cell line observed under *in vitro* infection conditions.

[00752] The results show that 786-O and HeLa cancer cell lines were sensitive to SKV-123v2 virus infection as evidenced by a decrease in cell viability in a dose dependent and time dependent manner (FIG. 56). 786-O cell viability decreased over time at all MOIs tested while HeLa cell viability decreased upon SKV-123v2 virus infection at an MOI of 1 and 0.1. Normal human PBMCs were resistant to infection as evidenced by high cell viability following SKV-123v2 virus infection at MOIs of 1, 0.1, and 0.01 (FIG. 56). Normal human PrECs were less sensitive to SKV-123v2 virus infection when compared to cancer cell lines. No decrease in cell viability was observed at any MOI (1, 0.1 and 0.01) up to 48 hours post-infection. By 72 hr post infection, decreased cell viability was noted upon SKV-123v2 virus infection at an MOI of 1 and 0.1 (FIG. 56).

[00753] SKV-123v2 viruses infected and replicated in cancer cell lines at higher rates when compared to normal human PrECs (FIG. 57). They infected and replicated in 786-O and HeLa cancer cell lines to levels greater than 10-fold when compared to normal human PrECs. SKV-123v2 viruses did not replicate in normal human PBMCs at MOIs of 1, 0.1, and 0.01 (FIG. 59).

[00754] Anti-CTLA-4 antibody and FLT3L (two transgene products produced by SKV-123v2 virus-infected cells) production was monitored in cell supernatant at each MOI and timepoint. SKV-123v2 virus infection resulted in greater production of anti-CTLA-4 antibody and FLT3L in cancer cells when compared to normal cells (PrEC cells or PBMCs) (FIGS. 58 and 59). No anti-CTLA-4 antibody or FLT3L could be detected in PBMC cell supernatant. FLT3L and anti-CTLA-4 antibody transgene product concentrations correlated with cell susceptibility to SKV-123v2 infection.

[00755] In the cytokine profiling experiment, higher levels of cytotoxicity were observed in SKV-123v2 virus-infected cancers cells than normal cells.

[00756] The cell line PrEC was particularly responsive to viral infection, producing EGF, G-CSF, IL-1a, IL-1RA, IL-4, and IL-18 in a context where only low or negligible concentrations of these cytokines were detectable from HeLa, 786-0, and PBMCs. PrEC and 786-0 were the only cell lines that produced IL-8, TGF-α, and TNFα in response to infection;

while only PrEC and PBMC produced IP-10. PrEC showed dose-dependent production of EGF, with increased production at higher MOI of virus infection. EGF concentration remained consistent within the same dosing group between 24 to 72 hours with a slight increase at 72 hours for cells infected with MOI 1 of virus. In PrEC cells, IL-1a production remained mostly consistent to baseline for 48 hours post-infection, and then increased at 72 hours, with the highest concentrations observed at MOI 1. Likewise, IL-1RA and IL-18 production by PrEC showed dramatic increases in concentration at 72 hours post-infection with low (slight IL-1RA increase at 24 hours in higher MOI 0.1 and 1 infection) or negligible prior to this time point. While production of IL-1RA seemed dose-dependent at 72 hours, MOI 1 of virus resulted in reduced IL-18 production compared to MOI 0.1. PrEC produced reduced IL-4 at 6 hours post-infection in all dosing groups compared to untreated control. However, this IL-4 production increased at 24 hours above baseline and remained high to 72 hours post-infection.

[00757] Alternatively, all cell lines, except PrEC, produced MCP-1. In HeLa and 786-0 cells, high concentrations of MCP-1 were produced at baseline and unaffected by viral infection. In PBMCs, MCP-1 was induced above baseline by high doses of virus: MOI 1 of virus at 24 hours and MOI 0.1 and 1 of virus at 72 hours post-infection.

[00758] Several cytokines increased at 24 and 72 hours post-infection, but not 48 hours (or only marginally), over baseline. In HeLa cells, these are FGF-2 (at MOI 1, while lower dosing was only able to induce production at 72 hours) and IL-6 (MOI 0.01 and 0.1 only; MOI 1 concentrations were consistent over time). In PrEC cells, these are G-CSF (at MOI 0.01 and 0.1 only; MOI 1 concentrations were consistent over time), TGF-α (at MOI 0.01 and 0.1 only; MOI 1 concentrations were consistent over time), TNFα (at MOI 0.01 and 0.1 only; MOI 1 increased over time), and IP-10 (MOI 0.1 and 0.1 only; MOI 1 produced low concentrations). In 786-0 cells, these are FGF-2 (in MOI 0.1 and 1 only; lowest dose MOI 0.01 only induced production at 72 hours), IL-8 (at MOI 0.01 and 0.1 only; MOI 1 concentrations were consistent over time) and TGF-α (at MOI 0.01 and 0.1 only), TNFα (MOI 0.01 and 0.1 only; MOI concentrations were baseline over time). In PBMCs, the cytokine is IP-10 (at MOI 1 only).

[00759] IFNα2 production in HeLa and 786-0 cells peaked at 24 hours post-infection and then dropped over the time-course, while in PrEC cells, IFNα2 production was highest at 72 hours. In all three cell lines, higher dosing at MOI 0.1 or 1 exhibited the lowest cytokine production among the dosing groups.

[00760] IFNγ production was low in all cell lines, with 786-0 exhibiting peak production at 24 hours and then decreasing over time.

6.32. Example 32 – Generation of recombinant vaccinia viruses

[00761] The methods and techniques described in this example were used to generate the vectors described in Table 45. As summarized in Table 45, each of the vectors has been demonstrated to be replication-competent, to express the transgene(s) contained in the vector, and to exhibit cytotoxicity in the cancer cell lines as indicated. Assays as described below were used to generate the data summarized in Table 45.

[00762] Recombination

[00763] Monolayers of nearly confluent (80-90%) U2OS cells are first infected for 2 hrs with vaccinia virus (*e.g.*. SKV virus) to be modified. Following infection, targeting DNA (FIG. 60) is transfected into infected cells. The following day (12-18 hrs post transfection), transfection media is removed and fresh media is added to cells. On the second day (~48 hrs post transfection) cells are frozen and thawed for plaque purification.

[00764] Plaque purification and amplification

[00765] To identify recombinant vaccinia viruses, plaques are screened using the fluorescent marker. Serial dilutions (1:10) of the infection/transfection mixture from the previous step are added to confluent monolayers of U2OS cells for 2hr after which the media is replaced with overlay media to allow plaque formation. Two days later, fluorescent plaques are picked, serially diluted and added to fresh monolayers of U2OS cells followed by overlay media. This process of plaque purification is repeated until all plaques are fluorescent. In order to remove the fluorescent marker, the appropriate recombinase is transfected with the fluorescent virus as outlined in the above step (*i.e.*, Recombination). The process of plaque purification is then continued to select for non-fluorescent plaques.

[00766] A plaque of a pure recombinant virus is then used to infect monolayers of another cell line (*e.g.*, HeLa cells) for expansion, at this step no overlay is added. Once visible cytopathic effect is seen on infected cells, cell lysate is collected and the recombinant virus concentration is determined by viral tittering.

[00767] Transgene expression

[00768] Recombinant viruses are used to infect a variety of cancer cells (*e.g.*, HeLa, U2OS, 786-O, etc.) at various concentrations (*e.g.*, MOI 0.01, 0.1 or 1) for various amounts of time (*e.g.*, 6 hrs, 24 hrs, 48 hrs and 72 hrs post infection). Cell lysates (for Western blot) and cell

supernatants (for ELISA) are frozen and stored at -80 °C for assays relating to transgene production. For transgenes encoding a soluble protein (*e.g.*, FLT3L, anti-CTLA-4 antibody) ELISA kits are used to quantify transgene production. For transgenes encoding cell restricted (*e.g.*, inside the cell or membrane bound) protein products (*e.g.*, membrane bound IL-12), western blots of cell lysates are used to quantify transgene production.

[00769] Cancer Cell Line Cytotoxicity

[00770] Cancer cell line cytotoxicity is determined by the visible cytopathic effect seen by light microscopy on infected cells. The cell lysate may be collected and the recombinant virus concentration determined by viral titering.

Some embodiments

All publications, patents, and patent applications mentioned in this specification are incorporated herein by reference to the same extent as if each independent publication or patent application was specifically and individually indicated to be incorporated by reference.

While the invention has been described in connection with specific embodiments thereof, it will be understood that it is capable of further modifications and this application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the invention that come within known or customary practice within the art to which the invention pertains and may be applied to the essential features hereinbefore set forth, and follows in the scope of the claims.

Some embodiments are within the claims.

Claims

What is claimed is:

1. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
   (a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;
   (b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to Cytotoxic T-lymphocyte Associated Protein 4 (CTLA-4), wherein the first nucleotide sequence is set forth in SEQ ID NO: 214;
   (c) a second transgene comprising a second nucleotide sequence encoding an Interleukin 12 (IL-12) polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215; and
   (d) a third transgene comprising a third nucleotide sequence encoding FMS-like tyrosine kinase 3 ligand (FLT3L), wherein the third nucleotide sequence is set forth in SEQ ID NO: 216.
2. The nucleic acid of claim 1, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.
3. The nucleic acid of claim 1 or 2, further comprising a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody.
4. The nucleic acid of claim 3, wherein the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an H5R promoter, a pS promoter, or a LEO promoter.
5. The nucleic acid of claim 3, wherein the at least one promoter operably linked to the first nucleotide sequence encoding the anti-CTLA-4 antibody is an H5R promoter.
6. The nucleic acid of any one of claims 1-5, further comprising a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide.

7. The nucleic acid of claim 6, wherein the at least one promoter operably linked to the second nucleotide sequence encoding the IL-12 polypeptide is a late promoter.
8. The nucleic acid of claim 7, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561, an F17R promoter, or a D13L promoter.
9. The nucleic acid of claim 7, wherein the late promoter comprises the nucleotide sequence of SEQ ID NO: 561.
10. The nucleic acid of any one of claims 1-9, further comprising a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence encoding FLT3L.
11. The nucleic acid of claim 10, wherein the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter, a B19R promoter, a E3L promoter, an F11L promoter, or a B2R promoter.
12. The nucleic acid of claim 10, wherein the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter.
13. The nucleic acid of claim 10, wherein the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B19R promoter.
14. The nucleic acid of claim 10, wherein the at least one promoter operably linked to the third nucleotide sequence encoding FLT3L is a B8R promoter and a B19R promoter.
15. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
16. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
17. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
18. The nucleic acid of any one of claims 1-14, wherein the first transgene is present in the locus of the deletion in the B8R gene.
19. The nucleic acid of any one of claims 1-14, wherein the second transgene is present in the locus of the deletion in the B8R gene.
20. The nucleic acid of any one of claims 1-14, wherein the third transgene is present in the locus of the deletion in the B8R gene.
21. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

22. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
23. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
24. The nucleic acid of any one of claims 1-14, wherein the first transgene and the second transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
25. The nucleic acid of any one of claims 1-14, wherein the first transgene and the second transgene are present in the locus of the deletion in the B8R gene.
26. The nucleic acid of any one of claims 1-14, wherein the first transgene and the second transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
27. The nucleic acid of any one of claims 1-14, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
28. The nucleic acid of any one of claims 1-14, wherein the first transgene and the third transgene are present in the locus of the deletion in the B8R gene.
29. The nucleic acid of any one of claims 1-14, wherein the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
30. The nucleic acid of any one of claims 1-14, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
31. The nucleic acid of any one of claims 1-14, wherein the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.
32. The nucleic acid of any one of claims 1-14, wherein the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
33. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present in the locus of the deletion in the B8R gene.

34. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present in the locus of the deletion in the B8R gene.
35. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present in the locus of the deletion in the B8R gene.
36. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present in the locus of the deletion in the B8R gene.
37. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present in the locus of the deletion in the B8R gene.
38. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present in the locus of the deletion in the B8R gene.
39. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
40. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
41. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
42. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
43. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third

transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

44. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
45. The nucleic acid of any one of claims 1-14, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
46. The nucleic acid of any one of claims 1-14, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
47. The nucleic acid of any one of claims 1-14, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
48. The nucleic acid of any one of claims 1-14, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
49. The nucleic acid of any one of claims 1-14, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
50. The nucleic acid of any one of claims 1-14, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
51. The nucleic acid of any one of claims 1-14, wherein the first transgene, the second transgene, and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210.
52. The nucleic acid of any one of claims 1-14, wherein the first transgene, the second transgene, and the third transgene are present in the locus of the deletion in the B8R gene.
53. The nucleic acid of any one of claims 1-14, wherein the first transgene, the second transgene, and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

54. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.
55. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene and the third transgene are present in the locus of the deletion in the B8R gene.
56. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene and the second transgene are present in the locus of the deletion in the B8R gene.
57. The nucleic acid of any one of claims 1-14, wherein the first transgene and the second transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present in the locus of the deletion in the B8R gene.
58. The nucleic acid of any one of claims 1-14, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present in the locus of the deletion in the B8R gene.
59. The nucleic acid of any one of claims 1-14, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present in the locus of the deletion in the B8R gene.
60. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
61. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
62. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first

transgene and the second transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

63. The nucleic acid of any one of claims 1-14, wherein the first transgene and the second transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
64. The nucleic acid of any one of claims 1-14, wherein the first transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
65. The nucleic acid of any one of claims 1-14, wherein the second transgene and the third transgene are present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
66. The nucleic acid of any one of claims 1-14, wherein the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
67. The nucleic acid of any one of claims 1-14, wherein the second transgene is present in the locus of the deletion in the B8R gene, and the first transgene and the third transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
68. The nucleic acid of any one of claims 1-14, wherein the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene and the second transgene are present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
69. The nucleic acid of any one of claims 1-14, wherein the first transgene and the second transgene are present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
70. The nucleic acid of any one of claims 1-14, wherein the first transgene and the third transgene are present in the locus of the deletion in the B8R gene, and the second

transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

71. The nucleic acid of any one of claims 1-14, wherein the second transgene and the third transgene are present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
72. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the second transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
73. The nucleic acid of any one of claims 1-14, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the third transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
74. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the first transgene is present in the locus of the deletion in the B8R gene, and the third transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
75. The nucleic acid of any one of claims 1-14, wherein the second transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the third transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
76. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the first transgene is present in the locus of the deletion in the B8R gene, and the second transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.
77. The nucleic acid of any one of claims 1-14, wherein the third transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, the second

transgene is present in the locus of the deletion in the B8R gene, and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210.

78. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;
(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214;
(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215; and
(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216;
wherein the nucleic acid further comprises:
(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;
(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and
(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

79. The nucleic acid of claim 78, wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence, the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence, and the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence.

80. The nucleic acid of claim 78 or 79, wherein the first transgene is present between the partial C2L and F3L vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.
81. The nucleic acid of claim 78 or 79, wherein the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210, and the second transgene and the third transgene are present in the locus of the deletion in the B8R gene.
82. The nucleic acid of claim 80 or 81, wherein the third transgene is upstream of the second transgene.
83. The nucleic acid of claim 80 or 81, wherein the third transgene is downstream of the second transgene.
84. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;
(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes the vaccinia virus nucleotide sequence of SEQ ID NO: 210;
(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and
(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

85. The nucleic acid of claim 84, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

86. The nucleic acid of claim 85, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

87. The nucleic acid of any one of claims 84-86, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

88. The nucleic acid of claim 87, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

89. The nucleic acid of claim 88, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

90. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the

first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

91. The nucleic acid of claim 90, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

92. The nucleic acid of claim 91, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

93. The nucleic acid of any one of claims 90-92, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.
94. The nucleic acid of claim 93, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.
95. The nucleic acid of claim 94, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.
96. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:
(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;
(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes in SEQ ID NO: 210;
(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and
(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;
wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

97. The nucleic acid of claim 96, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

98. The nucleic acid of claim 97, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

99. The nucleic acid of any one of claims 96-98, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

100. The nucleic acid of claim 99, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

101. The nucleic acid of claim 100, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

102. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the

first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

103. The nucleic acid of claim 102, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

104. The nucleic acid of claim 103, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

105. The nucleic acid of any one of claims 102-104, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

106. The nucleic acid of claim 105, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

107. The nucleic acid of claim 106, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

108. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

109. The nucleic acid of claim 108, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

110. The nucleic acid of claim 109, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

111. The nucleic acid of any one of claims 108-110, wherein the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

112. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second

transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

113. The nucleic acid of claim 112, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

114. The nucleic acid of claim 113, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

115. The nucleic acid of any one of claims 112-114, wherein the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

116. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

117. The nucleic acid of claim 116, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

118. The nucleic acid of claim 117, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

119. The nucleic acid of any one of claims 116-118, wherein the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

120. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

121. The nucleic acid of claim 120, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

122. The nucleic acid of claim 121, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

123. The nucleic acid of any one of claims 120-122, wherein the nucleotide sequence of the pS comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

124. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the

third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

125. The nucleic acid of claim 124, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

126. The nucleic acid of claim 125, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

127. The nucleic acid of any one of claims 124-126, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

128. The nucleic acid of claim 127, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

129. The nucleic acid of claim 128, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

130. The nucleic acid of any one of claims 124-129, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

131. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene, of the vaccinia virus nucleotide sequence of SEQ ID NO: 210 and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

132. The nucleic acid of claim 131, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

133. The nucleic acid of claim 132, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

134. The nucleic acid of any one of claims 131-133, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

135. The nucleic acid of claim 134, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

136. The nucleic acid of claim 135, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

137. The nucleic acid of any one of claims 131-136, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

138. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter or a B19R promoter.

139. The nucleic acid of claim 138, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

140. The nucleic acid of claim 139, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

141. The nucleic acid of any one of claims 138-140, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

142. The nucleic acid of claim 141, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

143. The nucleic acid of claim 142, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

144. The nucleic acid of any one of claims 138-143, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

145. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

146. The nucleic acid of claim 145, wherein the at least one promoter operably linked to the third nucleotide sequence is a B8R promoter and a B19R promoter.

147. The nucleic acid of claim 146, wherein the B8R promoter comprises the nucleotide sequence of SEQ ID NO: 564 and the B19R promoter comprises the nucleotide sequence of SEQ ID NO: 565.

148. The nucleic acid of any one of claims 145-147, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

149. The nucleic acid of claim 148, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

150. The nucleic acid of claim 149, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

151. The nucleic acid of any one of claims 145-150, nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

152. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

153. The nucleic acid of claim 152, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

154. The nucleic acid of claim 153, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

155. The nucleic acid of claim 154, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

156. The nucleic acid of any one of claims 152-155, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

157. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

158. The nucleic acid of claim 157, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

159. The nucleic acid of claim 158, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

160. The nucleic acid of claim 159, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

161. The nucleic acid of any one of claims 157-160, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

162. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

163. The nucleic acid of claim 162, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

164. The nucleic acid of claim 163, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

165. The nucleic acid of claim 164, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

166. The nucleic acid of any one of claims 162-165, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

167. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215,

and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is an H5R promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is a late promoter that comprises the nucleotide sequence of SEQ ID NO: 561; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

168. The nucleic acid of claim 167, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter or an H5R late promoter.

169. The nucleic acid of claim 168, wherein the at least one promoter operatively linked to the first nucleotide sequence is an H5R early promoter and an H5R late promoter.

170. The nucleic acid of claim 169, wherein the H5R early promoter comprises the nucleotide sequence of SEQ ID NO: 553 and the H5R late promoter comprises the nucleotide sequence of SEQ ID NO: 554.

171. The nucleic acid of any one of claims 167-170, nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

172. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

173. The nucleic acid of claim 172, wherein the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

174. The nucleic acid of claim 172 or 173, wherein the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

175. The nucleic acid of any one of claims 172-174, wherein the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

176. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial C2L and F3L vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

177. The nucleic acid of claim 176, wherein the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

178. The nucleic acid of claim 176 or 177, wherein the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

179. The nucleic acid of any one of claims 176-178, wherein the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

180. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is upstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

181. The nucleic acid of claim 180, wherein the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

182. The nucleic acid of claim 170 or 181, wherein the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

183. The nucleic acid of any one of claims 180-182, wherein the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

184. A nucleic acid comprising a recombinant vaccinia virus genome, comprising:

(a) a vaccinia virus nucleotide sequence of SEQ ID NO: 210, which comprises partial C2L, F3L, B14R, and B29R vaccinia genes and which comprises a deletion in the B8R gene;

(b) a first transgene comprising a first nucleotide sequence encoding an antibody that specifically binds to CTLA-4, wherein the first nucleotide sequence is set forth in SEQ ID NO: 214, and wherein the first nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the first nucleotide sequence and the

first transgene is present between the partial B14R and B29R vaccinia genes of the vaccinia virus nucleotide sequence of SEQ ID NO: 210;

(c) a second transgene comprising a second nucleotide sequence encoding an IL-12 polypeptide, wherein the second nucleotide sequence is set forth in SEQ ID NO: 215, and wherein the second nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the second nucleotide sequence and the second transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210; and

(d) a third transgene comprising a third nucleotide sequence encoding FLT3L, wherein the third nucleotide sequence is set forth in SEQ ID NO: 216, wherein the third nucleotide sequence is in the same orientation as endogenous vaccinia virus genes that flank the third nucleotide sequence and the third transgene is present in the locus of the deletion in the B8R gene of the vaccinia virus nucleotide sequence of SEQ ID NO: 210, and wherein the third transgene is downstream of the second transgene;

wherein the nucleic acid further comprises:

(i) a nucleotide sequence comprising at least one promoter operably linked to the first nucleotide sequence, wherein the at least one promoter operably linked to the first nucleotide sequence is a pS promoter;

(ii) a nucleotide sequence comprising at least one promoter operably linked to the second nucleotide sequence, wherein the at least one promoter operably linked to the second nucleotide sequence is an F17R promoter; and

(iii) a nucleotide sequence comprising at least one promoter operably linked to the third nucleotide sequence, wherein the at least one promoter operably linked to the third nucleotide sequence is a E3L promoter.

185. The nucleic acid of claim 184, wherein the nucleotide sequence of the pS promoter comprises the nucleotide sequence of SEQ ID NO: 555, SEQ ID NO: 556, or SEQ ID NO: 557.

186. The nucleic acid of claim 174 or 185, wherein the nucleotide sequence of the F17R promoter comprises the nucleotide sequence of SEQ ID NO: 563.

187. The nucleic acid of any one of claims 184-186, wherein the nucleotide sequence of the E3L promoter comprises the nucleotide sequence of SEQ ID NO: 567.

188. A virus comprising the nucleic acid comprising a recombinant vaccinia virus genome of any one of claims 1-187.

189. A packaging cell line comprising the nucleic acid of any one of claims 1-187.

190. A packaging cell line comprising the virus of claim 188.

191. A pharmaceutical composition comprising the virus of claim 188 and a physiologically acceptable carrier.

192. A kit comprising the nucleic acid of any one of claims 1-187 and a package insert instructing a user of the kit to express the nucleic acid in a host cell.

193. A kit comprising the virus of claim 188 and a package insert instructing a user of the kit to express the virus in a host cell.

194. A kit comprising the virus of claim 188 and a package insert instructing a user to administer a therapeutically effective amount of the virus to a mammalian patient having cancer, thereby treating the cancer.

195. The kit of claim 194, wherein the mammalian patient is a human patient.

196. A method of treating cancer in a mammalian patient, the method comprising administering to the mammalian patient a therapeutically effective amount of the virus of claim 188.

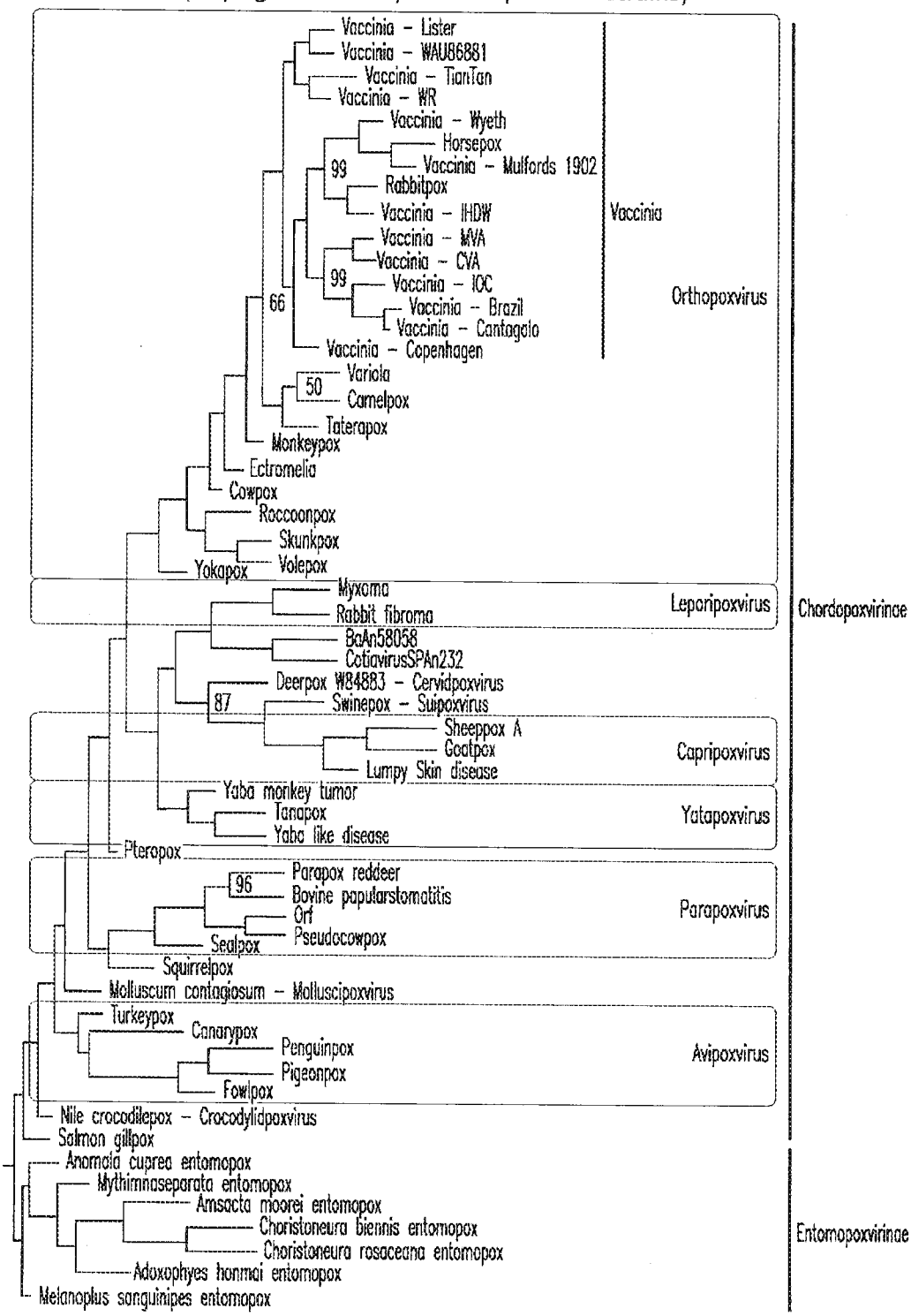
197. A method of treating cancer in a mammalian patient, the method comprising administering to the mammalian patient a therapeutically effective amount of the pharmaceutical composition of claim 191.

198. The method of claim 196 or 197, wherein the mammalian patient is a human patient.

199. The method of any one of claims 196-198, wherein the cancer is selected from the group consisting of leukemia, lymphoma, liver cancer, bone cancer, lung cancer, brain cancer, bladder cancer, gastrointestinal cancer, breast cancer, cardiac cancer, cervical cancer, uterine cancer, head and neck cancer, gallbladder cancer, laryngeal cancer, lip and oral cavity cancer, ocular cancer, melanoma, pancreatic cancer, prostate cancer, colorectal cancer, testicular cancer, and throat cancer.

200. The method of claim 199, wherein the method further comprises administering to the mammalian patient an anti-PD1 antibody or an anti-PD-L1 antibody.

FIG. 1
(Phylogenetic analysis of 59 poxvirus strains)



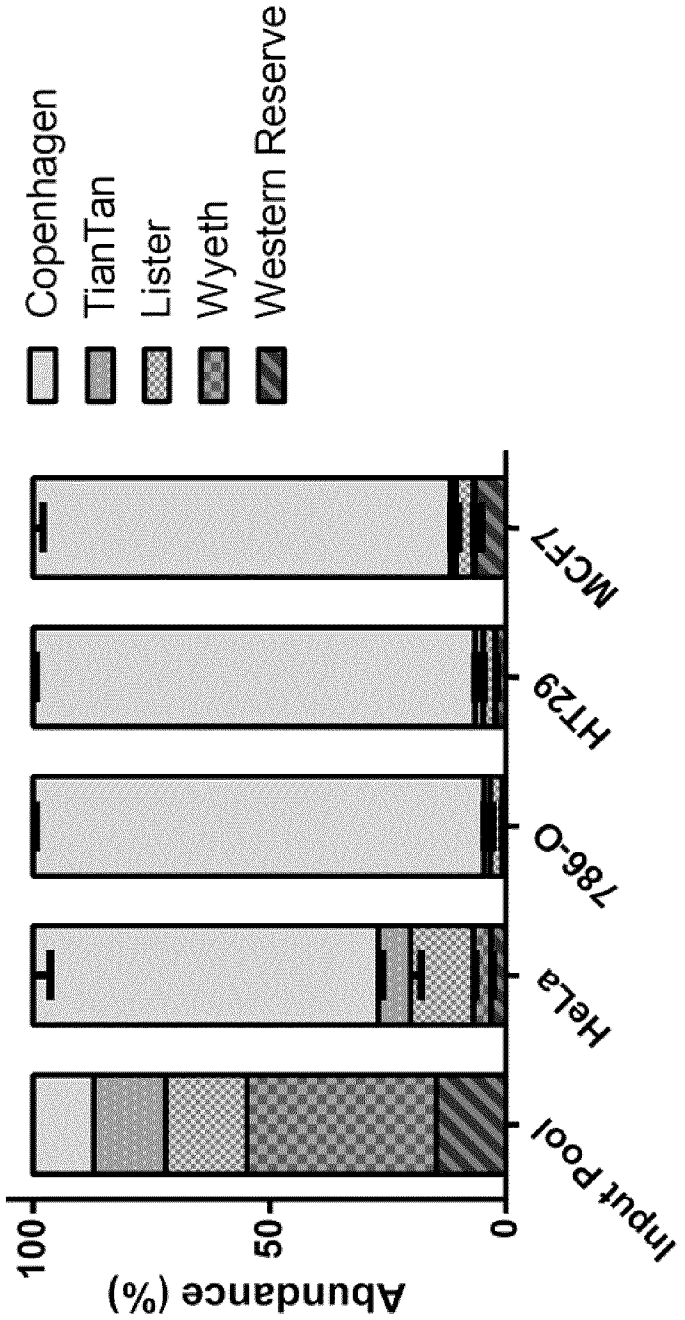


FIG. 2
(Fitness competition)

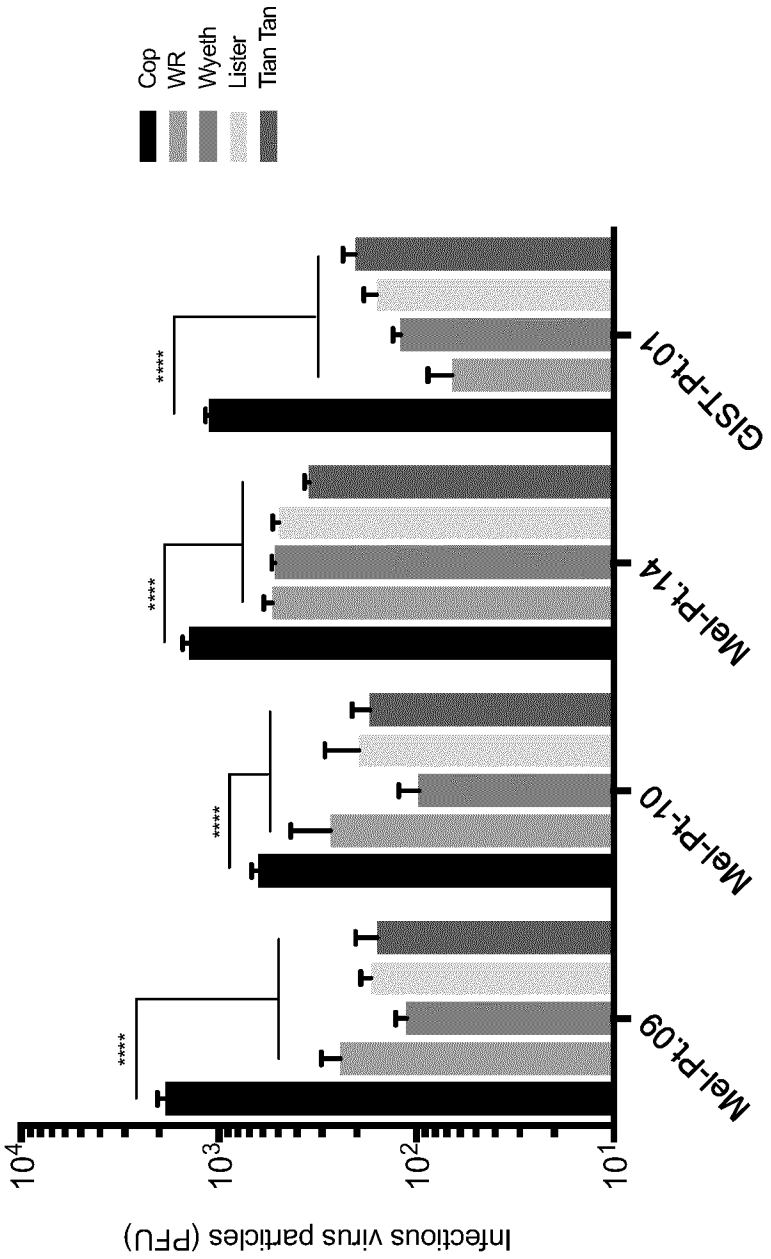


FIG. 3
(Replication in patient tumor cores)

FIG. 4
(Vaccinia plaque size formation)

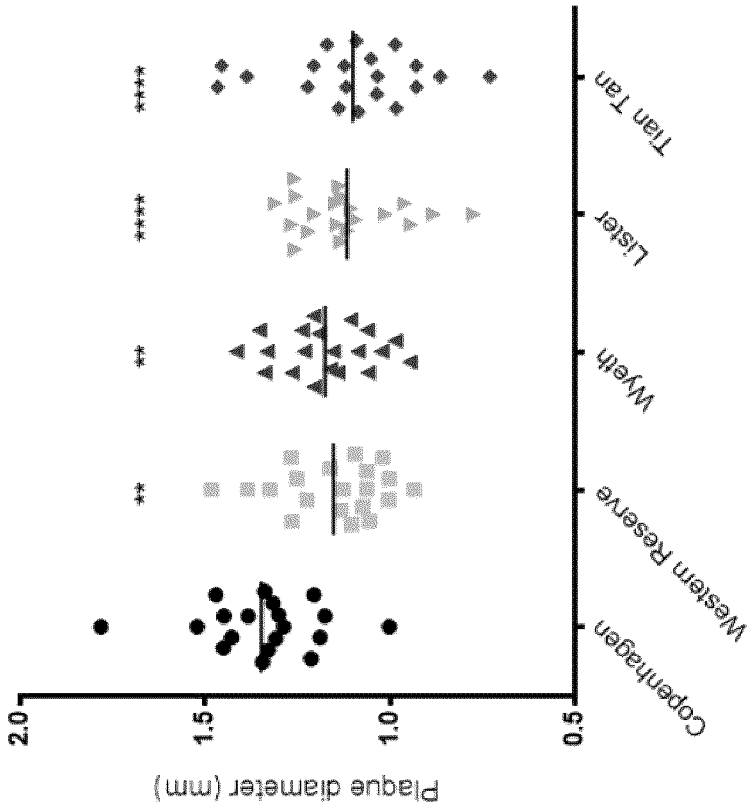
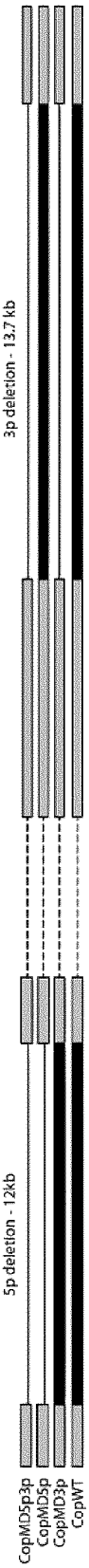


FIG. 5
(Major deletions)



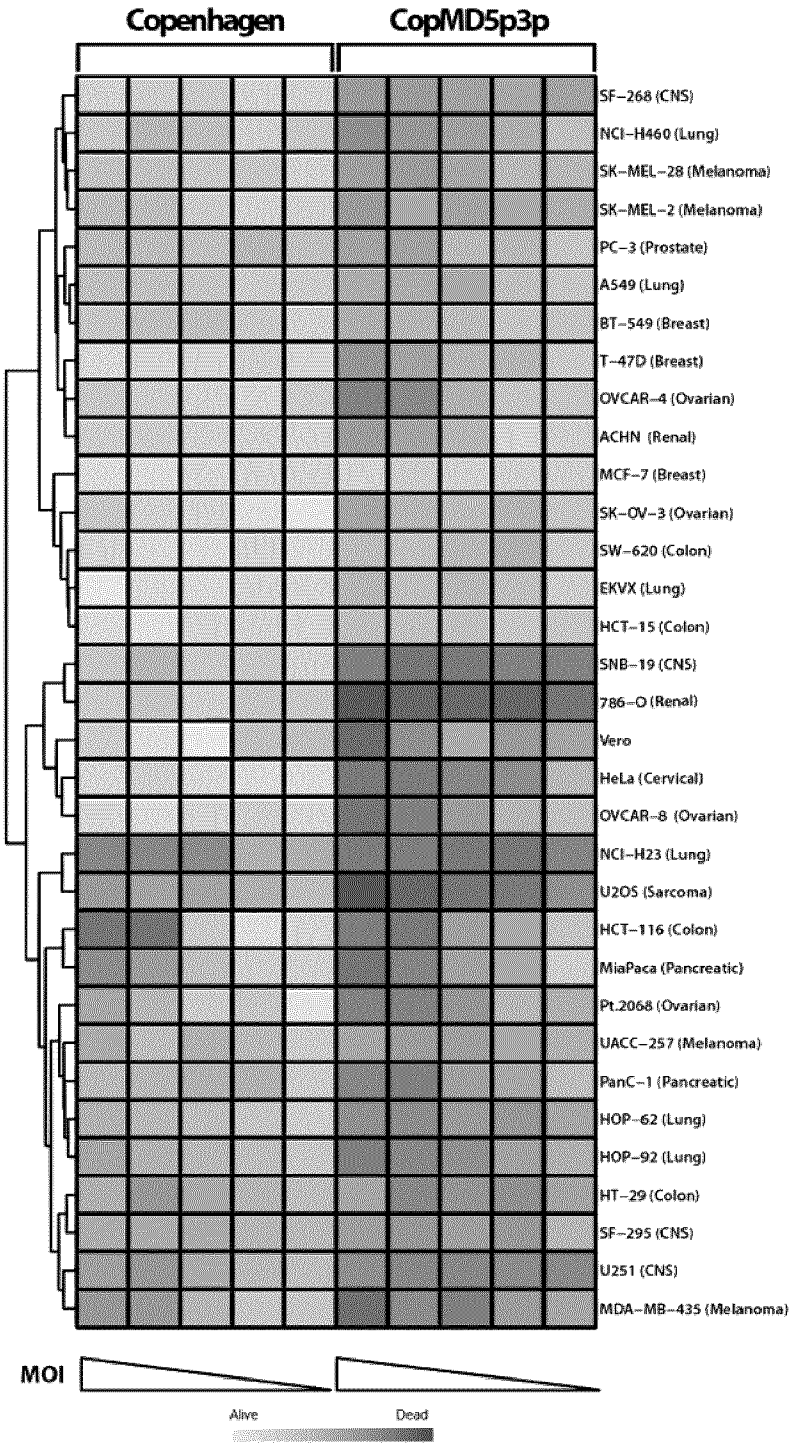
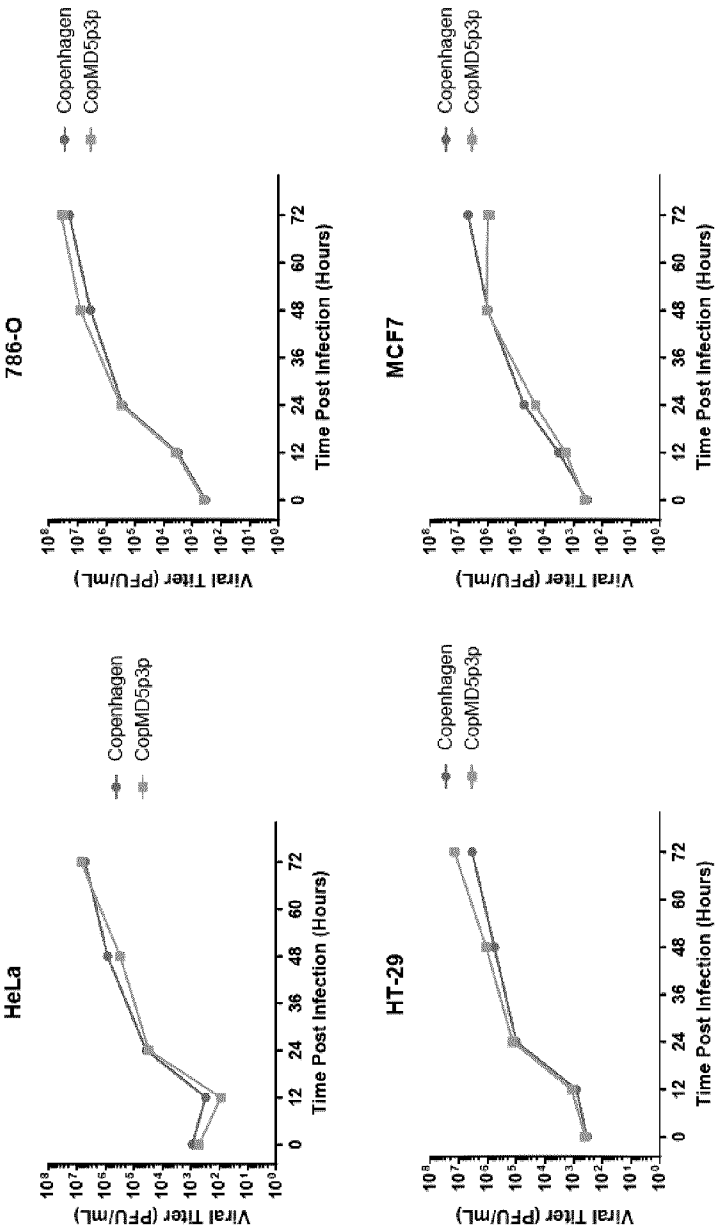


FIG. 6
(Cancer cell killing)

FIG. 7
(Growth in cancer cells)



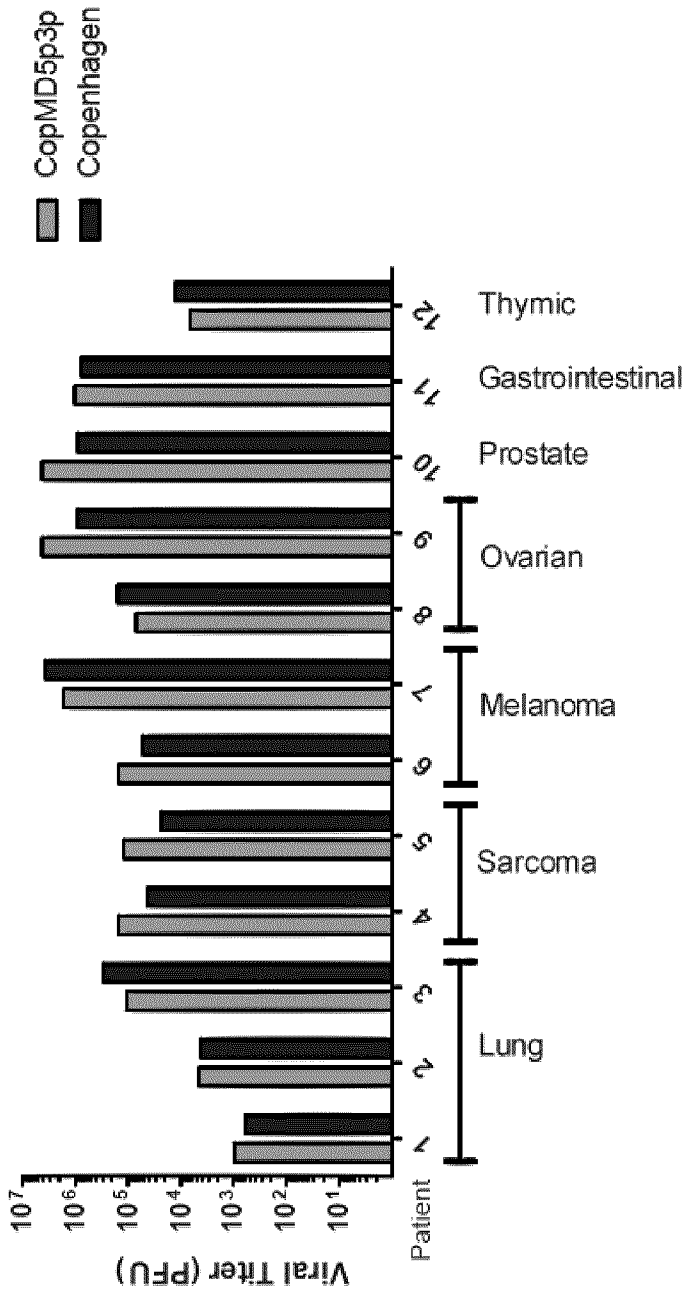
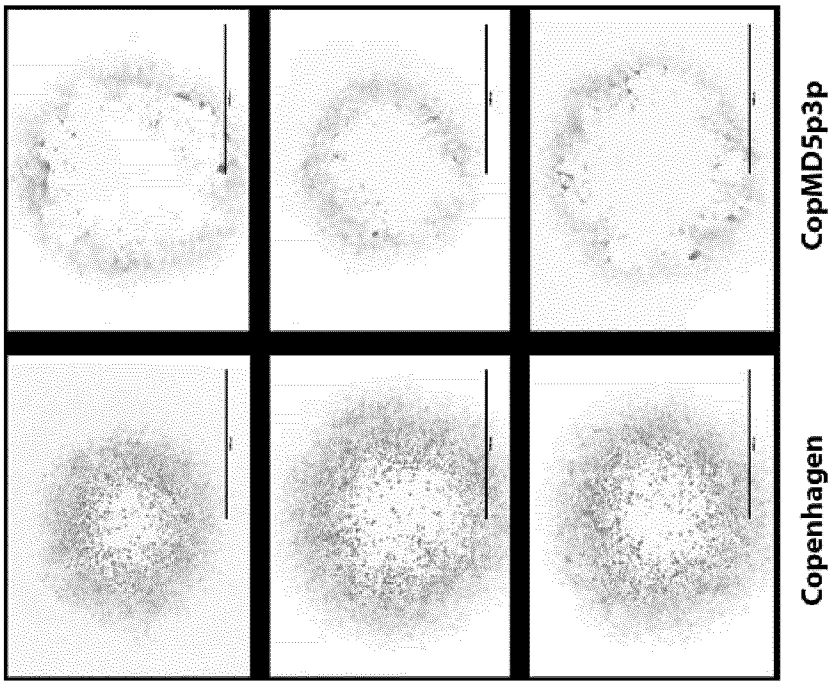


FIG. 8
(Growth in patient tumor samples)

FIG. 9
(Plaque difference, syncytia)



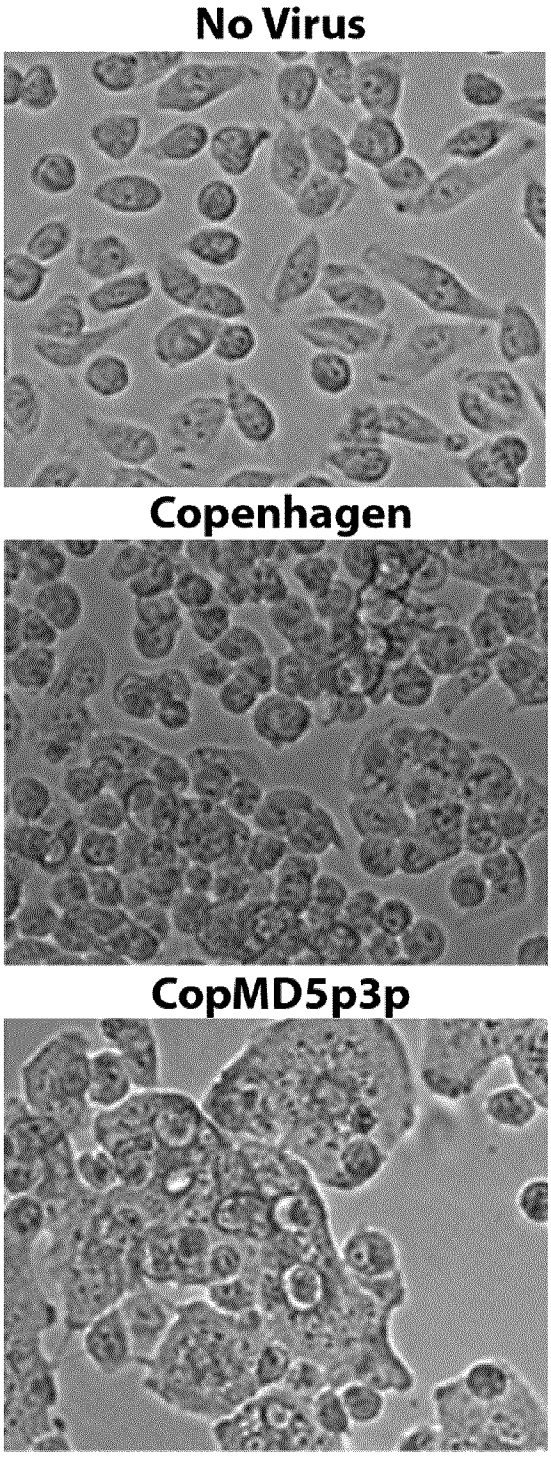


FIG. 10
(Syncytia)

FIG. 11
(Tumor control and weight loss)

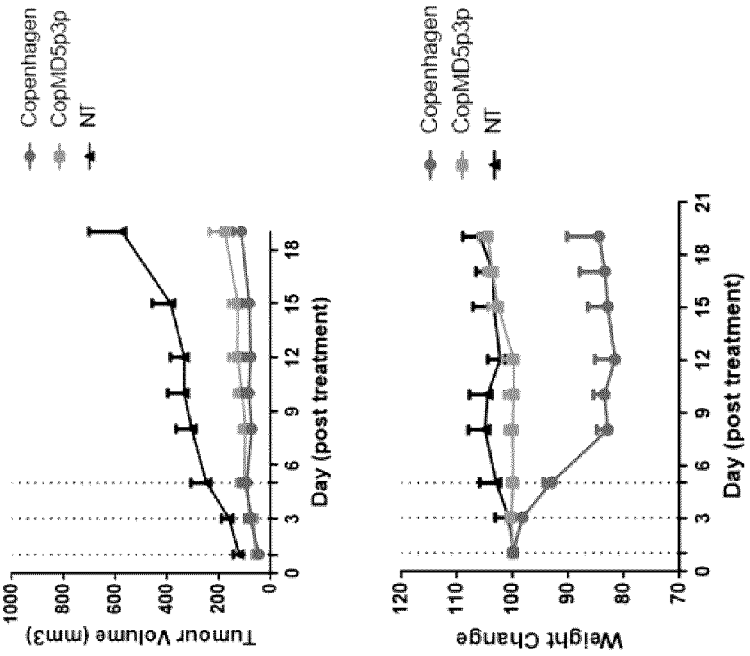
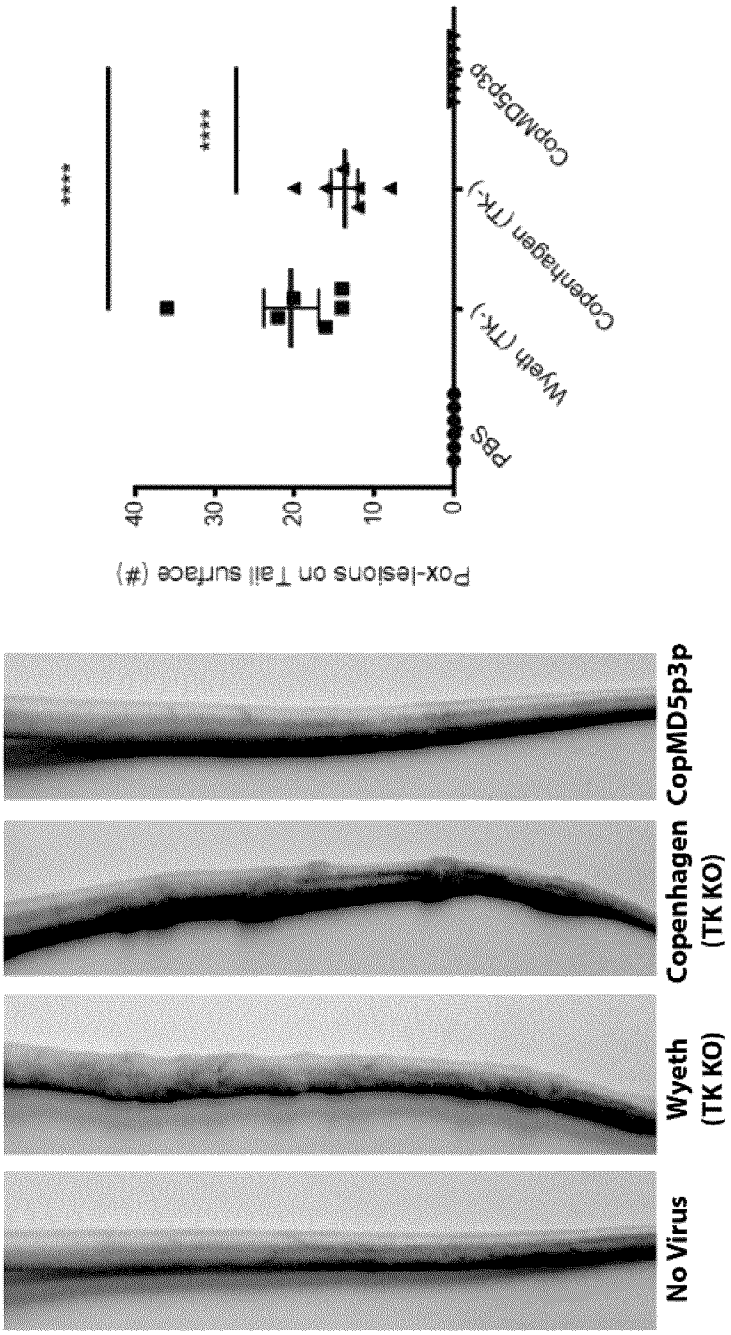


FIG. 12
(Pox lesion formation)



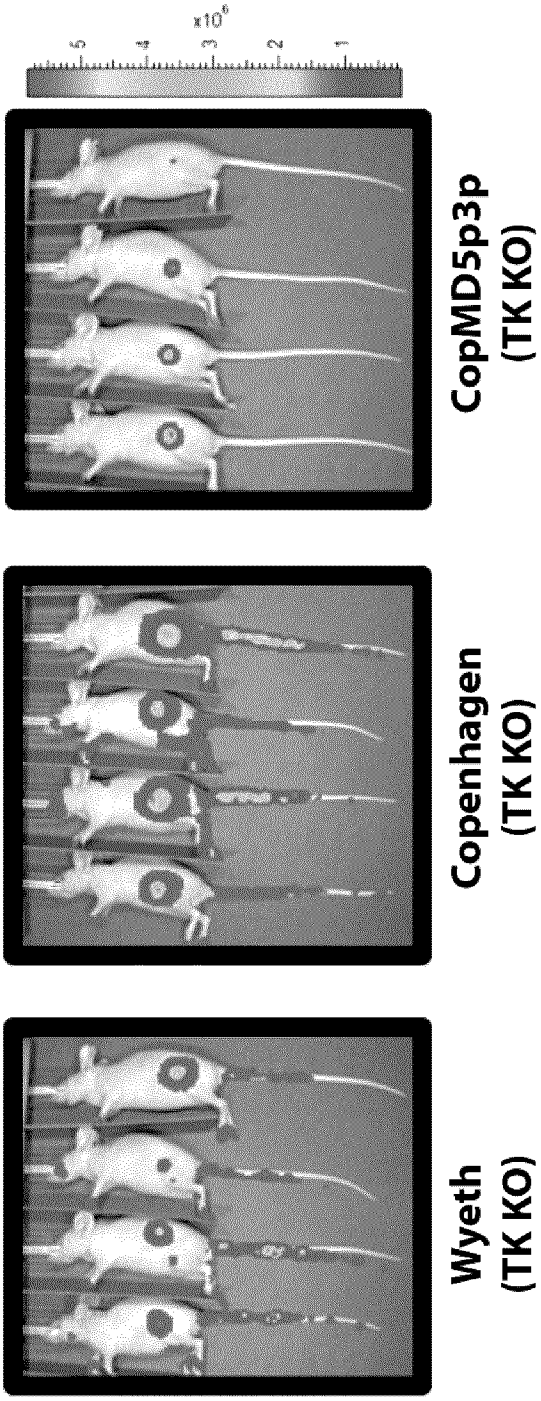


FIG. 13
(IVIS Bio-distribution of Vaccinia after systemic administration)

FIG. 14
(Bio-distribution of Vaccinia after systemic administration (titer))

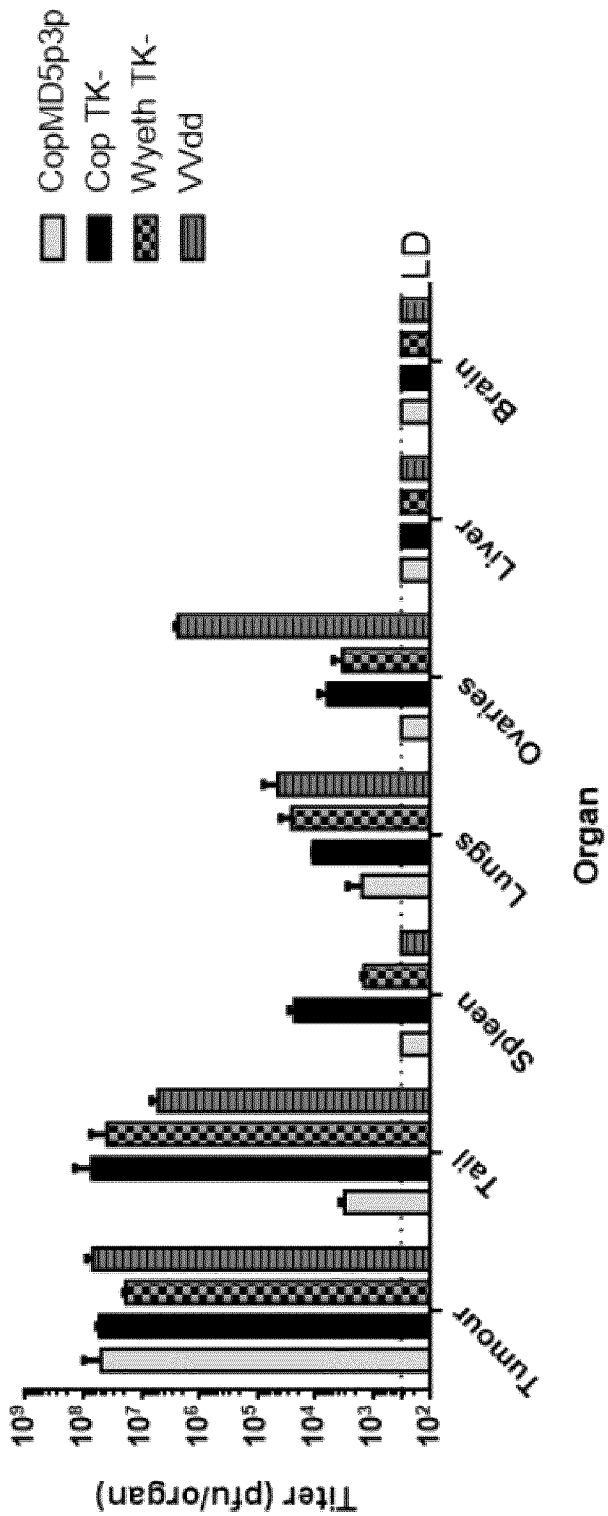


FIG. 15
(Immunogenicity of Vaccinia in Human PBMCs)

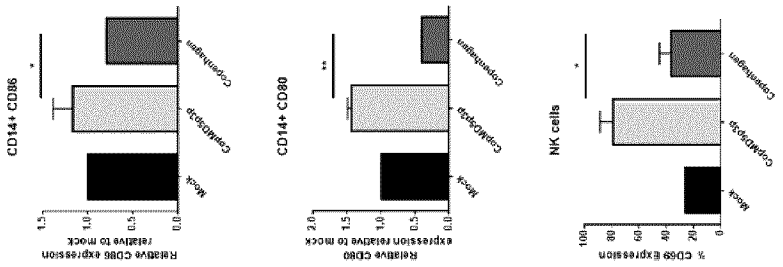


FIG. 16
(immunogenicity of Vaccinia in Mouse Splenocytes)

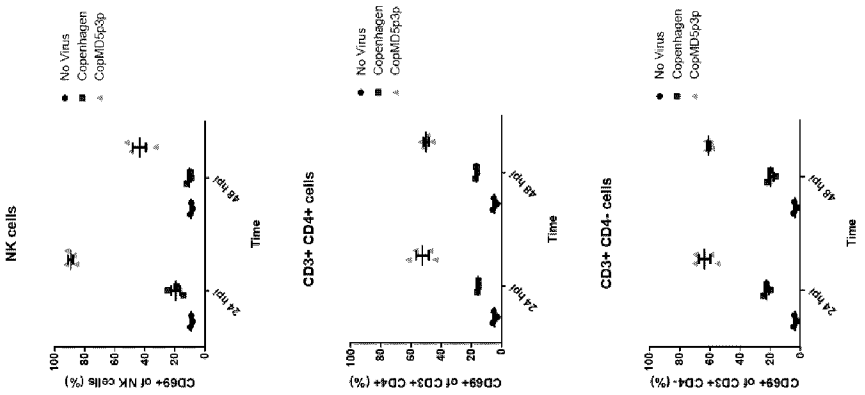


FIG. 17
(immunogenicity of Vaccinia in Human cells)

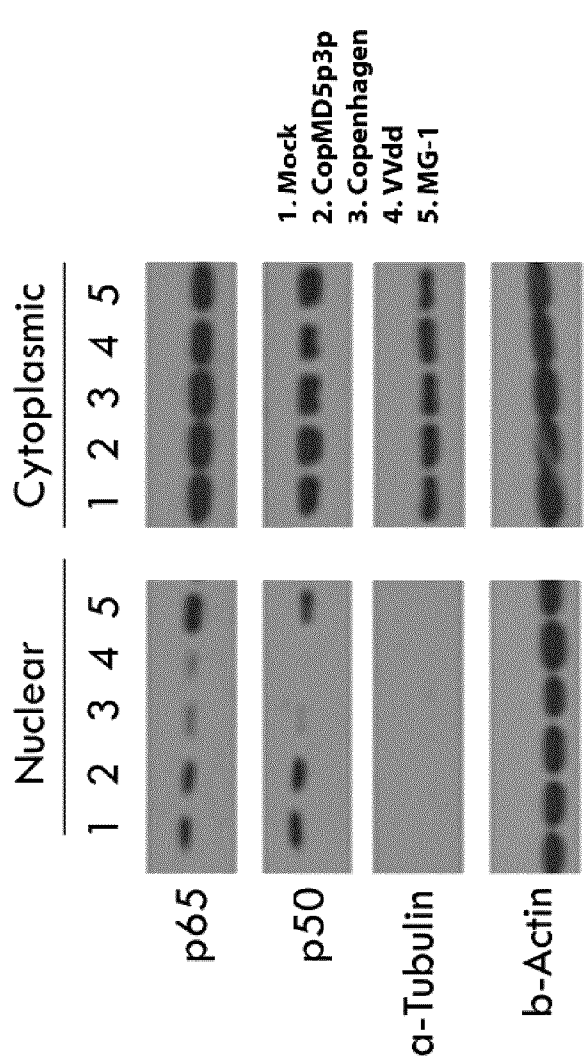


FIG. 18
(Synergy with immune checkpoint inhibitor Anti-CTLA-4 in an aggressive melanoma model)

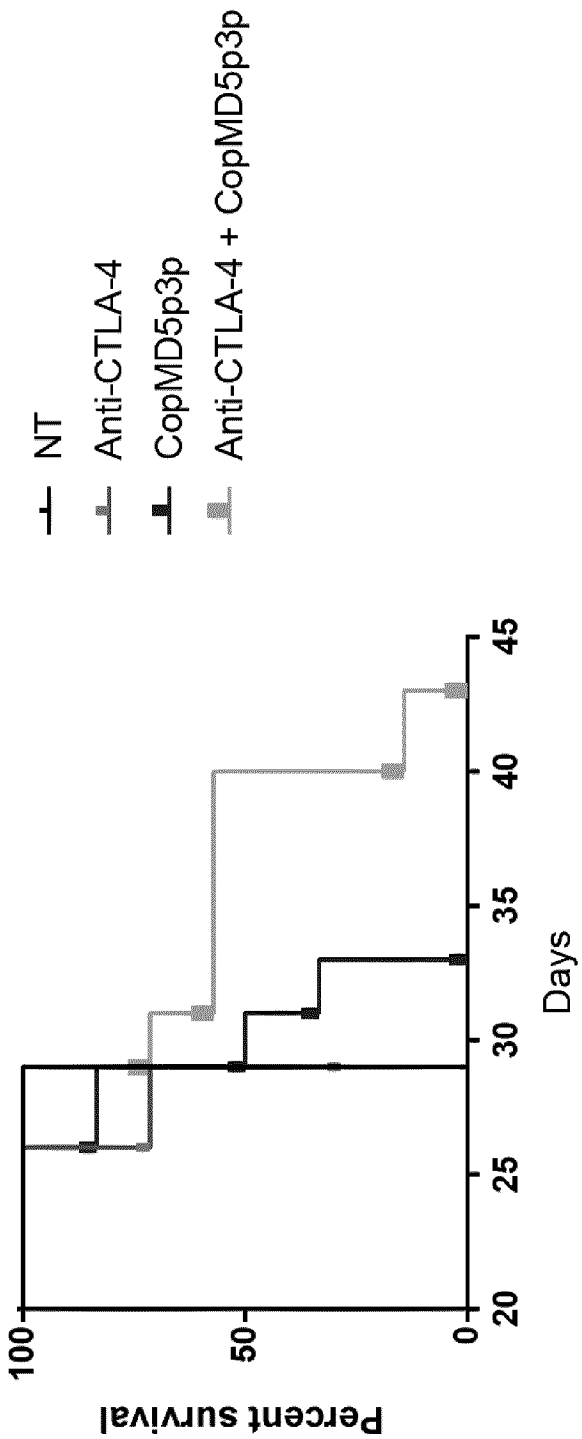


FIG. 19
(synergy with immune checkpoint inhibitor Anti-CTLA4)

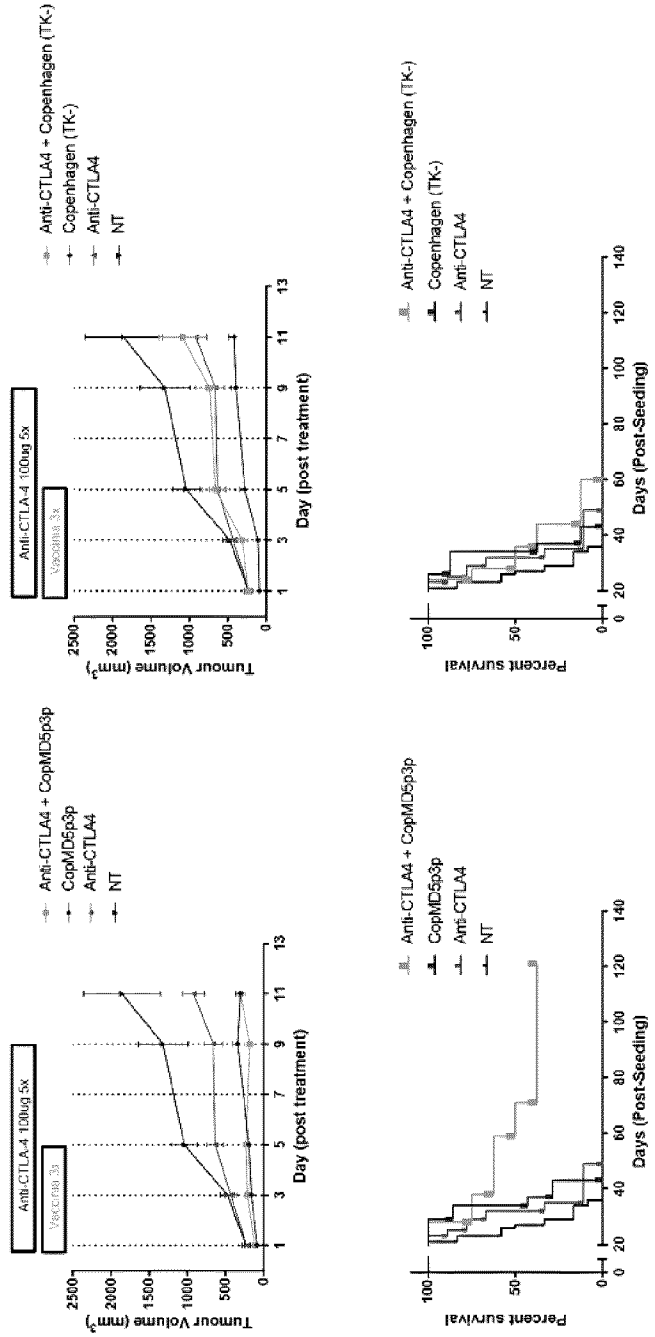


FIG. 20
(synergy with immune checkpoint inhibitor Anti-PD1)

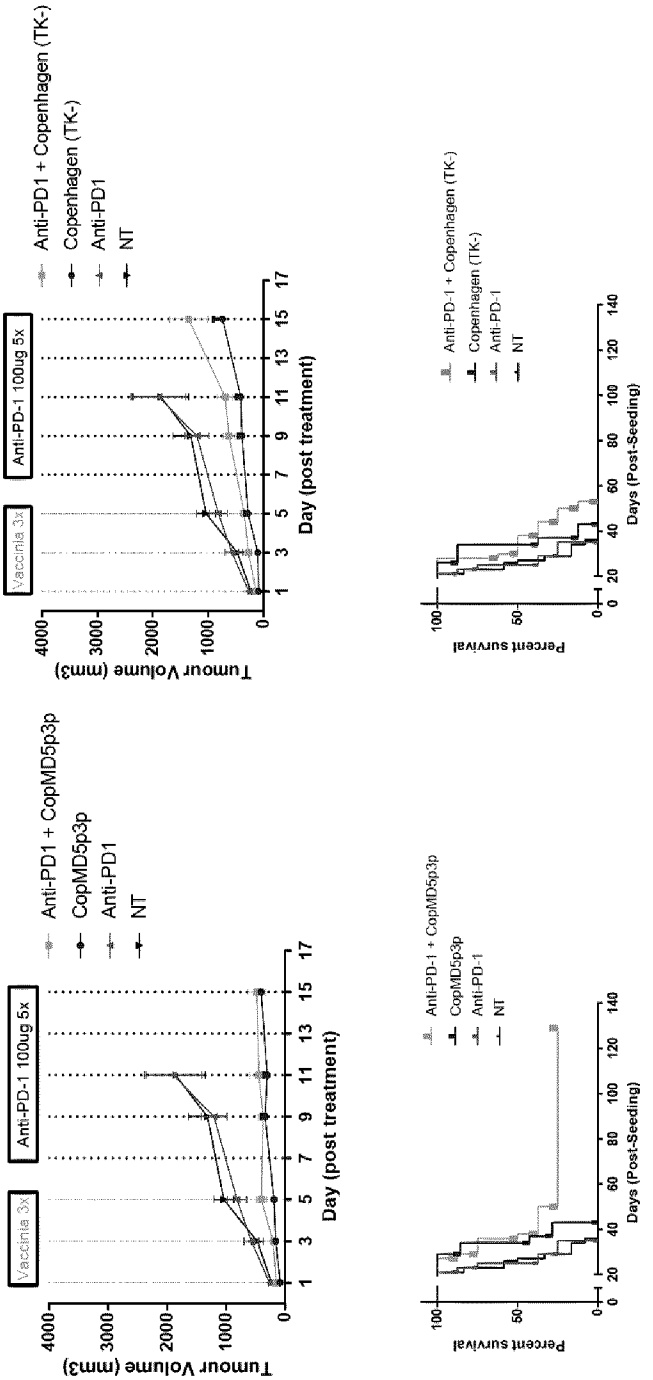


FIG. 21
(synergy with immune checkpoint inhibitors Anti-PD1 and Anti-CTLA-4)

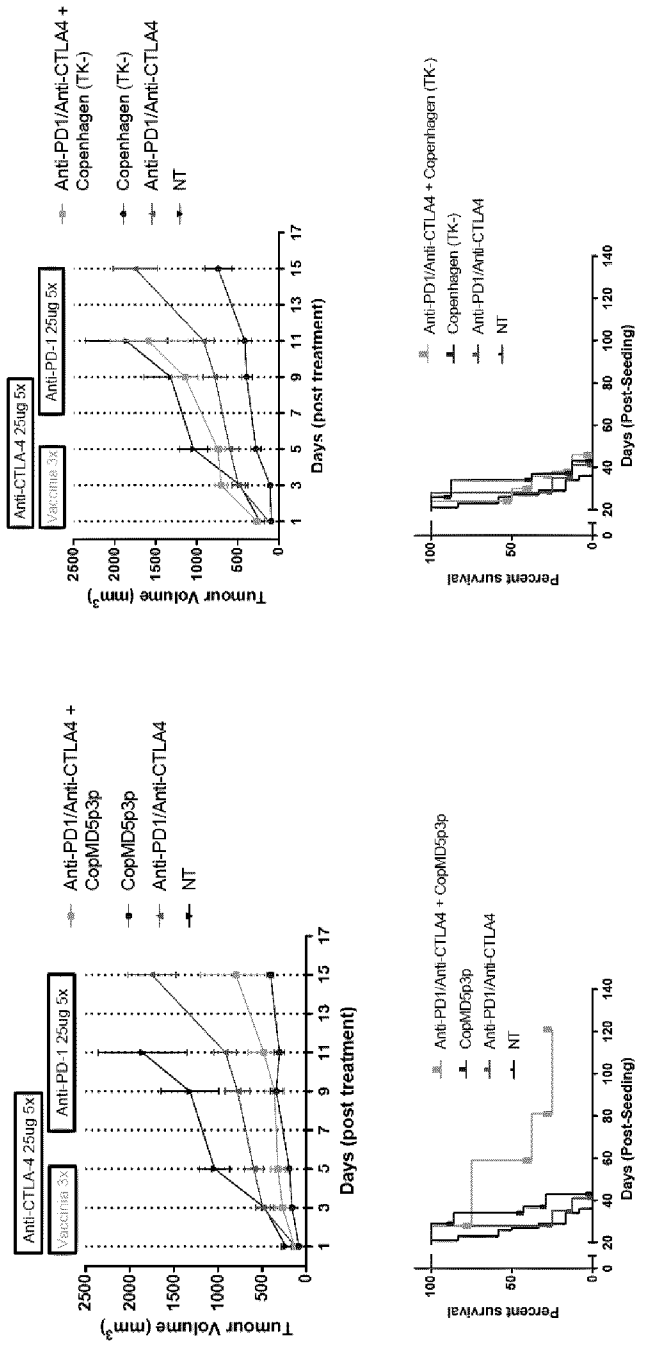


FIG. 22

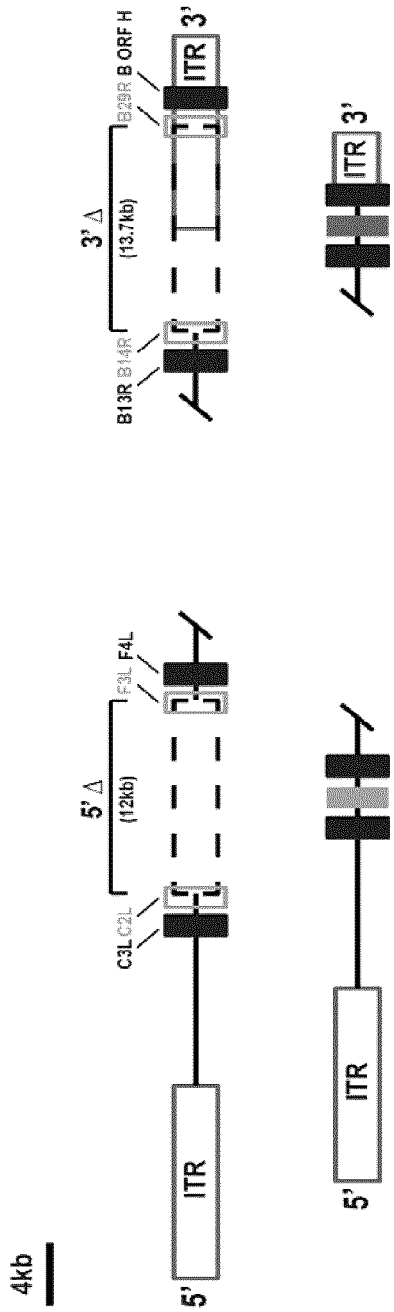

4kb
5'
ITR
C3L C2L
5' Δ
(12kb)
F3L F4L
5'
ITR
B13R B14R
3' Δ
(13.7kb)
B29R B ORF H
3'
ITR
3'
ITR

FIG. 23

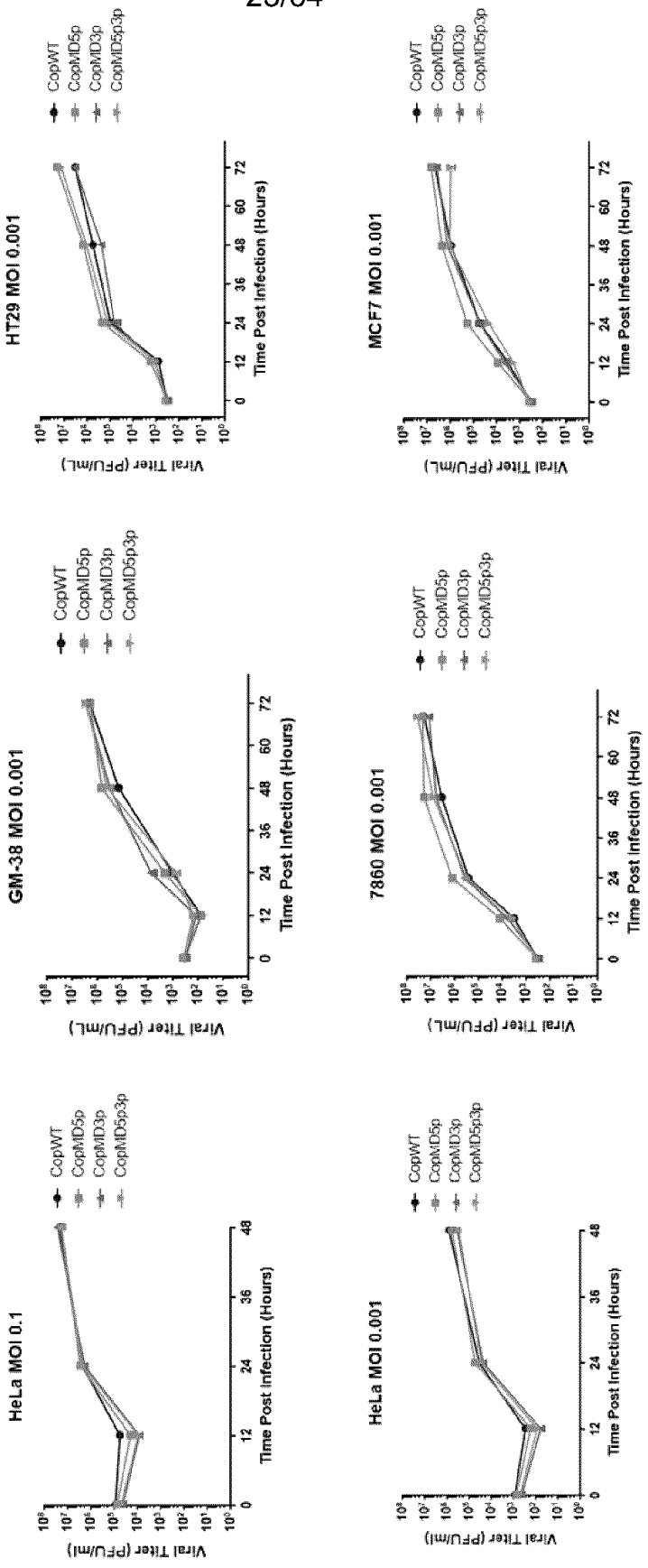

HeLa MOI 0.1
GM-38 MOI 0.001
HT29 MOI 0.001
HeLa MOI 0.001
7860 MOI 0.001
MCF7 MOI 0.001
CopWT
CopMD5p
CopMD3p
CopMD5p3p
Viral Titer (PFU/mL)
Viral Titer (PFU/ml)
Time Post Infection (Hours)

FIG. 24

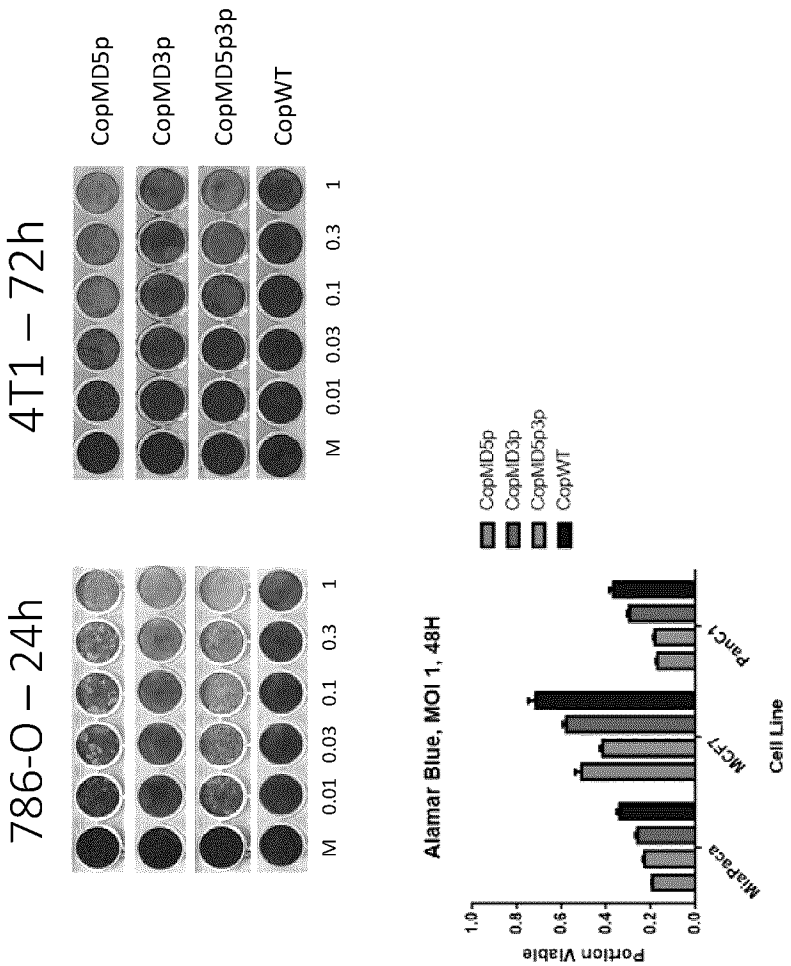

HeLa– 24h
786-O – 24h
4T1 – 72h
CopMD5p
CopMD3p
CopMD5p3p
CopWT
M 0.01 0.03 0.1 0.3 1
Alamar Blue, MOI 1, 48H
Portion Viable
1.0
0.8
0.6
0.4
0.2
0.0
MiaPaca
MCF7
Panc1
Cell Line

FIG. 25

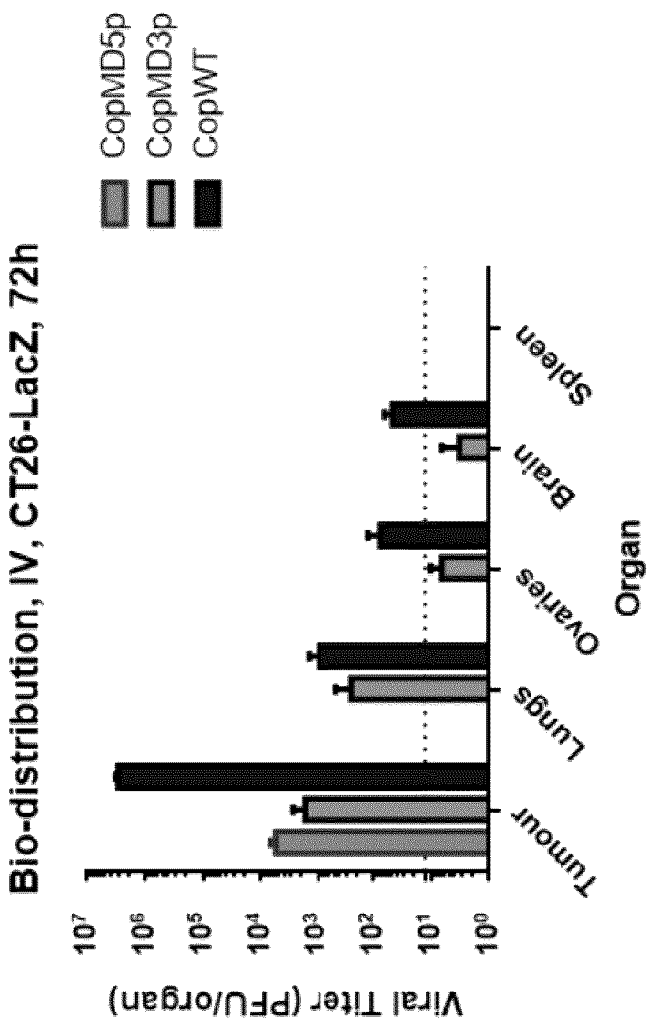

Bio-distribution, IV, CT26-LacZ, 72h
CopMD5p
CopMD3p
CopWT
Viral Titer (PFU/organ)
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
Tumour
Lungs
Ovaries
Brain
Spleen
Organ

FIG. 26

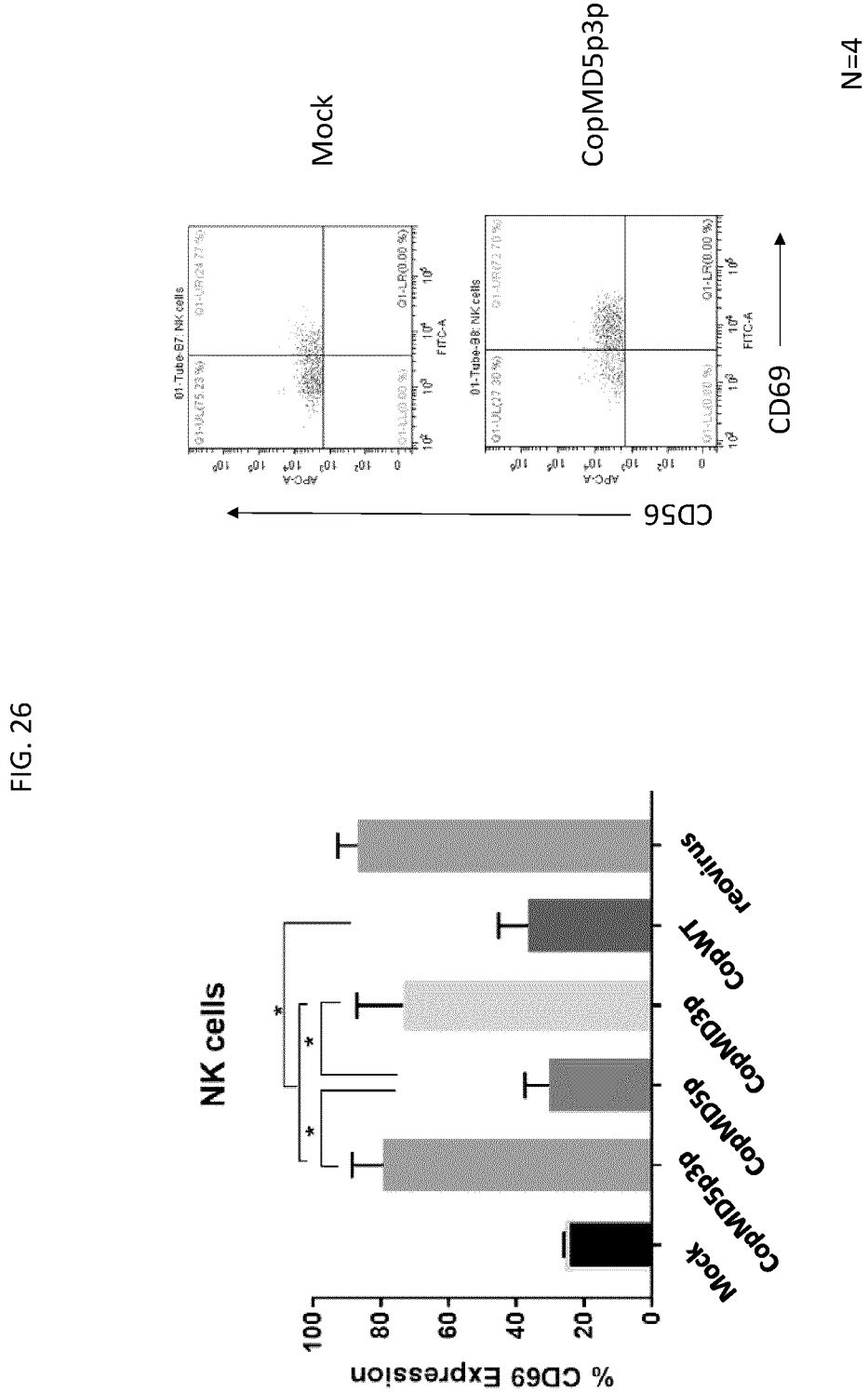

Mock
CopMD5p3p
N=4
CD56
CD69
01-Tube-B7: NK cells
01-Tube-B8: NK cells
APC-A
FITC-A
NK cells
% CD69 Expression
0
20
40
60
80
100
Mock
CopMD5p3p
CopMD5p
CopMD3p
CopWT
reovirus
*
*
*

FIG. 27

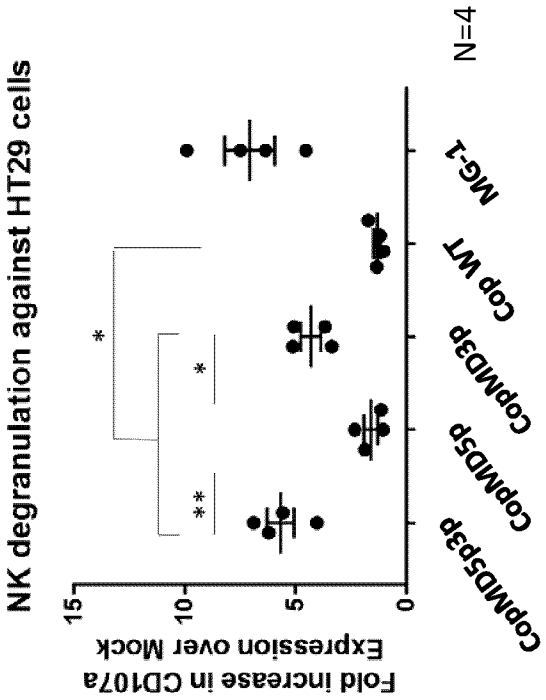

NK degranulation against HT29 cells
Fold increase in CD107a Expression over Mock
15
10
5
0
**
*
*
N=4
CopMD5p3p
CopMD5p
CopMD3p
Cop WT
MG-1

FIG. 28

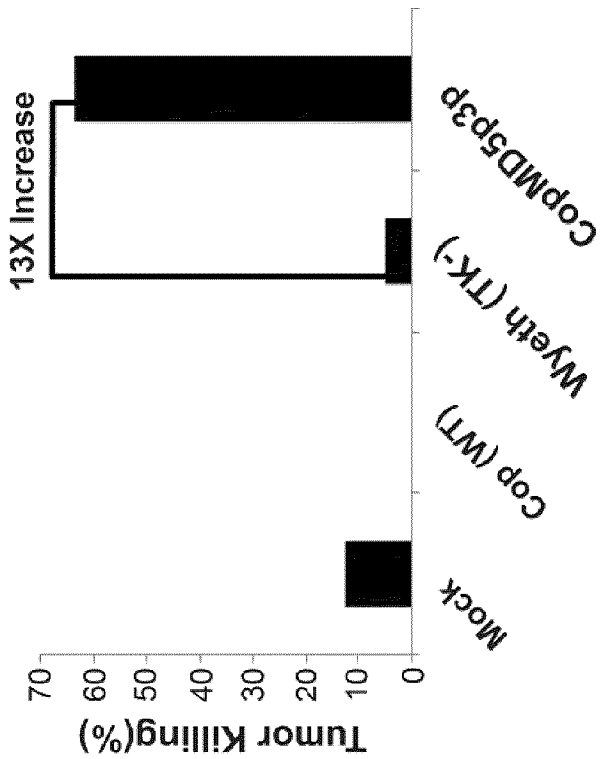

Tumor Killing(%)
0
10
20
30
40
50
60
70
Mock
Cop (WT)
Weth (TK-)
CopMD53p
13X Increase

FIG. 29

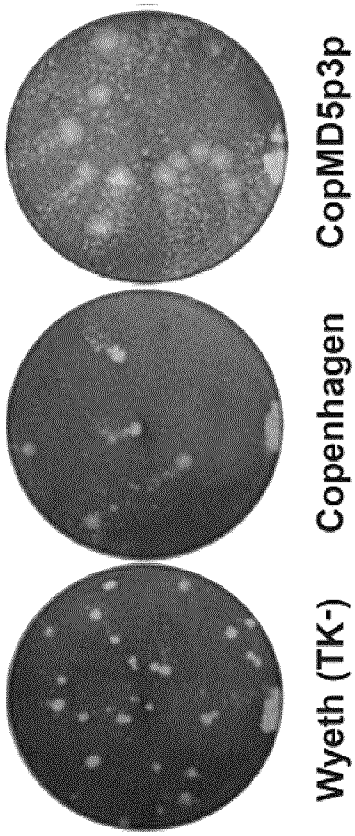


FIG. 30

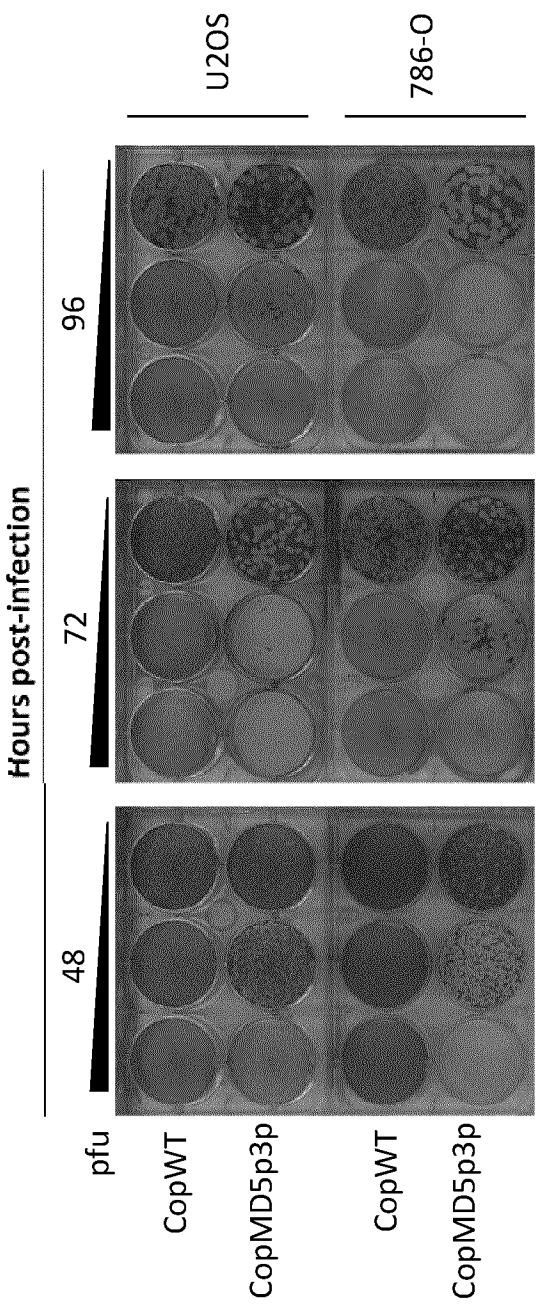
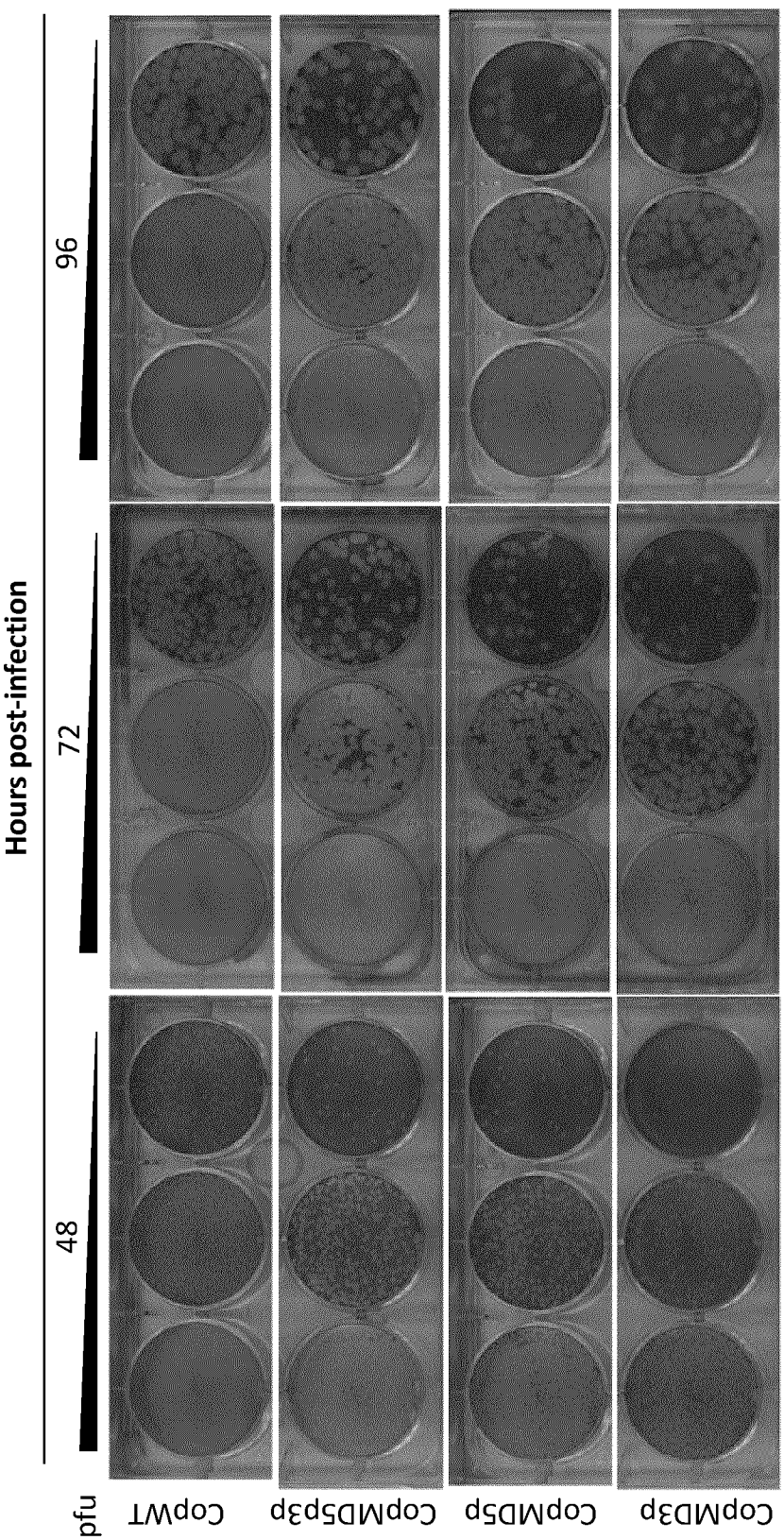

U2OS
786-O
Hours post-infection
96
72
48
pfu
CopWT
CopMD5p3p
CopWT
CopMD5p3p

FIG. 31


U2OS
Hours post-infection
48
72
96
pfu
CopWT
CopMD5p3p
CopMD5p
CopMD3p

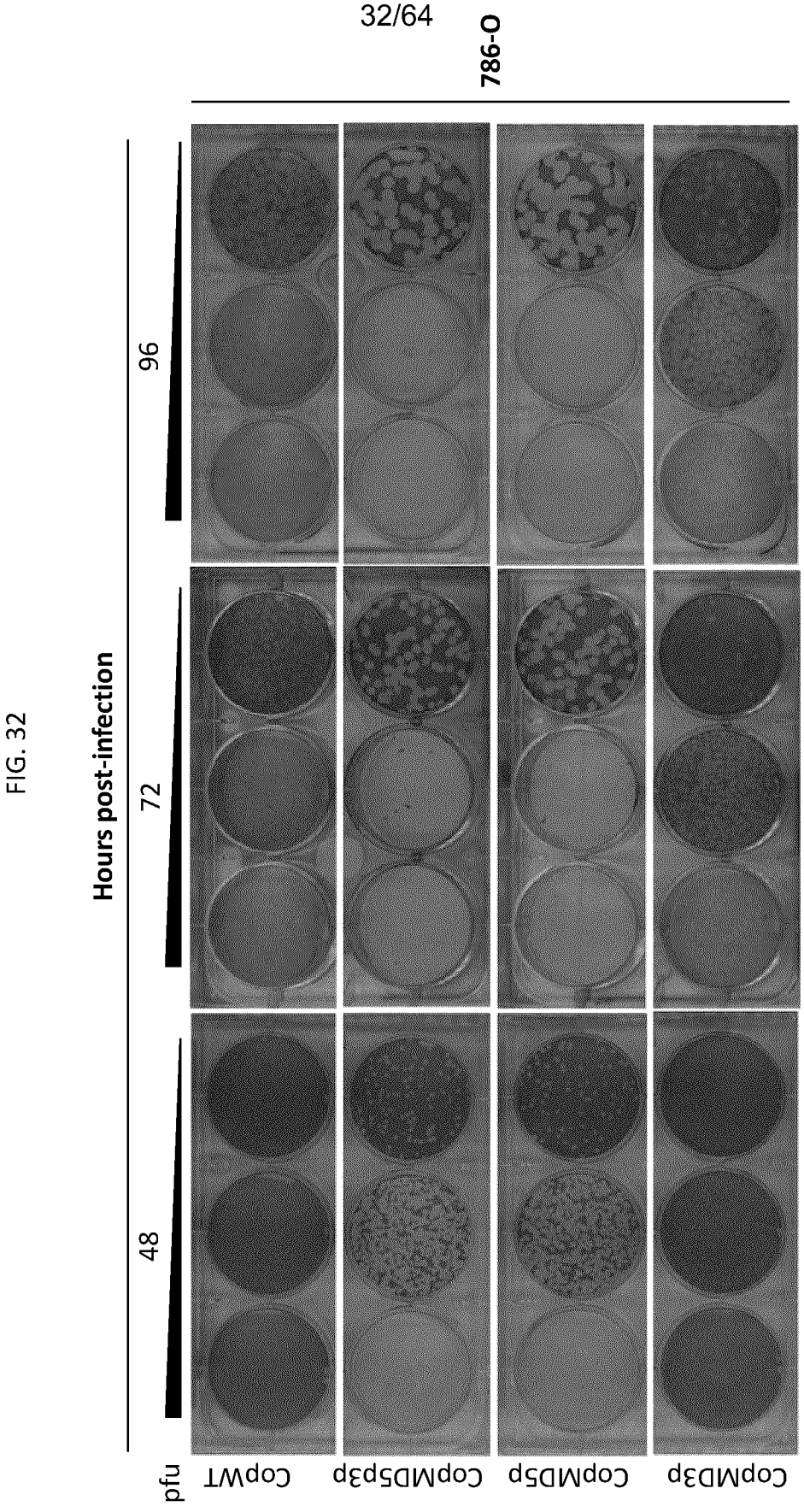

786-O
Hours post-infection
48
72
96
pfu
CopWT
CopMD5p3p
CopMD5p
CopMD3p

FIG. 32

FIG. 33

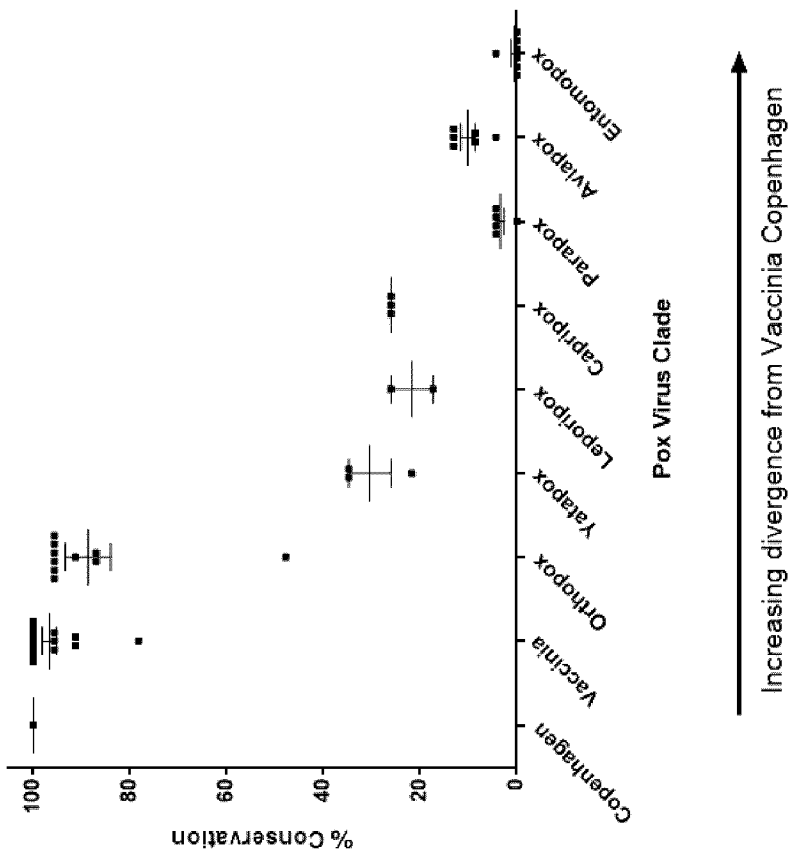
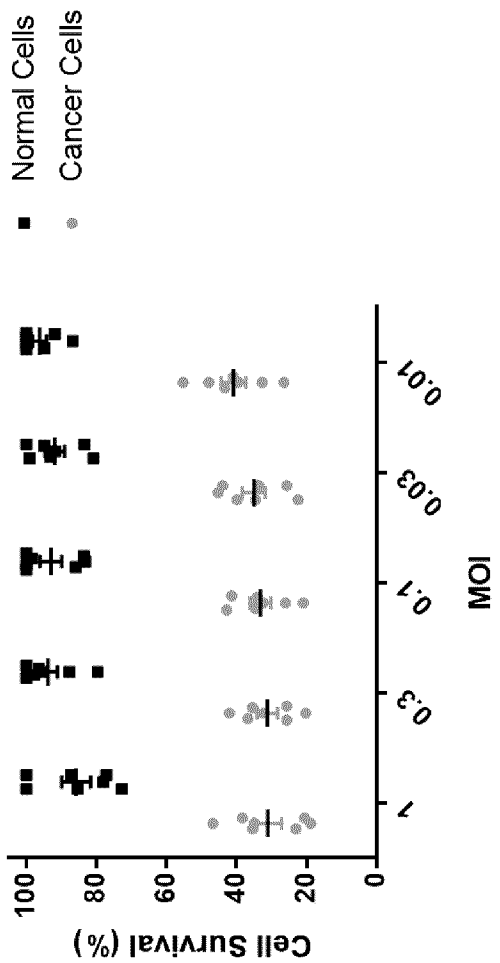

% Conservation
100
80
60
40
20
0
Copenhagen
Vaccinia
Orthopox
Yatapox
Leporipox
Capripox
Parapox
Avipox
Entomopox
Pox Virus Clade
Increasing divergence from Vaccinia Copenhagen

FIG. 34



Cancer Cells:
HeLa - Cervical
SNB-19 - Glioblastoma
786-O - Renal
M14 - Melanoma
U-251 - Glioblastoma
NCI-H23 - Lung
U2OS - Osteosarcoma

Normal Cells:
PrEC - Prostate Epithelial Cells
PBMC - Immune Cells
BdSMC - Bladder Smooth Muscle Cells
HSMM - Skeletal Muscle Myoblasts
HMEC - Mammary Epithelial Cells
NHDF - Dermal Fibroblasts
NHEM - Epidermal Melanocytes

FIG. 35

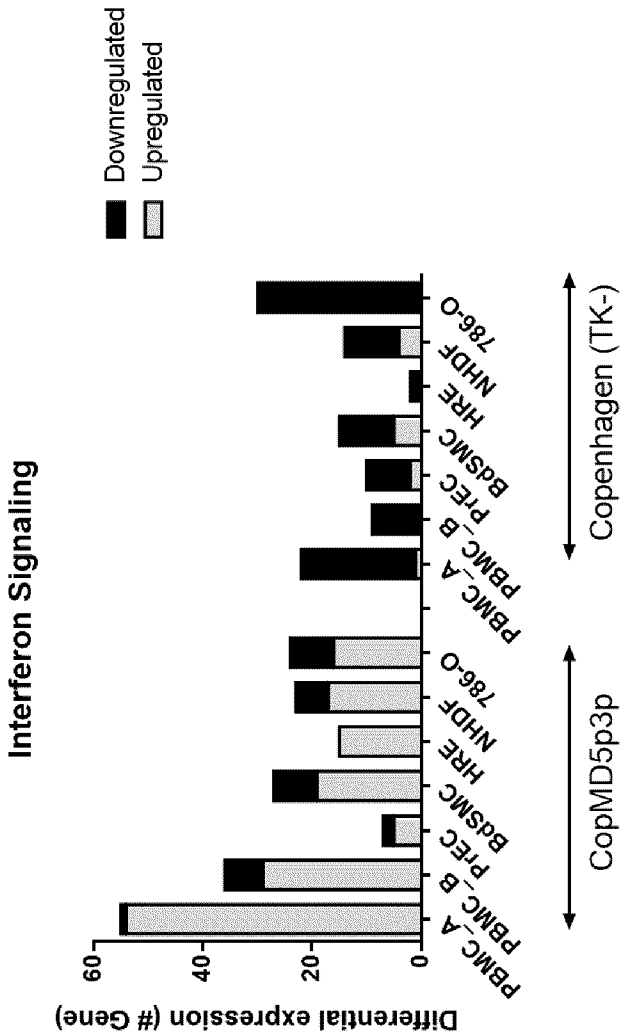

Interferon Signaling
Downregulated
Upregulated
Differential expression (# Gene)
60
40
20
0
PBMC_A
PBMC_B
PrEC
BdSMC
HRE
NHDF
786-O
PBMC_A
PBMC_B
PrEC
BdSMC
HRE
NHDF
786-O
CopMD5p3p
Copenhagen (TK-)

FIG. 36

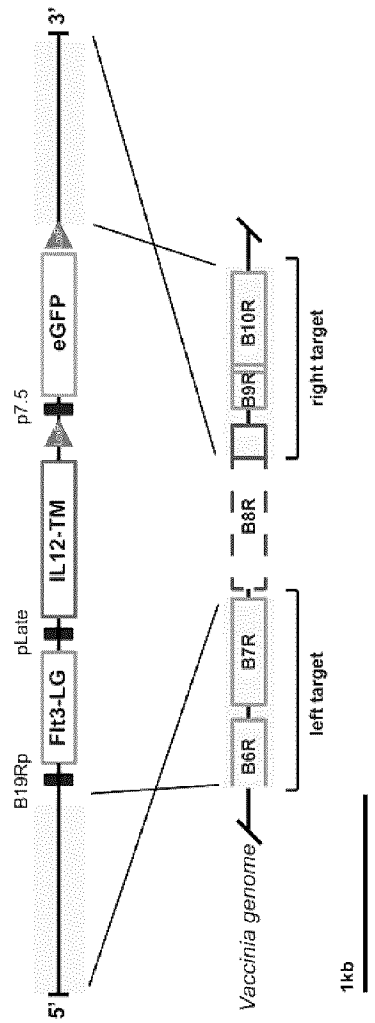

5'
B19Rp
Flt3-LG
pLate
IL12-TM
p7.5
eGFP
3'
B6R
B7R
B8R
B9R
B10R
left target
right target
Vaccinia genome
1kb

FIG. 37

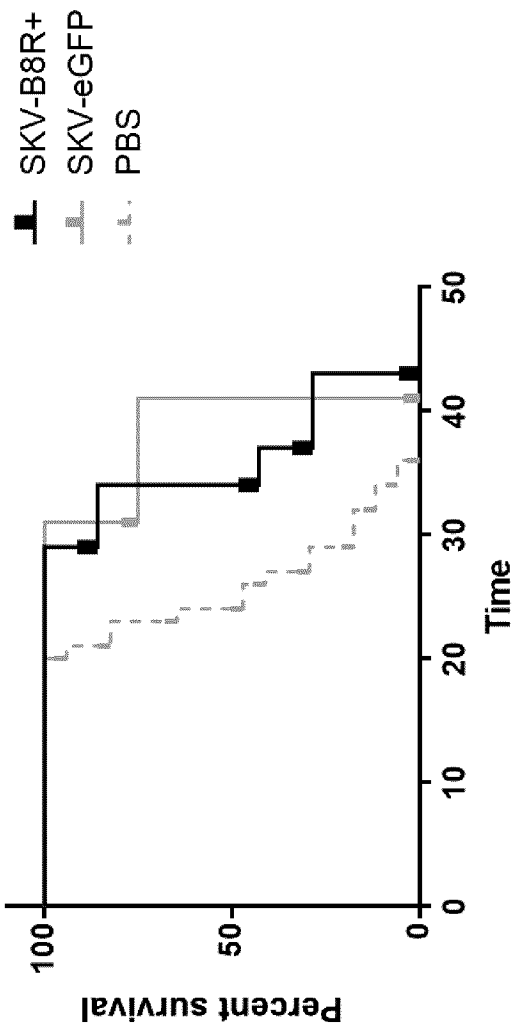

SKV-B8R+
SKV-eGFP
PBS
Percent survival
100
50
0
0
10
20
30
40
50
Time

FIG. 38

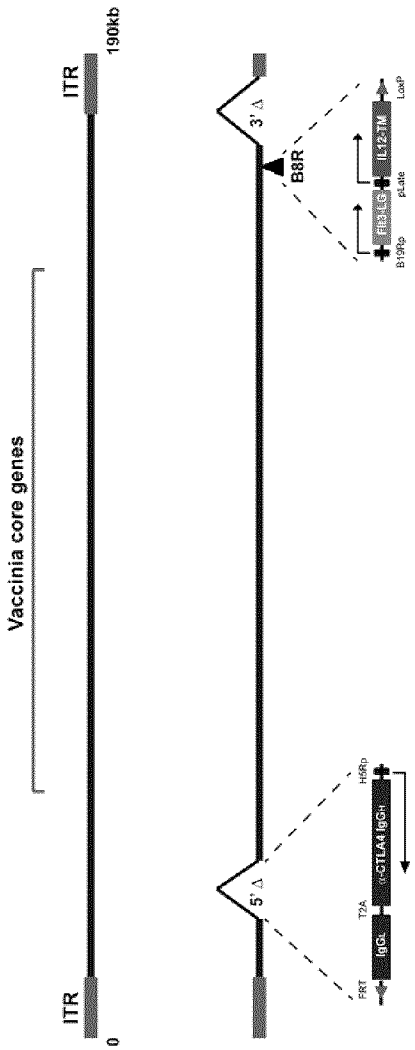
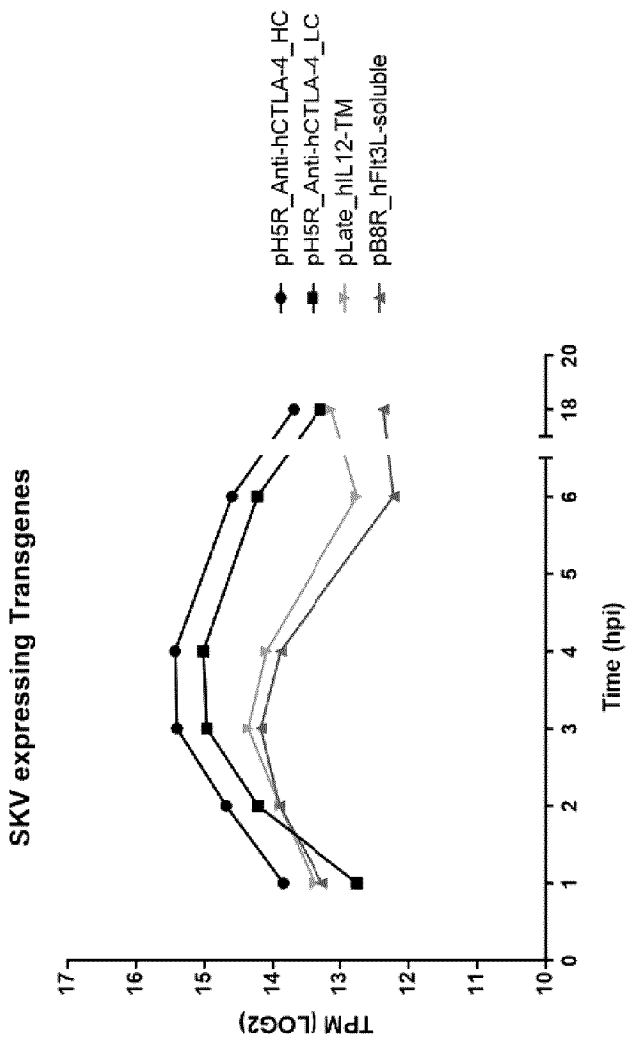

190kb
ITR
ITR
0
Vaccinia core genes
3' Δ
B8R
LoxP
pLate
B19Rp
5' Δ
H6Rp
T2A
FRT

FIG. 39


SKV expressing Transgenes
pH5R_Anti-hCTLA-4_HC
pH5R_Anti-hCTLA-4_LC
pLate_hIL12-TM
pB8R_hFlt3L-soluble
TPM (LOG2)
Time (hpi)
17
16
15
14
13
12
11
10
0
1
2
3
4
5
6
18
20

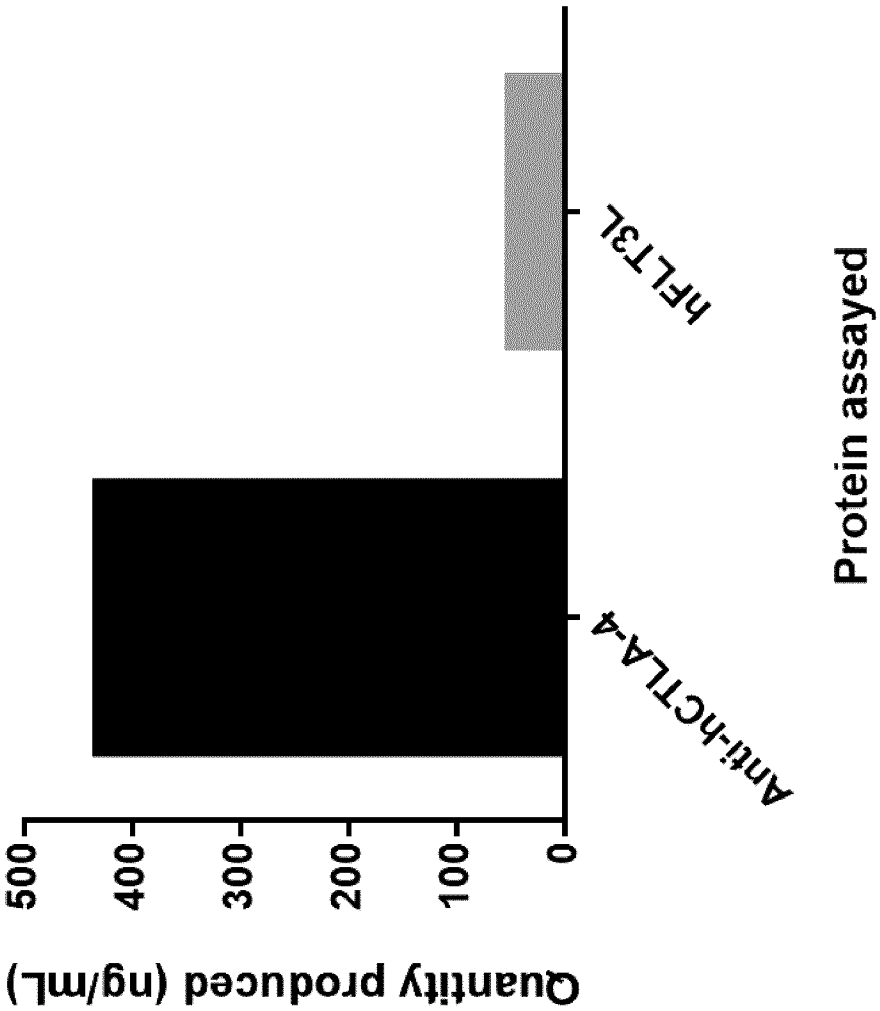

Quantity produced (ng/mL)
500
400
300
200
100
0
Anti-hCTLA-4
hFLT3L
Protein assayed

FIG. 40

FIG. 41

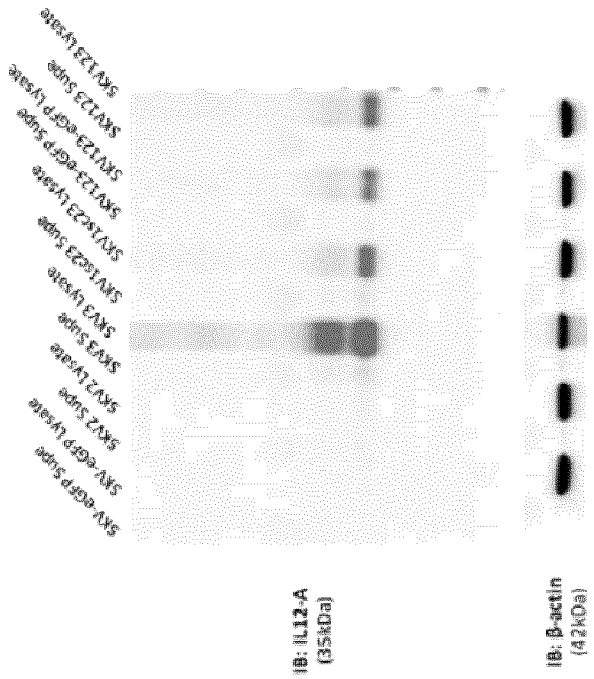

SKV-eGFP Supe
SKV-eGFP Lysate
SKV2 Supe
SKV2 Lysate
SKV3 Supe
SKV3 Lysate
SKV1&23 Supe
SKV1&23 Lysate
SKV123-eGFP Supe
SKV123-eGFP Lysate
SKV123 Supe
SKV123 Lysate
IB: IL12-A (35kDa)
IB: β-actin (42kDa)

FIG. 42

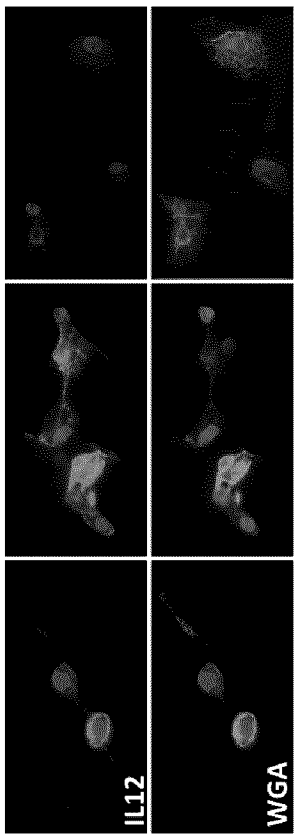


FIG. 43

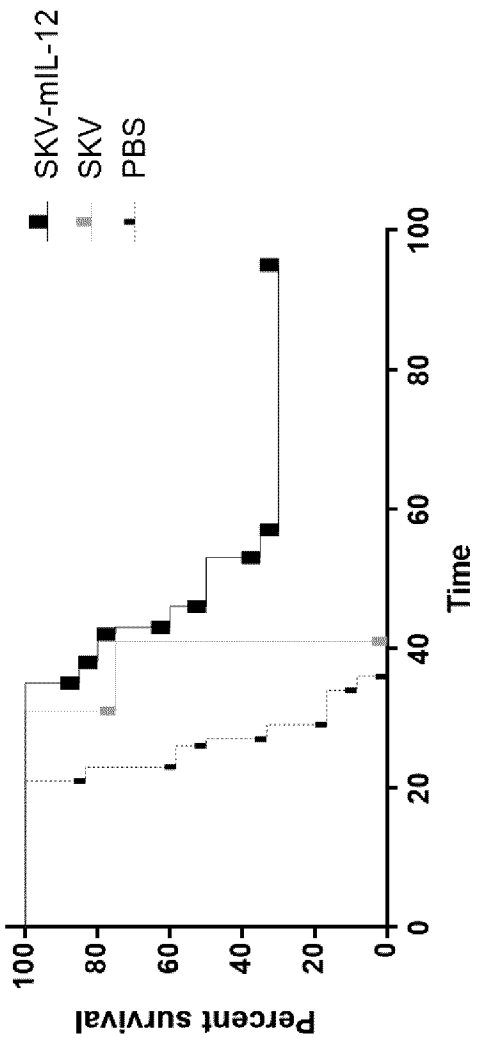

SKV-mIL-12
SKV
PBS
Percent survival
100
80
60
40
20
0
0
20
40
60
80
100
Time

FIG. 44

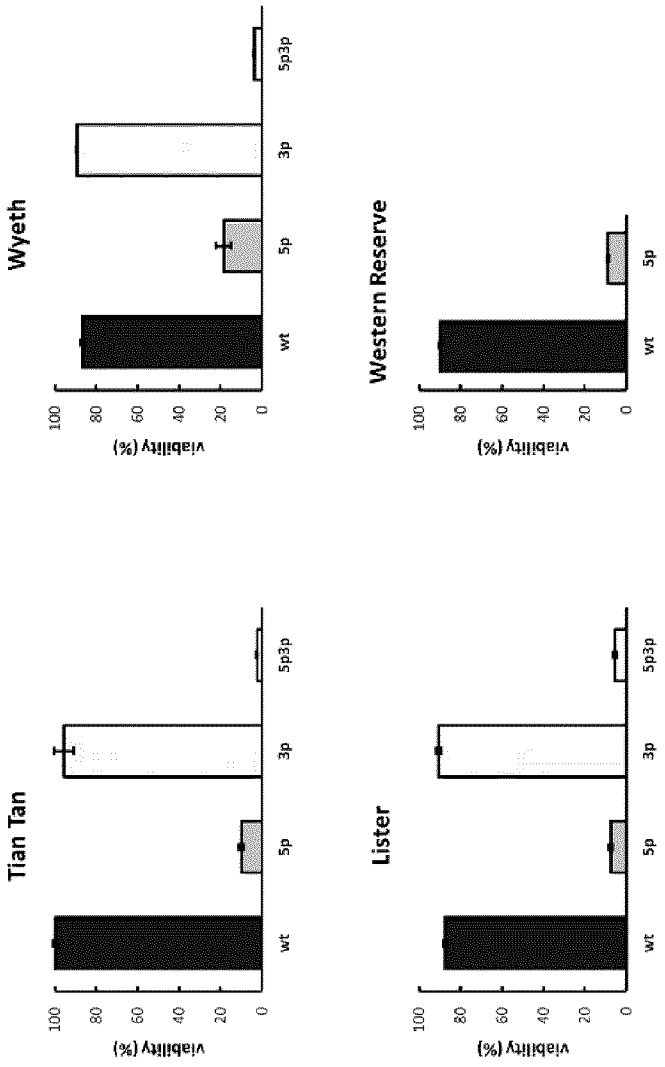

Wyeth
Western Reserve
Tian Tan
Lister
viability (%)
0
20
40
60
80
100
wt
5p
3p
5p3p

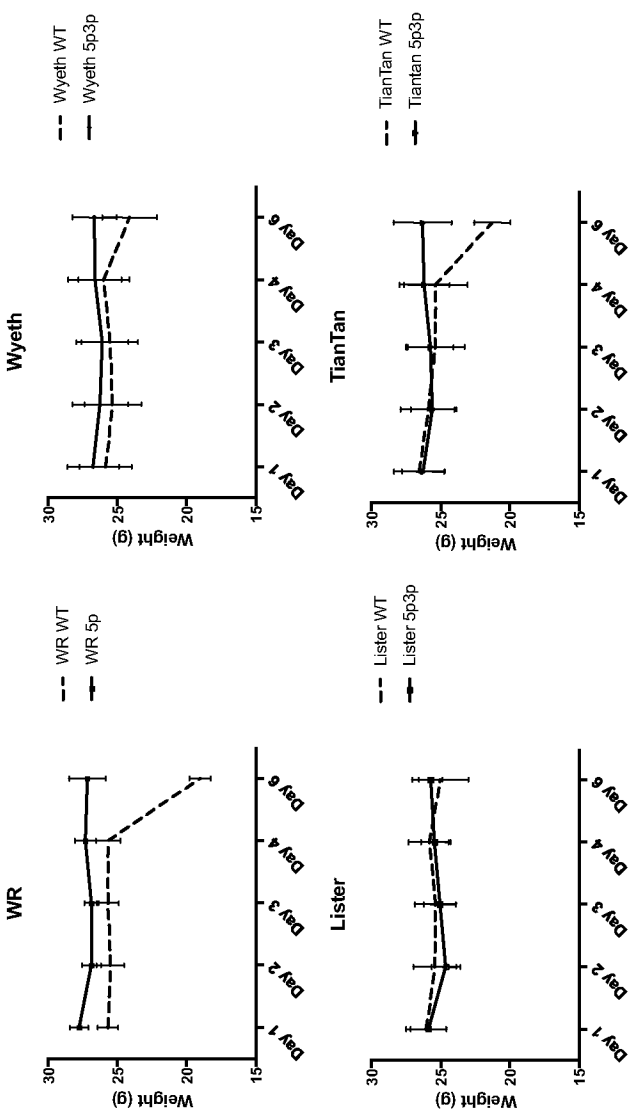
FIG. 45

Virus	Deletion	Syncytia	Cytotoxicity (HeLa)	Replication
Wyeth	NP	no	+	yes
Wyeth	5p	yes	+++	yes
Wyeth	3p	no	+	yes
Wyeth	5p3p	yes	+++	yes
TianTan	NP	No	+	yes
TianTan	5p	yes	+++	yes
TianTan	3p	no	+	yes
TianTan	5p3p	yes	+++	yes
Lister	NP	no	+	yes
Lister	5p	yes	+++	yes
Lister	3p	no	+	yes
Lister	5p3p	yes	+++	yes
Western Reserve	NP	no	+	yes
Western Reserve	5p	yes	+++	yes
Western Reserve	3p	ND	ND	ND
Western Reserve	5p3p	ND	ND	ND

NP: Wildtype virus with no major deletions present
ND: Not determined

Phenotypic characterization of HeLa cells infected with various vaccinia strains.

FIG. 46



Mouse body mass measurements. CD-1 nude mice were treated with 1 x 10^7 pfu via intravenously tail vein injection and measured at the indicated timepoints.
Conclusion: 5p3p vaccinia strains do not induce weight loss compared to wildtype strains.

FIG. 47

Vaccinia strain	WR	Wyeth	Lister	TianTan
WT	++	+++	+++	+++
5p3p	ND	-	-	-
5p	+	ND	ND	ND

-	no pox lesions
+	Tail only
++	Tail and paws
+++	Tail, paws, and parts of Body
ND	Not determined

Table assessing the presence of pox lesions. CD-1 nude mice were treated with 1×10^7 pfu with indicated vaccinia virus strains via intravenously tail vein injection. Mice were examined for pox lesions 6 days post-injection. **Conclusion:** 5p3p vaccinia strains do not induce pox lesions compared to wildtype strains.

FIG. 48

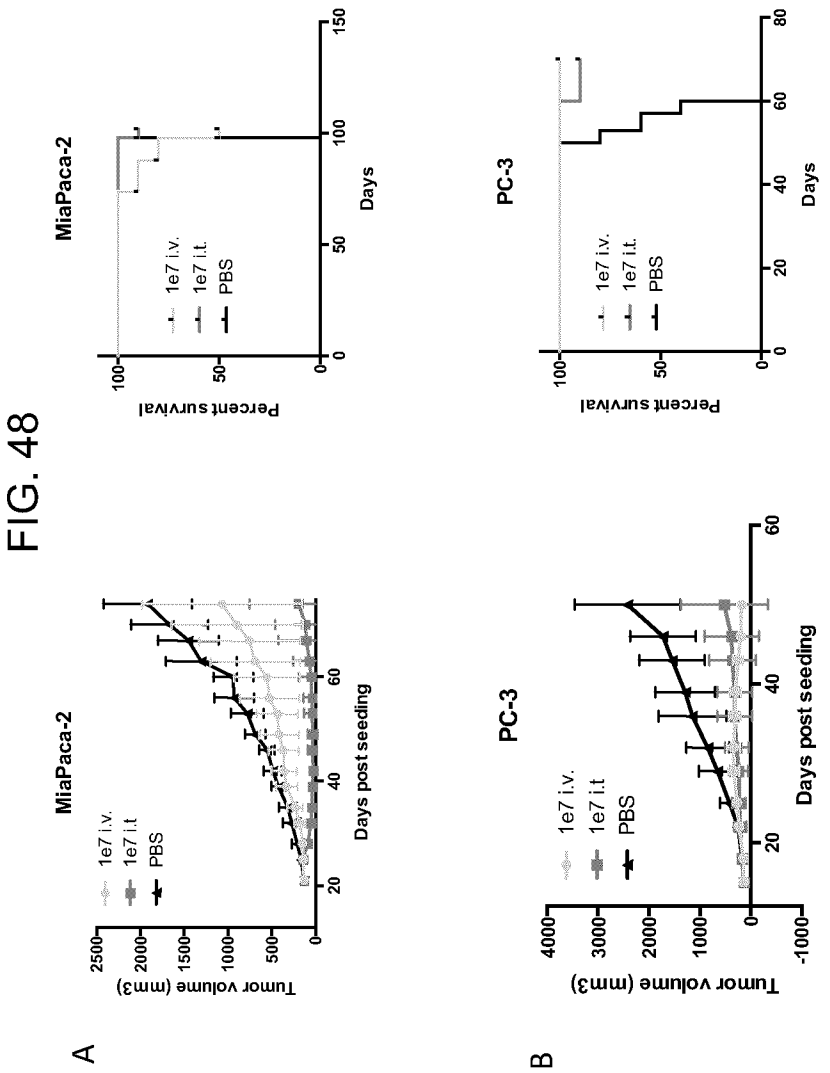

A
MiaPaca-2
Tumor volume (mm3)
Days post seeding
1e7 i.v.
1e7 i.t
PBS
MiaPaca-2
Percent survival
Days
1e7 i.v.
1e7 i.t.
PBS
B
PC-3
Tumor volume (mm3)
Days post seeding
1e7 i.v.
1e7 i.t
PBS
PC-3
Percent survival
Days
1e7 i.v.
1e7 i.t.
PBS

FIG. 48

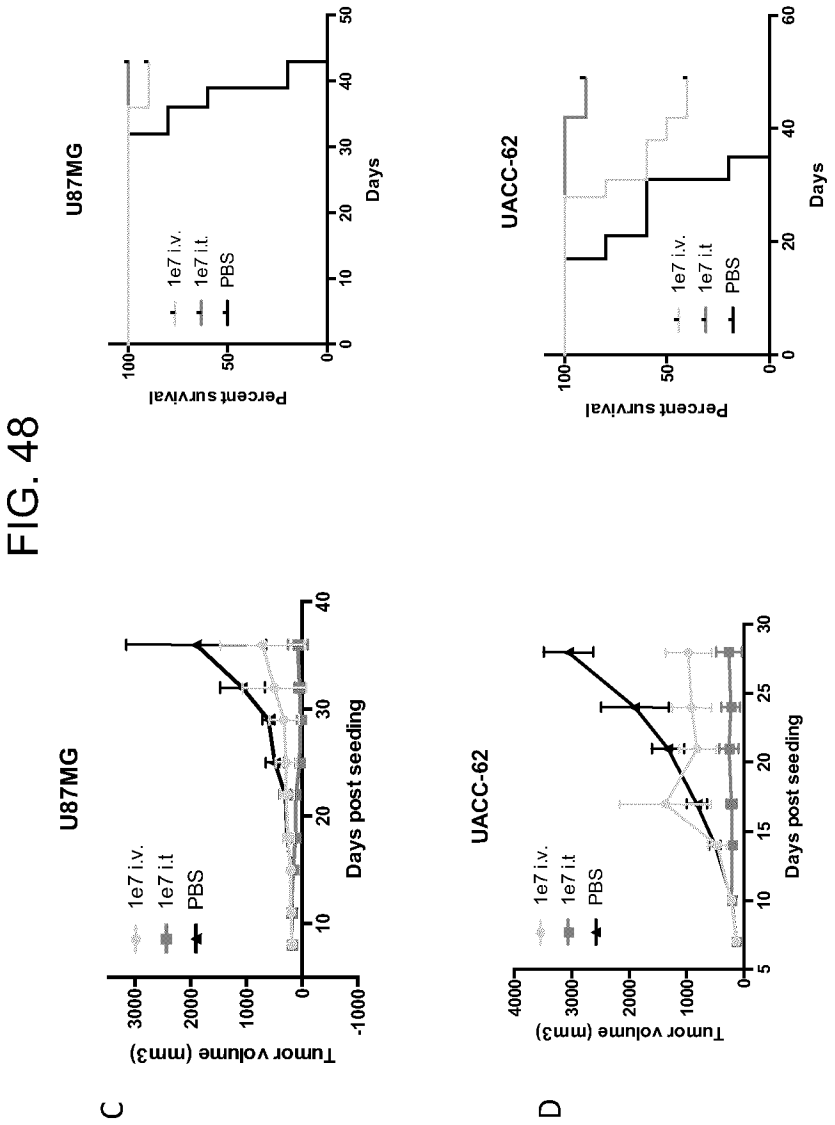

U87MG
Percent survival
Days
1e7 i.v.
1e7 i.t.
PBS
UACC-62
Percent survival
Days
1e7 i.v.
1e7 i.t
PBS
C
U87MG
Tumor volume (mm3)
Days post seeding
1e7 i.v.
1e7 i.t
PBS
D
UACC-62
Tumor volume (mm3)
Days post seeding
1e7 i.v.
1e7 i.t
PBS

FIG. 48

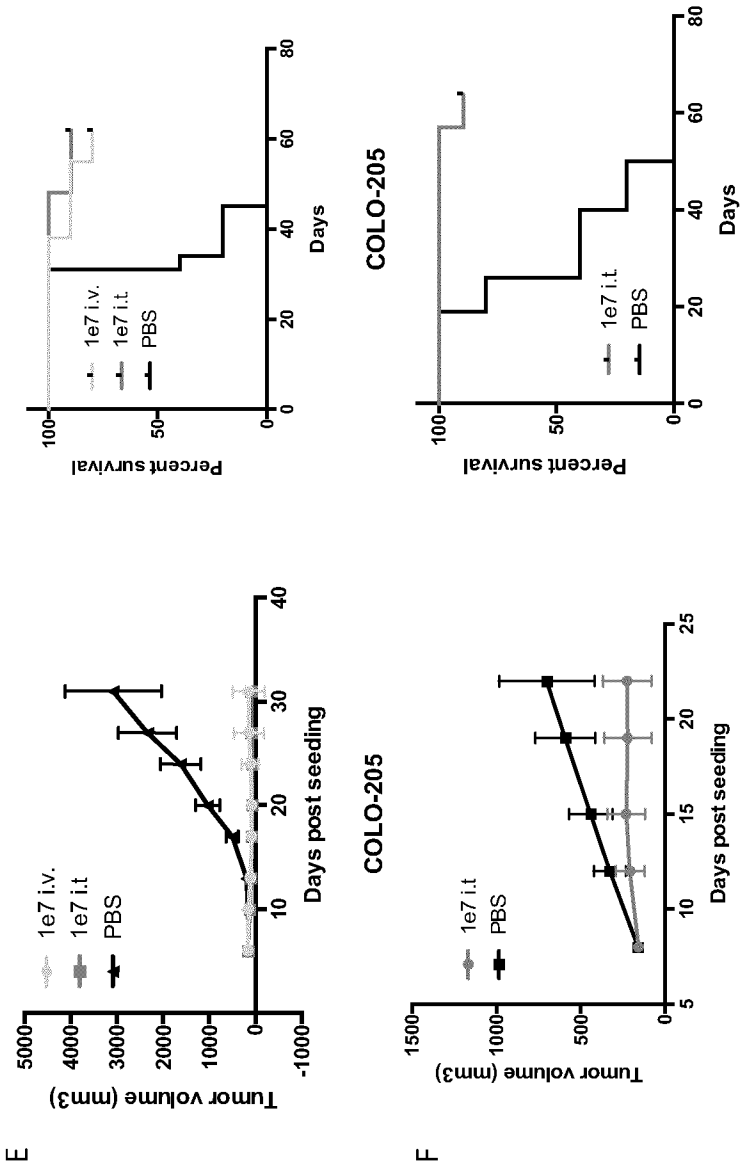

E
UM-UC-3
Tumor volume (mm3)
Days post seeding
1e7 i.v.
1e7 i.t
PBS
UM-UC-3
Percent survival
Days
1e7 i.v.
1e7 i.t
PBS
F
COLO-205
Tumor volume (mm3)
Days post seeding
1e7 i.t
PBS
COLO-205
Percent survival
Days
1e7 i.t
PBS

FIG. 48

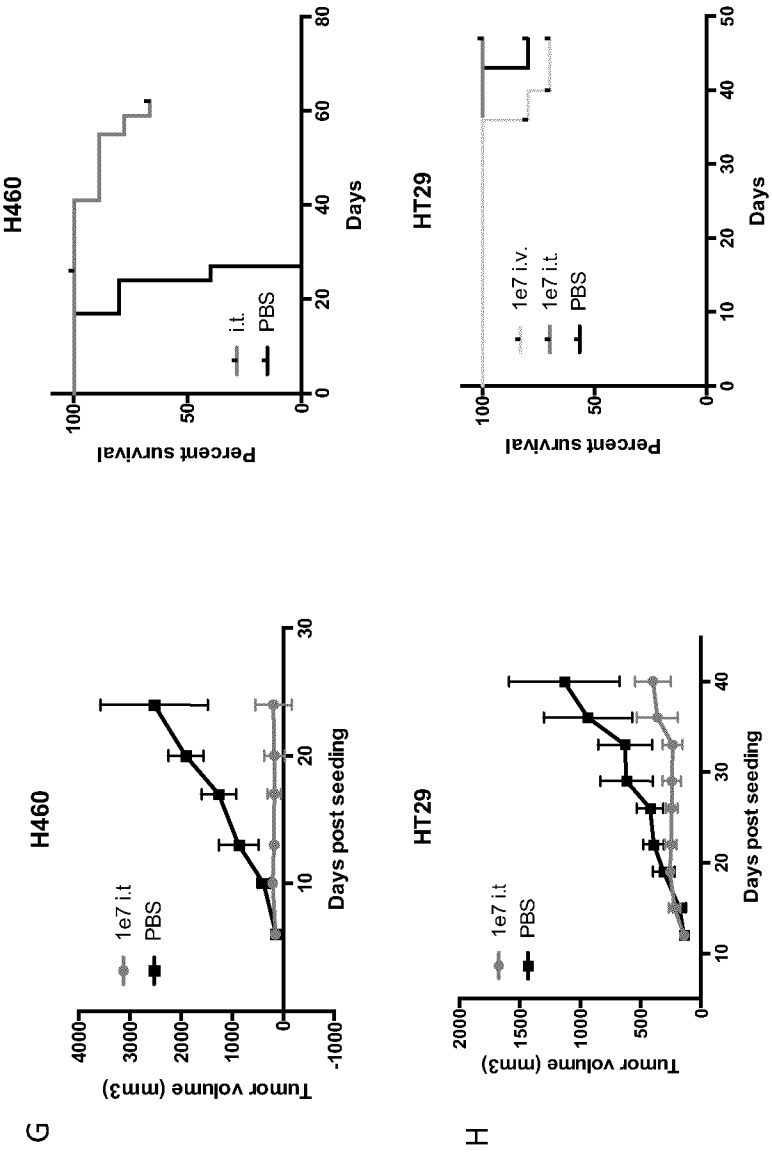
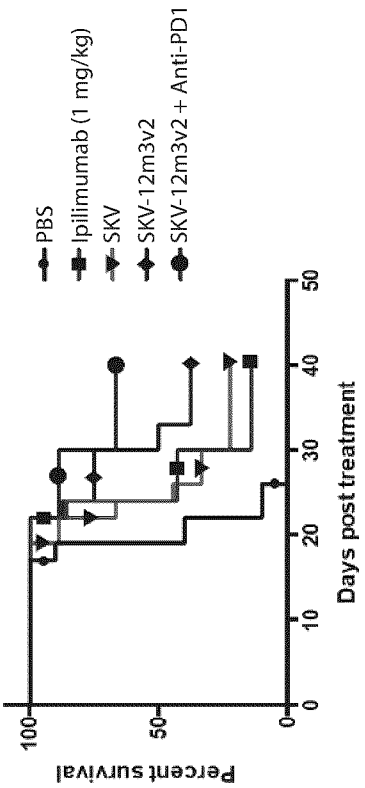

G
H460
Percent survival
Days
i.t.
PBS
HT29
1e7 i.v.
1e7 i.t
PBS
H
Tumor volume (mm3)
Days post seeding
1e7 i.t
PBS

FIG. 49


PBS
Ipilimumab (1 mg/kg)
SKV
SKV-12m3v2
SKV-12m3v2 + Anti-PD1
Percent survival
100
50
0
0
10
20
30
40
50
Days post treatment

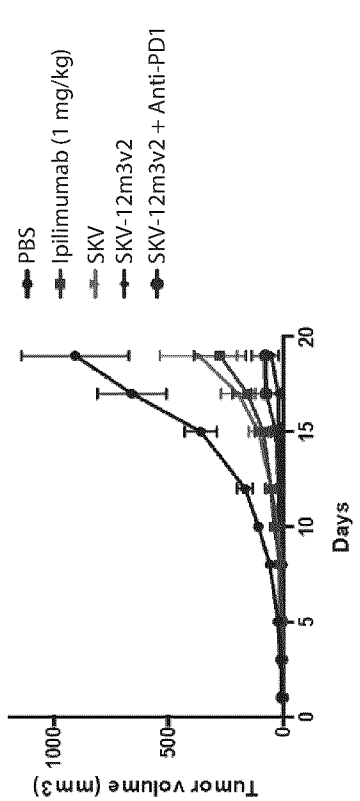

PBS
Ipilimumab (1 mg/kg)
SKV
SKV-12m3v2
SKV-12m3v2 + Anti-PD1
Tumor volume (mm3)
1000
500
0
0
5
10
15
20
Days

FIG. 50

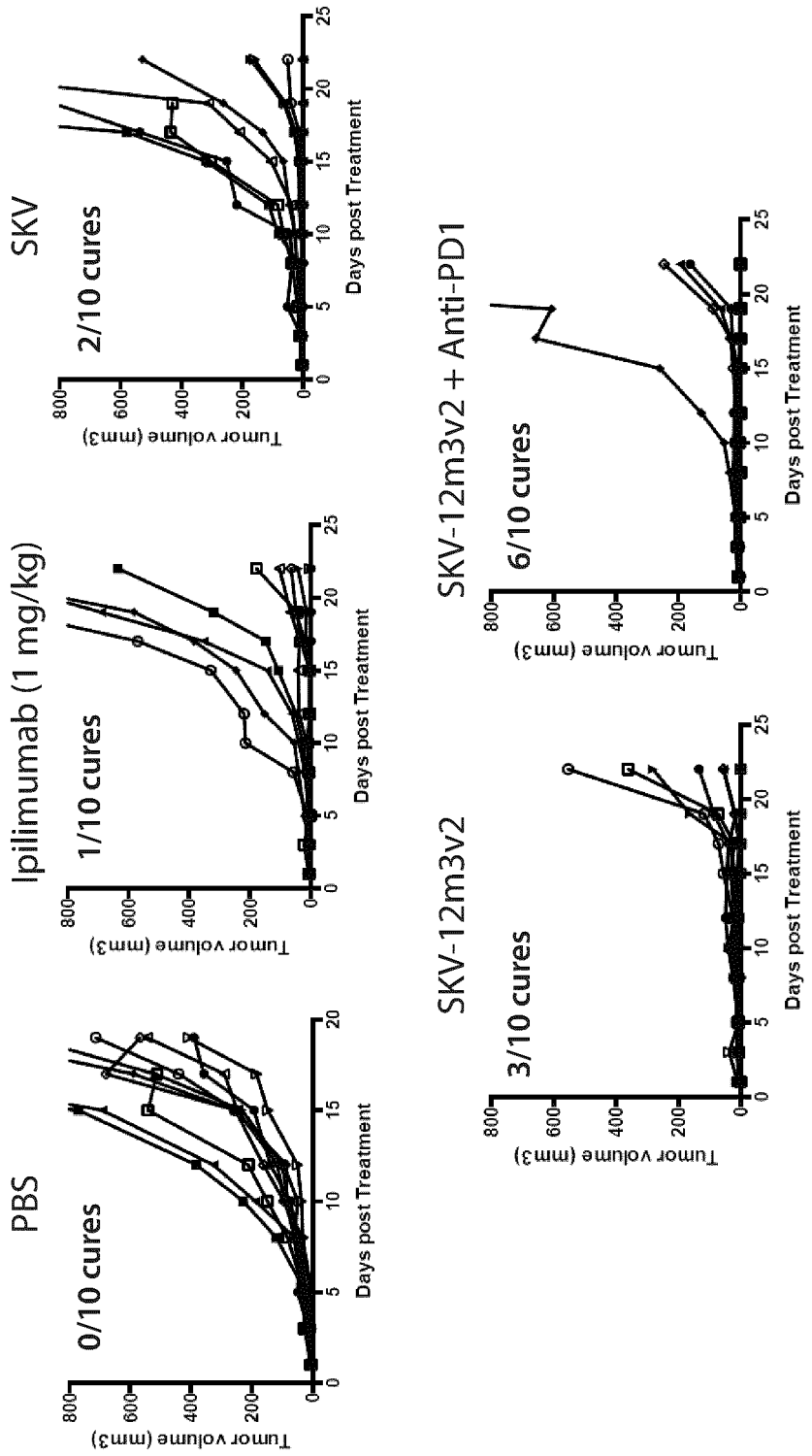

PBS
0/10 cures
Ipilimumab (1 mg/kg)
1/10 cures
SKV
2/10 cures
SKV-12m3v2
3/10 cures
SKV-12m3v2 + Anti-PD1
6/10 cures
Tumor volume (mm3)
Days post Treatment

FIG. 51

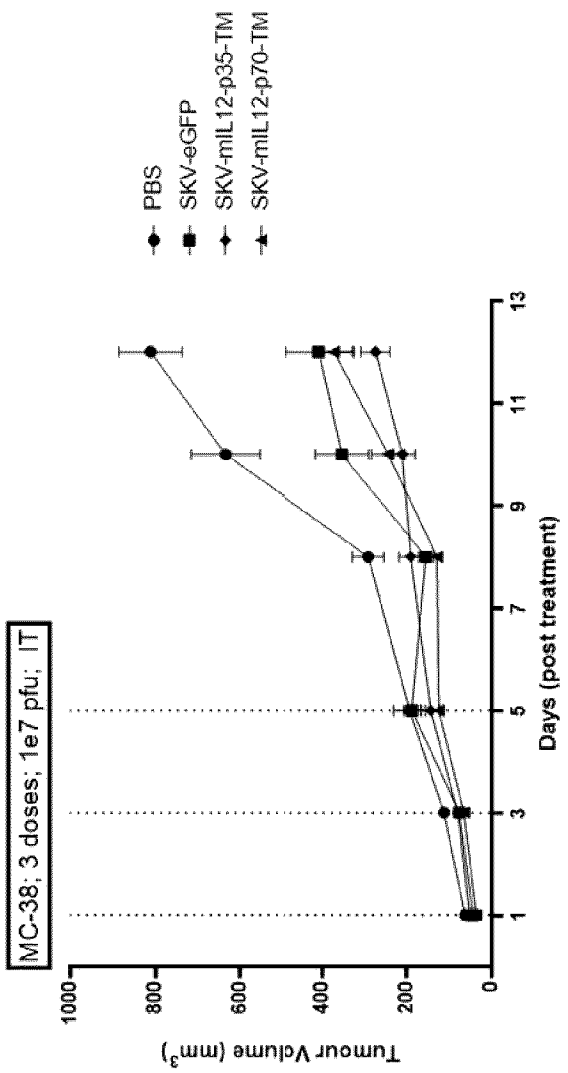

PBS
SKV-eGFP
SKV-mIL12-p35-TM
SKV-mIL12-p70-TM
MC-38; 3 doses; 1e7 pfu; IT
Tumour Volume (mm3)
Days (post treatment)
0
200
400
600
800
1000
1
3
5
7
9
11
13

FIG. 52

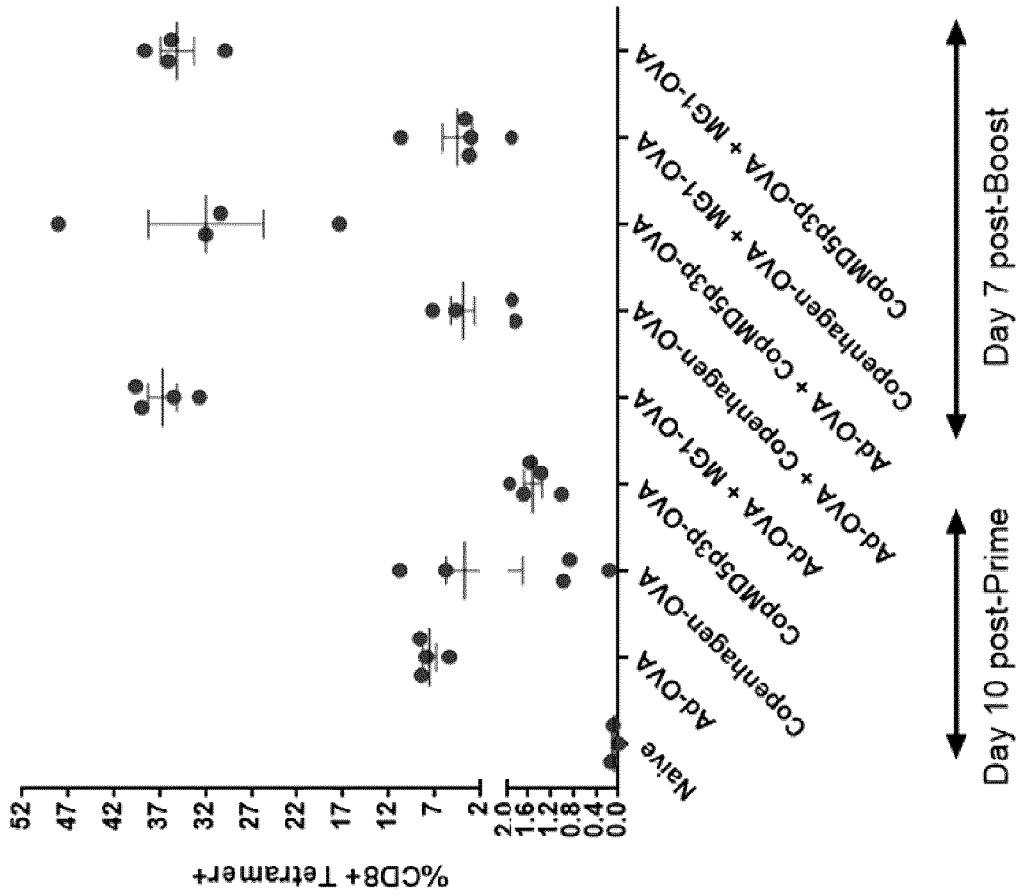

%CD8+ Tetramer+
52
47
42
37
32
27
22
17
12
7
2
2.0
1.6
1.2
0.8
0.4
0.0
Naive
Ad-OVA
Copenhagen-OVA
CopMD5p3p-OVA
Ad-OVA + MG1-OVA
Ad-OVA + Copenhagen-OVA
Ad-OVA + CopMD5p3p-OVA
Copenhagen-OVA + MG1-OVA
CopMD5p3p-OVA + MG1-OVA
Day 10 post-Prime
Day 7 post-Boost

FIG. 53

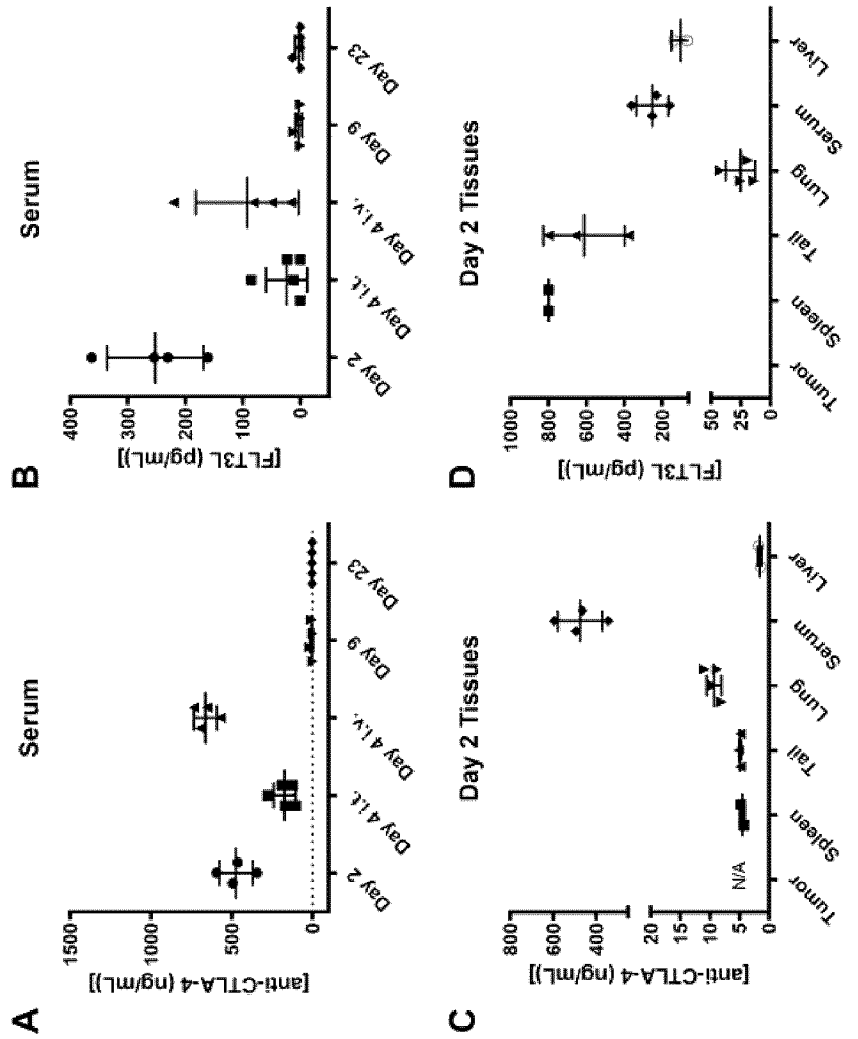

A
Serum
[anti-CTLA-4 (ng/mL)]
1500
1000
500
0
Day 2
Day 4 i.t.
Day 4 i.v.
Day 9
Day 23
B
Serum
[FLT3L (pg/mL)]
400
300
200
100
0
Day 2
Day 4 i.t.
Day 4 i.v.
Day 9
Day 23
C
Day 2 Tissues
[anti-CTLA-4 (ng/mL)]
800
600
400
20
15
10
5
0
N/A
Tumor
Spleen
Tail
Lung
Serum
Liver
D
Day 2 Tissues
[FLT3L (pg/mL)]
1000
800
600
400
200
50
25
0
Tumor
Spleen
Tail
Lung
Serum
Liver

FIG. 53

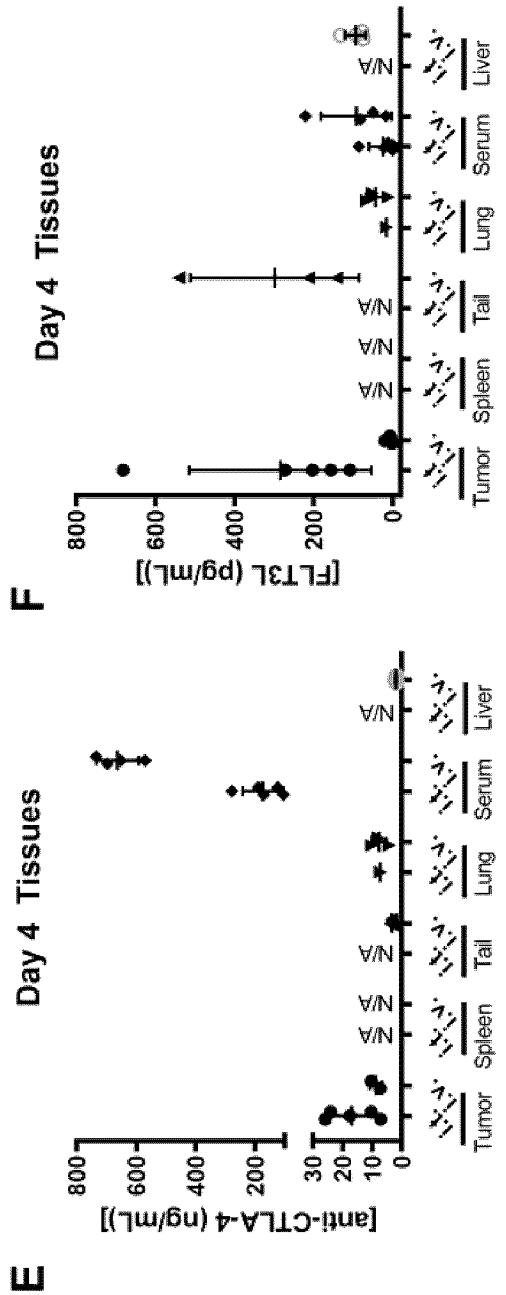
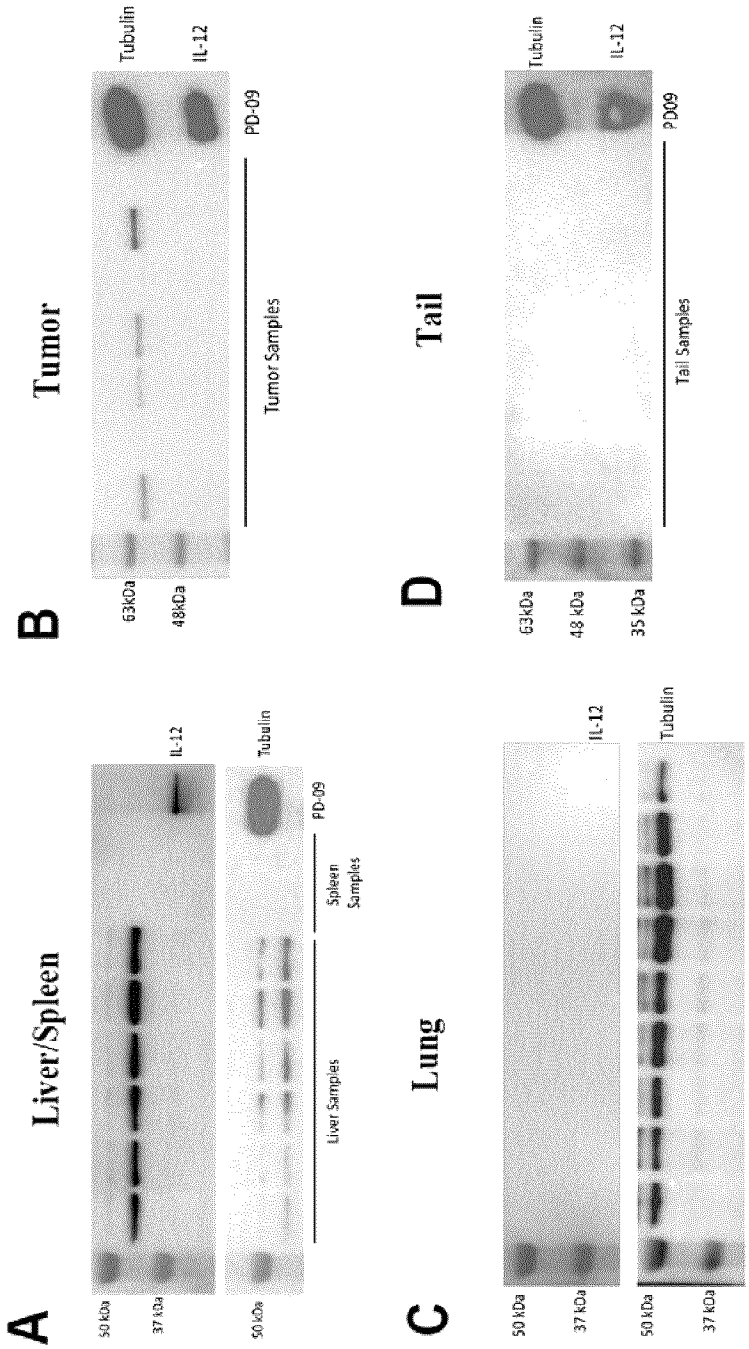

E
Day 4 Tissues
[anti-CTLA-4 (ng/mL)]
800
600
400
200
30
20
10
0
N/A
N/A
N/A
N/A
Tumor
Spleen
Tail
Lung
Serum
Liver
F
Day 4 Tissues
[FLT3L (pg/mL)]
800
600
400
200
0
N/A
N/A
N/A
N/A
Tumor
Spleen
Tail
Lung
Serum
Liver

FIG. 54


A
Liver/Spleen
IL-12
50 kDa
37 kDa
Tubulin
50 kDa
PD-09
Liver Samples
Spleen Samples
B
Tumor
Tubulin
IL-12
63kDa
48kDa
PD-09
Tumor Samples
C
Lung
IL-12
50 kDa
37 kDa
Tubulin
50 kDa
37 kDa
D
Tail
Tubulin
IL-12
63kDa
48 kDa
35 kDa
PD09
Tail Samples

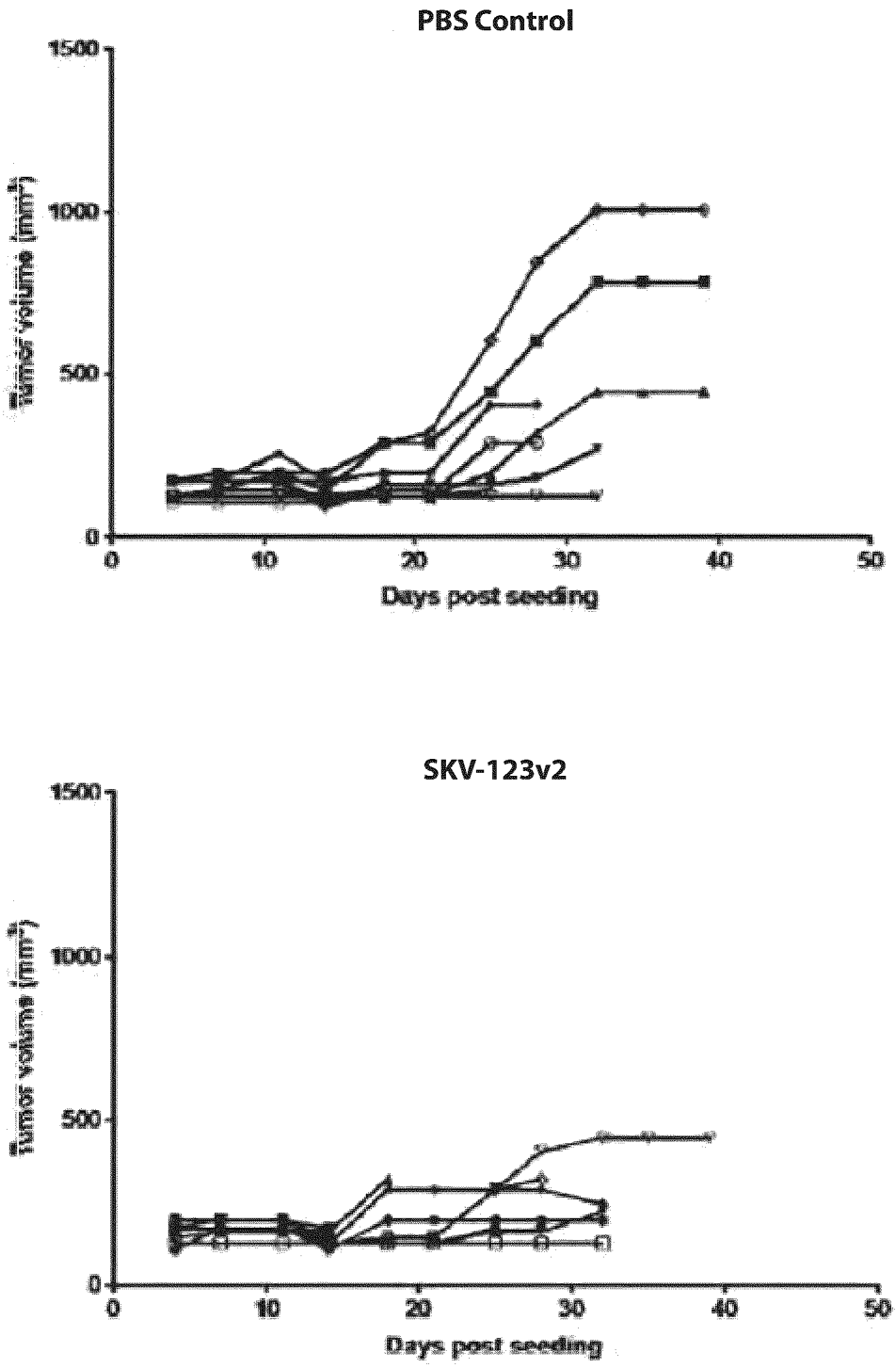

PBS Control
Tumor volume (mm³)
1500
1000
500
0
0
10
20
30
40
50
Days post seeding
SKV-123v2
Tumor volume (mm³)
1500
1000
500
0
0
10
20
30
40
50
Days post seeding

FIG. 55

FIG. 56

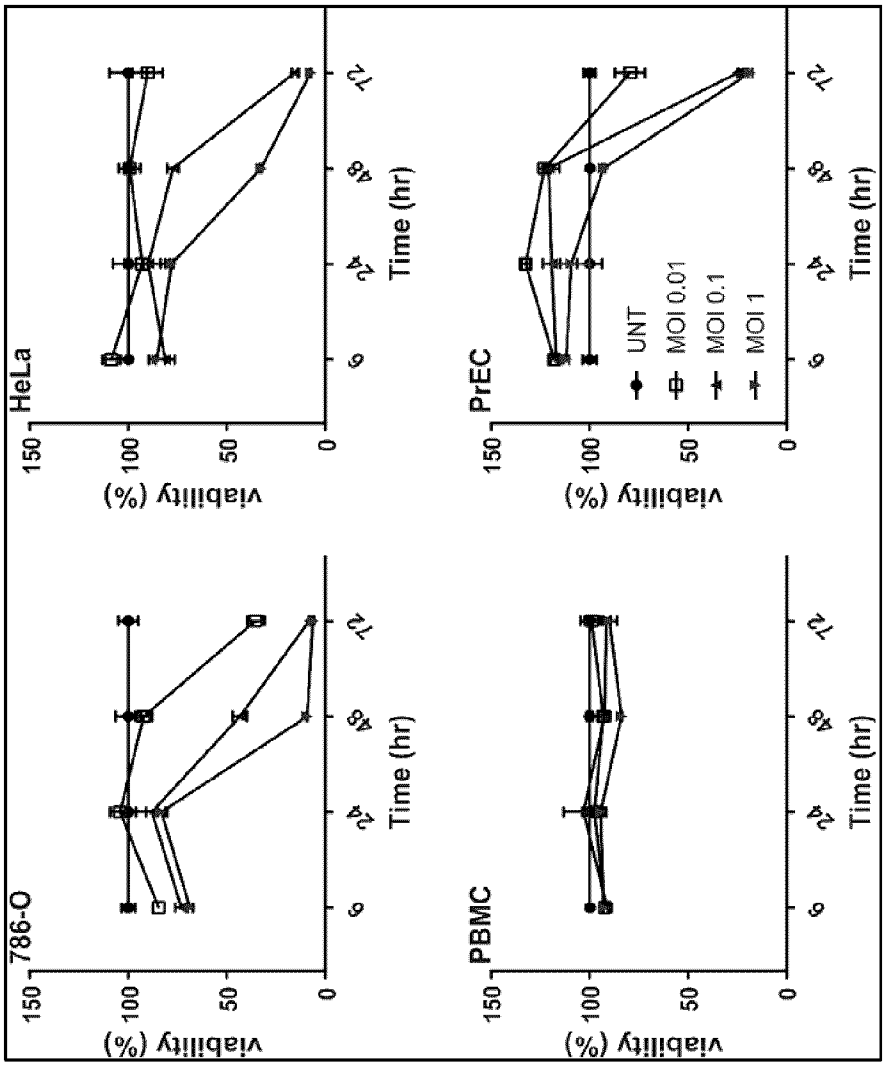

786-O
HeLa
PBMC
PrEC
viability (%)
Time (hr)
0
50
100
150
6
24
48
72
UNT
MOI 0.01
MOI 0.1
MOI 1

FIG. 57

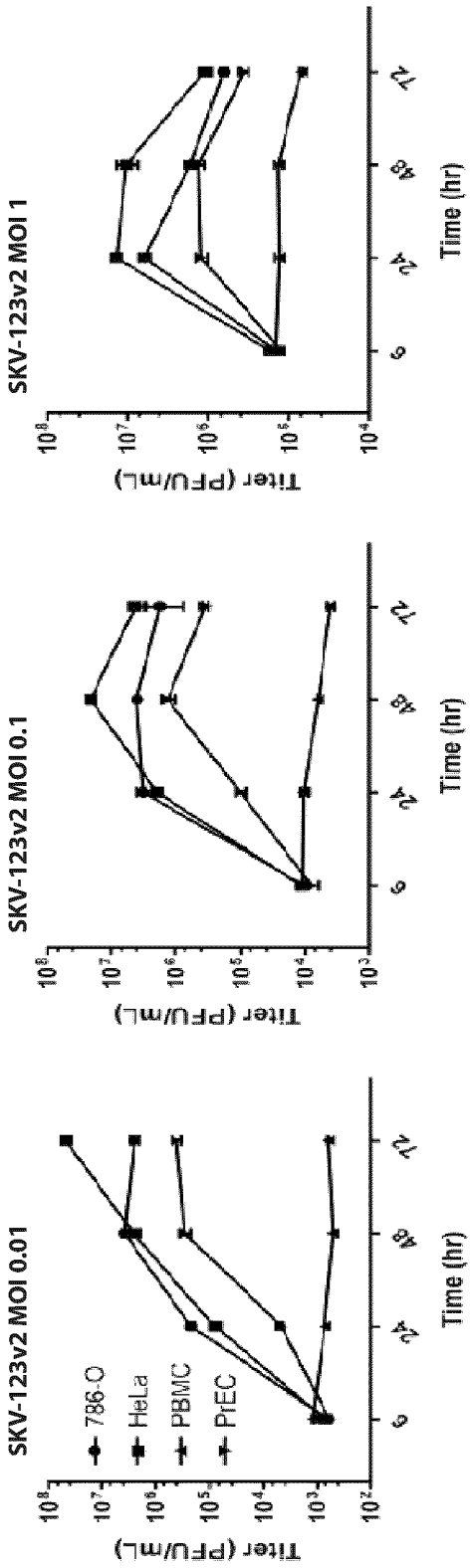

SKV-123v2 MOI 1
SKV-123v2 MOI 0.1
SKV-123v2 MOI 0.01
Titer (PFU/mL)
Time (hr)
786-O
HeLa
PBMC
PrEC

FIG. 58

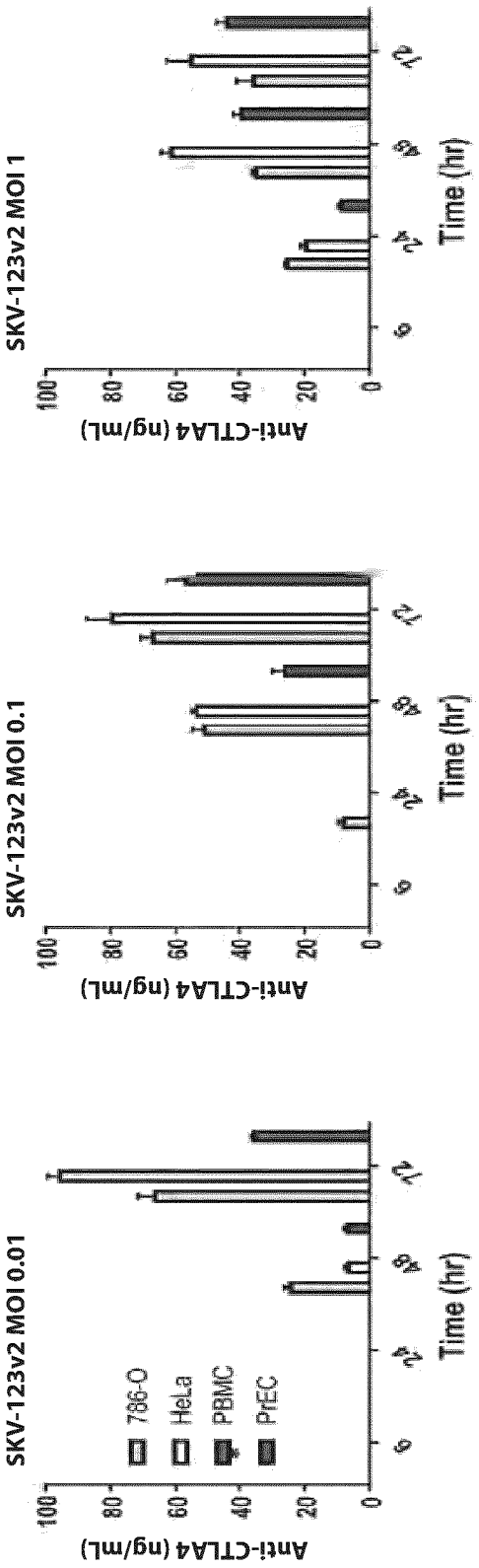

SKV-123v2 MOI 0.01
SKV-123v2 MOI 0.1
SKV-123v2 MOI 1
Anti-CTLA4 (ng/mL)
Time (hr)
0
20
40
60
80
100
6
24
48
72
786-O
HeLa
PBMC
PrEC

FIG. 59

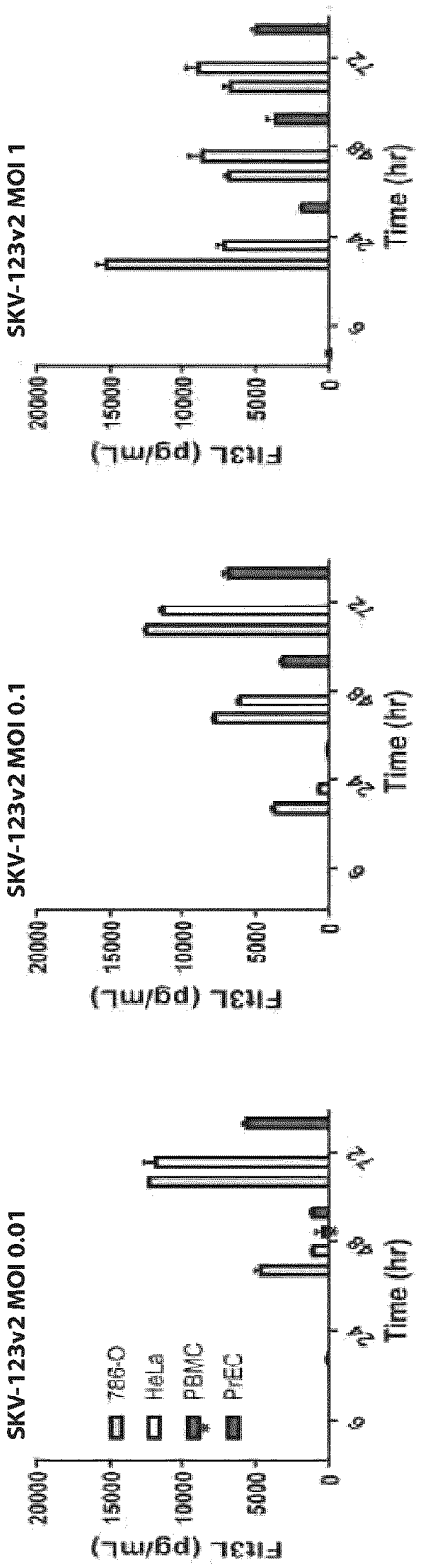

SKV-123v2 MOI 0.01
SKV-123v2 MOI 0.1
SKV-123v2 MOI 1
Flt3L (pg/mL)
20000
15000
10000
5000
0
Time (hr)
6
24
48
72
786-O
HeLa
PBMC
PrEC

FIG. 60

500-1000bp to the left of target insertion site
pEarly or pLate
Transgene (ex. FLT3L)
pEarly or pLate
Transgene (ex. IL-12)
Recombinase motif
(ex. loxP)
pEarly (ex. p7.5)
Fluorescent marker (ex. eGFP)
Recombinase motif
(ex. loxP)
500-1000bp to the right of target insertion site

SEQUENCE LISTING

<110> OTTAWA HOSPITAL RESEARCH INSTITUTE
TURNSTONE BIOLOGICS CORP

<120> MODIFIED ORTHOPOXVIRUS VECTORS

<130> 14596-050-228

<140>
<141>

<150> 62/930,524
<151> 2019-11-04

<150> 62/872,699
<151> 2019-07-10

<150> 62/784,372
<151> 2018-12-21

<160> 632

<170> PatentIn version 3.5

<210> 1
<211> 272
<212> PRT
<213> Vaccinia virus

<400> 1
Met Arg Tyr Ile Ile Ile Leu Ala Val Leu Phe Ile Asn Ser Ile His
1 5 10 15

Ala Lys Ile Thr Ser Tyr Lys Phe Glu Ser Val Asn Phe Asp Ser Lys
20 25 30

Ile Glu Trp Thr Gly Asp Gly Leu Tyr Asn Ile Ser Leu Lys Asn Tyr
35 40 45

Gly Ile Lys Thr Trp Gln Thr Met Tyr Thr Asn Val Pro Glu Gly Thr
50 55 60

Tyr Asp Ile Ser Ala Phe Pro Lys Asn Asp Phe Val Ser Phe Trp Val
65 70 75 80

```
Lys Phe Glu Gln Gly Asp Tyr Lys Val Glu Glu Tyr Cys Thr Gly Leu
                85                  90                  95

Cys Val Glu Val Lys Ile Gly Pro Pro Thr Val Thr Leu Thr Glu Tyr
            100                 105                 110

Asp Asp His Ile Asn Leu Tyr Ile Glu His Pro Tyr Ala Thr Arg Gly
        115                 120                 125

Ser Lys Lys Ile Pro Ile Tyr Lys Arg Gly Asp Met Cys Asp Ile Tyr
    130                 135                 140

Leu Leu Tyr Thr Ala Asn Phe Thr Phe Gly Asp Ser Glu Glu Pro Val
145                 150                 155                 160

Thr Tyr Asp Ile Asp Asp Tyr Asp Cys Thr Ser Thr Gly Cys Ser Ile
                165                 170                 175

Asp Phe Ala Thr Thr Glu Lys Val Cys Val Thr Ala Gln Gly Ala Thr
            180                 185                 190

Glu Gly Phe Leu Glu Lys Ile Thr Pro Trp Ser Ser Glu Val Cys Leu
        195                 200                 205

Thr Pro Lys Lys Asn Val Tyr Thr Cys Ala Ile Arg Ser Lys Glu Asp
    210                 215                 220

Val Pro Asn Phe Lys Asp Lys Met Ala Arg Val Ile Lys Arg Lys Phe
225                 230                 235                 240

Asn Lys Gln Ser Gln Ser Tyr Leu Thr Lys Phe Leu Gly Ser Thr Ser
                245                 250                 255

Asn Asp Val Thr Thr Phe Leu Ser Met Leu Asn Leu Thr Lys Tyr Ser
            260                 265                 270
```

<210> 2

<211> 222
<212> PRT
<213> Vaccinia virus

<400> 2
Met Asn His Cys Leu Leu Ala Ile Ser Ala Val Tyr Phe Lys Ala Lys
1   5   10   15

Trp Leu Thr Pro Phe Glu Lys Glu Phe Thr Ser Asp Tyr Pro Phe Tyr
            20   25   30

Val Ser Pro Thr Glu Met Val Asp Val Ser Met Met Ser Met Tyr Gly
        35   40   45

Glu Leu Phe Asn His Ala Ser Val Lys Glu Ser Phe Gly Asn Phe Ser
    50   55   60

Ile Ile Glu Leu Pro Tyr Val Gly Asp Thr Ser Met Met Val Ile Leu
65   70   75   80

Pro Asp Lys Ile Asp Gly Leu Glu Ser Ile Glu Gln Asn Leu Thr Asp
                85   90   95

Thr Asn Phe Lys Lys Trp Cys Asn Ser Leu Asp Ala Met Phe Ile Asp
            100   105   110

Val His Ile Pro Lys Phe Lys Val Thr Gly Ser Tyr Asn Leu Val Asp
        115   120   125

Thr Leu Val Lys Ser Gly Leu Thr Glu Val Phe Gly Ser Thr Gly Asp
    130   135   140

Tyr Ser Asn Met Cys Asn Leu Asp Val Ser Val Asp Ala Met Ile His
145   150   155   160

Lys Thr Tyr Ile Asp Val Asn Glu Glu Tyr Thr Glu Ala Ala Ala Ala
                165   170   175

Thr Cys Ala Leu Val Ser Asp Cys Ala Ser Thr Ile Thr Asn Glu Phe

```
            180                 185                 190

Cys Val Asp His Pro Phe Ile Tyr Val Ile Arg His Val Asp Gly Lys
        195                 200                 205

Ile Leu Phe Val Gly Arg Tyr Cys Ser Pro Thr Thr Asn Cys
    210                 215                 220
```

<210> 3
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 3

```
Met Thr Ala Asn Phe Ser Thr His Val Phe Ser Pro Gln His Cys Gly
1               5                   10                  15

Cys Asp Arg Leu Thr Ser Ile Asp Asp Val Lys Gln Cys Leu Thr Glu
            20                  25                  30

Tyr Ile Tyr Trp Ser Ser Tyr Ala Tyr Arg Asn Arg Gln Cys Ala Gly
        35                  40                  45

Gln Leu Tyr Ser Thr Leu Leu Ser Phe Arg Asp Asp Ala Glu Leu Val
    50                  55                  60

Phe Ile Asp Ile Arg Glu Leu Val Lys Asn Met Pro Trp Asp Asp Val
65                  70                  75                  80

Lys Asp Cys Thr Glu Ile Ile Arg Cys Tyr Ile Pro Asp Glu Gln Lys
                85                  90                  95

Thr Ile Arg Glu Ile Ser Ala Ile Ile Gly Leu Cys Ala Tyr Ala Ala
            100                 105                 110

Thr Tyr Trp Gly Gly Glu Asp His Pro Thr Ser Asn Ser Leu Asn Ala
        115                 120                 125

Leu Phe Val Met Leu Glu Met Leu Asn Tyr Val Asp Tyr Asn Ile Ile
```

130 135 140

Phe Arg Arg Met Asn
145

<210> 4
<211> 30
<212> PRT
<213> Vaccinia virus

<400> 4
Met Ser Ile Leu Pro Val Ile Phe Leu Pro Ile Phe Phe Tyr Ser Ser
1 5 10 15

Phe Val Gln Thr Phe Asn Ala Ser Glu Cys Ile Asp Lys Gly
20 25 30

<210> 5
<211> 340
<212> PRT
<213> Vaccinia virus

<400> 5
Met Ser Arg Lys Phe Met Gln Val Tyr Glu Tyr Asp Arg Glu Gln Tyr
1 5 10 15

Leu Asp Glu Phe Ile Glu Asp Arg Tyr Asn Asp Ser Phe Ile Thr Ser
20 25 30

Pro Glu Tyr Tyr Ser Ala Glu Lys Tyr Met Cys Arg Tyr Thr Thr Leu
35 40 45

Asn His Asn Cys Val Asn Val Arg Arg Cys Ala Leu Asp Ser Lys Leu
50 55 60

Leu His Asp Ile Ile Thr Asn Cys Lys Ile Tyr Asn Asn Ile Glu Leu
65 70 75 80

Val Arg Ala Thr Lys Phe Val Tyr Tyr Leu Asp Leu Ile Lys Cys Asn
85 90 95

```
Trp Val Ser Lys Val Gly Asp Ser Val Leu Tyr Pro Val Ile Phe Ile
            100                 105                 110

Thr His Thr Ser Thr Arg Asn Leu Asp Lys Val Ser Val Lys Thr Tyr
        115                 120                 125

Lys Gly Val Lys Val Lys Lys Leu Asn Arg Cys Ala Asp His Ala Ile
    130                 135                 140

Val Ile Asn Pro Phe Val Lys Phe Lys Leu Thr Leu Pro Asn Lys Thr
145                 150                 155                 160

Ser His Ala Lys Val Leu Val Thr Phe Cys Lys Leu Arg Thr Asp Ile
                165                 170                 175

Thr Pro Val Glu Ala Pro Leu Pro Gly Asn Val Leu Val Tyr Thr Phe
            180                 185                 190

Pro Asp Ile Asn Lys Arg Ile Pro Gly Tyr Ile His Val Asn Ile Glu
        195                 200                 205

Gly Cys Ile Asp Gly Met Ile Tyr Ile Asn Ser Ser Lys Phe Ala Cys
    210                 215                 220

Val Leu Lys Leu His Arg Ser Met Tyr Arg Ile Pro Pro Phe Pro Ile
225                 230                 235                 240

Asp Ile Cys Ser Cys Cys Ser Gln Tyr Thr Asn Asp Asp Ile Glu Ile
                245                 250                 255

Pro Ile His Asp Leu Ile Lys Asp Val Ala Ile Phe Lys Asn Lys Glu
            260                 265                 270

Thr Val Tyr Tyr Leu Lys Leu Asn Asn Lys Thr Ile Ala Arg Phe Thr
        275                 280                 285

Tyr Phe Asn Asn Ile Asp Thr Ala Ile Thr Gln Glu His Glu Tyr Val
```

290 295 300

Lys Ile Ala Leu Gly Ile Val Cys Lys Leu Met Ile Asn Asn Met His
305 310 315 320

Ser Ile Val Gly Val Asn His Ser Asn Thr Phe Val Asn Cys Leu Leu
325 330 335

Glu Asp Asn Val
340

<210> 6
<211> 574
<212> PRT
<213> Vaccinia virus

<400> 6
Met Ser Arg Arg Leu Ile Tyr Val Leu Asn Ile Asn Arg Lys Ser Thr
1 5 10 15

His Lys Ile Gln Glu Asn Glu Ile Tyr Thr Tyr Phe Ser His Cys Asn
20 25 30

Ile Asp His Thr Ser Thr Glu Leu Asp Phe Val Val Lys Asn Tyr Asp
35 40 45

Leu Asn Arg Arg Gln His Val Thr Gly Tyr Thr Ala Leu His Cys Tyr
50 55 60

Leu Tyr Asn Asn Tyr Phe Thr Asn Asp Val Leu Lys Ile Leu Leu Asn
65 70 75 80

His Asp Val Asn Val Thr Met Lys Thr Ser Ser Gly Arg Met Pro Val
85 90 95

Tyr Ile Leu Leu Thr Arg Cys Cys Asn Ile Ser His Asp Val Val Ile
100 105 110

Asp Met Ile Asp Lys Asp Lys Asn His Leu Ser His Arg Asp Tyr Ser

```
        115                 120                 125

Asn Leu Leu Leu Glu Tyr Ile Lys Ser Arg Tyr Met Leu Leu Lys Glu
    130                 135                 140

Glu Asp Ile Asp Glu Asn Ile Val Ser Thr Leu Leu Asp Lys Gly Ile
145                 150                 155                 160

Asp Pro Asn Phe Lys Gln Asp Gly Tyr Thr Ala Leu His Tyr Tyr Tyr
                165                 170                 175

Leu Cys Leu Ala His Val Tyr Lys Pro Gly Glu Cys Arg Lys Pro Ile
            180                 185                 190

Thr Ile Lys Lys Ala Lys Arg Ile Ile Ser Leu Phe Ile Gln His Gly
        195                 200                 205

Ala Asn Leu Asn Ala Leu Asp Asn Cys Gly Asn Thr Pro Phe His Leu
    210                 215                 220

Tyr Leu Ser Ile Glu Met Cys Asn Asn Ile His Met Thr Lys Met Leu
225                 230                 235                 240

Leu Thr Phe Asn Pro Asn Phe Lys Ile Cys Asn Asn His Gly Leu Thr
                245                 250                 255

Pro Ile Leu Cys Tyr Ile Thr Ser Asp Tyr Ile Gln His Asp Ile Leu
            260                 265                 270

Val Met Leu Ile His His Tyr Glu Thr Asn Val Gly Glu Met Pro Ile
        275                 280                 285

Asp Glu Arg Arg Met Ile Val Phe Glu Phe Ile Lys Thr Tyr Ser Thr
    290                 295                 300

Arg Pro Ala Asp Ser Ile Thr Tyr Leu Met Asn Arg Phe Lys Asn Ile
305                 310                 315                 320
```

```
Asn Ile Tyr Thr Arg Tyr Glu Gly Lys Thr Leu Leu His Val Ala Cys
                325                 330                 335

Glu Tyr Asn Asn Thr Gln Val Ile Asp Tyr Leu Ile Arg Ile Asn Gly
            340                 345                 350

Asp Ile Asn Ala Leu Thr Asp Asn Asn Lys His Ala Thr Gln Leu Ile
        355                 360                 365

Ile Asp Asn Lys Glu Asn Ser Pro Tyr Thr Ile Asn Cys Leu Leu Tyr
    370                 375                 380

Ile Leu Arg Tyr Ile Val Asp Lys Asn Val Ile Arg Ser Leu Val Asp
385                 390                 395                 400

Gln Leu Pro Ser Leu Pro Ile Phe Asp Ile Lys Ser Phe Glu Lys Phe
                405                 410                 415

Ile Ser Tyr Cys Ile Leu Leu Asp Asp Thr Phe Tyr Asp Arg His Val
            420                 425                 430

Lys Asn Arg Asp Ser Lys Thr Tyr Arg Tyr Ala Phe Ser Lys Tyr Met
        435                 440                 445

Ser Phe Asp Lys Tyr Asp Gly Ile Ile Thr Lys Cys His Asp Glu Thr
    450                 455                 460

Met Leu Leu Lys Leu Ser Thr Val Leu Asp Thr Thr Leu Tyr Ala Val
465                 470                 475                 480

Leu Arg Cys His Asn Ser Arg Lys Leu Arg Arg Tyr Leu Thr Glu Leu
                485                 490                 495

Lys Lys Tyr Asn Asn Asp Lys Ser Phe Lys Ile Tyr Ser Asn Ile Met
            500                 505                 510

Asn Glu Arg Tyr Leu Asn Val Tyr Tyr Lys Asp Met Tyr Val Ser Lys
```

```
        515                 520                 525

Val Tyr Asp Lys Leu Phe Pro Val Phe Thr Asp Lys Asn Cys Leu Leu
    530                 535                 540

Thr Leu Leu Pro Ser Glu Ile Ile Tyr Glu Ile Leu Tyr Met Leu Thr
545                 550                 555                 560

Ile Asn Asp Leu Tyr Asn Ile Ser Tyr Pro Pro Thr Lys Val
                565                 570
```

<210> 7
<211> 353
<212> PRT
<213> Vaccinia virus

<400> 7

```
Met Thr Met Lys Met Met Val His Ile Tyr Phe Val Ser Leu Ser Leu
1               5                   10                  15

Leu Leu Leu Leu Phe His Ser Tyr Ala Ile Asp Ile Glu Asn Glu Ile
            20                  25                  30

Thr Glu Phe Phe Asn Lys Met Arg Asp Thr Leu Pro Ala Lys Asp Ser
        35                  40                  45

Lys Trp Leu Asn Pro Ala Cys Met Phe Gly Gly Thr Met Asn Asp Met
    50                  55                  60

Ala Thr Leu Gly Glu Pro Phe Ser Ala Lys Cys Pro Pro Ile Glu Asp
65                  70                  75                  80

Ser Leu Leu Ser His Arg Tyr Lys Asp Tyr Val Val Lys Trp Glu Arg
                85                  90                  95

Leu Glu Lys Asn Arg Arg Arg Gln Val Ser Asn Lys Arg Val Lys His
            100                 105                 110

Gly Asp Leu Trp Ile Ala Asn Tyr Thr Ser Lys Phe Ser Asn Arg Arg
```

```
        115                 120                 125

Tyr Leu Cys Thr Val Thr Thr Lys Asn Gly Asp Cys Val Gln Gly Ile
    130                 135                 140

Val Arg Ser His Ile Lys Lys Pro Pro Ser Cys Ile Pro Lys Thr Tyr
145                 150                 155                 160

Glu Leu Gly Thr His Asp Lys Tyr Gly Ile Asp Leu Tyr Cys Gly Ile
                165                 170                 175

Leu Tyr Ala Lys His Tyr Asn Asn Ile Thr Trp Tyr Lys Asp Asn Lys
            180                 185                 190

Glu Ile Asn Ile Asp Asp Ile Lys Tyr Ser Gln Thr Gly Lys Glu Leu
        195                 200                 205

Ile Ile His Asn Pro Glu Leu Glu Asp Ser Gly Arg Tyr Asp Cys Tyr
    210                 215                 220

Val His Tyr Asp Asp Val Arg Ile Lys Asn Asp Ile Val Val Ser Arg
225                 230                 235                 240

Cys Lys Ile Leu Thr Val Ile Pro Ser Gln Asp His Arg Phe Lys Leu
                245                 250                 255

Ile Leu Asp Pro Lys Ile Asn Val Thr Ile Gly Glu Pro Ala Asn Ile
            260                 265                 270

Thr Cys Thr Ala Val Ser Thr Ser Leu Leu Ile Asp Asp Val Leu Ile
        275                 280                 285

Glu Trp Glu Asn Pro Ser Gly Trp Leu Ile Gly Phe Asp Phe Asp Val
    290                 295                 300

Tyr Ser Val Leu Thr Ser Arg Gly Gly Ile Thr Glu Ala Thr Leu Tyr
305                 310                 315                 320
```

```
Phe Glu Asn Val Thr Glu Glu Tyr Ile Gly Asn Thr Tyr Lys Cys Arg
                325                 330                 335

Gly His Asn Tyr Tyr Phe Glu Lys Thr Leu Thr Thr Thr Val Val Leu
            340                 345                 350

Glu
```

<210> 8
<211> 127
<212> PRT
<213> Vaccinia virus

<400> 8

```
Met Asp Glu Asp Thr Arg Leu Ser Arg Tyr Leu Tyr Leu Thr Asp Arg
1               5                   10                  15

Glu His Ile Asn Val Asp Ser Ile Lys Gln Leu Cys Lys Ile Ser Asp
            20                  25                  30

Pro Asn Ala Cys Tyr Arg Cys Gly Cys Thr Ala Leu His Glu Tyr Phe
        35                  40                  45

Tyr Asn Tyr Arg Ser Val Asn Gly Lys Tyr Lys Tyr Arg Tyr Asn Gly
    50                  55                  60

Tyr Tyr Gln Tyr Tyr Ser Ser Ser Asp Tyr Glu Asn Tyr Asn Glu Tyr
65                  70                  75                  80

Tyr Tyr Asp Asp Tyr Asp Arg Thr Gly Met Asn Ser Glu Ser Asp Ser
                85                  90                  95

Glu Ser Asp Asn Ile Ser Ile Lys Thr Glu Tyr Glu Asn Glu Tyr Glu
            100                 105                 110

Phe Tyr Asp Glu Thr Gln Asp Gln Ser Thr Gln His Asn Asp Leu
        115                 120                 125
```

<210> 9
<211> 224
<212> PRT
<213> Vaccinia virus

<400> 9
Met Val Lys Asn Asn Lys Ile Ser Asn Ser Cys Arg Met Ile Met Ser
1   5   10   15

Thr Asn Pro Asn Asn Ile Leu Met Arg His Leu Lys Asn Leu Thr Asp
            20   25   30

Asp Glu Phe Lys Cys Ile Ile His Arg Ser Ser Asp Phe Leu Tyr Leu
        35   40   45

Ser Asp Ser Asp Tyr Thr Ser Ile Thr Lys Glu Thr Leu Val Ser Glu
    50   55   60

Ile Val Glu Glu Tyr Pro Asp Asp Cys Asn Lys Ile Leu Ala Ile Ile
65   70   75   80

Phe Leu Val Leu Asp Lys Asp Ile Asp Val Asp Ile Glu Thr Lys Leu
                85   90   95

Lys Pro Lys Pro Ala Val Arg Phe Ala Ile Leu Asp Lys Met Thr Glu
            100   105   110

Asp Ile Lys Leu Thr Asp Leu Val Arg His Tyr Phe Arg Tyr Ile Glu
        115   120   125

Gln Asp Ile Pro Leu Gly Pro Leu Phe Lys Lys Ile Asp Ser Tyr Arg
    130   135   140

Thr Arg Ala Ile Asn Lys Tyr Ser Lys Glu Leu Gly Leu Ala Thr Glu
145   150   155   160

Tyr Phe Asn Lys Tyr Gly His Leu Met Phe Tyr Thr Leu Pro Ile Pro
                165   170   175

```
Tyr Asn Arg Phe Phe Cys Arg Asn Ser Ile Gly Phe Leu Ala Val Leu
            180                 185                 190


Ser Pro Thr Ile Gly His Val Lys Ala Phe Tyr Lys Phe Ile Glu Tyr
        195                 200                 205


Val Ser Ile Asp Asp Arg Arg Lys Phe Lys Lys Glu Leu Met Ser Lys
    210                 215                 220


<210> 10
<211> 512
<212> PRT
<213> Vaccinia virus

<400> 10
Met Glu Ser Val Ile Phe Ser Ile Asn Gly Glu Ile Ile Gln Val Asn
1               5                   10                  15


Lys Glu Ile Ile Thr Ala Ser Pro Tyr Asn Phe Phe Lys Arg Ile Gln
            20                  25                  30


Asp His His Leu Lys Asp Glu Ala Ile Ile Leu Asn Gly Ile Asn Tyr
        35                  40                  45


His Ala Phe Glu Ser Leu Leu Asp Tyr Met Arg Trp Lys Lys Ile Asn
    50                  55                  60


Ile Thr Ile Asn Asn Val Glu Met Ile Leu Val Ala Ala Val Ile Ile
65                  70                  75                  80


Asp Val Pro Pro Val Val Asp Leu Cys Val Lys Thr Met Ile His Asn
                85                  90                  95


Ile Asn Ser Thr Asn Cys Ile Arg Met Phe Asn Phe Ser Lys Arg Tyr
            100                 105                 110


Gly Ile Lys Lys Leu Tyr Asn Ala Ser Met Ser Glu Ile Ile Asn Asn
        115                 120                 125
```

```
Ile Thr Ala Val Thr Ser Asp Pro Glu Phe Gly Lys Leu Ser Lys Asp
    130                 135                 140

Glu Leu Thr Thr Ile Leu Ser His Glu Asp Val Asn Val Asn His Glu
145                 150                 155                 160

Asp Val Thr Ala Met Ile Leu Leu Lys Trp Ile His Lys Asn Pro Asn
                165                 170                 175

Asp Val Asp Ile Ile Asn Ile Leu His Pro Lys Phe Met Thr Asn Thr
            180                 185                 190

Met Arg Asn Ala Ile Ser Leu Leu Gly Leu Thr Ile Ser Lys Ser Thr
        195                 200                 205

Lys Pro Val Thr Arg Asn Gly Ile Lys His Asn Ile Val Val Ile Lys
    210                 215                 220

Asn Ser Asp Tyr Ile Ser Thr Ile Thr His Tyr Ser Pro Arg Thr Glu
225                 230                 235                 240

Tyr Trp Thr Ile Val Gly Asn Thr Asp Arg Gln Phe Tyr Asn Ala Asn
                245                 250                 255

Val Leu His Asn Cys Leu Tyr Ile Ile Gly Gly Met Ile Asn Asn Arg
            260                 265                 270

His Val Tyr Ser Val Ser Arg Val Asp Leu Glu Thr Lys Lys Trp Lys
        275                 280                 285

Thr Val Thr Asn Met Ser Ser Leu Lys Ser Glu Val Ser Thr Cys Val
    290                 295                 300

Asn Asp Gly Lys Leu Tyr Val Ile Gly Gly Leu Glu Phe Ser Ile Ser
305                 310                 315                 320

Thr Gly Val Ala Glu Tyr Leu Lys His Gly Thr Ser Lys Trp Ile Arg
```

```
                325                 330                 335

Leu Pro Asn Leu Ile Thr Pro Arg Tyr Ser Gly Ala Ser Val Phe Val
            340                 345                 350

Asn Asp Asp Ile Tyr Val Met Gly Gly Val Tyr Thr Thr Tyr Glu Lys
        355                 360                 365

Tyr Val Val Leu Asn Asp Val Glu Cys Phe Thr Lys Asn Arg Trp Ile
    370                 375                 380

Lys Lys Ser Pro Met Pro Arg His His Ser Ile Val Tyr Ala Val Glu
385                 390                 395                 400

Tyr Asp Gly Asp Ile Tyr Val Ile Thr Gly Ile Thr His Glu Thr Arg
                405                 410                 415

Asn Tyr Leu Tyr Lys Tyr Ile Val Lys Glu Asp Lys Trp Ile Glu Leu
            420                 425                 430

Tyr Met Tyr Phe Asn His Val Gly Lys Met Phe Val Cys Ser Cys Gly
        435                 440                 445

Asp Tyr Ile Leu Ile Ile Ala Asp Ala Lys Tyr Glu Tyr Tyr Pro Lys
    450                 455                 460

Ser Asn Thr Trp Asn Leu Phe Asp Met Ser Thr Arg Asn Ile Glu Tyr
465                 470                 475                 480

Tyr Asp Met Phe Thr Lys Asp Glu Thr Pro Lys Cys Asn Val Thr His
                485                 490                 495

Lys Ser Leu Pro Ser Phe Leu Ser Asn Cys Glu Lys Gln Phe Leu Gln
            500                 505                 510
```

<210> 11
<211> 226
<212> PRT

<213> Vaccinia virus

<400> 11

```
Met Leu Ser Met Phe Met Cys Asn Asn Ile Val Asp Tyr Val Asp Asp
1               5                  10                  15

Ile Asp Asn Gly Ile Val Gln Asp Ile Glu Asp Glu Ala Ser Asn Asn
            20                  25                  30

Val Asp His Asp Tyr Val Tyr Pro Leu Pro Glu Asn Met Val Tyr Arg
        35                  40                  45

Phe Asp Lys Ser Thr Asn Ile Leu Asp Tyr Leu Ser Thr Glu Arg Asp
    50                  55                  60

His Val Met Met Ala Val Arg Tyr Tyr Met Ser Lys Gln Arg Leu Asp
65                  70                  75                  80

Asp Leu Tyr Arg Gln Leu Pro Thr Lys Thr Arg Ser Tyr Ile Asp Ile
                85                  90                  95

Ile Asn Ile Tyr Cys Asp Lys Val Ser Asn Asp Tyr Asn Arg Asp Met
            100                 105                 110

Asn Ile Met Tyr Asp Met Ala Ser Thr Lys Ser Phe Thr Val Tyr Asp
        115                 120                 125

Ile Asn Asn Glu Val Asn Thr Ile Leu Met Asp Asn Lys Gly Leu Gly
    130                 135                 140

Val Arg Leu Ala Thr Ile Ser Phe Ile Thr Glu Leu Gly Arg Arg Cys
145                 150                 155                 160

Met Asn Pro Val Lys Thr Ile Lys Met Phe Thr Leu Leu Ser His Thr
                165                 170                 175

Ile Cys Asp Asp Cys Phe Val Asp Tyr Ile Thr Asp Ile Ser Pro Pro
            180                 185                 190
```

```
Asp Asn Thr Ile Pro Asn Thr Ser Thr Arg Glu Tyr Leu Lys Leu Ile
        195                 200                 205


Gly Ile Thr Ala Ile Met Phe Ala Thr Tyr Lys Thr Leu Lys Tyr Met
    210                 215                 220


Ile Gly
225


<210> 12
<211> 147
<212> PRT
<213> Vaccinia virus

<400> 12
Met Phe Asn Met Asn Ile Asn Ser Pro Val Arg Phe Val Lys Glu Thr
1               5                   10                  15


Asn Arg Ala Lys Ser Pro Thr Arg Gln Ser Pro Gly Ala Ala Gly Tyr
            20                  25                  30


Asp Leu Tyr Ser Ala Tyr Asp Tyr Thr Ile Pro Pro Gly Glu Arg Gln
        35                  40                  45


Leu Ile Lys Thr Asp Ile Ser Met Ser Met Pro Lys Ile Cys Tyr Gly
    50                  55                  60


Arg Ile Ala Pro Arg Ser Gly Leu Ser Leu Lys Gly Ile Asp Ile Gly
65                  70                  75                  80


Gly Gly Val Ile Asp Glu Asp Tyr Arg Gly Asn Ile Gly Val Ile Leu
                85                  90                  95


Ile Asn Asn Gly Lys Cys Thr Phe Asn Val Asn Thr Gly Asp Arg Ile
            100                 105                 110


Ala Gln Leu Ile Tyr Gln Arg Ile Tyr Tyr Pro Glu Leu Glu Glu Val
        115                 120                 125
```

Gln Ser Leu Asp Ser Thr Asn Arg Gly Asp Gln Gly Phe Gly Ser Thr
130 135 140

Gly Leu Arg
145

<210> 13
<211> 480
<212> PRT
<213> Vaccinia virus

<400> 13
Met Pro Ile Phe Val Asn Thr Val Tyr Cys Lys Asn Ile Leu Ala Leu
1 5 10 15

Ser Met Thr Lys Lys Phe Lys Thr Ile Ile Asp Ala Ile Gly Gly Asn
20 25 30

Ile Ile Val Asn Ser Thr Ile Leu Lys Lys Leu Ser Pro Tyr Phe Arg
35 40 45

Thr His Leu Arg Gln Lys Tyr Thr Lys Asn Lys Asp Pro Val Thr Arg
50 55 60

Val Cys Leu Asp Leu Asp Ile His Ser Leu Thr Ser Ile Val Ile Tyr
65 70 75 80

Ser Tyr Thr Gly Lys Val Tyr Ile Asp Ser His Asn Val Val Asn Leu
85 90 95

Leu Arg Ala Ser Ile Leu Thr Ser Val Glu Phe Ile Ile Tyr Thr Cys
100 105 110

Ile Asn Phe Ile Leu Arg Asp Phe Arg Lys Glu Tyr Cys Val Glu Cys
115 120 125

Tyr Met Met Gly Ile Glu Tyr Gly Leu Ser Asn Leu Leu Cys His Thr
130 135 140

```
Lys Asn Phe Ile Ala Lys His Phe Leu Glu Leu Glu Asp Asp Ile Ile
145                 150                 155                 160


Asp Asn Phe Asp Tyr Leu Ser Met Lys Leu Ile Leu Glu Ser Asp Glu
                165                 170                 175


Leu Asn Val Pro Asp Glu Asp Tyr Val Val Asp Phe Val Ile Lys Trp
            180                 185                 190


Tyr Ile Lys Arg Arg Asn Lys Leu Gly Asn Leu Leu Leu Leu Ile Lys
        195                 200                 205


Asn Val Ile Arg Ser Asn Tyr Leu Ser Pro Arg Gly Ile Asn Asn Val
    210                 215                 220


Lys Trp Ile Leu Asp Cys Thr Lys Ile Phe His Cys Asp Lys Gln Pro
225                 230                 235                 240


Arg Lys Ser Tyr Lys Tyr Pro Phe Ile Glu Tyr Pro Met Asn Met Asp
                245                 250                 255


Gln Ile Ile Asp Ile Phe His Met Cys Thr Ser Thr His Val Gly Glu
            260                 265                 270


Val Val Tyr Leu Ile Gly Gly Trp Met Asn Asn Glu Ile His Asn Asn
        275                 280                 285


Ala Ile Ala Val Asn Tyr Ile Ser Asn Asn Trp Ile Pro Ile Pro Pro
    290                 295                 300


Met Asn Ser Pro Arg Leu Tyr Ala Thr Gly Ile Pro Ala Asn Asn Lys
305                 310                 315                 320


Leu Tyr Val Val Gly Gly Leu Pro Asn Pro Thr Ser Val Glu Arg Trp
                325                 330                 335


Phe His Gly Asp Ala Ala Trp Val Asn Met Pro Ser Leu Leu Lys Pro
```

```
            340                 345                 350

Arg Cys Asn Pro Ala Val Ala Ser Ile Asn Asn Val Ile Tyr Val Met
        355                 360                 365

Gly Gly His Ser Glu Thr Asp Thr Thr Thr Glu Tyr Leu Leu Pro Asn
    370                 375                 380

His Asp Gln Trp Gln Phe Gly Pro Ser Thr Tyr Tyr Pro His Tyr Lys
385                 390                 395                 400

Ser Cys Ala Leu Val Phe Gly Arg Arg Leu Phe Leu Val Gly Arg Asn
                405                 410                 415

Ala Glu Phe Tyr Cys Glu Ser Ser Asn Thr Trp Thr Leu Ile Asp Asp
            420                 425                 430

Pro Ile Tyr Pro Arg Asp Asn Pro Glu Leu Ile Ile Val Asp Asn Lys
        435                 440                 445

Leu Leu Leu Ile Gly Gly Phe Tyr Arg Gly Ser Tyr Ile Asp Thr Ile
    450                 455                 460

Glu Val Tyr Asn His His Thr Tyr Ser Trp Asn Ile Trp Asp Gly Lys
465                 470                 475                 480


<210> 14
<211> 284
<212> PRT
<213> Vaccinia virus

<400> 14
Met Asp Leu Ser Arg Ile Asn Thr Trp Lys Ser Lys Gln Leu Lys Ser
1               5                   10                  15

Phe Leu Ser Ser Lys Asp Thr Phe Lys Ala Asp Val His Gly His Ser
            20                  25                  30

Ala Leu Tyr Tyr Ala Ile Ala Asp Asn Asn Val Arg Leu Val Cys Thr
```

```
        35                  40                  45

Leu Leu Asn Ala Gly Ala Leu Lys Asn Leu Leu Glu Asn Glu Phe Pro
    50                  55                  60

Leu His Gln Ala Ala Thr Leu Glu Asp Thr Lys Ile Val Lys Ile Leu
65                  70                  75                  80

Leu Phe Ser Gly Met Asp Asp Ser Gln Phe Asp Asp Lys Gly Asn Thr
                85                  90                  95

Ala Leu Tyr Tyr Ala Val Asp Ser Gly Asn Met Gln Thr Val Lys Leu
            100                 105                 110

Phe Val Lys Lys Asn Trp Arg Leu Met Phe Tyr Gly Lys Thr Gly Trp
        115                 120                 125

Lys Thr Ser Phe Tyr His Ala Val Met Leu Asn Asp Val Ser Ile Val
    130                 135                 140

Ser Tyr Phe Leu Ser Glu Ile Pro Ser Thr Phe Asp Leu Ala Ile Leu
145                 150                 155                 160

Leu Ser Cys Ile His Thr Thr Ile Lys Asn Gly His Val Asp Met Met
                165                 170                 175

Ile Leu Leu Leu Asp Tyr Met Thr Ser Thr Asn Thr Asn Asn Ser Leu
            180                 185                 190

Leu Phe Ile Pro Asp Ile Lys Leu Ala Ile Asp Asn Lys Asp Ile Glu
        195                 200                 205

Met Leu Gln Ala Leu Phe Lys Tyr Asp Ile Asn Ile Tyr Ser Val Asn
    210                 215                 220

Leu Glu Asn Val Leu Leu Asp Asp Ala Glu Ile Thr Lys Met Ile Ile
225                 230                 235                 240
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```
Glu Lys His Val Glu Tyr Lys Ser Asp Ser Tyr Thr Lys Asp Leu Asp
                245                 250                 255


Ile Val Lys Asn Asn Lys Leu Asp Glu Ile Ile Ser Lys Asn Lys Glu
            260                 265                 270


Leu Arg Leu Met Tyr Val Asn Cys Val Lys Lys Asn
        275                 280


<210> 15
<211> 369
<212> PRT
<213> Vaccinia virus

<400> 15
Met Ile Ala Leu Leu Ile Leu Ser Leu Thr Cys Ser Val Ser Thr Tyr
1               5                   10                  15


Arg Leu Gln Gly Phe Thr Asn Ala Gly Ile Val Ala Tyr Lys Asn Ile
            20                  25                  30


Gln Asp Asp Asn Ile Val Phe Ser Pro Phe Gly Tyr Ser Phe Ser Met
        35                  40                  45


Phe Met Ser Leu Leu Pro Ala Ser Gly Asn Thr Arg Ile Glu Leu Leu
    50                  55                  60


Lys Thr Met Asp Leu Arg Lys Arg Asp Leu Gly Pro Ala Phe Thr Glu
65                  70                  75                  80


Leu Ile Ser Gly Leu Ala Lys Leu Lys Thr Ser Lys Tyr Thr Tyr Thr
                85                  90                  95


Asp Leu Thr Tyr Gln Ser Phe Val Asp Asn Thr Val Cys Ile Lys Pro
            100                 105                 110


Leu Tyr Tyr Gln Gln Tyr His Arg Phe Gly Leu Tyr Arg Leu Asn Phe
        115                 120                 125
```

```
Arg Arg Asp Ala Val Asn Lys Ile Asn Ser Ile Val Glu Arg Arg Ser
    130                 135                 140

Gly Met Ser Asn Val Val Asp Ser Asn Met Leu Asp Asn Asn Thr Leu
145                 150                 155                 160

Trp Ala Ile Ile Asn Thr Ile Tyr Phe Lys Gly Thr Trp Gln Tyr Pro
                165                 170                 175

Phe Asp Ile Thr Lys Thr Arg Asn Ala Ser Phe Thr Asn Lys Tyr Gly
            180                 185                 190

Thr Lys Thr Val Pro Met Met Asn Val Val Thr Lys Leu Gln Gly Asn
        195                 200                 205

Thr Ile Thr Ile Asp Asp Glu Glu Tyr Asp Met Val Arg Leu Pro Tyr
    210                 215                 220

Lys Asp Ala Asn Ile Ser Met Tyr Leu Ala Ile Gly Asp Asn Met Thr
225                 230                 235                 240

His Phe Thr Asp Ser Ile Thr Ala Ala Lys Leu Asp Tyr Trp Ser Phe
                245                 250                 255

Gln Leu Gly Asn Lys Val Tyr Asn Leu Lys Leu Pro Lys Phe Ser Ile
            260                 265                 270

Glu Asn Lys Arg Asp Ile Lys Ser Ile Ala Glu Met Met Ala Pro Ser
        275                 280                 285

Met Phe Asn Pro Asp Asn Ala Ser Phe Lys His Met Thr Arg Asp Pro
    290                 295                 300

Leu Tyr Ile Tyr Lys Met Phe Gln Asn Ala Lys Ile Asp Val Asp Glu
305                 310                 315                 320

Gln Gly Thr Val Ala Glu Ala Ser Thr Ile Met Val Ala Thr Ala Arg
```

325 330 335

Ser Ser Pro Glu Lys Leu Glu Phe Asn Thr Pro Phe Val Phe Ile Ile
340 345 350

Arg His Asp Ile Thr Gly Phe Ile Leu Phe Met Gly Lys Val Glu Ser
355 360 365

Pro

<210> 16
<211> 88
<212> PRT
<213> Vaccinia virus

<400> 16
Met Leu Ala Phe Cys Tyr Ser Leu Pro Asn Ala Gly Asp Val Ile Lys
1 5 10 15

Gly Arg Val Tyr Glu Lys Asp Tyr Ala Leu Tyr Ile Tyr Leu Phe Asp
20 25 30

Tyr Pro His Ser Glu Ala Ile Leu Ala Glu Ser Val Lys Met His Met
35 40 45

Asp Arg Tyr Val Glu Tyr Arg Asp Lys Leu Val Gly Lys Thr Val Lys
50 55 60

Val Lys Val Ile Arg Val Asp Tyr Thr Lys Gly Tyr Ile Asp Val Asn
65 70 75 80

Tyr Lys Arg Met Cys Arg His Gln
85

<210> 17
<211> 424
<212> PRT
<213> Vaccinia virus

<400> 17
Met Asn Pro Asp Asn Thr Ile Ala Val Ile Thr Glu Thr Ile Pro Ile
1   5   10   15

Gly Met Gln Phe Asp Lys Val Tyr Leu Ser Thr Phe Asn Met Trp Arg
            20   25   30

Glu Ile Leu Ser Asn Thr Thr Lys Thr Leu Asp Ile Ser Ser Phe Tyr
        35   40   45

Trp Ser Leu Ser Asp Glu Val Gly Thr Asn Phe Gly Thr Ile Ile Leu
    50   55   60

Asn Glu Ile Val Gln Leu Pro Lys Arg Gly Val Arg Val Arg Val Ala
65   70   75   80

Val Asn Lys Ser Asn Lys Pro Leu Lys Asp Val Glu Arg Leu Gln Met
                85   90   95

Ala Gly Val Glu Val Arg Tyr Ile Asp Ile Thr Asn Ile Leu Gly Gly
            100   105   110

Val Leu His Thr Lys Phe Trp Ile Ser Asp Asn Thr His Ile Tyr Leu
        115   120   125

Gly Ser Ala Asn Met Asp Trp Arg Ser Leu Thr Gln Val Lys Glu Leu
    130   135   140

Gly Ile Ala Ile Phe Asn Asn Arg Asn Leu Ala Ala Asp Leu Thr Gln
145   150   155   160

Ile Phe Glu Val Tyr Trp Tyr Leu Gly Val Asn Asn Leu Pro Tyr Asn
                165   170   175

Trp Lys Asn Phe Tyr Pro Ser Tyr Tyr Asn Thr Asp His Pro Leu Ser
            180   185   190

Ile Asn Val Ser Gly Val Pro His Ser Val Phe Ile Ala Ser Ala Pro

```
        195                 200                 205

Gln Gln Leu Cys Thr Met Glu Arg Thr Asn Asp Leu Thr Ala Leu Leu
    210                 215                 220

Ser Cys Ile Arg Asn Ala Ser Lys Phe Val Tyr Val Ser Val Met Asn
225                 230                 235                 240

Phe Ile Pro Ile Ile Tyr Ser Lys Ala Gly Lys Ile Leu Phe Trp Pro
                245                 250                 255

Tyr Ile Glu Asp Glu Leu Arg Arg Ser Ala Ile Asp Arg Gln Val Ser
            260                 265                 270

Val Lys Leu Leu Ile Ser Cys Trp Gln Arg Ser Ser Phe Ile Met Arg
        275                 280                 285

Asn Phe Leu Arg Ser Ile Ala Met Leu Lys Ser Lys Asn Ile Asp Ile
    290                 295                 300

Glu Val Lys Leu Phe Ile Val Pro Asp Ala Asp Pro Pro Ile Pro Tyr
305                 310                 315                 320

Ser Arg Val Asn His Ala Lys Tyr Met Val Thr Asp Lys Thr Ala Tyr
                325                 330                 335

Ile Gly Thr Ser Asn Trp Thr Gly Asn Tyr Phe Thr Asp Thr Cys Gly
            340                 345                 350

Ala Ser Ile Asn Ile Thr Pro Asp Asp Gly Leu Gly Leu Arg Gln Gln
        355                 360                 365

Leu Glu Asp Ile Phe Met Arg Asp Trp Asn Ser Lys Tyr Ser Tyr Glu
    370                 375                 380

Leu Tyr Asp Thr Ser Pro Thr Lys Arg Cys Lys Leu Leu Lys Asn Met
385                 390                 395                 400
```

Lys Gln Cys Thr Asn Asp Ile Tyr Cys Asp Glu Ile Gln Pro Glu Lys
405 410 415

Glu Ile Pro Glu Tyr Ser Leu Glu
420

<210> 18
<211> 136
<212> PRT
<213> Vaccinia virus

<400> 18
Met Gly Ala Thr Ile Ser Ile Leu Ala Ser Tyr Asp Asn Pro Asn Leu
1 5 10 15

Phe Thr Ala Met Ile Leu Met Ser Pro Leu Val Asn Ala Asp Ala Val
20 25 30

Ser Arg Leu Asn Leu Leu Ala Ala Lys Leu Met Gly Thr Ile Thr Pro
35 40 45

Asn Ala Pro Val Gly Lys Leu Cys Pro Glu Ser Val Ser Arg Asp Met
50 55 60

Asp Lys Val Tyr Lys Tyr Gln Tyr Asp Pro Leu Ile Asn His Glu Lys
65 70 75 80

Ile Lys Ala Gly Phe Ala Ser Gln Val Leu Lys Ala Thr Asn Lys Val
85 90 95

Arg Lys Ile Ile Ser Lys Ile Asn Thr Pro Arg Leu Ser Tyr Ser Arg
100 105 110

Glu Gln Thr Met Arg Leu Val Met Phe Gln Val His Ile Ile Ser Cys
115 120 125

Asn Met Gln Ile Val Ile Glu Lys
130 135

<210> 19
<211> 81
<212> PRT
<213> Vaccinia virus

<400> 19
Met Ser Ala Asn Cys Met Phe Asn Leu Asp Asn Asp Tyr Ile Tyr Trp
1   5   10   15

Lys Pro Ile Thr Tyr Pro Lys Ala Leu Val Phe Ile Ser His Gly Ala
            20   25   30

Gly Lys His Ser Gly Arg Tyr Asp Glu Leu Ala Glu Asn Ile Ser Ser
        35   40   45

Leu Gly Ile Leu Val Phe Ser His Asp His Ile Gly His Gly Arg Ser
    50   55   60

Asn Gly Glu Lys Met Met Ile Asp Asp Phe Gly Thr Ala Arg Gly Asn
65   70   75   80

Tyr

<210> 20
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 20
Met Ala Thr Lys Leu Asp Tyr Glu Asp Ala Val Phe Tyr Phe Val Asp
1   5   10   15

Asp Asp Lys Ile Cys Ser Arg Asp Ser Ile Ile Asp Leu Ile Asp Glu
            20   25   30

Tyr Ile Thr Trp Arg Asn His Val Ile Val Phe Asn Lys Asp Ile Thr
        35   40   45

Ser Cys Gly Arg Leu Tyr Lys Glu Leu Met Lys Phe Asp Asp Val Ala

```
    50                  55                  60

Ile Arg Tyr Tyr Gly Ile Asp Lys Ile Asn Glu Ile Val Glu Ala Met
65                  70                  75                  80

Ser Glu Gly Asp His Tyr Ile Asn Phe Thr Lys Val His Asp Gln Glu
                85                  90                  95

Ser Leu Phe Ala Thr Ile Gly Ile Cys Ala Lys Ile Thr Glu His Trp
            100                 105                 110

Gly Tyr Lys Lys Ile Ser Glu Ser Arg Phe Gln Ser Leu Gly Asn Ile
        115                 120                 125

Thr Asp Leu Met Thr Asp Asp Asn Ile Asn Ile Leu Ile Leu Phe Leu
    130                 135                 140

Glu Lys Lys Leu Asn
145


<210> 21
<211> 472
<212> PRT
<213> Vaccinia virus

<400> 21
Met Ile Phe Val Ile Glu Ser Lys Leu Leu Gln Ile Tyr Arg Asn Arg
1               5                   10                  15

Asn Arg Asn Ile Asn Phe Tyr Thr Thr Met Asp Asn Ile Met Ser Ala
            20                  25                  30

Glu Tyr Tyr Leu Ser Leu Tyr Ala Lys Tyr Asn Ser Lys Asn Leu Asp
        35                  40                  45

Val Phe Arg Asn Met Leu Gln Ala Ile Glu Pro Ser Gly Asn Asn Tyr
    50                  55                  60

His Ile Leu His Ala Tyr Cys Gly Ile Lys Gly Leu Asp Glu Arg Phe
```

```
65                  70                  75                  80

Val Glu Glu Leu Leu His Arg Gly Tyr Ser Pro Asn Glu Thr Asp Asp
                85                  90                  95

Asp Gly Asn Tyr Pro Leu His Ile Ala Ser Lys Ile Asn Asn Asn Arg
            100                 105                 110

Ile Val Ala Met Leu Leu Thr His Gly Ala Asp Pro Asn Ala Cys Asp
        115                 120                 125

Lys His Asn Lys Thr Pro Leu Tyr Tyr Leu Ser Gly Thr Asp Asp Glu
    130                 135                 140

Val Ile Glu Arg Ile Asn Leu Leu Val Gln Tyr Gly Ala Lys Ile Asn
145                 150                 155                 160

Asn Ser Val Asp Glu Glu Gly Cys Gly Pro Leu Leu Ala Cys Thr Asp
                165                 170                 175

Pro Ser Glu Arg Val Phe Lys Lys Ile Met Ser Ile Gly Phe Glu Ala
            180                 185                 190

Arg Ile Val Asp Lys Phe Gly Lys Asn His Ile His Arg His Leu Met
        195                 200                 205

Ser Asp Asn Pro Lys Ala Ser Thr Ile Ser Trp Met Met Lys Leu Gly
    210                 215                 220

Ile Ser Pro Ser Lys Pro Asp His Asp Gly Asn Thr Pro Leu His Ile
225                 230                 235                 240

Val Cys Ser Lys Thr Val Lys Asn Val Asp Ile Ile Asp Leu Leu Leu
                245                 250                 255

Pro Ser Thr Asp Val Asn Lys Gln Asn Lys Phe Gly Asp Ser Pro Leu
            260                 265                 270
```

```
Thr Leu Leu Ile Lys Thr Leu Ser Pro Ala His Leu Ile Asn Lys Leu
        275                 280                 285

Leu Ser Thr Ser Asn Val Ile Thr Asp Gln Thr Val Asn Ile Cys Ile
    290                 295                 300

Phe Tyr Asp Arg Asp Asp Val Leu Glu Ile Ile Asn Asp Lys Gly Lys
305                 310                 315                 320

Gln Tyr Asp Ser Thr Asp Phe Lys Met Ala Val Glu Val Gly Ser Ile
                325                 330                 335

Arg Cys Val Lys Tyr Leu Leu Asp Asn Asp Ile Ile Cys Glu Asp Ala
            340                 345                 350

Met Tyr Tyr Ala Val Leu Ser Glu Tyr Glu Thr Met Val Asp Tyr Leu
        355                 360                 365

Leu Phe Asn His Phe Ser Val Asp Ser Val Val Asn Gly His Thr Cys
    370                 375                 380

Met Ser Glu Cys Val Arg Leu Asn Asn Pro Val Ile Leu Ser Lys Leu
385                 390                 395                 400

Met Leu His Asn Pro Thr Ser Glu Thr Met Tyr Leu Thr Met Lys Ala
                405                 410                 415

Ile Glu Lys Asp Lys Leu Asp Lys Ser Ile Ile Ile Pro Phe Ile Ala
            420                 425                 430

Tyr Phe Val Leu Met His Pro Asp Phe Cys Lys Asn Arg Arg Tyr Phe
        435                 440                 445

Thr Ser Tyr Lys Arg Phe Val Thr Asp Tyr Val His Glu Gly Val Ser
    450                 455                 460

Tyr Glu Val Phe Asp Asp Tyr Phe
```

465 470

<210> 22
<211> 220
<212> PRT
<213> Vaccinia virus

<400> 22
Met Val Tyr Lys Leu Val Leu Leu Phe Cys Ile Ala Ser Leu Gly Tyr
1 5 10 15

Ser Val Glu Tyr Lys Asn Thr Ile Cys Pro Pro Arg Gln Asp Tyr Arg
20 25 30

Tyr Trp Tyr Phe Ala Ala Glu Leu Thr Ile Gly Val Asn Tyr Asp Ile
35 40 45

Asn Ser Thr Ile Ile Gly Glu Cys His Met Ser Glu Ser Tyr Ile Asp
50 55 60

Arg Asn Ala Asn Ile Val Leu Thr Gly Tyr Gly Leu Glu Ile Asn Met
65 70 75 80

Thr Ile Met Asp Thr Asp Gln Arg Phe Val Ala Ala Ala Glu Gly Val
85 90 95

Gly Lys Asp Asn Lys Leu Ser Val Leu Leu Phe Thr Thr Gln Arg Leu
100 105 110

Asp Lys Val His His Asn Ile Ser Val Thr Ile Thr Cys Met Glu Met
115 120 125

Asn Cys Gly Thr Thr Lys Tyr Asp Ser Asp Leu Pro Glu Ser Ile His
130 135 140

Lys Ser Ser Ser Cys Asp Ile Thr Ile Asn Gly Ser Cys Val Thr Cys
145 150 155 160

Val Asn Leu Glu Thr Asp Pro Thr Lys Ile Asn Pro His Tyr Leu His

```
                165                 170                 175

Pro Lys Asp Lys Tyr Leu Tyr His Asn Ser Glu Tyr Gly Met Arg Gly
            180                 185                 190

Ser Tyr Gly Val Thr Phe Ile Asp Glu Leu Asn Gln Cys Leu Leu Asp
        195                 200                 205

Ile Lys Glu Leu Ser Tyr Asp Ile Cys Tyr Arg Glu
    210                 215                 220
```

<210> 23
<211> 117
<212> PRT
<213> Vaccinia virus

<400> 23

```
Met Arg Thr Leu Leu Ile Arg Tyr Ile Leu Trp Arg Asn Asp Asn Asp
1               5                   10                  15

Gln Thr Tyr Tyr Asn Asp Asp Phe Lys Lys Leu Met Leu Leu Asp Glu
            20                  25                  30

Leu Val Asp Asp Gly Asp Val Cys Thr Leu Ile Lys Asn Met Arg Met
        35                  40                  45

Thr Leu Ser Asp Gly Pro Leu Leu Asp Arg Leu Asn Gln Pro Val Asn
    50                  55                  60

Asn Ile Glu Asp Ala Lys Arg Met Ile Ala Ile Ser Ala Lys Val Ala
65                  70                  75                  80

Arg Asp Ile Gly Glu Arg Ser Glu Ile Arg Trp Glu Glu Ser Phe Thr
                85                  90                  95

Ile Leu Phe Arg Met Ile Glu Thr Tyr Phe Asp Asp Leu Met Ile Asp
            100                 105                 110

Leu Tyr Gly Glu Lys
```

115

<210> 24
<211> 224
<212> PRT
<213> Vaccinia virus

<400> 24
Met Val Lys Asn Asn Lys Ile Ser Asn Ser Cys Arg Met Ile Met Ser
1 5 10 15

Thr Asn Pro Asn Asn Ile Leu Met Arg His Leu Lys Asn Leu Thr Asp
20 25 30

Asp Glu Phe Lys Cys Ile Ile His Arg Ser Ser Asp Phe Leu Tyr Leu
35 40 45

Ser Asp Ser Asp Tyr Thr Ser Ile Thr Lys Glu Thr Leu Val Ser Glu
50 55 60

Ile Val Glu Glu Tyr Pro Asp Asp Cys Asn Lys Ile Leu Ala Ile Ile
65 70 75 80

Phe Leu Val Leu Asp Lys Asp Ile Asp Val Asp Ile Glu Thr Lys Leu
85 90 95

Lys Pro Lys Pro Ala Val Arg Phe Ala Ile Leu Asp Lys Met Thr Glu
100 105 110

Asp Ile Lys Leu Thr Asp Leu Val Arg His Tyr Phe Arg Tyr Ile Glu
115 120 125

Gln Asp Ile Pro Leu Gly Pro Leu Phe Lys Lys Ile Asp Ser Tyr Arg
130 135 140

Thr Arg Ala Ile Asn Lys Tyr Ser Lys Glu Leu Gly Leu Ala Thr Glu
145 150 155 160

Tyr Phe Asn Lys Tyr Gly His Leu Met Phe Tyr Thr Leu Pro Ile Pro

```
                165                 170                 175

Tyr Asn Arg Phe Phe Cys Arg Asn Ser Ile Gly Phe Leu Ala Val Leu
            180                 185                 190

Ser Pro Thr Ile Gly His Val Lys Ala Phe Tyr Lys Phe Ile Glu Tyr
        195                 200                 205

Val Ser Ile Asp Asp Arg Arg Lys Phe Lys Lys Glu Leu Met Ser Lys
    210                 215                 220
```

<210> 25
<211> 117
<212> PRT
<213> Vaccinia virus

<400> 25

```
Met Arg Thr Leu Leu Ile Arg Tyr Ile Leu Trp Arg Asn Asp Asn Asp
1               5                   10                  15

Gln Thr Tyr Tyr Asn Asp Asp Phe Lys Lys Leu Met Leu Leu Asp Glu
            20                  25                  30

Leu Val Asp Asp Gly Asp Val Cys Thr Leu Ile Lys Asn Met Arg Met
        35                  40                  45

Thr Leu Ser Asp Gly Pro Leu Leu Asp Arg Leu Asn Gln Pro Val Asn
    50                  55                  60

Asn Ile Glu Asp Ala Lys Arg Met Ile Ala Ile Ser Ala Lys Val Ala
65                  70                  75                  80

Arg Asp Ile Gly Glu Arg Ser Glu Ile Arg Trp Glu Glu Ser Phe Thr
                85                  90                  95

Ile Leu Phe Arg Met Ile Glu Thr Tyr Phe Asp Asp Leu Met Ile Asp
            100                 105                 110

Leu Tyr Gly Glu Lys
```

115

<210> 26
<211> 175
<212> PRT
<213> Vaccinia virus

<400> 26
Met Thr Ser Ser Ala Met Asp Asn Asn Glu Pro Lys Val Leu Glu Met
1   5   10   15

Val Tyr Asp Ala Thr Ile Leu Pro Glu Gly Ser Ser Met Asp Pro Asn
            20   25   30

Ile Met Asp Cys Ile Asn Arg His Ile Asn Met Cys Ile Gln Arg Thr
        35   40   45

Tyr Ser Ser Ser Ile Ile Ala Ile Leu Asn Arg Phe Leu Thr Met Asn
    50   55   60

Lys Asp Glu Leu Asn Asn Thr Gln Cys His Ile Ile Lys Glu Phe Met
65   70   75   80

Thr Tyr Glu Gln Met Ala Ile Asp His Tyr Gly Glu Tyr Val Asn Ala
                85   90   95

Ile Leu Tyr Gln Ile Arg Lys Arg Pro Asn Gln His His Thr Ile Asp
            100   105   110

Leu Phe Lys Lys Ile Lys Arg Thr Pro Tyr Asp Thr Phe Lys Val Asp
        115   120   125

Pro Val Glu Phe Val Lys Lys Val Ile Gly Phe Val Ser Ile Leu Asn
    130   135   140

Lys Tyr Lys Pro Val Tyr Ser Tyr Val Leu Tyr Glu Asn Val Leu Tyr
145   150   155   160

Asp Glu Phe Lys Cys Phe Ile Asn Tyr Val Glu Thr Lys Tyr Phe

```
                165                 170                 175


<210> 27
<211> 472
<212> PRT
<213> Vaccinia virus

<400> 27
Met Ile Phe Val Ile Glu Ser Lys Leu Leu Gln Ile Tyr Arg Asn Arg
1               5                   10                  15


Asn Arg Asn Ile Asn Phe Tyr Thr Thr Met Asp Asn Ile Met Ser Ala
            20                  25                  30


Glu Tyr Tyr Leu Ser Leu Tyr Ala Lys Tyr Asn Ser Lys Asn Leu Asp
        35                  40                  45


Val Phe Arg Asn Met Leu Gln Ala Ile Glu Pro Ser Gly Asn Asn Tyr
    50                  55                  60


His Ile Leu His Ala Tyr Cys Gly Ile Lys Gly Leu Asp Glu Arg Phe
65                  70                  75                  80


Val Glu Glu Leu Leu His Arg Gly Tyr Ser Pro Asn Glu Thr Asp Asp
                85                  90                  95


Asp Gly Asn Tyr Pro Leu His Ile Ala Ser Lys Ile Asn Asn Asn Arg
            100                 105                 110


Ile Val Ala Met Leu Leu Thr His Gly Ala Asp Pro Asn Ala Cys Asp
        115                 120                 125


Lys His Asn Lys Thr Pro Leu Tyr Tyr Leu Ser Gly Thr Asp Asp Glu
    130                 135                 140


Val Ile Glu Arg Ile Asn Leu Leu Val Gln Tyr Gly Ala Lys Ile Asn
145                 150                 155                 160


Asn Ser Val Asp Glu Glu Gly Cys Gly Pro Leu Leu Ala Cys Thr Asp
```

```
                165                 170                 175

Pro Ser Glu Arg Val Phe Lys Lys Ile Met Ser Ile Gly Phe Glu Ala
            180                 185                 190

Arg Ile Val Asp Lys Phe Gly Lys Asn His Ile His Arg His Leu Met
        195                 200                 205

Ser Asp Asn Pro Lys Ala Ser Thr Ile Ser Trp Met Met Lys Leu Gly
    210                 215                 220

Ile Ser Pro Ser Lys Pro Asp His Asp Gly Asn Thr Pro Leu His Ile
225                 230                 235                 240

Val Cys Ser Lys Thr Val Lys Asn Val Asp Ile Ile Asp Leu Leu Leu
                245                 250                 255

Pro Ser Thr Asp Val Asn Lys Gln Asn Lys Phe Gly Asp Ser Pro Leu
            260                 265                 270

Thr Leu Leu Ile Lys Thr Leu Ser Pro Ala His Leu Ile Asn Lys Leu
        275                 280                 285

Leu Ser Thr Ser Asn Val Ile Thr Asp Gln Thr Val Asn Ile Cys Ile
    290                 295                 300

Phe Tyr Asp Arg Asp Asp Val Leu Glu Ile Ile Asn Asp Lys Gly Lys
305                 310                 315                 320

Gln Tyr Asp Ser Thr Asp Phe Lys Met Ala Val Glu Val Gly Ser Ile
                325                 330                 335

Arg Cys Val Lys Tyr Leu Leu Asp Asn Asp Ile Ile Cys Glu Asp Ala
            340                 345                 350

Met Tyr Tyr Ala Val Leu Ser Glu Tyr Glu Thr Met Val Asp Tyr Leu
        355                 360                 365
```

```
Leu Phe Asn His Phe Ser Val Asp Ser Val Val Asn Gly His Thr Cys
    370                 375                 380

Met Ser Glu Cys Val Arg Leu Asn Asn Pro Val Ile Leu Ser Lys Leu
385                 390                 395                 400

Met Leu His Asn Pro Thr Ser Glu Thr Met Tyr Leu Thr Met Lys Ala
                405                 410                 415

Ile Glu Lys Asp Lys Leu Asp Lys Ser Ile Ile Ile Pro Phe Ile Ala
            420                 425                 430

Tyr Phe Val Leu Met His Pro Asp Phe Cys Lys Asn Arg Arg Tyr Phe
        435                 440                 445

Thr Ser Tyr Lys Arg Phe Val Thr Asp Tyr Val His Glu Gly Val Ser
    450                 455                 460

Tyr Glu Val Phe Asp Asp Tyr Phe
465                 470
```

<210> 28
<211> 220
<212> PRT
<213> Vaccinia virus

<400> 28

```
Met Val Tyr Lys Leu Val Leu Leu Phe Cys Ile Ala Ser Leu Gly Tyr
1               5                   10                  15

Ser Val Glu Tyr Lys Asn Thr Ile Cys Pro Pro Arg Gln Asp Tyr Arg
            20                  25                  30

Tyr Trp Tyr Phe Ala Ala Glu Leu Thr Ile Gly Val Asn Tyr Asp Ile
        35                  40                  45

Asn Ser Thr Ile Ile Gly Glu Cys His Met Ser Glu Ser Tyr Ile Asp
    50                  55                  60
```

```
Arg Asn Ala Asn Ile Val Leu Thr Gly Tyr Gly Leu Glu Ile Asn Met
65                  70                  75                  80


Thr Ile Met Asp Thr Asp Gln Arg Phe Val Ala Ala Ala Glu Gly Val
                85                  90                  95


Gly Lys Asp Asn Lys Leu Ser Val Leu Leu Phe Thr Thr Gln Arg Leu
            100                 105                 110


Asp Lys Val His His Asn Ile Ser Val Thr Ile Thr Cys Met Glu Met
        115                 120                 125


Asn Cys Gly Thr Thr Lys Tyr Asp Ser Asp Leu Pro Glu Ser Ile His
    130                 135                 140


Lys Ser Ser Ser Cys Asp Ile Thr Ile Asn Gly Ser Cys Val Thr Cys
145                 150                 155                 160


Val Asn Leu Glu Thr Asp Pro Thr Lys Ile Asn Pro His Tyr Leu His
                165                 170                 175


Pro Lys Asp Lys Tyr Leu Tyr His Asn Ser Glu Tyr Gly Met Arg Gly
            180                 185                 190


Ser Tyr Gly Val Thr Phe Ile Asp Glu Leu Asn Gln Cys Leu Leu Asp
        195                 200                 205


Ile Lys Glu Leu Ser Tyr Asp Ile Cys Tyr Arg Glu
    210                 215                 220


<210> 29
<211> 284
<212> PRT
<213> Vaccinia virus

<400> 29
Met Asp Leu Ser Arg Ile Asn Thr Trp Lys Ser Lys Gln Leu Lys Ser
1               5                   10                  15
```

```
Phe Leu Ser Ser Lys Asp Thr Phe Lys Ala Asp Val His Gly His Ser
            20                  25                  30

Ala Leu Tyr Tyr Ala Ile Ala Asp Asn Asn Val Arg Leu Val Cys Thr
        35                  40                  45

Leu Leu Asn Ala Gly Ala Leu Lys Asn Leu Leu Glu Asn Glu Phe Pro
    50                  55                  60

Leu His Gln Ala Ala Thr Leu Glu Asp Thr Lys Ile Val Lys Ile Leu
65                  70                  75                  80

Leu Phe Ser Gly Met Asp Asp Ser Gln Phe Asp Asp Lys Gly Asn Thr
                85                  90                  95

Ala Leu Tyr Tyr Ala Val Asp Ser Gly Asn Met Gln Thr Val Lys Leu
            100                 105                 110

Phe Val Lys Lys Asn Trp Arg Leu Met Phe Tyr Gly Lys Thr Gly Trp
        115                 120                 125

Lys Thr Ser Phe Tyr His Ala Val Met Leu Asn Asp Val Ser Ile Val
    130                 135                 140

Ser Tyr Phe Leu Ser Glu Ile Pro Ser Thr Phe Asp Leu Ala Ile Leu
145                 150                 155                 160

Leu Ser Cys Ile His Thr Thr Ile Lys Asn Gly His Val Asp Met Met
                165                 170                 175

Ile Leu Leu Leu Asp Tyr Met Thr Ser Thr Asn Thr Asn Asn Ser Leu
            180                 185                 190

Leu Phe Ile Pro Asp Ile Lys Leu Ala Ile Asp Asn Lys Asp Ile Glu
        195                 200                 205

Met Leu Gln Ala Leu Phe Lys Tyr Asp Ile Asn Ile Tyr Ser Val Asn
```

```
    210                 215                 220

Leu Glu Asn Val Leu Leu Asp Asp Ala Glu Ile Thr Lys Met Ile Ile
225                 230                 235                 240

Glu Lys His Val Glu Tyr Lys Ser Asp Ser Tyr Thr Lys Asp Leu Asp
                245                 250                 255

Ile Val Lys Asn Asn Lys Leu Asp Glu Ile Ile Ser Lys Asn Lys Glu
            260                 265                 270

Leu Arg Leu Met Tyr Val Asn Cys Val Lys Lys Asn
        275                 280
```

<210> 30
<211> 369
<212> PRT
<213> Vaccinia virus

<400> 30

```
Met Ile Ala Leu Leu Ile Leu Ser Leu Thr Cys Ser Val Ser Thr Tyr
1               5                   10                  15

Arg Leu Gln Gly Phe Thr Asn Ala Gly Ile Val Ala Tyr Lys Asn Ile
            20                  25                  30

Gln Asp Asp Asn Ile Val Phe Ser Pro Phe Gly Tyr Ser Phe Ser Met
        35                  40                  45

Phe Met Ser Leu Leu Pro Ala Ser Gly Asn Thr Arg Ile Glu Leu Leu
    50                  55                  60

Lys Thr Met Asp Leu Arg Lys Arg Asp Leu Gly Pro Ala Phe Thr Glu
65                  70                  75                  80

Leu Ile Ser Gly Leu Ala Lys Leu Lys Thr Ser Lys Tyr Thr Tyr Thr
                85                  90                  95

Asp Leu Thr Tyr Gln Ser Phe Val Asp Asn Thr Val Cys Ile Lys Pro
```

```
            100                 105                 110

Leu Tyr Tyr Gln Gln Tyr His Arg Phe Gly Leu Tyr Arg Leu Asn Phe
        115                 120                 125

Arg Arg Asp Ala Val Asn Lys Ile Asn Ser Ile Val Glu Arg Arg Ser
    130                 135                 140

Gly Met Ser Asn Val Val Asp Ser Asn Met Leu Asp Asn Asn Thr Leu
145                 150                 155                 160

Trp Ala Ile Ile Asn Thr Ile Tyr Phe Lys Gly Thr Trp Gln Tyr Pro
                165                 170                 175

Phe Asp Ile Thr Lys Thr Arg Asn Ala Ser Phe Thr Asn Lys Tyr Gly
            180                 185                 190

Thr Lys Thr Val Pro Met Met Asn Val Val Thr Lys Leu Gln Gly Asn
        195                 200                 205

Thr Ile Thr Ile Asp Asp Glu Glu Tyr Asp Met Val Arg Leu Pro Tyr
    210                 215                 220

Lys Asp Ala Asn Ile Ser Met Tyr Leu Ala Ile Gly Asp Asn Met Thr
225                 230                 235                 240

His Phe Thr Asp Ser Ile Thr Ala Ala Lys Leu Asp Tyr Trp Ser Phe
                245                 250                 255

Gln Leu Gly Asn Lys Val Tyr Asn Leu Lys Leu Pro Lys Phe Ser Ile
            260                 265                 270

Glu Asn Lys Arg Asp Ile Lys Ser Ile Ala Glu Met Met Ala Pro Ser
        275                 280                 285

Met Phe Asn Pro Asp Asn Ala Ser Phe Lys His Met Thr Arg Asp Pro
    290                 295                 300
```

```
Leu Tyr Ile Tyr Lys Met Phe Gln Asn Ala Lys Ile Asp Val Asp Glu
305                 310                 315                 320


Gln Gly Thr Val Ala Glu Ala Ser Thr Ile Met Val Ala Thr Ala Arg
                325                 330                 335


Ser Ser Pro Glu Lys Leu Glu Phe Asn Thr Pro Phe Val Phe Ile Ile
            340                 345                 350


Arg His Asp Ile Thr Gly Phe Ile Leu Phe Met Gly Lys Val Glu Ser
        355                 360                 365


Pro
```

<210> 31
<211> 81
<212> PRT
<213> Vaccinia virus

<400> 31

```
Met Gly His Ile Ile Thr Tyr Cys Gln Val His Thr Asn Ile Ser Ile
1               5                   10                  15


Leu Ile Arg Lys Ala His His Ile Ile Phe Phe Val Ile Asp Cys Asp
            20                  25                  30


Cys Ile Ser Leu Gln Phe Ser Asn Tyr Val His His Gly Asn Arg Phe
        35                  40                  45


Arg Thr Val Leu Ile Ser Lys Thr Ser Ile Ala Cys Phe Ser Asp Ile
    50                  55                  60


Lys Arg Ile Leu Pro Cys Thr Phe Lys Ile Tyr Ser Ile Asn Asp Cys
65                  70                  75                  80


Pro
```

<210> 32
<211> 79
<212> PRT
<213> Vaccinia virus

<400> 32
Met Gly Thr Val Phe Val Pro Tyr Leu Leu Val Lys Leu Ala Leu Arg
1   5   10   15

Val Leu Val Ile Ser Asn Gly Tyr Cys His Val Pro Leu Lys Tyr Ile
            20   25   30

Val Leu Met Ile Ala His Arg Val Leu Leu Ser Ser Ile Leu Glu Ser
        35   40   45

Thr Thr Leu Asp Ile Pro Asp Leu Arg Ser Thr Ile Glu Leu Ile Leu
    50   55   60

Leu Thr Ala Ser Arg Leu Lys Phe Asn Leu Tyr Arg Pro Asn Leu
65   70   75

<210> 33
<211> 88
<212> PRT
<213> Vaccinia virus

<400> 33
Met Leu Ala Phe Cys Tyr Ser Leu Pro Asn Ala Gly Asp Val Ile Lys
1   5   10   15

Gly Arg Val Tyr Glu Lys Asp Tyr Ala Leu Tyr Ile Tyr Leu Phe Asp
            20   25   30

Tyr Pro His Ser Glu Ala Ile Leu Ala Glu Ser Val Lys Met His Met
        35   40   45

Asp Arg Tyr Val Glu Tyr Arg Asp Lys Leu Val Gly Lys Thr Val Lys
    50   55   60

Val Lys Val Ile Arg Val Asp Tyr Thr Lys Gly Tyr Ile Asp Val Asn

65 70 75 80

Tyr Lys Arg Met Cys Arg His Gln
85

<210> 34
<211> 424
<212> PRT
<213> Vaccinia virus

<400> 34
Met Asn Pro Asp Asn Thr Ile Ala Val Ile Thr Glu Thr Ile Pro Ile
1 5 10 15

Gly Met Gln Phe Asp Lys Val Tyr Leu Ser Thr Phe Asn Met Trp Arg
20 25 30

Glu Ile Leu Ser Asn Thr Thr Lys Thr Leu Asp Ile Ser Ser Phe Tyr
35 40 45

Trp Ser Leu Ser Asp Glu Val Gly Thr Asn Phe Gly Thr Ile Ile Leu
50 55 60

Asn Glu Ile Val Gln Leu Pro Lys Arg Gly Val Arg Val Arg Val Ala
65 70 75 80

Val Asn Lys Ser Asn Lys Pro Leu Lys Asp Val Glu Arg Leu Gln Met
85 90 95

Ala Gly Val Glu Val Arg Tyr Ile Asp Ile Thr Asn Ile Leu Gly Gly
100 105 110

Val Leu His Thr Lys Phe Trp Ile Ser Asp Asn Thr His Ile Tyr Leu
115 120 125

Gly Ser Ala Asn Met Asp Trp Arg Ser Leu Thr Gln Val Lys Glu Leu
130 135 140

Gly Ile Ala Ile Phe Asn Asn Arg Asn Leu Ala Ala Asp Leu Thr Gln

```
145                 150                 155                 160

Ile Phe Glu Val Tyr Trp Tyr Leu Gly Val Asn Asn Leu Pro Tyr Asn
                165                 170                 175

Trp Lys Asn Phe Tyr Pro Ser Tyr Tyr Asn Thr Asp His Pro Leu Ser
            180                 185                 190

Ile Asn Val Ser Gly Val Pro His Ser Val Phe Ile Ala Ser Ala Pro
        195                 200                 205

Gln Gln Leu Cys Thr Met Glu Arg Thr Asn Asp Leu Thr Ala Leu Leu
    210                 215                 220

Ser Cys Ile Arg Asn Ala Ser Lys Phe Val Tyr Val Ser Val Met Asn
225                 230                 235                 240

Phe Ile Pro Ile Ile Tyr Ser Lys Ala Gly Lys Ile Leu Phe Trp Pro
                245                 250                 255

Tyr Ile Glu Asp Glu Leu Arg Arg Ser Ala Ile Asp Arg Gln Val Ser
            260                 265                 270

Val Lys Leu Leu Ile Ser Cys Trp Gln Arg Ser Ser Phe Ile Met Arg
        275                 280                 285

Asn Phe Leu Arg Ser Ile Ala Met Leu Lys Ser Lys Asn Ile Asp Ile
    290                 295                 300

Glu Val Lys Leu Phe Ile Val Pro Asp Ala Asp Pro Pro Ile Pro Tyr
305                 310                 315                 320

Ser Arg Val Asn His Ala Lys Tyr Met Val Thr Asp Lys Thr Ala Tyr
                325                 330                 335

Ile Gly Thr Ser Asn Trp Thr Gly Asn Tyr Phe Thr Asp Thr Cys Gly
            340                 345                 350
```

```
Ala Ser Ile Asn Ile Thr Pro Asp Asp Gly Leu Gly Leu Arg Gln Gln
        355                 360                 365

Leu Glu Asp Ile Phe Met Arg Asp Trp Asn Ser Lys Tyr Ser Tyr Glu
    370                 375                 380

Leu Tyr Asp Thr Ser Pro Thr Lys Arg Cys Lys Leu Leu Lys Asn Met
385                 390                 395                 400

Lys Gln Cys Thr Asn Asp Ile Tyr Cys Asp Glu Ile Gln Pro Glu Lys
                405                 410                 415

Glu Ile Pro Glu Tyr Ser Leu Glu
            420
```

<210> 35
<211> 135
<212> PRT
<213> Vaccinia virus

<400> 35

```
Met Gly Ala Thr Ile Ser Ile Leu Ala Ser Tyr Asp Asn Pro Asn Leu
1               5                   10                  15

Phe Thr Ala Met Ile Leu Met Ser Pro Leu Val Asn Ala Asp Ala Val
            20                  25                  30

Ser Arg Leu Asn Leu Leu Ala Ala Lys Leu Met Gly Thr Ile Thr Pro
        35                  40                  45

Asn Ala Pro Val Gly Lys Leu Cys Pro Glu Ser Val Ser Arg Asp Met
    50                  55                  60

Asp Lys Val Tyr Lys Tyr Gln Tyr Asp Pro Leu Ile Asn His Glu Lys
65                  70                  75                  80

Ile Lys Ala Gly Phe Ala Ser Gln Val Leu Lys Ala Thr Asn Lys Val
                85                  90                  95
```

Arg Lys Ile Ile Ser Lys Ile Asn Thr Pro Arg Leu Ser Tyr Ser Arg
100 105 110

Glu Gln Thr Met Arg Leu Val Met Phe Gln Val His Ile Ile Ser Cys
115 120 125

Asn Met Gln Ile Val Ile Glu
130 135

<210> 36
<211> 81
<212> PRT
<213> Vaccinia virus

<400> 36
Met Ser Ala Asn Cys Met Phe Asn Leu Asp Asn Asp Tyr Ile Tyr Trp
1 5 10 15

Lys Pro Ile Thr Tyr Pro Lys Ala Leu Val Phe Ile Ser His Gly Ala
20 25 30

Gly Lys His Ser Gly Arg Tyr Asp Glu Leu Ala Glu Asn Ile Ser Ser
35 40 45

Leu Gly Ile Leu Val Phe Ser His Asp His Ile Gly His Gly Arg Ser
50 55 60

Asn Gly Glu Lys Met Met Ile Asp Asp Phe Gly Thr Ala Arg Gly Asn
65 70 75 80

Tyr

<210> 37
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 37
Met Ala Thr Lys Leu Asp Tyr Glu Asp Ala Val Phe Tyr Phe Val Asp

1 5 10 15

Asp Asp Lys Ile Cys Ser Arg Asp Ser Ile Ile Asp Leu Ile Asp Glu
20 25 30

Tyr Ile Thr Trp Arg Asn His Val Ile Val Phe Asn Lys Asp Ile Thr
35 40 45

Ser Cys Gly Arg Leu Tyr Lys Glu Leu Met Lys Phe Asp Asp Val Ala
50 55 60

Ile Arg Tyr Tyr Gly Ile Asp Lys Ile Asn Glu Ile Val Glu Ala Met
65 70 75 80

Ser Glu Gly Asp His Tyr Ile Asn Phe Thr Lys Val His Asp Gln Glu
85 90 95

Ser Leu Phe Ala Thr Ile Gly Ile Cys Ala Lys Ile Thr Glu His Trp
100 105 110

Gly Tyr Lys Lys Ile Ser Glu Ser Arg Phe Gln Ser Leu Gly Asn Ile
115 120 125

Thr Asp Leu Met Thr Asp Asp Asn Ile Asn Ile Leu Ile Leu Phe Leu
130 135 140

Glu Lys Lys Leu Asn
145

<210> 38
<211> 226
<212> PRT
<213> Vaccinia virus

<400> 38
Met Leu Ser Met Phe Met Cys Asn Asn Ile Val Asp Tyr Val Asp Asp
1 5 10 15

Ile Asp Asn Gly Ile Val Gln Asp Ile Glu Asp Glu Ala Ser Asn Asn

```
            20                  25                  30

Val Asp His Asp Tyr Val Tyr Pro Leu Pro Glu Asn Met Val Tyr Arg
        35                  40                  45

Phe Asp Lys Ser Thr Asn Ile Leu Asp Tyr Leu Ser Thr Glu Arg Asp
    50                  55                  60

His Val Met Met Ala Val Arg Tyr Tyr Met Ser Lys Gln Arg Leu Asp
65                  70                  75                  80

Asp Leu Tyr Arg Gln Leu Pro Thr Lys Thr Arg Ser Tyr Ile Asp Ile
                85                  90                  95

Ile Asn Ile Tyr Cys Asp Lys Val Ser Asn Asp Tyr Asn Arg Asp Met
            100                 105                 110

Asn Ile Met Tyr Asp Met Ala Ser Thr Lys Ser Phe Thr Val Tyr Asp
        115                 120                 125

Ile Asn Asn Glu Val Asn Thr Ile Leu Met Asp Asn Lys Gly Leu Gly
    130                 135                 140

Val Arg Leu Ala Thr Ile Ser Phe Ile Thr Glu Leu Gly Arg Arg Cys
145                 150                 155                 160

Met Asn Pro Val Lys Thr Ile Lys Met Phe Thr Leu Leu Ser His Thr
                165                 170                 175

Ile Cys Asp Asp Cys Phe Val Asp Tyr Ile Thr Asp Ile Ser Pro Pro
            180                 185                 190

Asp Asn Thr Ile Pro Asn Thr Ser Thr Arg Glu Tyr Leu Lys Leu Ile
        195                 200                 205

Gly Ile Thr Ala Ile Met Phe Ala Thr Tyr Lys Thr Leu Lys Tyr Met
    210                 215                 220
```

Ile Gly
225

<210> 39
<211> 147
<212> PRT
<213> Vaccinia virus

<400> 39
Met Phe Asn Met Asn Ile Asn Ser Pro Val Arg Phe Val Lys Glu Thr
1 5 10 15

Asn Arg Ala Lys Ser Pro Thr Arg Gln Ser Pro Gly Ala Ala Gly Tyr
20 25 30

Asp Leu Tyr Ser Ala Tyr Asp Tyr Thr Ile Pro Pro Gly Glu Arg Gln
35 40 45

Leu Ile Lys Thr Asp Ile Ser Met Ser Met Pro Lys Ile Cys Tyr Gly
50 55 60

Arg Ile Ala Pro Arg Ser Gly Leu Ser Leu Lys Gly Ile Asp Ile Gly
65 70 75 80

Gly Gly Val Ile Asp Glu Asp Tyr Arg Gly Asn Ile Gly Val Ile Leu
85 90 95

Ile Asn Asn Gly Lys Cys Thr Phe Asn Val Asn Thr Gly Asp Arg Ile
100 105 110

Ala Gln Leu Ile Tyr Gln Arg Ile Tyr Tyr Pro Glu Leu Glu Glu Val
115 120 125

Gln Ser Leu Asp Ser Thr Asn Arg Gly Asp Gln Gly Phe Gly Ser Thr
130 135 140

Gly Leu Arg
145

<210> 40
<211> 480
<212> PRT
<213> Vaccinia virus

<400> 40
Met Pro Ile Phe Val Asn Thr Val Tyr Cys Lys Asn Ile Leu Ala Leu
1   5   10   15

Ser Met Thr Lys Lys Phe Lys Thr Ile Ile Asp Ala Ile Gly Gly Asn
            20   25   30

Ile Ile Val Asn Ser Thr Ile Leu Lys Lys Leu Ser Pro Tyr Phe Arg
        35   40   45

Thr His Leu Arg Gln Lys Tyr Thr Lys Asn Lys Asp Pro Val Thr Arg
    50   55   60

Val Cys Leu Asp Leu Asp Ile His Ser Leu Thr Ser Ile Val Ile Tyr
65   70   75   80

Ser Tyr Thr Gly Lys Val Tyr Ile Asp Ser His Asn Val Val Asn Leu
                85   90   95

Leu Arg Ala Ser Ile Leu Thr Ser Val Glu Phe Ile Ile Tyr Thr Cys
            100   105   110

Ile Asn Phe Ile Leu Arg Asp Phe Arg Lys Glu Tyr Cys Val Glu Cys
        115   120   125

Tyr Met Met Gly Ile Glu Tyr Gly Leu Ser Asn Leu Leu Cys His Thr
    130   135   140

Lys Asn Phe Ile Ala Lys His Phe Leu Glu Leu Glu Asp Asp Ile Ile
145   150   155   160

Asp Asn Phe Asp Tyr Leu Ser Met Lys Leu Ile Leu Glu Ser Asp Glu
                165   170   175

```
Leu Asn Val Pro Asp Glu Asp Tyr Val Val Asp Phe Val Ile Lys Trp
            180                 185                 190

Tyr Ile Lys Arg Arg Asn Lys Leu Gly Asn Leu Leu Leu Leu Ile Lys
        195                 200                 205

Asn Val Ile Arg Ser Asn Tyr Leu Ser Pro Arg Gly Ile Asn Asn Val
    210                 215                 220

Lys Trp Ile Leu Asp Cys Thr Lys Ile Phe His Cys Asp Lys Gln Pro
225                 230                 235                 240

Arg Lys Ser Tyr Lys Tyr Pro Phe Ile Glu Tyr Pro Met Asn Met Asp
                245                 250                 255

Gln Ile Ile Asp Ile Phe His Met Cys Thr Ser Thr His Val Gly Glu
            260                 265                 270

Val Val Tyr Leu Ile Gly Gly Trp Met Asn Asn Glu Ile His Asn Asn
        275                 280                 285

Ala Ile Ala Val Asn Tyr Ile Ser Asn Asn Trp Ile Pro Ile Pro Pro
    290                 295                 300

Met Asn Ser Pro Arg Leu Tyr Ala Thr Gly Ile Pro Ala Asn Asn Lys
305                 310                 315                 320

Leu Tyr Val Val Gly Gly Leu Pro Asn Pro Thr Ser Val Glu Arg Trp
                325                 330                 335

Phe His Gly Asp Ala Ala Trp Val Asn Met Pro Ser Leu Leu Lys Pro
            340                 345                 350

Arg Cys Asn Pro Ala Val Ala Ser Ile Asn Asn Val Ile Tyr Val Met
        355                 360                 365

Gly Gly His Ser Glu Thr Asp Thr Thr Thr Glu Tyr Leu Leu Pro Asn
```

```
    370                 375                 380

His Asp Gln Trp Gln Phe Gly Pro Ser Thr Tyr Tyr Pro His Tyr Lys
385                 390                 395                 400

Ser Cys Ala Leu Val Phe Gly Arg Arg Leu Phe Leu Val Gly Arg Asn
                405                 410                 415

Ala Glu Phe Tyr Cys Glu Ser Ser Asn Thr Trp Thr Leu Ile Asp Asp
            420                 425                 430

Pro Ile Tyr Pro Arg Asp Asn Pro Glu Leu Ile Ile Val Asp Asn Lys
        435                 440                 445

Leu Leu Leu Ile Gly Gly Phe Tyr Arg Gly Ser Tyr Ile Asp Thr Ile
    450                 455                 460

Glu Val Tyr Asn His His Thr Tyr Ser Trp Asn Ile Trp Asp Gly Lys
465                 470                 475                 480
```

<210> 41
<211> 512
<212> PRT
<213> Vaccinia virus

<400> 41

```
Met Glu Ser Val Ile Phe Ser Ile Asn Gly Glu Ile Ile Gln Val Asn
1               5                   10                  15

Lys Glu Ile Ile Thr Ala Ser Pro Tyr Asn Phe Phe Lys Arg Ile Gln
            20                  25                  30

Asp His His Leu Lys Asp Glu Ala Ile Ile Leu Asn Gly Ile Asn Tyr
        35                  40                  45

His Ala Phe Glu Ser Leu Leu Asp Tyr Ile Arg Trp Lys Lys Ile Asn
    50                  55                  60

Ile Thr Ile Asn Asn Val Glu Met Ile Leu Val Ala Ala Ile Ile Ile
```

```
65                  70                  75                  80

Asp Val Pro Pro Val Val Asp Leu Cys Val Lys Thr Met Ile His Asn
                85                  90                  95

Ile Asn Ser Thr Asn Cys Ile Arg Met Phe Asn Phe Ser Lys Arg Tyr
            100                 105                 110

Gly Ile Lys Lys Leu Tyr Asn Ala Ser Met Ser Glu Ile Ile Asn Asn
        115                 120                 125

Ile Thr Ala Val Thr Ser Asp Pro Glu Phe Gly Lys Leu Ser Lys Asp
    130                 135                 140

Glu Leu Thr Thr Ile Leu Ser His Glu Asn Val Asn Val Asn His Glu
145                 150                 155                 160

Asp Val Thr Ala Met Ile Leu Leu Lys Trp Ile His Lys Asn Pro Asn
                165                 170                 175

Asp Val Asp Ile Ile Asn Ile Leu His Pro Lys Phe Met Thr Asn Thr
            180                 185                 190

Met Arg Asn Ala Ile Ser Leu Leu Gly Leu Thr Ile Ser Lys Ser Thr
        195                 200                 205

Lys Pro Val Thr Arg Asn Gly Ile Lys His Asn Ile Val Val Ile Lys
    210                 215                 220

Asn Ser Asp Tyr Ile Ser Thr Ile Thr His Tyr Ser Pro Arg Thr Glu
225                 230                 235                 240

Tyr Trp Thr Ile Val Gly Asn Thr Asp Arg Gln Phe Tyr Asn Ala Asn
                245                 250                 255

Val Leu His Asn Cys Leu Tyr Ile Ile Gly Gly Met Ile Asn Asn Arg
            260                 265                 270
```

```
His Val Tyr Ser Val Ser Arg Val Asp Leu Glu Thr Lys Lys Trp Lys
        275                 280                 285

Thr Val Thr Asn Met Ser Ser Leu Lys Ser Glu Val Ser Thr Cys Val
    290                 295                 300

Asn Asp Gly Lys Leu Tyr Val Ile Gly Gly Leu Glu Phe Ser Ile Ser
305                 310                 315                 320

Thr Gly Val Ala Glu Tyr Leu Lys His Gly Thr Ser Lys Trp Ile Arg
                325                 330                 335

Leu Pro Asn Leu Ile Thr Pro Arg Tyr Ser Gly Ala Ser Val Phe Val
            340                 345                 350

Asn Asp Asp Ile Tyr Val Met Gly Gly Val Tyr Thr Thr Tyr Glu Lys
        355                 360                 365

Tyr Val Val Leu Asn Asp Val Glu Cys Phe Thr Lys Asn Arg Trp Ile
    370                 375                 380

Lys Lys Ser Pro Met Pro Arg His His Ser Ile Val Tyr Ala Val Glu
385                 390                 395                 400

Tyr Asp Gly Asp Ile Tyr Val Ile Thr Gly Ile Thr His Glu Thr Arg
                405                 410                 415

Asn Tyr Leu Tyr Lys Tyr Ile Val Lys Glu Asp Lys Trp Ile Glu Leu
            420                 425                 430

Tyr Met Tyr Phe Asn His Val Gly Lys Met Phe Val Cys Ser Cys Gly
        435                 440                 445

Asp Tyr Ile Leu Ile Ile Ala Asp Ala Lys Tyr Glu Tyr Tyr Pro Lys
    450                 455                 460

Ser Asn Thr Trp Asn Leu Phe Asp Met Ser Thr Arg Asn Ile Glu Tyr
```

```
465                 470                 475                 480

Tyr Asp Met Phe Thr Lys Asp Glu Thr Pro Lys Cys Asn Val Thr His
                485                 490                 495

Lys Ser Leu Pro Ser Phe Leu Ser Asn Cys Glu Lys Gln Phe Leu Gln
            500                 505                 510


<210> 42
<211> 229
<212> PRT
<213> Vaccinia virus

<400> 42
Met Val Lys Asn Asn Lys Ile Gln Lys Asn Lys Ile Ser Asn Ser Cys
1               5                   10                  15

Arg Met Ile Met Ser Thr Asp Pro Asn Asn Ile Leu Met Arg His Leu
            20                  25                  30

Lys Asn Leu Thr Asp Asp Glu Phe Lys Cys Ile Ile His Arg Ser Ser
        35                  40                  45

Asp Phe Leu Tyr Leu Ser Asp Ser Asp Tyr Thr Ser Ile Thr Lys Glu
    50                  55                  60

Thr Leu Val Ser Glu Ile Val Glu Glu Tyr Pro Asp Asp Cys Asn Lys
65                  70                  75                  80

Ile Leu Ala Ile Ile Phe Leu Val Leu Asp Lys Asp Ile Asp Val Asp
                85                  90                  95

Ile Lys Thr Lys Leu Lys Pro Lys Pro Ala Val Arg Phe Ala Ile Leu
            100                 105                 110

Asp Lys Met Thr Glu Asp Ile Lys Leu Thr Asp Leu Val Arg His Tyr
        115                 120                 125

Phe Arg Tyr Ile Glu Gln Asp Ile Pro Leu Gly Pro Leu Phe Lys Lys
```

```
    130                 135                 140

Ile Asp Ser Tyr Arg Thr Arg Ala Ile Asn Lys Tyr Ser Lys Glu Leu
145                 150                 155                 160

Gly Leu Ala Thr Glu Tyr Phe Asn Lys Tyr Gly His Leu Met Phe Tyr
                165                 170                 175

Thr Leu Pro Ile Pro Tyr Asn Arg Phe Phe Cys Arg Asn Ser Ile Gly
            180                 185                 190

Phe Leu Ala Val Leu Ser Pro Thr Ile Gly His Val Lys Ala Phe Tyr
        195                 200                 205

Lys Phe Ile Glu Tyr Val Ser Ile Asp Asp Arg Arg Lys Phe Lys Lys
    210                 215                 220

Glu Leu Met Ser Lys
225


<210> 43
<211> 117
<212> PRT
<213> Vaccinia virus

<400> 43
Met Arg Thr Leu Leu Ile Arg Tyr Ile Leu Trp Arg Asn Asp Asn Asp
1               5                   10                  15

Gln Thr Tyr Tyr Asn Asp Asn Phe Lys Lys Leu Met Leu Leu Asp Glu
            20                  25                  30

Leu Val Asp Asp Gly Asp Val Cys Thr Leu Ile Lys Asn Met Arg Met
        35                  40                  45

Thr Leu Ser Asp Gly Pro Leu Leu Asp Arg Leu Asn Gln Pro Val Asn
    50                  55                  60

Asn Ile Glu Asp Ala Lys Arg Met Ile Ala Ile Ser Ala Lys Val Ala
```

65 70 75 80

Arg Asp Ile Gly Glu Arg Ser Glu Ile Arg Trp Glu Glu Ser Phe Thr
85 90 95

Ile Leu Phe Arg Met Ile Glu Thr Tyr Phe Asp Asp Leu Met Ile Asp
100 105 110

Leu Tyr Gly Glu Lys
115

<210> 44
<211> 175
<212> PRT
<213> Vaccinia virus

<400> 44
Met Thr Ser Ser Ala Met Asp Asn Asn Glu Pro Lys Val Leu Glu Met
1 5 10 15

Val Tyr Asp Ala Thr Ile Leu Pro Glu Gly Ser Ser Met Asp Pro Asn
20 25 30

Ile Met Asp Cys Ile Asn Arg His Ile Asn Met Cys Ile Gln Arg Thr
35 40 45

Tyr Ser Ser Ser Ile Ile Ala Ile Leu Asp Arg Phe Leu Met Met Asn
50 55 60

Lys Asp Glu Leu Asn Asn Thr Gln Cys His Ile Ile Lys Glu Phe Met
65 70 75 80

Thr Tyr Glu Gln Met Ala Ile Asp His Tyr Gly Gly Tyr Val Asn Ala
85 90 95

Ile Leu Tyr Gln Ile Arg Lys Arg Pro Asn Gln His His Thr Ile Asp
100 105 110

Leu Phe Lys Arg Ile Lys Arg Thr Arg Tyr Asp Thr Phe Lys Val Asp

```
        115                 120                 125

Pro Val Glu Phe Val Lys Lys Val Ile Gly Phe Val Ser Ile Leu Asn
    130                 135                 140

Lys Tyr Lys Pro Val Tyr Ser Tyr Val Leu Tyr Glu Asn Val Leu Tyr
145                 150                 155                 160

Asp Glu Phe Lys Cys Phe Ile Asn Tyr Val Glu Thr Lys Tyr Phe
                165                 170                 175

<210> 45
<211> 472
<212> PRT
<213> Vaccinia virus

<400> 45
Met Ile Phe Val Ile Glu Ser Lys Leu Leu Gln Ile Tyr Arg Asn Arg
1               5                   10                  15

Asn Arg Asn Ile Asn Phe Tyr Thr Thr Met Asp Asn Ile Met Ser Ala
            20                  25                  30

Glu Tyr Tyr Leu Ser Leu Tyr Ala Lys Tyr Asn Ser Lys Asn Leu Asp
        35                  40                  45

Val Phe Arg Asn Met Leu Gln Ala Ile Glu Pro Ser Gly Asn Asn Tyr
    50                  55                  60

His Ile Leu His Ala Tyr Cys Gly Ile Lys Gly Leu Asp Glu Arg Phe
65                  70                  75                  80

Val Glu Glu Leu Leu His Arg Gly Tyr Ser Pro Asn Glu Thr Asp Asp
                85                  90                  95

Asp Gly Asn Tyr Pro Leu His Ile Ala Ser Lys Ile Asn Asn Asn Arg
            100                 105                 110

Ile Val Ala Met Leu Leu Thr His Gly Ala Asp Pro Asn Ala Cys Asp
```

```
        115                 120                 125

Lys His Asn Lys Thr Pro Leu Tyr Tyr Leu Ser Gly Thr Asp Asp Glu
    130                 135                 140

Val Ile Glu Arg Ile Asn Leu Leu Val Gln Tyr Gly Ala Lys Ile Asn
145                 150                 155                 160

Asn Ser Val Asp Glu Glu Gly Cys Gly Pro Leu Leu Ala Cys Thr Asp
                165                 170                 175

Pro Ser Glu Arg Val Phe Lys Lys Ile Met Ser Ile Gly Phe Glu Ala
            180                 185                 190

Arg Ile Val Asp Lys Phe Gly Lys Asn His Ile His Arg His Leu Met
        195                 200                 205

Ser Asp Asn Pro Lys Ala Ser Thr Ile Ser Trp Met Met Lys Leu Gly
    210                 215                 220

Ile Ser Pro Ser Lys Pro Asp His Asp Gly Asn Thr Pro Leu His Ile
225                 230                 235                 240

Val Cys Ser Lys Thr Val Lys Asn Val Asp Ile Ile Asp Leu Leu Leu
                245                 250                 255

Pro Ser Thr Asp Val Asn Lys Gln Asn Lys Phe Gly Asp Ser Pro Leu
            260                 265                 270

Thr Leu Leu Ile Lys Thr Leu Ser Pro Ala His Leu Ile Asn Lys Leu
        275                 280                 285

Leu Ser Thr Ser Asn Val Ile Thr Asp Gln Thr Val Asn Ile Cys Ile
    290                 295                 300

Phe Tyr Asp Arg Asp Asp Val Leu Glu Ile Ile Asn Asp Lys Gly Lys
305                 310                 315                 320
```

```
Gln Tyr Asp Ser Thr Asp Phe Lys Met Ala Val Glu Val Gly Ser Ile
                325                 330                 335

Arg Cys Val Lys Tyr Leu Leu Asp Asn Asp Ile Ile Cys Glu Asp Ala
            340                 345                 350

Met Tyr Tyr Ala Val Leu Ser Glu Tyr Glu Thr Met Val Asp Tyr Leu
        355                 360                 365

Leu Phe Asn His Phe Ser Val Asp Phe Val Val Asn Gly His Thr Cys
    370                 375                 380

Met Ser Glu Cys Val Arg Leu Asn Asn Pro Val Ile Leu Ser Lys Leu
385                 390                 395                 400

Met Leu His Asn Pro Thr Ser Glu Thr Met Tyr Leu Thr Met Lys Ala
                405                 410                 415

Ile Glu Lys Asp Arg Leu Asp Lys Ser Ile Ile Ile Pro Phe Ile Ala
            420                 425                 430

Tyr Phe Val Leu Met His Pro Asp Phe Cys Lys Asn Arg Arg Tyr Phe
        435                 440                 445

Thr Ser Tyr Lys Arg Phe Val Thr Asp Tyr Val His Glu Gly Val Ser
    450                 455                 460

Tyr Glu Val Phe Asp Asp Tyr Phe
465                 470
```

<210> 46
<211> 220
<212> PRT
<213> Vaccinia virus

<400> 46

```
Met Val Tyr Lys Leu Val Leu Leu Phe Cys Ile Ala Ser Leu Gly Tyr
1               5                   10                  15
```

```
Ser Val Glu Tyr Lys Asn Thr Ile Cys Pro Pro Arg Gln Asp Tyr Arg
            20                  25                  30

Tyr Trp Tyr Phe Ala Ala Glu Leu Thr Ile Gly Val Asn Tyr Asp Ile
        35                  40                  45

Asn Ser Thr Ile Ile Gly Glu Cys His Met Ser Glu Ser Tyr Ile Asp
    50                  55                  60

Arg Asn Ala Asn Ile Val Leu Thr Gly Tyr Gly Leu Glu Ile Asn Met
65                  70                  75                  80

Thr Ile Met Asp Thr Asp Gln Arg Phe Val Ala Ala Ala Glu Gly Val
                85                  90                  95

Gly Lys Asp Asn Lys Leu Ser Val Leu Leu Phe Thr Thr Gln Arg Leu
            100                 105                 110

Asp Lys Val His His Asn Ile Ser Val Thr Ile Thr Cys Met Glu Met
        115                 120                 125

Asn Cys Gly Thr Thr Lys Tyr Asp Ser Asp Leu Pro Glu Ser Ile His
    130                 135                 140

Lys Ser Ser Ser Cys Asp Ile Thr Ile Asn Gly Ser Cys Val Thr Cys
145                 150                 155                 160

Val Asn Leu Glu Thr Asp Pro Thr Lys Ile Asn Pro His Tyr Leu His
                165                 170                 175

Pro Lys Asp Lys Tyr Leu Tyr His Asn Ser Glu Tyr Ser Met Arg Gly
            180                 185                 190

Ser Tyr Gly Val Thr Phe Ile Asp Glu Leu Asn Gln Cys Leu Leu Asp
        195                 200                 205

Ile Lys Glu Leu Ser Tyr Asp Ile Cys Tyr Arg Glu
```

210 215 220

<210> 47
<211> 284
<212> PRT
<213> Vaccinia virus

<400> 47
Met Asp Leu Ser Arg Ile Asn Thr Trp Lys Ser Lys Gln Leu Lys Ser
1 5 10 15

Phe Leu Ser Ser Lys Asp Ala Phe Lys Ala Asp Val His Gly His Ser
20 25 30

Ala Leu Tyr Tyr Ala Ile Ala Asp Asn Asn Val Arg Leu Val Cys Thr
35 40 45

Leu Leu Asn Ala Gly Ala Leu Lys Asn Leu Leu Glu Asn Glu Phe Pro
50 55 60

Leu His Gln Ala Ala Thr Leu Glu Asp Thr Lys Ile Val Lys Ile Leu
65 70 75 80

Leu Phe Ser Gly Leu Asp Asp Ser Gln Phe Asp Asp Lys Gly Asn Thr
85 90 95

Ala Leu Tyr Tyr Ala Val Asp Ser Gly Asn Met Gln Thr Val Lys Leu
100 105 110

Phe Val Lys Lys Asn Trp Arg Leu Met Phe Tyr Gly Lys Thr Gly Trp
115 120 125

Lys Thr Ser Phe Tyr His Ala Val Met Leu Asn Asp Val Ser Ile Val
130 135 140

Ser Tyr Phe Leu Ser Glu Ile Pro Ser Thr Phe Asp Leu Ala Ile Leu
145 150 155 160

Leu Ser Cys Ile His Ile Thr Ile Lys Asn Gly His Val Asp Met Met

```
                165                 170                 175

Ile Leu Leu Leu Asp Tyr Met Thr Ser Thr Asn Thr Asn Asn Ser Leu
            180                 185                 190

Leu Phe Ile Pro Asp Ile Lys Leu Ala Ile Asp Asn Lys Asp Ile Glu
        195                 200                 205

Met Leu Gln Ala Leu Phe Lys Tyr Asp Ile Asn Ile Tyr Ser Ala Asn
    210                 215                 220

Leu Glu Asn Val Leu Leu Asp Asp Ala Glu Ile Ala Lys Met Ile Ile
225                 230                 235                 240

Glu Lys His Val Glu Tyr Lys Ser Asp Ser Tyr Thr Lys Asp Leu Asp
                245                 250                 255

Ile Val Lys Asn Asn Lys Leu Asp Glu Ile Ile Ser Lys Asn Lys Glu
            260                 265                 270

Leu Arg Leu Met Tyr Val Asn Cys Val Lys Lys Asn
        275                 280
```

<210> 48
<211> 369
<212> PRT
<213> Vaccinia virus

<400> 48

```
Met Ile Ala Leu Leu Ile Leu Ser Leu Thr Cys Ser Val Ser Thr Tyr
1               5                   10                  15

Arg Leu Gln Gly Phe Thr Asn Ala Gly Ile Val Ala Tyr Lys Asn Ile
            20                  25                  30

Gln Asp Asp Asn Ile Val Phe Ser Pro Phe Gly Tyr Ser Phe Ser Met
        35                  40                  45

Phe Met Ser Leu Leu Pro Ala Ser Gly Asn Thr Arg Ile Glu Leu Leu
```

```
    50                  55                  60

Lys Thr Met Asp Leu Arg Lys Arg Asp Leu Gly Pro Ala Phe Thr Glu
65                  70                  75                  80

Leu Ile Ser Gly Leu Ala Lys Leu Lys Thr Ser Lys Tyr Thr Tyr Thr
                85                  90                  95

Asp Leu Thr Tyr Gln Ser Phe Val Asp Asn Thr Val Cys Ile Lys Pro
            100                 105                 110

Ser Tyr Tyr Gln Gln Tyr His Arg Phe Gly Leu Tyr Arg Leu Asn Phe
        115                 120                 125

Arg Arg Asp Ala Val Asn Lys Ile Asn Ser Ile Val Glu Arg Arg Ser
    130                 135                 140

Gly Met Ser Asn Val Val Asp Ser Asn Met Leu Asp Asn Asn Thr Leu
145                 150                 155                 160

Trp Ala Ile Ile Asn Thr Ile Tyr Phe Lys Gly Ile Trp Gln Tyr Pro
                165                 170                 175

Phe Asp Ile Thr Lys Thr Arg Asn Ala Ser Phe Thr Asn Lys Tyr Gly
            180                 185                 190

Thr Lys Thr Val Pro Met Met Asn Val Val Thr Lys Leu Gln Gly Asn
        195                 200                 205

Thr Ile Thr Ile Asp Asp Glu Glu Tyr Asp Met Val Arg Leu Pro Tyr
    210                 215                 220

Lys Asp Ala Asn Ile Ser Met Tyr Leu Ala Ile Gly Asp Asn Met Thr
225                 230                 235                 240

His Phe Thr Asp Ser Ile Thr Ala Ala Lys Leu Asp Tyr Trp Ser Phe
                245                 250                 255
```

```
Gln Leu Gly Asn Lys Val Tyr Asn Leu Lys Leu Pro Lys Phe Ser Ile
            260                 265                 270

Glu Asn Lys Arg Asp Ile Lys Ser Ile Ala Glu Met Met Ala Pro Ser
        275                 280                 285

Met Phe Asn Pro Asp Asn Ala Ser Phe Lys His Met Thr Arg Asp Pro
    290                 295                 300

Leu Tyr Ile Tyr Lys Met Phe Gln Asn Ala Lys Ile Asp Val Asp Glu
305                 310                 315                 320

Gln Gly Thr Val Ala Glu Ala Ser Thr Ile Met Val Ala Thr Ala Arg
                325                 330                 335

Ser Ser Pro Glu Lys Leu Glu Phe Asn Thr Pro Phe Val Phe Ile Ile
            340                 345                 350

Arg His Asp Ile Thr Gly Phe Ile Leu Phe Met Gly Lys Val Glu Ser
        355                 360                 365

Pro
```

<210> 49
<211> 88
<212> PRT
<213> Vaccinia virus

<400> 49

```
Met Leu Ala Phe Cys Tyr Ser Leu Pro Asn Ala Gly Asp Val Ile Lys
1               5                   10                  15

Gly Arg Val Tyr Glu Lys Asp Tyr Ala Leu Tyr Ile Tyr Leu Phe Asp
            20                  25                  30

Tyr Pro His Phe Glu Ala Ile Leu Ala Glu Ser Val Lys Met His Met
        35                  40                  45
```

```
Asp Arg Tyr Val Glu Tyr Arg Asp Lys Leu Val Gly Lys Thr Val Lys
    50                  55                  60

Val Lys Val Ile Arg Val Asp Tyr Thr Lys Gly Tyr Ile Asp Val Asn
65                  70                  75                  80

Tyr Lys Arg Met Cys Arg His Gln
                85
```

<210> 50
<211> 424
<212> PRT
<213> Vaccinia virus

<400> 50

```
Met Asn Pro Asp Asn Thr Ile Ala Val Ile Thr Glu Thr Ile Pro Ile
1               5                   10                  15

Gly Met Gln Phe Asp Lys Val Tyr Leu Ser Thr Phe Asn Met Trp Arg
            20                  25                  30

Glu Ile Leu Ser Asn Thr Thr Lys Thr Leu Asp Ile Ser Ser Phe Tyr
        35                  40                  45

Trp Ser Leu Ser Asp Glu Val Gly Thr Asn Phe Gly Thr Ile Ile Leu
    50                  55                  60

Asn Lys Ile Val Gln Leu Pro Lys Arg Gly Val Arg Val Arg Val Ala
65                  70                  75                  80

Val Asn Lys Ser Asn Lys Pro Leu Lys Asp Val Glu Arg Leu Gln Met
                85                  90                  95

Ala Gly Val Glu Val Arg Tyr Ile Asp Ile Thr Asn Ile Leu Gly Gly
            100                 105                 110

Val Leu His Thr Lys Phe Trp Ile Ser Asp Asn Thr His Ile Tyr Leu
        115                 120                 125
```

```
Gly Ser Ala Asn Met Asp Trp Arg Ser Leu Thr Gln Val Lys Glu Leu
    130                 135                 140

Gly Ile Ala Ile Phe Asn Asn Arg Asn Leu Ala Ala Asp Leu Thr Gln
145                 150                 155                 160

Ile Phe Glu Val Tyr Trp Tyr Leu Gly Val Asn Asn Leu Pro Tyr Asn
                165                 170                 175

Trp Lys Asn Phe Tyr Pro Ser Tyr Tyr Asn Thr Asp His Pro Leu Ser
            180                 185                 190

Ile Asn Val Ser Gly Val Pro His Ser Val Phe Ile Ala Ser Ala Pro
        195                 200                 205

Gln Gln Leu Cys Thr Met Glu Arg Thr Asn Asp Leu Thr Ala Leu Leu
    210                 215                 220

Ser Cys Ile Arg Asn Ala Ser Lys Phe Val Tyr Val Ser Val Met Asn
225                 230                 235                 240

Phe Ile Pro Ile Ile Tyr Ser Lys Ala Gly Asn Ile Leu Phe Trp Pro
                245                 250                 255

Tyr Ile Glu Asp Glu Leu Arg Arg Ala Ala Ile Asp Arg Gln Val Ser
            260                 265                 270

Val Lys Leu Leu Ile Ser Cys Trp Gln Arg Ser Ser Phe Ile Met Arg
        275                 280                 285

Asn Phe Leu Arg Ser Ile Ala Met Leu Lys Ser Lys Asn Ile Asn Ile
    290                 295                 300

Glu Val Lys Leu Phe Ile Val Pro Asp Ala Asp Pro Pro Ile Pro Tyr
305                 310                 315                 320

Ser Arg Val Asn His Ala Lys Tyr Met Val Thr Asp Lys Thr Ala Tyr
```

```
                325                 330                 335

Ile Gly Thr Ser Asn Trp Thr Gly Asn Tyr Phe Thr Asp Thr Cys Gly
            340                 345                 350

Ala Ser Ile Asn Ile Thr Pro Asp Asp Gly Leu Gly Leu Arg Gln Gln
        355                 360                 365

Leu Glu Asp Ile Phe Met Arg Asp Trp Asn Ser Lys Tyr Ser Tyr Glu
    370                 375                 380

Leu Tyr Asp Thr Ser Pro Thr Lys Arg Cys Arg Leu Leu Lys Asn Met
385                 390                 395                 400

Lys Gln Cys Thr Asn Asp Ile Tyr Cys Asp Glu Ile Gln Pro Glu Lys
                405                 410                 415

Glu Ile Pro Glu Tyr Ser Leu Glu
            420


<210> 51
<211> 44
<212> PRT
<213> Vaccinia virus

<400> 51
Met Gln His Ala Asn Cys Asn Arg Glu Ile Lys Ile Tyr Glu Gly Ala
1               5                   10                  15

Lys His His Leu His Lys Glu Thr Asp Glu Val Lys Lys Ser Val Met
            20                  25                  30

Lys Glu Ile Glu Thr Trp Ile Phe Asn Arg Val Lys
        35                  40


<210> 52
<211> 134
<212> PRT
<213> Vaccinia virus
```

<400> 52
Met Thr Leu Val Gln His Val Val Thr Ile Lys Ser Thr Tyr Trp Val
1   5   10   15

Ile Pro Trp Glu Leu Ala Ser Tyr Asp Asn Pro Asn Leu Phe Thr Ala
            20   25   30

Met Ile Leu Met Ser Pro Leu Val Asn Ala Asp Ala Val Ser Lys Leu
        35   40   45

Asn Leu Leu Ala Ala Lys Leu Met Gly Thr Ile Thr Leu Asn Ala Pro
    50   55   60

Val Gly Lys Leu Cys Pro Glu Ser Val Ser Arg Asp Met Asp Lys Val
65   70   75   80

Tyr Lys Tyr Gln Tyr Asp Pro Leu Ile Asn His Glu Lys Ile Lys Ala
                85   90   95

Gly Phe Ala Ser Gln Val Leu Lys Ala Thr Asn Lys Val Arg Lys Ile
            100   105   110

Ile Ser Lys Ile Asn Thr Pro Arg Leu Ser Tyr Ser Arg Glu Gln Thr
        115   120   125

Ile Arg Leu Ala Met Phe
    130

<210> 53
<211> 81
<212> PRT
<213> Vaccinia virus

<400> 53
Met Ser Ala Asn Cys Met Phe Asn Leu Asp Asn Asp Tyr Ile Tyr Trp
1   5   10   15

Lys Pro Ile Thr Tyr Pro Lys Ala Leu Val Phe Ile Ser His Gly Ala
            20   25   30

```
Gly Lys His Ser Gly Arg Tyr Asp Glu Leu Ala Glu Asn Ile Ser Ser
        35                  40                  45

Leu Gly Ile Leu Val Phe Ser His Asp His Ile Gly His Gly Arg Ser
    50                  55                  60

Asn Gly Glu Lys Met Met Ile Asp Asp Phe Gly Thr Ala Arg Gly Asn
65                  70                  75                  80

Tyr
```

<210> 54
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 54

```
Met Ala Thr Lys Leu Asp Tyr Glu Asp Ala Val Phe Tyr Phe Val Asp
1               5                   10                  15

Asp Asp Lys Ile Cys Ser Arg Asp Ser Ile Ile Asp Leu Ile Asp Glu
            20                  25                  30

Tyr Ile Thr Trp Arg Asn His Val Ile Val Phe Asn Lys Asp Ile Thr
        35                  40                  45

Ser Cys Gly Arg Leu Tyr Lys Glu Leu Met Lys Phe Asp Asp Val Ala
    50                  55                  60

Ile Arg Tyr Tyr Gly Ile Asp Lys Ile Asn Glu Ile Val Glu Ala Met
65                  70                  75                  80

Ser Glu Gly Asp His Tyr Ile Asn Phe Thr Lys Val His Asp Gln Glu
                85                  90                  95

Ser Leu Phe Ala Thr Ile Gly Ile Cys Ala Lys Ile Thr Glu His Trp
            100                 105                 110
```

Gly Tyr Lys Lys Ile Ser Glu Ser Arg Phe Gln Ser Leu Gly Asn Ile
        115   120   125

Thr Asp Leu Met Thr Asp Asp Asn Ile Asn Ile Leu Ile Leu Phe Leu
    130   135   140

Glu Lys Lys Leu Asn
145

<210> 55
<211> 226
<212> PRT
<213> Vaccinia virus

<400> 55
Met Leu Ser Met Phe Met Cys Asn Asn Ile Val Asp Tyr Val Asp Asp
1   5   10   15

Ile Asp Asn Gly Ile Val Gln Asp Ile Glu Asp Glu Ala Ser Asn Asn
            20   25   30

Val Asp His Asp Tyr Val Tyr Pro Leu Pro Glu Asn Met Val Tyr Arg
        35   40   45

Phe Asp Lys Ser Thr Asn Ile Leu Asp Tyr Leu Ser Thr Glu Arg Asp
    50   55   60

His Val Met Met Ala Val Arg Tyr Tyr Met Ser Lys Gln Arg Leu Asp
65   70   75   80

Asp Leu Tyr Arg Gln Leu Pro Thr Lys Thr Arg Ser Tyr Ile Asp Ile
                85   90   95

Ile Asn Ile Tyr Cys Asp Lys Val Ser Asn Asp Tyr Asn Arg Asp Met
            100   105   110

Asn Ile Met Tyr Asp Met Ala Ser Thr Lys Ser Phe Thr Val Tyr Asp
        115   120   125

```
Ile Asn Asn Glu Val Asn Thr Ile Leu Met Asp Asn Lys Gly Leu Gly
    130                 135                 140

Val Arg Leu Ala Thr Ile Ser Phe Ile Thr Glu Leu Gly Arg Arg Cys
145                 150                 155                 160

Met Asn Pro Val Glu Thr Ile Lys Met Phe Thr Leu Leu Ser His Thr
                165                 170                 175

Ile Cys Asp Asp Tyr Phe Val Asp Tyr Ile Thr Asp Ile Ser Pro Pro
            180                 185                 190

Asp Asn Thr Ile Pro Asn Thr Ser Thr Arg Glu Tyr Leu Lys Leu Ile
        195                 200                 205

Gly Ile Thr Ala Ile Met Phe Ala Thr Tyr Lys Thr Leu Lys Tyr Met
    210                 215                 220

Ile Gly
225
```

<210> 56
<211> 147
<212> PRT
<213> Vaccinia virus

<400> 56

```
Met Phe Asn Met Asn Ile Asn Ser Pro Val Arg Phe Val Lys Glu Thr
1               5                   10                  15

Asn Arg Ala Lys Ser Pro Thr Arg Gln Ser Pro Tyr Ala Ala Gly Tyr
            20                  25                  30

Asp Leu Tyr Ser Ala Tyr Asp Tyr Thr Ile Pro Pro Gly Glu Arg Gln
        35                  40                  45

Leu Ile Lys Thr Asp Ile Ser Met Ser Met Pro Lys Phe Cys Tyr Gly
    50                  55                  60
```

```
Arg Ile Ala Pro Arg Ser Gly Leu Ser Leu Lys Gly Ile Asp Ile Gly
65                  70                  75                  80


Gly Gly Val Ile Asp Glu Asp Tyr Arg Gly Asn Ile Gly Val Ile Leu
                85                  90                  95


Ile Asn Asn Gly Lys Cys Thr Phe Asn Val Asn Thr Gly Asp Arg Ile
            100                 105                 110


Ala Gln Leu Ile Tyr Gln Arg Ile Tyr Tyr Pro Glu Leu Glu Glu Val
        115                 120                 125


Gln Ser Leu Asp Ser Thr Asn Arg Gly Asp Gln Gly Phe Gly Ser Thr
    130                 135                 140


Gly Leu Arg
145


<210> 57
<211> 480
<212> PRT
<213> Vaccinia virus

<400> 57
Met Pro Ile Phe Val Asn Thr Val Tyr Cys Lys Asn Ile Leu Ala Leu
1               5                   10                  15


Ser Met Thr Lys Lys Phe Lys Thr Ile Ile Asp Ala Ile Gly Gly Asn
            20                  25                  30


Ile Ile Val Asn Ser Thr Ile Leu Lys Lys Leu Ser Pro Tyr Phe Arg
        35                  40                  45


Thr His Leu Arg Gln Lys Tyr Thr Lys Asn Lys Asp Pro Val Thr Trp
    50                  55                  60


Val Cys Leu Asp Leu Asp Ile His Ser Leu Thr Ser Ile Val Ile Tyr
65                  70                  75                  80
```

```
Ser Tyr Thr Gly Lys Val Tyr Ile Asp Ser His Asn Val Val Asn Leu
                85                  90                  95

Leu Arg Ala Ser Ile Leu Thr Ser Val Glu Phe Ile Ile Tyr Thr Cys
            100                 105                 110

Ile Asn Phe Ile Leu Arg Asp Phe Arg Lys Glu Tyr Cys Val Glu Cys
        115                 120                 125

Tyr Met Met Gly Ile Glu Tyr Gly Leu Ser Asn Leu Leu Cys His Thr
    130                 135                 140

Lys Asn Phe Ile Ala Lys His Phe Leu Glu Leu Glu Asp Asp Ile Ile
145                 150                 155                 160

Asp Asn Phe Asp Tyr Leu Ser Met Lys Leu Ile Leu Glu Ser Asp Glu
                165                 170                 175

Leu Asn Val Pro Asp Glu Asp Tyr Val Val Asp Phe Val Ile Lys Trp
            180                 185                 190

Tyr Ile Lys Arg Arg Asn Lys Leu Gly Asn Leu Leu Leu Leu Ile Lys
        195                 200                 205

Asn Val Ile Arg Ser Asn Tyr Leu Ser Pro Arg Gly Ile Asn Asn Val
    210                 215                 220

Lys Trp Ile Leu Asp Cys Thr Lys Ile Phe His Cys Asp Lys Gln Pro
225                 230                 235                 240

Arg Lys Ser Tyr Lys Tyr Pro Phe Ile Glu Tyr Pro Met Asn Met Asp
                245                 250                 255

Gln Ile Ile Asp Ile Phe His Met Cys Thr Ser Thr His Val Gly Glu
            260                 265                 270

Val Val Tyr Leu Ile Gly Gly Trp Met Asn Asn Glu Ile His Asn Asn
```

```
        275                 280                 285

Ala Ile Ala Val Asn Tyr Ile Ser Asn Asn Trp Ile Pro Ile Pro Pro
    290                 295                 300

Met Asn Ser Pro Arg Leu Tyr Ala Ser Gly Ile Pro Ala Asn Asn Lys
305                 310                 315                 320

Leu Tyr Val Val Gly Gly Leu Pro Asn Pro Thr Ser Val Glu Arg Trp
                325                 330                 335

Phe His Gly Asp Ala Ala Trp Val Asn Met Pro Ser Leu Leu Lys Pro
            340                 345                 350

Arg Cys Asn Pro Ala Val Ala Ser Ile Asn Asn Val Ile Tyr Val Met
        355                 360                 365

Gly Gly His Ser Glu Thr Asp Thr Thr Thr Glu Tyr Leu Leu Pro Asn
    370                 375                 380

His Asp Gln Trp Gln Phe Gly Pro Ser Thr Tyr Tyr Pro His Tyr Lys
385                 390                 395                 400

Ser Cys Ala Leu Val Phe Gly Arg Arg Leu Phe Leu Val Gly Arg Asn
                405                 410                 415

Ala Glu Phe Tyr Cys Glu Ser Ser Asn Thr Trp Thr Leu Ile Asp Asp
            420                 425                 430

Pro Ile Tyr Pro Arg Asp Asn Pro Glu Leu Ile Ile Val Asp Asn Lys
        435                 440                 445

Leu Leu Leu Ile Gly Gly Phe Tyr Arg Glu Ser Tyr Ile Asp Thr Ile
    450                 455                 460

Glu Val Tyr Asn His His Thr Tyr Ser Trp Asn Ile Trp Asp Gly Lys
465                 470                 475                 480
```

<210> 58
<211> 512
<212> PRT
<213> Vaccinia virus

<400> 58
Met Glu Ser Val Ile Phe Ser Ile Asn Gly Glu Ile Ile Gln Val Asn
1   5   10   15

Lys Glu Ile Ile Thr Ala Ser Pro Tyr Asn Phe Phe Lys Arg Ile Gln
            20   25   30

Asp His His Leu Lys Asp Glu Ala Ile Ile Leu Asn Gly Ile Asn Tyr
        35   40   45

His Ala Phe Glu Ser Leu Leu Asp Tyr Ile Arg Trp Lys Lys Ile Asn
    50   55   60

Ile Thr Ile Asn Asn Val Glu Met Ile Leu Val Ala Ala Ile Ile Ile
65   70   75   80

Asp Val Pro Pro Val Val Asp Leu Cys Val Lys Thr Met Ile His Asn
                85   90   95

Ile Asn Ser Thr Asn Cys Ile Arg Met Phe Asn Phe Ser Lys Gln Tyr
            100   105   110

Gly Ile Lys Lys Leu Tyr Asn Ala Ser Met Ser Glu Ile Ile Asn Asn
        115   120   125

Ile Thr Ala Val Thr Ser Asp Pro Glu Phe Gly Lys Leu Ser Lys Asp
    130   135   140

Glu Leu Thr Thr Ile Leu Ser His Glu Asp Val Asn Val Asn His Glu
145   150   155   160

Asp Val Thr Ala Met Ile Leu Leu Lys Trp Ile His Lys Asn Pro Asn
                165   170   175

```
Asp Val Asp Ile Ile Asn Ile Leu His Pro Lys Phe Met Thr Asn Thr
            180                 185                 190

Met Arg Asn Ala Ile Ser Leu Leu Gly Leu Thr Ile Ser Lys Ser Thr
        195                 200                 205

Lys Pro Val Thr Arg Asn Gly Ile Lys His Asn Ile Val Val Ile Lys
    210                 215                 220

Asn Ser Asp Tyr Ile Ser Thr Ile Thr His Tyr Ser Pro Arg Thr Glu
225                 230                 235                 240

Tyr Trp Thr Ile Val Gly Asn Thr Asp Arg Gln Phe Tyr Asn Ala Asn
                245                 250                 255

Val Leu His Asn Cys Leu Tyr Ile Ile Gly Gly Met Ile Asn Asn Arg
            260                 265                 270

His Val Tyr Ser Val Ser Arg Val Asp Leu Glu Thr Lys Lys Trp Lys
        275                 280                 285

Thr Val Thr Asn Met Ser Ser Leu Lys Ser Glu Val Ser Thr Cys Val
    290                 295                 300

Asn Asn Gly Lys Leu Tyr Val Ile Gly Gly Leu Glu Phe Ser Ile Ser
305                 310                 315                 320

Thr Gly Val Ala Glu Tyr Leu Lys His Gly Thr Ser Lys Trp Ile Arg
                325                 330                 335

Leu Pro Asn Leu Ile Thr Pro Arg Tyr Ser Gly Ala Ser Val Phe Val
            340                 345                 350

Asn Asp Asp Ile Tyr Val Met Gly Gly Val Tyr Thr Thr Tyr Glu Lys
        355                 360                 365

Tyr Val Val Leu Asn Asp Val Glu Cys Phe Thr Lys Asn Arg Trp Ile
```

```
    370                 375                 380

Lys Lys Ser Pro Met Pro Arg His His Ser Ile Val Tyr Ala Val Glu
385                 390                 395                 400

Tyr Asp Gly Asp Ile Tyr Val Ile Thr Gly Ile Thr His Glu Thr Arg
                405                 410                 415

Asn Tyr Leu Tyr Lys Tyr Ile Val Lys Glu Asp Lys Trp Ile Glu Leu
            420                 425                 430

Tyr Met Tyr Phe Asn His Val Gly Lys Met Phe Val Cys Ser Cys Gly
        435                 440                 445

Asp Tyr Ile Leu Ile Ile Ala Asp Ala Lys Tyr Glu Tyr Tyr Pro Lys
    450                 455                 460

Ser Asn Thr Trp Asn Leu Phe Asp Met Ser Thr Arg Asn Ile Glu Tyr
465                 470                 475                 480

Tyr Asp Met Phe Thr Lys Asp Glu Thr Pro Lys Cys Asn Val Thr His
                485                 490                 495

Lys Ser Leu Pro Ser Phe Leu Ser Asn Cys Glu Lys Gln Phe Leu Gln
            500                 505                 510


<210> 59
<211> 224
<212> PRT
<213> Vaccinia virus

<400> 59
Met Val Lys Asn Asn Lys Ile Ser Asn Ser Cys Arg Met Ile Met Ser
1               5                   10                  15

Thr Asp Pro Asn Asn Ile Leu Met Arg His Leu Lys Asn Leu Thr Asp
            20                  25                  30

Asp Glu Phe Lys Cys Ile Ile His Arg Ser Ser Asp Phe Leu Tyr Leu
```

```
        35                  40                  45

Ser Asp Ser Asp Tyr Thr Ser Ile Thr Lys Glu Thr Leu Val Ser Glu
    50                  55                  60

Ile Val Glu Glu Tyr Pro Asp Asp Cys Asn Lys Ile Leu Ala Ile Ile
65                  70                  75                  80

Phe Leu Val Leu Asp Lys Asp Ile Asp Val Asp Ile Lys Thr Lys Leu
                85                  90                  95

Lys Pro Lys Pro Ala Val Arg Phe Ala Ile Leu Asp Lys Met Thr Glu
            100                 105                 110

Asp Ile Lys Leu Thr Asp Leu Val Arg His Tyr Phe Arg Tyr Ile Glu
        115                 120                 125

Gln Asp Ile Pro Leu Gly Pro Leu Phe Lys Lys Ile Asp Ser Tyr Arg
    130                 135                 140

Thr Arg Ala Ile Asn Lys Tyr Ser Lys Glu Leu Gly Leu Ala Thr Glu
145                 150                 155                 160

Tyr Phe Asn Lys Tyr Gly His Leu Met Phe Tyr Thr Leu Pro Ile Pro
                165                 170                 175

Tyr Asn Arg Phe Phe Cys Arg Asn Ser Ile Gly Phe Leu Ala Val Leu
            180                 185                 190

Ser Pro Thr Ile Gly His Val Lys Ala Phe Tyr Lys Phe Ile Glu Tyr
        195                 200                 205

Val Ser Ile Asp Asp Arg Arg Lys Phe Lys Lys Glu Leu Met Ser Lys
    210                 215                 220

<210> 60
<211> 117
<212> PRT
```

<213> Vaccinia virus

<400> 60
Met Arg Thr Leu Leu Ile Arg Tyr Ile Leu Trp Arg Asn Asp Asn Asp
1   5   10   15

Gln Thr Tyr Tyr Asn Asp Asp Phe Lys Lys Leu Met Leu Leu Asp Glu
            20   25   30

Leu Val Asp Asp Gly Asp Val Cys Thr Leu Ile Lys Asn Met Arg Met
        35   40   45

Thr Leu Ser Asp Gly Pro Leu Leu Asp Arg Leu Asn Gln Pro Val Asn
    50   55   60

Asn Ile Glu Asp Ala Lys Arg Met Ile Ala Ile Ser Ala Lys Val Ala
65   70   75   80

Arg Asp Ile Gly Glu Arg Ser Glu Ile Arg Trp Glu Glu Ser Phe Thr
                85   90   95

Ile Leu Phe Arg Met Ile Glu Thr Tyr Phe Asp Asp Leu Met Ile Asp
            100   105   110

Leu Tyr Gly Glu Lys
        115

<210> 61
<211> 79
<212> PRT
<213> Vaccinia virus

<400> 61
Met Thr Ser Ser Ala Met Asp Asn Asn Glu Pro Lys Val Leu Glu Met
1   5   10   15

Val Tyr Asp Ala Thr Ile Leu Pro Glu Gly Ser Ser Met Asp Pro Tyr
            20   25   30

Ile Met Asp Cys Ile Asn Arg His Ile Asn Met Cys Ile Gln Arg Thr

```
        35                  40                  45

Tyr Ser Ser Ser Ile Ile Ala Ile Leu Asp Arg Phe Leu Met Met Asn
    50                  55                  60

Lys Asp Glu Leu Asn Asn Thr Gln Cys His Ile Ile Lys Asn Leu
65                  70                  75

<210> 62
<211> 472
<212> PRT
<213> Vaccinia virus

<400> 62
Met Ile Phe Val Ile Glu Ser Lys Leu Leu Gln Ile Tyr Arg Asn Arg
1               5                   10                  15

Asn Arg Asn Ile Asn Phe Tyr Thr Thr Met Asp Asn Ile Met Ser Ala
            20                  25                  30

Glu Tyr Tyr Leu Ser Leu Tyr Ala Lys Tyr Asn Ser Lys Asn Leu Asp
        35                  40                  45

Val Phe Arg Asn Met Leu Gln Ala Ile Glu Pro Ser Gly Asn Asn Tyr
    50                  55                  60

His Ile Leu His Ala Tyr Cys Gly Ile Lys Gly Leu Asp Glu Arg Phe
65                  70                  75                  80

Val Glu Glu Leu Leu His Arg Gly Tyr Ser Pro Asn Glu Thr Asp Asp
                85                  90                  95

Asp Gly Asn Tyr Pro Leu His Ile Ala Ser Lys Ile Asn Asn Asn Arg
            100                 105                 110

Ile Val Ala Met Leu Leu Thr His Gly Ala Asp Pro Asn Ala Cys Asp
        115                 120                 125

Lys His Asn Lys Thr Pro Leu Tyr Tyr Leu Ser Gly Thr Asp Asp Glu
```

```
    130                 135                 140

Val Ile Glu Arg Ile Asn Leu Leu Val Gln Tyr Gly Ala Lys Ile Asn
145                 150                 155                 160

Asn Ser Val Asp Glu Glu Gly Cys Gly Pro Leu Leu Ala Cys Thr Asp
                165                 170                 175

Pro Ser Glu Arg Val Phe Lys Lys Ile Met Ser Ile Gly Phe Glu Ala
            180                 185                 190

Arg Ile Val Asp Lys Phe Gly Lys Asn His Ile His Arg His Leu Met
        195                 200                 205

Ser Asp Asn Pro Lys Ala Ser Thr Ile Ser Trp Met Met Lys Leu Gly
    210                 215                 220

Ile Ser Pro Ser Lys Pro Asp His Asp Gly Asn Thr Pro Leu His Ile
225                 230                 235                 240

Val Cys Ser Lys Thr Val Lys Asn Val Asp Ile Ile Asp Leu Leu Leu
                245                 250                 255

Pro Ser Thr Asp Val Asn Lys Gln Asn Lys Phe Gly Asp Ser Pro Leu
            260                 265                 270

Thr Leu Leu Ile Lys Thr Leu Ser Pro Ala His Leu Ile Asn Lys Leu
        275                 280                 285

Leu Ser Thr Ser Asn Val Ile Thr Asp Gln Thr Val Asn Ile Cys Ile
    290                 295                 300

Phe Tyr Asp Arg Asp Asp Val Leu Glu Ile Ile Asn Asp Lys Gly Lys
305                 310                 315                 320

Gln Tyr Asp Ser Thr Asp Phe Lys Met Ala Val Glu Val Gly Ser Ile
                325                 330                 335
```

```
Arg Cys Val Lys Tyr Leu Leu Asp Asn Asp Ile Ile Cys Glu Asp Ala
            340                 345                 350


Met Tyr Tyr Ala Val Leu Ser Glu Tyr Glu Thr Met Val Asp Tyr Leu
        355                 360                 365


Leu Phe Asn His Phe Ser Val Asp Phe Val Val Asn Gly His Thr Cys
    370                 375                 380


Met Ser Glu Cys Val Arg Leu Asn Asn Pro Val Ile Leu Ser Lys Leu
385                 390                 395                 400


Met Leu His Asn Leu Thr Ser Glu Thr Met Tyr Leu Thr Met Lys Ala
                405                 410                 415


Ile Glu Lys Asp Arg Leu Asp Lys Ser Ile Ile Ile Pro Phe Ile Ala
            420                 425                 430


Tyr Phe Val Leu Met His Pro Asp Phe Cys Lys Asn Arg Arg Tyr Phe
        435                 440                 445


Thr Ser Tyr Lys Arg Phe Val Thr Asp Tyr Val His Glu Gly Val Ser
    450                 455                 460


Tyr Glu Val Phe Asp Asp Tyr Phe
465                 470


<210> 63
<211> 196
<212> PRT
<213> Vaccinia virus

<400> 63
Met Ser Ser Ser Thr Arg Leu Pro Val Leu Val Leu Ala Ala Glu Leu
1               5                   10                  15


Thr Ile Gly Val Asn Tyr Asp Ile Asn Ser Thr Ile Ile Gly Glu Cys
            20                  25                  30
```

```
His Met Ser Glu Ser Tyr Ile Asp Arg Asn Ala Asn Ile Val Leu Thr
        35                  40                  45

Gly Tyr Gly Leu Glu Ile Asn Met Thr Ile Met Asp Thr Asp Gln Arg
    50                  55                  60

Phe Val Ala Ala Ala Glu Gly Val Gly Lys Asp Asn Lys Leu Ser Val
65                  70                  75                  80

Leu Leu Phe Thr Thr Gln Arg Leu Asp Lys Val His His Asn Ile Ser
                85                  90                  95

Val Thr Ile Thr Cys Met Glu Met Asn Cys Gly Thr Thr Lys Tyr Asp
            100                 105                 110

Ser Asp Leu Pro Glu Ser Ile His Lys Ser Ser Ser Cys Asp Ile Thr
        115                 120                 125

Ile Asn Gly Ser Cys Val Thr Cys Val Asn Leu Glu Thr Asp Pro Thr
    130                 135                 140

Lys Ile Asn Pro His Tyr Leu His Pro Lys Asp Lys Tyr Leu Tyr His
145                 150                 155                 160

Asn Ser Glu Tyr Gly Met Arg Gly Ser Tyr Gly Val Thr Phe Ile Asp
                165                 170                 175

Glu Leu Asn Gln Cys Leu Leu Asp Ile Lys Glu Leu Ser Tyr Asp Ile
            180                 185                 190

Cys Tyr Arg Glu
        195
```

<210> 64
<211> 76
<212> PRT
<213> Vaccinia virus

<400> 64
Met Leu Gln Ala Leu Phe Lys Tyr Asp Ile Asn Ile Tyr Ser Ala Asn
1   5   10   15

Leu Glu Asn Val Leu Leu Asp Asp Ala Glu Ile Ala Lys Met Ile Ile
            20   25   30

Glu Lys His Val Glu Tyr Lys Ser Asp Ser Tyr Thr Lys Asp Leu Asp
        35   40   45

Ile Val Lys Asn Asn Lys Leu Asp Glu Ile Ile Ser Lys Asn Lys Glu
    50   55   60

Leu Arg Leu Met Tyr Val Asn Cys Val Lys Lys Asn
65   70   75

<210> 65
<211> 189
<212> PRT
<213> Vaccinia virus

<400> 65
Met Asp Leu Ser Arg Ile Asn Thr Trp Lys Ser Lys Gln Leu Lys Ser
1   5   10   15

Phe Leu Ser Ser Lys Asp Thr Phe Lys Ala Asp Val His Gly His Ser
            20   25   30

Ala Leu Tyr Tyr Ala Ile Ala Asp Asn Asn Val Arg Leu Val Cys Thr
        35   40   45

Leu Leu Asn Ser Gly Ala Leu Lys Asn Leu Leu Glu Asn Glu Phe Pro
    50   55   60

Leu His Gln Ala Ala Thr Leu Glu Asp Thr Lys Ile Val Lys Ile Leu
65   70   75   80

Leu Phe Ser Gly Leu Asp Asp Ser Gln Phe Asp Asp Lys Gly Asn Thr
                85   90   95

```
Ala Leu Tyr Tyr Ala Val Asp Ser Gly Asn Met Gln Thr Val Lys Leu
            100                 105                 110


Phe Val Lys Lys Asn Trp Arg Leu Met Phe Tyr Gly Lys Thr Gly Trp
        115                 120                 125


Lys Thr Ser Phe Tyr His Ala Val Met Leu Asn Asp Val Ser Ile Val
    130                 135                 140


Ser Tyr Phe Leu Ser Glu Ile Pro Ser Thr Phe Asp Leu Ala Ile Leu
145                 150                 155                 160


Leu Ser Cys Ile His Ile Thr Ile Lys Asn Gly His Val Asp Met Met
                165                 170                 175


Ile Leu Leu Leu Asp Tyr Met Thr Val Asp Lys His Gln
            180                 185


<210> 66
<211> 368
<212> PRT
<213> Vaccinia virus

<400> 66
Met Ile Ala Leu Leu Ile Leu Ser Leu Ala Cys Ser Ala Ser Ala Tyr
1               5                   10                  15


Arg Leu Gln Gly Phe Thr Asn Ala Gly Ile Val Ala Tyr Lys Asn Ile
            20                  25                  30


Gln Asp Asp Asn Ile Val Phe Ser Pro Phe Gly Tyr Ser Phe Ser Met
        35                  40                  45


Phe Met Ser Leu Leu Pro Ala Ser Gly Asn Thr Arg Ile Glu Leu Leu
    50                  55                  60


Lys Thr Met Asp Leu Arg Lys Arg Asp Leu Gly Pro Ala Phe Thr Glu
65                  70                  75                  80
```

```
Leu Ile Ser Gly Leu Ala Lys Leu Lys Thr Ser Lys Tyr Thr Tyr Thr
                85                  90                  95

Asp Leu Thr Tyr Gln Ser Phe Val Asp Asn Thr Val Cys Ile Lys Pro
            100                 105                 110

Ser Tyr Tyr Gln Gln Tyr His Arg Phe Gly Leu Tyr Arg Leu Asn Phe
        115                 120                 125

Arg Arg Asp Ala Val Asn Lys Ile Asn Ser Ile Val Glu Arg Arg Ser
    130                 135                 140

Gly Met Ser Asn Val Val Asp Ser Asn Met Leu Asp Asn Asn Thr Leu
145                 150                 155                 160

Trp Ala Ile Ile Asn Thr Ile Tyr Phe Lys Gly Thr Trp Gln Tyr Pro
                165                 170                 175

Phe Asp Ile Thr Lys Thr Arg Asn Ala Ser Phe Thr Asn Lys Tyr Gly
            180                 185                 190

Thr Lys Thr Val Pro Met Met Asn Val Val Thr Lys Leu Gln Gly Asn
        195                 200                 205

Thr Ile Thr Ile Asp Asp Glu Glu Tyr Asp Met Val Arg Leu Pro Tyr
    210                 215                 220

Lys Asp Ala Asn Ile Ser Met Tyr Leu Ala Ile Gly Asp Asn Met Thr
225                 230                 235                 240

His Phe Thr Asp Ser Ile Thr Ala Ala Lys Asp Tyr Trp Ser Phe Gln
                245                 250                 255

Leu Gly Asn Lys Val Tyr Asn Leu Lys Leu Pro Lys Phe Ser Ile Glu
            260                 265                 270

Asn Lys Arg Asp Ile Lys Ser Ile Ala Glu Met Met Ala Pro Ser Met
```

```
        275                 280                 285

Phe Asn Pro Asp Asn Ala Ser Phe Lys His Met Thr Arg Asp Pro Leu
    290                 295                 300

Tyr Ile Tyr Lys Met Phe Gln Asn Ala Lys Ile Asp Val Asp Glu Gln
305                 310                 315                 320

Gly Thr Val Ala Glu Ala Ser Thr Ile Met Val Ala Thr Ala Arg Ser
                325                 330                 335

Ser Pro Glu Glu Leu Glu Phe Asn Thr Pro Phe Val Phe Ile Ile Arg
            340                 345                 350

His Asp Ile Thr Gly Phe Ile Leu Phe Met Gly Lys Val Glu Ser Pro
        355                 360                 365
```

<210> 67
<211> 81
<212> PRT
<213> Vaccinia virus

<400> 67

```
Met Gly His Ile Ile Thr Tyr Cys Gln Val His Thr Asn Ile Ser Ile
1               5                   10                  15

Leu Ile Arg Lys Ala Tyr His Ile Ile Phe Phe Val Ile Asp Cys Asp
            20                  25                  30

Cys Ile Ser Leu Gln Phe Ser Asn Tyr Val His His Gly Asn Arg Phe
        35                  40                  45

Arg Thr Val Leu Ile Ser Lys Thr Ser Ile Ala Cys Phe Ser Asp Ile
    50                  55                  60

Lys Arg Ile Leu Pro Cys Thr Phe Lys Ile Tyr Ser Ile Asn Asp Cys
65                  70                  75                  80

Pro
```

<210> 68
<211> 88
<212> PRT
<213> Vaccinia virus

<400> 68
Met Leu Ala Phe Cys Tyr Ser Leu Pro Asn Ala Gly Asp Val Ile Lys
1   5   10   15

Gly Arg Val Tyr Glu Lys Asp Tyr Ala Leu Tyr Ile Tyr Leu Phe Asp
            20   25   30

Tyr Pro His Ser Glu Ala Ile Leu Ala Glu Ser Val Lys Met His Met
        35   40   45

Asp Arg Tyr Val Glu Tyr Arg Asp Lys Leu Val Gly Lys Thr Val Lys
    50   55   60

Val Lys Val Ile Arg Val Asp Tyr Thr Lys Gly Tyr Ile Asp Val Asn
65   70   75   80

Tyr Lys Arg Met Cys Arg His Gln
                85

<210> 69
<211> 134
<212> PRT
<213> Vaccinia virus

<400> 69
Met Thr Leu Val Gln His Val Val Thr Ile Lys Ser Thr Tyr Trp Val
1   5   10   15

Ile Pro Trp Glu Leu Ala Ser Tyr Asp Asn Pro Asn Leu Phe Thr Ala
            20   25   30

Met Ile Leu Met Ser Pro Leu Val Asn Ala Asp Ala Val Ser Lys Leu
        35   40   45

```
Asn Leu Leu Ala Ala Lys Leu Met Gly Thr Ile Thr Leu Asn Ala Pro
    50                  55                  60

Val Gly Lys Leu Cys Pro Glu Ser Val Ser Arg Asp Met Asp Lys Val
65                  70                  75                  80

Tyr Lys Tyr Gln Tyr Asp Pro Leu Ile Asn His Glu Lys Ile Lys Ala
                85                  90                  95

Gly Phe Ala Ser Gln Val Leu Lys Ala Thr Asn Lys Val Arg Lys Ile
            100                 105                 110

Ile Ser Lys Ile Asn Thr Pro Arg Leu Ser Tyr Ser Arg Glu Gln Thr
        115                 120                 125

Ile Arg Leu Ala Met Phe
    130
```

<210> 70
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 70

```
Met Ala Thr Lys Leu Asp Tyr Glu Asp Ala Val Phe Tyr Phe Val Asp
1               5                   10                  15

Asp Asp Lys Ile Cys Ser Arg Asp Ser Ile Ile Asp Leu Ile Asp Glu
            20                  25                  30

Tyr Ile Thr Trp Arg Asn His Val Ile Val Phe Asn Lys Asp Ile Thr
        35                  40                  45

Ser Cys Gly Arg Leu Tyr Lys Glu Leu Met Lys Phe Asp Asp Val Ala
    50                  55                  60

Ile Arg Tyr Tyr Gly Ile Asp Lys Ile Asn Glu Ile Val Glu Ala Met
65                  70                  75                  80
```

```
Ser Glu Gly Asp His Tyr Ile Asn Phe Thr Lys Val His Asp Gln Glu
                85                  90                  95


Ser Leu Phe Ala Thr Ile Gly Ile Cys Ala Lys Ile Thr Glu His Trp
            100                 105                 110


Gly Tyr Lys Lys Ile Ser Glu Ser Arg Phe Gln Ser Leu Gly Asn Ile
        115                 120                 125


Thr Asp Leu Met Thr Asp Asp Asn Ile Asn Ile Leu Ile Leu Phe Leu
    130                 135                 140


Glu Lys Lys Leu Asn
145


<210> 71
<211> 226
<212> PRT
<213> Vaccinia virus

<400> 71
Met Leu Ser Met Phe Met Cys Asn Asn Ile Val Asp Tyr Val Asp Asp
1               5                   10                  15


Ile Asp Asn Gly Ile Val Gln Asp Ile Glu Asp Glu Ala Ser Asn Asn
            20                  25                  30


Val Asp Arg Asp Tyr Val Tyr Pro Leu Pro Glu Asn Met Val Tyr Arg
        35                  40                  45


Phe Asp Lys Ser Thr Asn Ile Leu Asp Tyr Leu Ser Thr Glu Arg Asp
    50                  55                  60


His Val Met Met Ala Val Arg Tyr Tyr Met Ser Lys Gln Arg Leu Asp
65                  70                  75                  80


Asp Leu Tyr Arg Gln Leu Pro Thr Lys Thr Arg Ser Tyr Ile Asp Ile
                85                  90                  95
```

```
Ile Asn Ile Tyr Cys Asp Lys Val Ser Asn Asp Tyr Asn Arg Asp Met
            100                 105                 110

Asn Ile Met Tyr Asp Met Ala Ser Thr Lys Ser Phe Thr Val Tyr Asp
        115                 120                 125

Ile Asn Asn Glu Val Asn Thr Ile Leu Met Asp Asn Lys Gly Leu Gly
    130                 135                 140

Val Arg Leu Ala Thr Ile Ser Phe Ile Thr Glu Leu Gly Arg Arg Cys
145                 150                 155                 160

Met Asn Pro Val Lys Thr Ile Lys Met Phe Thr Leu Leu Ser His Thr
                165                 170                 175

Ile Cys Asp Asp Cys Phe Val Asp Tyr Ile Thr Asp Ile Ser Pro Pro
            180                 185                 190

Asp Asn Thr Ile Pro Asn Thr Ser Thr Arg Glu Tyr Leu Lys Leu Ile
        195                 200                 205

Gly Ile Thr Ala Ile Met Phe Ala Thr Tyr Lys Thr Leu Lys Tyr Met
    210                 215                 220

Ile Gly
225


<210> 72
<211> 147
<212> PRT
<213> Vaccinia virus

<400> 72
Met Phe Asn Met Asn Ile Asn Ser Pro Val Arg Phe Val Lys Glu Thr
1               5                   10                  15

Asn Arg Ala Lys Ser Pro Thr Arg Gln Ser Pro Gly Ala Ala Gly Tyr
            20                  25                  30
```

```
Asp Leu Tyr Ser Ala Tyr Asp Tyr Thr Ile Pro Pro Gly Glu Arg Gln
        35                  40                  45

Leu Ile Lys Thr Asp Ile Ser Met Ser Met Pro Lys Ile Cys Tyr Gly
    50                  55                  60

Arg Ile Ala Pro Arg Ser Gly Leu Ser Leu Lys Gly Ile Asp Ile Gly
65                  70                  75                  80

Gly Gly Val Ile Asp Glu Asp Tyr Arg Gly Asn Ile Gly Val Ile Leu
                85                  90                  95

Ile Asn Asn Gly Lys Cys Thr Phe Asn Val Asn Thr Gly Asp Arg Ile
            100                 105                 110

Ala Gln Leu Ile Tyr Gln Arg Ile Tyr Tyr Pro Glu Leu Glu Glu Val
        115                 120                 125

Gln Ser Leu Asp Ser Thr Asp Arg Gly Asp Gln Gly Phe Gly Ser Thr
    130                 135                 140

Gly Leu Arg
145
```

<210> 73
<211> 480
<212> PRT
<213> Vaccinia virus

<400> 73

```
Met Pro Ile Phe Val Asn Thr Val Tyr Cys Lys Asn Ile Leu Ala Leu
1               5                   10                  15

Ser Met Thr Lys Lys Phe Lys Thr Ile Ile Asp Ala Ile Gly Gly Asn
            20                  25                  30

Ile Ile Val Asn Ser Thr Ile Leu Lys Lys Leu Ser Pro Tyr Phe Arg
        35                  40                  45
```

```
Thr His Leu Arg Gln Lys Tyr Thr Lys Asn Lys Asp Pro Val Thr Arg
    50                  55                  60

Val Cys Leu Asp Leu Asp Ile His Ser Leu Thr Ser Ile Val Ile Tyr
65                  70                  75                  80

Ser Tyr Thr Gly Lys Val Tyr Ile Asp Ser His Asn Val Val Asn Leu
                85                  90                  95

Leu Arg Ala Ser Ile Leu Thr Ser Val Glu Phe Ile Ile Tyr Thr Cys
            100                 105                 110

Ile Asn Phe Ile Leu Arg Asp Phe Arg Lys Glu Tyr Cys Val Glu Cys
        115                 120                 125

Tyr Met Met Gly Ile Glu Tyr Gly Leu Ser Asn Leu Leu Cys His Thr
    130                 135                 140

Lys Asn Phe Ile Ala Lys His Phe Leu Glu Leu Glu Asp Asp Ile Ile
145                 150                 155                 160

Asp Asn Phe Asp Tyr Leu Ser Met Lys Leu Ile Leu Glu Ser Asp Glu
                165                 170                 175

Leu Asn Val Pro Asp Glu Asp Tyr Val Val Asp Phe Val Ile Lys Trp
            180                 185                 190

Tyr Ile Lys Arg Arg Asn Lys Leu Gly Asn Leu Leu Leu Leu Ile Lys
        195                 200                 205

Asn Val Ile Arg Ser Asn Tyr Leu Ser Pro Arg Gly Ile Asn Asn Val
    210                 215                 220

Lys Trp Ile Leu Asp Cys Thr Lys Ile Phe His Cys Asp Lys Gln Pro
225                 230                 235                 240

Arg Lys Ser Tyr Lys Tyr Pro Phe Ile Glu Tyr Pro Met Asn Met Asp
```

```
               245                 250                 255

Gln Ile Ile Asp Ile Phe His Met Cys Thr Ser Thr His Val Gly Glu
            260                 265                 270

Val Val Tyr Leu Ile Gly Gly Trp Met Asn Asn Glu Ile His Asn Asn
        275                 280                 285

Ala Ile Ala Val Asn Tyr Ile Ser Asn Asn Trp Ile Pro Ile Pro Pro
    290                 295                 300

Met Asn Ser Pro Arg Leu Tyr Ala Ser Gly Ile Pro Ala Asn Asn Lys
305                 310                 315                 320

Leu Tyr Val Val Gly Gly Leu Pro Asn Pro Thr Ser Val Glu Arg Trp
                325                 330                 335

Phe His Gly Asp Ala Ala Trp Val Asn Met Pro Ser Leu Leu Lys Pro
            340                 345                 350

Arg Cys Asn Pro Ala Val Ala Ser Ile Asn Asn Val Ile Tyr Val Met
        355                 360                 365

Gly Gly His Ser Glu Thr Asp Thr Thr Thr Glu Tyr Leu Leu Pro Asn
    370                 375                 380

His Asp Gln Trp Gln Phe Gly Pro Ser Thr Tyr Tyr Pro His Tyr Lys
385                 390                 395                 400

Ser Cys Ala Leu Val Phe Gly Arg Arg Leu Phe Leu Val Gly Arg Asn
                405                 410                 415

Ala Glu Phe Tyr Cys Glu Ser Ser Asn Thr Trp Thr Leu Ile Asp Asp
            420                 425                 430

Pro Ile Tyr Pro Arg Asp Asn Pro Glu Leu Ile Ile Val Asp Asn Lys
        435                 440                 445
```

```
Leu Leu Leu Ile Gly Gly Phe Tyr Arg Glu Ser Tyr Ile Asp Thr Ile
    450                 455                 460

Glu Val Tyr Asn His His Thr Tyr Ser Trp Asn Ile Trp Asp Gly Lys
465                 470                 475                 480
```

<210> 74
<211> 506
<212> PRT
<213> Vaccinia virus

<400> 74

```
Met Glu Ser Val Thr Phe Ser Ile Asn Gly Glu Ile Ile Gln Val Asn
1               5                   10                  15

Lys Glu Ile Ile Thr Ala Ser Pro Tyr Asn Phe Phe Lys Arg Ile Gln
            20                  25                  30

Glu His His Ile Asn Asp Glu Val Ile Ile Leu Asn Gly Ile Asn Tyr
        35                  40                  45

His Ala Phe Glu Ser Leu Leu Asp Tyr Met Arg Trp Lys Lys Ile Asn
    50                  55                  60

Ile Thr Ile Asn Asn Val Glu Met Ile Leu Val Ala Ala Val Ile Ile
65                  70                  75                  80

Asp Val Thr Pro Val Val Asp Leu Cys Val Lys Thr Met Ile His Asn
                85                  90                  95

Ile Asn Ser Thr Asn Cys Ile Arg Met Phe Asn Phe Ser Lys Arg Tyr
            100                 105                 110

Gly Ile Lys Lys Leu Tyr Asn Ala Ser Met Ser Glu Ile Ile Asn Asn
        115                 120                 125

Ile Thr Ala Val Thr Ser Asp Pro Glu Phe Gly Lys Leu Ser Lys Asp
    130                 135                 140
```

```
Glu Leu Thr Thr Ile Leu Ser His Glu Asp Val Asn Val Asn His Glu
145                 150                 155                 160

Asp Val Thr Ala Met Ile Leu Leu Lys Trp Ile His Lys Asn Pro Asn
                165                 170                 175

Asp Val Asp Ile Ile Asn Ile Leu His Pro Lys Phe Met Thr Asn Thr
            180                 185                 190

Met Arg Asn Ala Ile Ser Leu Leu Gly Leu Thr Ile Ser Lys Ser Thr
        195                 200                 205

Lys Pro Val Thr Arg Asn Gly Ile Lys His Asn Ile Val Val Ile Lys
    210                 215                 220

Asn Ser Asp Tyr Ile Ser Thr Ile Thr His Tyr Ser Pro Arg Thr Glu
225                 230                 235                 240

Tyr Trp Thr Ile Val Gly Asn Thr Asp Arg Gln Phe Tyr Asn Ala Asn
                245                 250                 255

Val Leu His Asn Cys Leu Tyr Ile Ile Gly Gly Met Ile Asn Asn Arg
            260                 265                 270

His Val Tyr Ser Val Ser Arg Val Asp Leu Glu Thr Lys Lys Trp Lys
        275                 280                 285

Thr Val Thr Asn Met Ser Ser Leu Lys Ser Glu Val Ser Thr Cys Val
    290                 295                 300

Asn Asn Gly Lys Leu Tyr Val Ile Gly Gly Leu Glu Phe Ser Ile Ser
305                 310                 315                 320

Thr Gly Val Ala Glu Tyr Leu Lys His Gly Thr Ser Lys Trp Ile Arg
                325                 330                 335

Leu Pro Asn Leu Ile Thr Pro Arg Tyr Ser Gly Ala Ser Val Phe Val
```

```
            340                 345                 350

Asn Asp Asp Ile Tyr Val Met Gly Gly Val Tyr Thr Thr Tyr Glu Lys
        355                 360                 365

Tyr Val Val Leu Asn Asp Val Glu Cys Phe Thr Lys Asn Arg Trp Ile
    370                 375                 380

Lys Lys Ser Pro Met Pro Arg His His Ser Ile Val Tyr Ala Val Glu
385                 390                 395                 400

Tyr Asp Gly Asp Ile Tyr Ala Ile Thr Gly Ile Thr His Glu Thr Arg
                405                 410                 415

Asn Tyr Leu Tyr Lys Tyr Ile Val Lys Glu Asp Lys Trp Ile Glu Leu
            420                 425                 430

Tyr Met Tyr Phe Asn His Val Gly Lys Met Phe Val Cys Ser Cys Gly
        435                 440                 445

Asp Tyr Ile Leu Ile Ile Ala Asp Ala Lys Tyr Glu Tyr Tyr Pro Lys
    450                 455                 460

Ser Asn Thr Trp Asn Leu Phe Asp Met Ser Thr Arg Asn Ile Glu Tyr
465                 470                 475                 480

Tyr Asp Met Phe Thr Lys Asp Glu Thr His Lys Ser Leu Pro Ser Phe
                485                 490                 495

Leu Ser Asn Cys Glu Lys Gln Phe Leu Gln
            500                 505


<210> 75
<211> 224
<212> PRT
<213> Vaccinia virus

<400> 75
Met Val Lys Asn Asn Lys Ile Ser Asn Ser Cys Arg Met Ile Met Ser
```

```
1               5                   10                  15

Thr Asn Pro Asn Asn Ile Leu Met Arg His Leu Lys Asn Leu Thr Asp
            20                  25                  30

Asp Glu Phe Lys Cys Ile Ile His Arg Ser Ser Asp Phe Leu Tyr Leu
        35                  40                  45

Ser Asp Arg Asp Tyr Thr Ser Ile Thr Lys Glu Thr Leu Val Ser Glu
    50                  55                  60

Ile Val Glu Glu Tyr Pro Asp Asp Cys Asn Lys Ile Leu Ala Ile Ile
65                  70                  75                  80

Phe Leu Val Leu Asp Lys Asp Ile Asp Val Asp Ile Lys Thr Lys Leu
                85                  90                  95

Lys Pro Lys Pro Ala Val Arg Phe Ala Ile Leu Asp Lys Met Thr Glu
            100                 105                 110

Asp Ile Lys Leu Thr Asp Leu Val Arg His Tyr Phe Arg Tyr Ile Glu
        115                 120                 125

Gln Asp Ile Pro Leu Gly Pro Leu Phe Lys Lys Ile Asp Ser Tyr Arg
    130                 135                 140

Thr Arg Ala Ile Asn Lys Tyr Ser Lys Glu Leu Gly Leu Ala Thr Glu
145                 150                 155                 160

Tyr Phe Asn Lys Tyr Gly His Leu Met Phe Tyr Thr Leu Pro Ile Pro
                165                 170                 175

Tyr Asn Arg Phe Phe Cys Arg Asn Ser Ile Gly Phe Leu Ala Val Leu
            180                 185                 190

Ser Pro Thr Ile Gly His Val Lys Ala Phe Tyr Lys Phe Ile Glu Tyr
        195                 200                 205
```

Val Ser Ile Asp Asp Arg Arg Lys Phe Lys Lys Glu Leu Met Ser Lys
210 215 220

<210> 76
<211> 117
<212> PRT
<213> Vaccinia virus

<400> 76
Met Arg Thr Leu Leu Ile Arg Tyr Ile Leu Trp Arg Asn Asp Asn Asp
1 5 10 15

Gln Thr Tyr Tyr Asn Asp Asp Phe Lys Lys Leu Met Leu Leu Asp Glu
20 25 30

Leu Val Asp Asp Gly Asp Val Cys Thr Leu Ile Lys Asn Met Arg Met
35 40 45

Thr Leu Ser Asp Gly Pro Leu Leu Asp Arg Leu Asn Gln Pro Val Asn
50 55 60

Asn Ile Glu Asp Ala Lys Arg Met Ile Ala Ile Ser Ala Lys Val Ala
65 70 75 80

Arg Asp Ile Gly Glu Arg Ser Glu Ile Arg Trp Glu Glu Ser Phe Thr
85 90 95

Ile Leu Phe Arg Met Ile Glu Thr Tyr Phe Asp Asp Leu Met Ile Asp
100 105 110

Leu Tyr Gly Glu Lys
115

<210> 77
<211> 175
<212> PRT
<213> Vaccinia virus

<400> 77
Met Thr Ser Ser Ala Met Asp Asn Asn Glu Pro Lys Val Leu Glu Met

```
1               5                   10                  15

Val Tyr Asp Ala Thr Ile Leu Pro Glu Gly Ser Ser Met Asp Pro Asn
            20                  25                  30

Ile Ile Asp Cys Ile Asn Arg His Ile Asn Met Cys Ile Gln Arg Thr
        35                  40                  45

Tyr Ser Ser Ser Ile Ile Ala Ile Leu Asp Arg Phe Leu Thr Met Asn
    50                  55                  60

Lys Asp Glu Leu Asn Asn Thr Gln Cys His Ile Ile Lys Glu Phe Met
65                  70                  75                  80

Thr Tyr Glu Gln Met Ala Ile Asp His Tyr Gly Gly Tyr Val Asn Ala
                85                  90                  95

Ile Leu Tyr Gln Ile Arg Lys Arg Pro Asn Gln His His Thr Ile Asp
            100                 105                 110

Leu Phe Lys Lys Ile Lys Arg Thr Arg Tyr Asp Thr Phe Lys Val Asp
        115                 120                 125

Pro Val Glu Phe Val Lys Lys Val Ile Gly Phe Val Ser Ile Leu Asn
    130                 135                 140

Lys Tyr Lys Pro Val Tyr Ser Tyr Val Leu Tyr Glu Asn Val Leu Tyr
145                 150                 155                 160

Asp Glu Phe Lys Cys Phe Ile Asp Tyr Val Glu Thr Lys Tyr Phe
                165                 170                 175


<210> 78
<211> 72
<212> PRT
<213> Vaccinia virus

<400> 78
Met Leu His Asn Pro Thr Ser Glu Thr Met Tyr Leu Thr Met Asn Ala
```

```
1               5                   10                  15


Ile Lys Lys Asp Lys Leu Asp Lys Ser Ile Ile Ile Pro Phe Ile Ala
            20                  25                  30


Tyr Phe Val Leu Met His Pro Asp Phe Cys Lys Asn Arg Arg Tyr Phe
        35                  40                  45


Thr Ser Tyr Lys Arg Phe Val Thr Asp Tyr Val His Glu Gly Val Ser
    50                  55                  60


Tyr Glu Val Phe Asp Asp Tyr Phe
65                  70


<210> 79
<211> 214
<212> PRT
<213> Vaccinia virus

<400> 79
Met Ser Ile Gly Phe Glu Ala Arg Ile Val Asp Lys Phe Gly Lys Asn
1               5                   10                  15


His Ile His Arg His Leu Met Ser Asp Asn Pro Lys Ala Ser Thr Ile
            20                  25                  30


Ser Trp Met Met Lys Leu Gly Ile Ser Pro Ser Lys Pro Asp His Asp
        35                  40                  45


Gly Asn Thr Pro Leu His Ile Val Cys Ser Lys Thr Val Lys Tyr Val
    50                  55                  60


Asp Ile Ile Asp Leu Leu Leu Pro Ser Thr Asp Val Asn Lys Gln Asn
65                  70                  75                  80


Lys Phe Gly Asp Ser Pro Leu Thr Leu Leu Ile Lys Thr Leu Ser Leu
                85                  90                  95


Ala His Leu Ile Asn Lys Leu Leu Ser Thr Ser Asn Val Ile Thr Asp
```

```
            100                 105                 110

Gln Thr Val Asn Ile Cys Ile Phe Tyr Asp Arg Asp Asp Val Leu Glu
        115                 120                 125

Ile Ile Asn Asp Lys Gly Lys Gln Tyr Asp Phe Lys Met Ala Val Glu
    130                 135                 140

Val Gly Ser Ile Lys Cys Val Lys Tyr Leu Leu Asp Asn Asp Ile Ile
145                 150                 155                 160

Cys Glu Asp Ala Met Tyr Tyr Ala Val Leu Ser Glu Tyr Lys Thr Met
                165                 170                 175

Val Asp Tyr Leu Leu Phe Asn His Phe Ser Val Asp Ser Val Val Asn
            180                 185                 190

Gly His Thr Cys Met Ser Glu Cys Val Lys Leu Asn Asn Arg His Phe
        195                 200                 205

Ile Glu Ala Asp Val Thr
    210
```

<210> 80
<211> 161
<212> PRT
<213> Vaccinia virus

<400> 80

```
Met Ile Phe Val Ile Glu Ser Lys Leu Leu Gln Ile Tyr Arg Asn Arg
1               5                   10                  15

Asn Arg Asn Ile Asn Phe Tyr Thr Thr Met Asp Asn Ile Met Ser Ala
            20                  25                  30

Glu Tyr Tyr Leu Ser Leu Tyr Ala Lys Tyr Asn Ser Lys Asn Leu Asp
        35                  40                  45

Val Phe Arg Asn Met Leu Gln Ala Ile Glu Pro Ser Gly Asn Asn Tyr
```

```
    50                  55                  60

His Ile Leu His Ala Tyr Cys Gly Ile Lys Gly Leu Asp Glu Arg Phe
65                  70                  75                  80

Val Glu Glu Leu Leu His Arg Gly Tyr Ser Pro Asn Glu Thr Asp Asp
                85                  90                  95

Asp Gly Asn Tyr Pro Leu His Ile Ala Ser Lys Ile Asn Asn Asn Arg
            100                 105                 110

Ile Val Ala Met Leu Leu Thr His Gly Ala Asp Pro Asn Ala Cys Asp
        115                 120                 125

Lys His Asn Lys Thr Pro Leu Tyr Tyr Leu Ser Gly Thr Asp Asp Glu
    130                 135                 140

Val Ile Glu Arg Ile Asn Leu Leu Val Gln Tyr Gly Ala Lys Ile Asn
145                 150                 155                 160

Asn
```

<210> 81
<211> 220
<212> PRT
<213> Vaccinia virus

<400> 81

```
Met Val Tyr Lys Leu Val Leu Leu Phe Cys Ile Ala Ser Leu Gly Tyr
1               5                   10                  15

Ser Val Glu Tyr Lys Asn Thr Ile Cys Pro Pro Arg Gln Asp Tyr Arg
            20                  25                  30

Tyr Trp Tyr Phe Ala Ala Glu Leu Thr Ile Gly Val Asn Tyr Asp Ile
        35                  40                  45

Asn Ser Thr Ile Ile Gly Glu Cys His Met Ser Glu Ser Tyr Ile Asp
```

```
    50                  55                  60

Arg Asn Ala Asn Ile Val Leu Thr Gly Tyr Gly Leu Glu Ile Asn Met
65                  70                  75                  80

Thr Ile Met Asp Thr Asp Gln Arg Phe Val Ala Ala Ala Glu Gly Val
                85                  90                  95

Gly Lys Asp Asn Lys Leu Ser Val Leu Leu Phe Thr Thr Gln Arg Leu
            100                 105                 110

Asp Lys Val His His Asn Ile Ser Val Thr Ile Thr Cys Met Glu Met
        115                 120                 125

Asn Cys Gly Thr Thr Lys Tyr Asp Ser Asp Leu Pro Glu Ser Ile His
    130                 135                 140

Lys Ser Ser Ser Cys Asp Ile Thr Ile Asn Gly Ser Cys Val Thr Cys
145                 150                 155                 160

Val Asn Leu Glu Thr Asp Pro Thr Lys Ile Asn Pro His Tyr Leu His
                165                 170                 175

Pro Lys Asp Lys Tyr Leu Tyr His Asn Ser Glu Tyr Gly Met Arg Gly
            180                 185                 190

Ser Tyr Gly Val Thr Phe Ile Asp Glu Leu Asn Gln Cys Leu Leu Asp
        195                 200                 205

Ile Lys Glu Leu Ser Tyr Asp Ile Cys Tyr Arg Glu
    210                 215                 220


<210> 82
<211> 284
<212> PRT
<213> Vaccinia virus

<400> 82
Met Asp Leu Ser Arg Ile Asn Thr Trp Lys Ser Lys Gln Leu Lys Ser
```

```
1               5                   10                  15

Phe Leu Ser Ser Lys Asp Thr Phe Lys Ala Asp Val His Gly His Ser
            20                  25                  30

Ala Leu Tyr Tyr Ala Ile Ala Asp Asn Asn Val Arg Leu Val Cys Thr
        35                  40                  45

Leu Leu Asn Ala Gly Ala Leu Lys Asn Leu Leu Glu Asn Glu Phe Pro
    50                  55                  60

Leu His Gln Ala Ala Thr Leu Glu Asp Thr Lys Ile Val Lys Ile Leu
65                  70                  75                  80

Leu Phe Ser Gly Leu Asp Asp Ser Gln Phe Asp Asp Lys Gly Asn Thr
                85                  90                  95

Ala Leu Tyr Tyr Ala Val Asp Ser Gly Asn Met Gln Thr Val Lys Leu
            100                 105                 110

Phe Val Lys Lys Asn Trp Arg Leu Met Phe Tyr Gly Lys Thr Gly Trp
        115                 120                 125

Lys Thr Ser Phe Tyr His Ala Val Met Leu Asn Asp Val Ser Ile Val
    130                 135                 140

Ser Tyr Phe Leu Ser Glu Ile Pro Ser Thr Phe Asp Leu Ala Ile Leu
145                 150                 155                 160

Leu Ser Cys Ile His Ile Thr Ile Lys Asn Gly His Val Asp Met Met
                165                 170                 175

Ile Leu Leu Leu Asp Tyr Met Thr Ser Thr Asn Thr Asn Asn Ser Leu
            180                 185                 190

Leu Phe Ile Pro Asp Ile Lys Leu Ala Ile Asp Asn Lys Asp Ile Glu
        195                 200                 205
```

```
Met Leu Gln Ala Leu Phe Lys Tyr Asp Ile Asn Ile Tyr Ser Ala Asn
    210                 215                 220

Leu Glu Asn Val Leu Leu Asp Asp Ala Glu Ile Ala Lys Met Ile Ile
225                 230                 235                 240

Glu Lys His Val Glu Tyr Lys Ser Asp Ser Tyr Thr Lys Asp Leu Asp
                245                 250                 255

Ile Val Lys Asn Asn Lys Leu Asp Glu Ile Ile Ser Lys Asn Lys Glu
            260                 265                 270

Leu Arg Leu Met Tyr Val Asn Cys Val Lys Lys Asn
        275                 280
```

<210> 83
<211> 364
<212> PRT
<213> Vaccinia virus

<400> 83

```
Met Ile Ala Leu Leu Ile Leu Ser Leu Thr Cys Ser Val Ser Thr Tyr
1               5                   10                  15

Arg Leu Gln Gly Phe Thr Asn Ala Gly Ile Val Ala Tyr Lys Asn Ile
            20                  25                  30

Gln Asp Asp Asn Ile Val Phe Ser Pro Phe Gly Tyr Ser Phe Ser Met
        35                  40                  45

Phe Met Ser Leu Leu Pro Ala Ser Gly Asn Thr Arg Ile Glu Leu Leu
    50                  55                  60

Lys Thr Met Asp Leu Arg Lys Arg Asp Leu Gly Pro Ala Phe Thr Glu
65                  70                  75                  80

Leu Ile Ser Gly Leu Ala Lys Leu Lys Thr Ser Lys Tyr Thr Tyr Thr
                85                  90                  95
```

```
Asp Leu Thr Tyr Gln Ser Phe Val Asp Asn Thr Val Cys Ile Lys Pro
            100                 105                 110

Ser Tyr Tyr Gln Gln Tyr His Arg Leu Asn Phe Arg Arg Asp Ala Val
        115                 120                 125

Asn Lys Ile Asn Ser Ile Val Glu Arg Arg Ser Gly Met Ser Asn Val
    130                 135                 140

Val Asp Ser Asn Met Leu Asp Asn Asn Thr Leu Trp Ala Ile Ile Asn
145                 150                 155                 160

Thr Ile Tyr Phe Lys Gly Ile Trp Gln Tyr Pro Phe Asp Ile Thr Lys
                165                 170                 175

Thr Arg Asn Ala Ser Phe Thr Asn Lys Tyr Gly Thr Lys Thr Val Pro
            180                 185                 190

Met Met Asn Val Val Thr Lys Leu Gln Gly Asn Thr Ile Thr Ile Asp
        195                 200                 205

Asp Lys Glu Tyr Asp Met Val Arg Leu Pro Tyr Lys Asp Ala Asn Ile
    210                 215                 220

Ser Met Tyr Leu Ala Ile Gly Asp Asn Met Thr His Phe Thr Asp Ser
225                 230                 235                 240

Ile Thr Ala Ala Lys Leu Asp Tyr Trp Ser Phe Gln Leu Gly Asn Lys
                245                 250                 255

Val Tyr Asn Leu Lys Leu Pro Lys Phe Ser Ile Glu Asn Lys Arg Asp
            260                 265                 270

Ile Lys Ser Ile Ala Glu Met Met Ala Pro Ser Met Phe Asn Pro Asp
        275                 280                 285

Asn Ala Ser Phe Lys His Met Thr Arg Asp Pro Leu Tyr Ile Tyr Lys
```

```
    290                 295                 300

Met Phe Gln Asn Ala Lys Ile Asp Val Asp Glu Gln Gly Thr Val Ala
305                 310                 315                 320

Glu Ala Ser Thr Ile Met Val Ala Thr Ala Arg Ser Ser Pro Glu Lys
                325                 330                 335

Leu Glu Phe Asn Thr Pro Phe Val Phe Ile Ile Arg His Asp Ile Thr
            340                 345                 350

Gly Phe Ile Leu Phe Met Gly Lys Val Glu Ser Pro
        355                 360
```

<210> 84
<211> 88
<212> PRT
<213> Vaccinia virus

<400> 84

```
Met Leu Ala Phe Cys Tyr Ser Leu Pro Asn Ala Gly Asp Val Ile Lys
1               5                   10                  15

Gly Arg Val Tyr Glu Asn Asp Tyr Ala Leu Tyr Ile Tyr Leu Phe Asp
            20                  25                  30

Tyr Pro His Phe Glu Ala Ile Leu Ala Glu Ser Val Lys Met His Met
        35                  40                  45

Asp Arg Tyr Val Glu Tyr Arg Asp Lys Leu Val Gly Lys Thr Val Lys
    50                  55                  60

Val Lys Val Ile Arg Val Asp Tyr Thr Lys Gly Tyr Ile Asp Val Asn
65                  70                  75                  80

Tyr Lys Arg Met Cys Arg His Gln
                85
```

<210> 85

<211> 424
<212> PRT
<213> Vaccinia virus

<400> 85
Met Asn Pro Asp Asn Thr Ile Ala Val Ile Thr Glu Thr Ile Pro Ile
1   5   10   15

Gly Met Gln Phe Asp Lys Val Tyr Leu Ser Thr Phe Asn Met Trp Arg
            20   25   30

Glu Ile Leu Ser Asn Thr Thr Lys Thr Leu Asp Ile Ser Ser Phe Tyr
        35   40   45

Trp Ser Leu Ser Asp Glu Val Gly Thr Asn Phe Gly Thr Ile Ile Leu
    50   55   60

Asn Glu Ile Val Gln Leu Pro Lys Arg Gly Val Arg Val Arg Val Ala
65   70   75   80

Val Asn Lys Ser Asn Lys Pro Leu Lys Asp Val Glu Arg Leu Gln Met
                85   90   95

Ala Gly Val Glu Val Arg Tyr Ile Asp Ile Thr Asn Ile Leu Gly Gly
            100   105   110

Val Leu His Thr Lys Phe Trp Ile Ser Asp Asn Thr His Ile Tyr Leu
        115   120   125

Gly Ser Ala Asn Met Asp Trp Arg Ser Leu Thr Gln Val Lys Glu Leu
    130   135   140

Gly Ile Ala Ile Phe Asn Asn Arg Asn Leu Ala Ala Asp Leu Thr Gln
145   150   155   160

Ile Phe Glu Val Tyr Trp Tyr Leu Gly Val Asn Asn Leu Pro Tyr Asn
                165   170   175

Trp Lys Asn Phe Tyr Pro Ser Tyr Tyr Asn Thr Asp His Pro Leu Ser

```
            180                 185                 190

Ile Asn Val Ser Gly Val Pro His Ser Val Phe Ile Ala Ser Ala Pro
        195                 200                 205

Gln Gln Leu Cys Thr Met Glu Arg Thr Asn Asp Leu Thr Ala Leu Leu
    210                 215                 220

Ser Cys Ile Arg Asn Ala Ser Lys Phe Val Tyr Val Ser Val Met Asn
225                 230                 235                 240

Phe Ile Pro Ile Ile Tyr Ser Lys Ala Gly Lys Ile Leu Phe Trp Pro
                245                 250                 255

Tyr Ile Glu Asp Glu Leu Arg Arg Ser Ala Ile Asp Arg Gln Val Ser
            260                 265                 270

Val Lys Leu Leu Ile Ser Cys Trp Gln Arg Ser Ser Phe Ile Met Arg
        275                 280                 285

Asn Phe Leu Arg Ser Ile Ala Met Leu Lys Ser Lys Asn Ile Asn Ile
    290                 295                 300

Glu Val Lys Leu Phe Ile Val Pro Asp Ala Asp Pro Pro Ile Pro Tyr
305                 310                 315                 320

Ser Arg Val Asn His Ala Lys Tyr Met Val Thr Asp Lys Thr Ala Tyr
                325                 330                 335

Ile Gly Thr Ser Asn Trp Thr Gly Asn Tyr Phe Thr Asp Thr Cys Gly
            340                 345                 350

Ala Ser Ile Asn Ile Thr Pro Asp Asp Gly Leu Gly Leu Arg Gln Gln
        355                 360                 365

Leu Glu Asp Ile Phe Met Arg Asp Trp Asn Ser Lys Tyr Ser Tyr Glu
    370                 375                 380
```

```
Leu Tyr Asp Thr Ser Pro Thr Lys Arg Cys Lys Leu Leu Lys Asn Met
385                 390                 395                 400


Lys Gln Cys Thr Asn Asp Ile Tyr Cys Asp Glu Ile Gln Pro Glu Lys
                405                 410                 415


Glu Ile Pro Glu Tyr Ser Leu Glu
            420


<210> 86
<211> 171
<212> PRT
<213> Vaccinia virus

<400> 86
Met Gly Ala Thr Ile Ser Ile Leu Ala Ser Tyr Asp Asn Pro Asn Leu
1               5                   10                  15


Phe Thr Ala Met Ile Leu Met Ser Pro Leu Val Asn Ala Asp Ala Val
            20                  25                  30


Ser Lys Leu Asn Leu Leu Ala Ala Lys Leu Met Gly Thr Ile Thr Pro
        35                  40                  45


Asn Ala Pro Val Gly Lys Leu Cys Pro Glu Ser Val Ser Arg Asp Met
    50                  55                  60


Asp Lys Val Tyr Lys Tyr Gln Tyr Asp Pro Leu Ile Asn His Glu Lys
65                  70                  75                  80


Ile Lys Ala Gly Phe Ala Ser Gln Val Leu Lys Ala Thr Asn Lys Val
                85                  90                  95


Arg Lys Ile Ile Ser Lys Ile Asn Thr Pro Pro Thr Leu Ile Leu Gln
            100                 105                 110


Gly Thr Asn Asn Glu Ile Ser Asp Val Leu Gly Ala Tyr Tyr Phe Met
        115                 120                 125
```

Gln His Ala Asn Cys Asn Arg Glu Ile Lys Ile Tyr Glu Gly Ala Lys
130 135 140

His His Leu His Lys Glu Thr Asp Glu Val Lys Lys Ser Val Met Lys
145 150 155 160

Glu Ile Glu Thr Trp Ile Phe Asn Arg Val Lys
165 170

<210> 87
<211> 81
<212> PRT
<213> Vaccinia virus

<400> 87
Met Ser Ala Asn Cys Met Phe Asn Leu Asp Asn Asp Tyr Ile Tyr Trp
1 5 10 15

Lys Pro Ile Thr Tyr Pro Lys Ala Leu Val Phe Ile Ser His Gly Ala
20 25 30

Gly Lys His Ser Gly Arg Tyr Asp Glu Leu Ala Glu Asn Ile Ser Ser
35 40 45

Leu Gly Ile Leu Val Phe Ser His Asp His Ile Gly His Gly Arg Ser
50 55 60

Asn Gly Glu Lys Met Met Ile Asp Asp Phe Gly Thr Ala Arg Gly Asn
65 70 75 80

Tyr

<210> 88
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 88
Met Ala Thr Lys Leu Asp Tyr Glu Asp Ala Val Phe Tyr Phe Val Asp

1 5 10 15

Asp Asp Lys Ile Cys Ser Arg Asp Ser Ile Ile Asp Leu Ile Asp Glu
20 25 30

Tyr Ile Thr Trp Arg Asn His Val Ile Val Phe Asn Lys Asp Ile Thr
35 40 45

Ser Cys Gly Arg Leu Tyr Lys Glu Leu Met Lys Phe Asp Asp Val Ala
50 55 60

Ile Arg Tyr Tyr Gly Ile Asp Lys Ile Asn Glu Ile Val Glu Ala Met
65 70 75 80

Ser Glu Gly Asp His Tyr Ile Asn Phe Thr Lys Val His Asp Gln Glu
85 90 95

Ser Leu Phe Ala Thr Ile Gly Ile Cys Ala Lys Ile Thr Glu His Trp
100 105 110

Gly Tyr Lys Lys Ile Ser Glu Ser Arg Phe Gln Ser Leu Gly Asn Ile
115 120 125

Thr Asp Leu Met Thr Asp Asp Asn Ile Asn Ile Leu Ile Leu Phe Leu
130 135 140

Glu Lys Lys Leu Asn
145

<210> 89
<211> 226
<212> PRT
<213> Vaccinia virus

<400> 89
Met Leu Ser Met Phe Met Cys Asn Asn Ile Val Asp Tyr Val Asp Asp
1 5 10 15

Ile Asp Asn Gly Ile Val Gln Asp Ile Glu Asp Glu Ala Ser Asn Asn

```
            20                  25                  30

Val Asp His Asp Tyr Val Tyr Pro Leu Pro Glu Asn Met Val Tyr Arg
        35                  40                  45

Phe Asp Lys Ser Thr Asn Ile Leu Asp Tyr Leu Ser Thr Glu Arg Asp
    50                  55                  60

His Val Met Met Ala Val Arg Tyr Tyr Met Ser Lys Gln Arg Leu Asp
65                  70                  75                  80

Asp Leu Tyr Arg Gln Leu Pro Thr Lys Thr Arg Ser Tyr Ile Asp Ile
                85                  90                  95

Ile Asn Ile Tyr Cys Asp Lys Val Ser Asn Asp Tyr Asn Arg Asp Met
            100                 105                 110

Asn Ile Met Tyr Asp Met Ala Ser Thr Lys Ser Phe Thr Val Tyr Asp
        115                 120                 125

Ile Asn Asn Glu Val Asn Thr Ile Leu Met Asp Asn Lys Gly Leu Gly
    130                 135                 140

Val Arg Leu Ala Thr Ile Ser Phe Ile Thr Lys Leu Gly Arg Arg Cys
145                 150                 155                 160

Met Asn Pro Val Lys Thr Ile Lys Met Phe Thr Leu Leu Ser His Thr
                165                 170                 175

Ile Cys Asp Asp Cys Phe Val Asp Tyr Ile Thr Asp Ile Ser Pro Pro
            180                 185                 190

Asp Asn Thr Ile Pro Asn Thr Ser Thr Arg Glu Tyr Leu Lys Leu Ile
        195                 200                 205

Gly Ile Thr Ala Ile Met Phe Ala Thr Tyr Lys Thr Leu Lys Tyr Met
    210                 215                 220
```

Ile Gly
225

<210> 90
<211> 147
<212> PRT
<213> Vaccinia virus

<400> 90
Met Phe Asn Met Asn Ile Asn Ser Pro Val Arg Phe Val Lys Glu Thr
1 5 10 15

Asn Arg Ala Lys Ser Pro Thr Arg Gln Ser Pro Gly Ala Ala Gly Tyr
20 25 30

Asp Leu Tyr Ser Ala Tyr Asp Tyr Thr Ile Pro Pro Gly Glu Arg Gln
35 40 45

Leu Ile Lys Thr Asp Ile Ser Met Ser Met Pro Lys Ile Cys Tyr Gly
50 55 60

Arg Ile Ala Pro Arg Ser Gly Leu Ser Leu Lys Gly Ile Asp Ile Gly
65 70 75 80

Gly Gly Val Ile Asp Glu Asp Tyr Arg Gly Asn Ile Gly Val Ile Leu
85 90 95

Ile Asn Asn Gly Lys Cys Thr Phe Asn Val Asn Thr Gly Asp Arg Ile
100 105 110

Ala Gln Leu Ile Tyr Gln Arg Ile Tyr Tyr Pro Glu Leu Glu Glu Val
115 120 125

Gln Ser Leu Asp Ser Thr Asn Arg Gly Asp Gln Gly Phe Gly Ser Thr
130 135 140

Gly Leu Arg
145

<210> 91
<211> 480
<212> PRT
<213> Vaccinia virus

<400> 91
Met Pro Ile Phe Val Asn Thr Val Tyr Cys Lys Asn Ile Leu Ala Leu
1   5   10   15

Ser Met Thr Lys Lys Phe Lys Thr Ile Ile Asp Ala Ile Gly Gly Asn
            20   25   30

Ile Ile Val Asn Ser Thr Ile Leu Lys Lys Leu Ser Pro Tyr Phe Arg
        35   40   45

Thr His Leu Arg Gln Lys Tyr Thr Lys Asn Lys Asp Pro Val Thr Arg
    50   55   60

Val Cys Leu Asp Leu Asp Ile His Ser Leu Thr Ser Ile Val Ile Tyr
65   70   75   80

Ser Tyr Thr Gly Lys Val Tyr Ile Asp Ser His Asn Val Val Asn Leu
                85   90   95

Leu Arg Ala Ser Ile Leu Thr Ser Val Glu Phe Ile Ile Tyr Thr Cys
            100   105   110

Ile Asn Phe Ile Leu Arg Asp Phe Arg Lys Glu Tyr Cys Val Glu Cys
        115   120   125

Tyr Met Met Gly Ile Glu Tyr Gly Leu Ser Asn Leu Leu Cys His Thr
    130   135   140

Lys Asn Phe Ile Ala Lys His Phe Leu Glu Leu Glu Asp Asp Ile Ile
145   150   155   160

Asp Asn Phe Asp Tyr Leu Ser Met Lys Leu Ile Leu Glu Ser Asp Glu
                165   170   175

```
Leu Asn Val Pro Asp Glu Asp Tyr Val Val Asp Phe Val Ile Lys Trp
            180                 185                 190

Tyr Ile Lys Arg Arg Asn Lys Leu Gly Asn Leu Leu Leu Leu Ile Lys
        195                 200                 205

Asn Val Ile Arg Ser Asn Tyr Leu Ser Pro Arg Gly Ile Asn Asn Val
    210                 215                 220

Lys Trp Ile Leu Asp Cys Thr Lys Ile Phe His Cys Asp Lys Gln Pro
225                 230                 235                 240

Arg Lys Ser Tyr Lys Tyr Pro Phe Ile Glu Tyr Pro Met Asn Met Asp
                245                 250                 255

Gln Ile Ile Asp Ile Phe His Met Cys Thr Ser Thr His Val Gly Glu
            260                 265                 270

Val Val Tyr Leu Ile Gly Gly Trp Met Asn Asn Glu Ile His Asn Asn
        275                 280                 285

Ala Ile Ala Val Asn Tyr Ile Ser Asn Asn Trp Ile Pro Ile Pro Pro
    290                 295                 300

Met Asn Ser Pro Arg Leu Tyr Ala Ser Gly Ile Pro Ala Asn Asn Lys
305                 310                 315                 320

Leu Tyr Val Val Gly Gly Leu Pro Asn Pro Thr Ser Val Glu Arg Trp
                325                 330                 335

Phe His Gly Asp Ala Ala Trp Val Asn Met Pro Ser Leu Leu Lys Pro
            340                 345                 350

Arg Cys Asn Pro Ala Val Ala Ser Ile Asn Asn Val Ile Tyr Val Met
        355                 360                 365

Gly Gly His Ser Glu Thr Asp Thr Thr Thr Glu Tyr Leu Leu Pro Asn
```

```
    370                 375                 380

His Asp Gln Trp Gln Phe Gly Pro Ser Thr Tyr Tyr Pro His Tyr Lys
385                 390                 395                 400

Ser Cys Ala Leu Val Phe Gly Arg Arg Leu Phe Leu Val Gly Arg Asn
                405                 410                 415

Ala Glu Phe Tyr Cys Glu Ser Ser Asn Thr Trp Thr Leu Ile Asp Asp
            420                 425                 430

Pro Ile Tyr Pro Arg Asp Asn Pro Glu Leu Ile Ile Val Asp Asn Lys
        435                 440                 445

Leu Leu Leu Ile Gly Gly Phe Tyr Arg Glu Ser Tyr Ile Asp Thr Ile
    450                 455                 460

Glu Val Tyr Asn His His Thr Tyr Ser Trp Asn Ile Trp Asp Gly Lys
465                 470                 475                 480
```

<210> 92
<211> 512
<212> PRT
<213> Vaccinia virus

<400> 92

```
Met Glu Ser Val Ile Phe Ser Ile Asn Gly Glu Ile Ile Gln Val Asn
1               5                   10                  15

Lys Glu Ile Ile Thr Ala Ser Pro Tyr Asn Phe Phe Lys Arg Ile Gln
            20                  25                  30

Asp His His Leu Lys Asp Glu Ala Ile Ile Leu Asn Gly Ile Asn Tyr
        35                  40                  45

His Ala Phe Glu Ser Leu Leu Asp Tyr Met Arg Trp Lys Lys Ile Asn
    50                  55                  60

Ile Thr Ile Asn Asn Val Glu Met Ile Leu Val Ala Ala Ile Ile Ile
```

```
65                  70                  75                  80

Asp Val Pro Pro Val Val Asp Leu Cys Val Lys Thr Met Ile His Asn
                85                  90                  95

Ile Asn Phe Thr Asn Cys Ile Arg Met Phe Asn Phe Ser Lys Arg Tyr
            100                 105                 110

Gly Ile Lys Lys Leu Tyr Asn Ala Ser Met Ser Glu Ile Ile Asn Asn
        115                 120                 125

Ile Thr Ala Val Thr Ser Asp Pro Glu Phe Gly Lys Leu Ser Lys Asp
    130                 135                 140

Glu Leu Thr Thr Ile Leu Ser His Glu Asp Val Asn Val Asn His Glu
145                 150                 155                 160

Asp Val Thr Ala Met Ile Leu Leu Lys Trp Ile His Lys Asn Pro Asn
                165                 170                 175

Asp Val Asp Ile Ile Asn Ile Leu His Pro Lys Phe Met Thr Asn Thr
            180                 185                 190

Met Arg Asn Ala Ile Ser Leu Leu Gly Leu Thr Ile Ser Lys Ser Thr
        195                 200                 205

Lys Pro Val Thr Arg Asn Gly Ile Lys His Asn Ile Val Val Ile Lys
    210                 215                 220

Asn Ser Asp Tyr Ile Ser Thr Ile Thr His Tyr Ser Pro Arg Thr Glu
225                 230                 235                 240

Tyr Trp Thr Ile Val Gly Asn Thr Asp Arg Gln Phe Tyr Asn Ala Asn
                245                 250                 255

Val Leu His Asn Cys Leu Tyr Ile Ile Gly Gly Met Ile Asn Asn Arg
            260                 265                 270
```

```
His Val Tyr Ser Val Ser Arg Val Asp Leu Lys Thr Lys Lys Trp Lys
        275                 280                 285

Thr Val Thr Asn Met Ser Ser Leu Lys Ser Glu Val Ser Thr Cys Val
    290                 295                 300

Asn Asp Gly Lys Leu Tyr Val Ile Gly Gly Leu Glu Phe Ser Ile Ser
305                 310                 315                 320

Thr Gly Val Ala Glu Tyr Leu Lys His Gly Thr Ser Lys Trp Ile Arg
                325                 330                 335

Leu Pro Asn Leu Ile Thr Pro Arg Tyr Ser Gly Ala Ser Val Phe Val
            340                 345                 350

Asn Asp Asp Ile Tyr Val Met Gly Gly Val Tyr Thr Thr Tyr Glu Lys
        355                 360                 365

Tyr Val Val Leu Asn Asp Val Glu Cys Phe Thr Lys Asn Arg Trp Ile
    370                 375                 380

Lys Lys Ser Pro Met Pro Arg His His Ser Ile Val Tyr Ala Val Glu
385                 390                 395                 400

Tyr Asp Gly Asp Ile Tyr Val Ile Thr Gly Ile Thr His Glu Thr Arg
                405                 410                 415

Asn Tyr Leu Tyr Lys Tyr Ile Val Lys Glu Asp Lys Trp Ile Glu Leu
            420                 425                 430

Tyr Met Tyr Phe Asn His Val Gly Lys Met Phe Val Cys Ser Cys Gly
        435                 440                 445

Asp Tyr Ile Leu Ile Ile Ala Asp Ala Lys Tyr Glu Tyr Tyr Pro Lys
    450                 455                 460

Ser Asn Thr Trp Asn Leu Phe Asp Met Ser Thr Arg Asn Ile Glu Tyr
```

```
465                 470                 475                 480

Tyr Asp Met Phe Thr Lys Asp Glu Thr Pro Lys Cys Asn Val Thr His
                485                 490                 495

Lys Ser Leu Pro Ser Phe Leu Ser Asn Cys Glu Lys Gln Phe Leu Gln
            500                 505                 510


<210> 93
<211> 224
<212> PRT
<213> Vaccinia virus

<400> 93
Met Val Lys Asn Asn Lys Ile Ser Asn Ser Cys Arg Met Ile Met Ser
1               5                   10                  15

Thr Asn Pro Asn Asn Ile Leu Met Arg His Leu Lys Asn Leu Thr Asp
            20                  25                  30

Asp Glu Phe Lys Cys Ile Ile His Arg Ser Ser Asp Phe Leu Tyr Leu
        35                  40                  45

Ser Asp Ser Asp Tyr Thr Ser Ile Thr Lys Glu Thr Leu Val Ser Glu
    50                  55                  60

Ile Val Glu Glu Tyr Pro Asp Asp Cys Asn Lys Ile Leu Ala Ile Ile
65                  70                  75                  80

Phe Leu Val Leu Asp Lys Asp Ile Asp Val Asp Ile Glu Thr Lys Leu
                85                  90                  95

Lys Pro Lys Pro Ala Val Arg Phe Ala Ile Leu Asp Lys Met Thr Ala
            100                 105                 110

Asp Ile Lys Leu Thr Asp Leu Val Arg His Tyr Phe Arg Tyr Ile Glu
        115                 120                 125

Gln Asp Ile Pro Leu Gly Pro Leu Phe Lys Lys Ile Asp Ser Tyr Arg
```

```
    130                 135                 140

Thr Arg Ala Ile Asn Lys Tyr Ser Lys Glu Leu Gly Leu Ala Thr Glu
145                 150                 155                 160

Tyr Phe Asn Lys Tyr Gly His Leu Met Phe Tyr Thr Leu Pro Ile Pro
                165                 170                 175

Tyr Asn Arg Phe Phe Cys Arg Asn Ser Ile Gly Phe Leu Ala Val Leu
            180                 185                 190

Ser Pro Thr Ile Gly His Val Lys Ala Phe Tyr Lys Phe Ile Glu Tyr
        195                 200                 205

Val Ser Ile Asp Asp Arg Arg Lys Phe Lys Lys Glu Leu Met Ser Lys
    210                 215                 220
```

<210> 94
<211> 117
<212> PRT
<213> Vaccinia virus

<400> 94

```
Met Arg Thr Leu Leu Ile Arg Tyr Ile Leu Trp Arg Asn Asp Asn Asp
1               5                   10                  15

Gln Thr Tyr Tyr Asn Asp Asp Phe Lys Lys Leu Met Leu Leu Asp Glu
            20                  25                  30

Leu Val Asp Asp Gly Asp Val Cys Thr Leu Ile Lys Asn Met Arg Met
        35                  40                  45

Thr Leu Ser Asp Gly Pro Leu Leu Asp Arg Leu Asn Gln Pro Val Asn
    50                  55                  60

Asn Ile Glu Asp Ala Lys Arg Met Ile Ala Ile Ser Ala Lys Val Ala
65                  70                  75                  80

Arg Asp Ile Gly Glu Arg Ser Glu Ile Arg Trp Glu Glu Ser Phe Thr
```

```
                85                  90                  95

Ile Leu Phe Arg Met Ile Glu Thr Tyr Phe Asp Asp Leu Met Ile Asp
            100                 105                 110

Leu Tyr Gly Glu Lys
        115
```

<210> 95
<211> 175
<212> PRT
<213> Vaccinia virus

<400> 95

```
Met Thr Ser Ser Ala Met Asp Asn Asn Glu Pro Lys Val Leu Glu Met
1               5                   10                  15

Val Tyr Asp Ala Thr Ile Leu Pro Glu Gly Ser Ser Met Asp Pro Asn
            20                  25                  30

Ile Met Asp Cys Ile Asn Arg His Ile Asn Met Cys Ile Gln Arg Thr
        35                  40                  45

Tyr Ser Ser Ser Ile Ile Ala Ile Leu Asp Arg Phe Leu Thr Met Asn
    50                  55                  60

Lys Asp Glu Leu Asn Asn Thr Gln Cys His Ile Ile Lys Glu Phe Met
65                  70                  75                  80

Thr Tyr Glu Gln Met Ala Ile Asp His Tyr Gly Glu Tyr Val Asn Ala
                85                  90                  95

Ile Leu Tyr Gln Ile Arg Lys Arg Pro Asn Gln His His Thr Ile Asp
            100                 105                 110

Leu Phe Lys Lys Ile Lys Arg Thr Arg Tyr Asp Thr Phe Lys Val Asp
        115                 120                 125

Pro Val Glu Phe Val Lys Lys Val Ile Gly Phe Val Ser Ile Leu Asn
```

130 135 140

Lys Tyr Lys Pro Val Tyr Ser Tyr Val Leu Tyr Glu Asn Val Leu Tyr
145 150 155 160

Asp Glu Phe Lys Cys Phe Ile Asp Tyr Val Glu Thr Lys Tyr Phe
165 170 175

<210> 96
<211> 470
<212> PRT
<213> Vaccinia virus

<400> 96
Met Ile Phe Val Ile Glu Ser Lys Leu Leu Gln Ile Tyr Arg Asn Arg
1 5 10 15

Asn Ile Asn Phe Tyr Thr Thr Met Asp Asn Ile Met Ser Ala Glu Tyr
20 25 30

Tyr Leu Ser Leu Tyr Ala Lys Tyr Asn Ser Lys Asn Leu Asp Val Phe
35 40 45

Arg Asn Met Leu Gln Ala Ile Glu Pro Ser Gly Asn Asn Tyr His Ile
50 55 60

Leu His Ala Tyr Cys Gly Ile Lys Gly Leu Asp Glu Arg Phe Val Glu
65 70 75 80

Glu Leu Leu His Arg Gly Tyr Ser Pro Asn Glu Thr Asp Asp Asp Gly
85 90 95

Asn Tyr Pro Leu His Ile Ala Ser Lys Ile Asn Asn Asn Arg Ile Val
100 105 110

Ala Met Leu Leu Thr His Gly Ala Asp Pro Asn Ala Cys Asp Lys Gln
115 120 125

His Lys Thr Pro Leu Tyr Tyr Leu Ser Gly Thr Asp Asp Glu Val Ile

```
    130                 135                 140

Glu Arg Ile Asn Leu Leu Val Gln Tyr Gly Ala Lys Ile Asn Asn Ser
145                 150                 155                 160

Val Asp Glu Glu Gly Cys Gly Pro Leu Leu Ala Cys Thr Asp Pro Ser
                165                 170                 175

Glu Arg Val Phe Lys Lys Ile Met Ser Ile Gly Phe Glu Ala Arg Ile
            180                 185                 190

Val Asp Lys Phe Gly Lys Asn His Ile His Arg His Leu Met Ser Asp
        195                 200                 205

Asn Pro Lys Ala Ser Thr Ile Ser Trp Met Met Lys Leu Gly Ile Ser
    210                 215                 220

Pro Ser Lys Pro Asp His Asp Gly Asn Thr Pro Leu His Ile Val Cys
225                 230                 235                 240

Ser Lys Thr Val Lys Asn Val Asp Ile Ile Asp Leu Leu Leu Pro Ser
                245                 250                 255

Thr Asp Val Asn Lys Gln Asn Lys Phe Gly Asp Ser Pro Leu Thr Leu
            260                 265                 270

Leu Ile Lys Thr Leu Ser Pro Ala His Leu Ile Asn Lys Leu Leu Ser
        275                 280                 285

Thr Ser Asn Val Ile Thr Asp Gln Thr Val Asn Ile Cys Ile Phe Tyr
    290                 295                 300

Asp Arg Asp Asp Val Leu Glu Ile Ile Asn Asp Lys Gly Lys Gln Tyr
305                 310                 315                 320

Asp Ser Thr Asp Phe Lys Met Ala Val Glu Val Gly Ser Ile Arg Cys
                325                 330                 335
```

```
Val Lys Tyr Leu Leu Asp Asn Asp Ile Ile Cys Glu Asp Ala Met Tyr
            340                 345                 350

Tyr Ala Val Leu Ser Glu Tyr Glu Thr Met Val Asp Tyr Leu Leu Phe
        355                 360                 365

Asn His Phe Ser Val Asp Ser Val Val Asn Gly His Thr Cys Met Ser
    370                 375                 380

Glu Cys Val Arg Leu Asn Asn Pro Val Ile Leu Ser Lys Leu Met Leu
385                 390                 395                 400

His Asn Pro Thr Ser Glu Thr Met Tyr Leu Thr Met Lys Ala Ile Glu
                405                 410                 415

Lys Asp Arg Leu Asp Lys Ser Ile Ile Ile Pro Phe Ile Ala Tyr Phe
            420                 425                 430

Val Leu Met His Pro Asp Phe Cys Lys Asn Arg Arg Tyr Phe Thr Ser
        435                 440                 445

Tyr Lys Arg Phe Val Thr Asp Tyr Val His Glu Gly Val Ser Tyr Glu
    450                 455                 460

Val Phe Asp Asp Tyr Phe
465                 470
```

<210> 97
<211> 220
<212> PRT
<213> Vaccinia virus

<400> 97

```
Met Val Tyr Lys Leu Val Leu Leu Phe Cys Ile Ala Ser Leu Gly Tyr
1               5                   10                  15

Ser Val Glu Tyr Lys Asn Thr Ile Cys Pro Pro Arg Gln Asp Tyr Arg
            20                  25                  30
```

```
Tyr Trp Tyr Phe Ala Ala Glu Leu Thr Ile Gly Val Asn Tyr Asp Ile
        35                  40                  45

Asn Ser Thr Ile Ile Gly Glu Cys His Met Ser Glu Ser Tyr Ile Asp
    50                  55                  60

Arg Asn Ala Asn Ile Val Leu Thr Gly Tyr Gly Leu Glu Ile Asn Met
65                  70                  75                  80

Thr Ile Met Asp Thr Asp Gln Arg Phe Val Ala Ala Ala Glu Gly Val
                85                  90                  95

Gly Lys Asp Asn Lys Leu Ser Val Leu Leu Phe Thr Thr Gln Arg Leu
            100                 105                 110

Asp Lys Val His His Asn Ile Ser Val Thr Ile Thr Cys Met Glu Met
        115                 120                 125

Asn Cys Gly Thr Thr Lys Tyr Asp Ser Asp Leu Pro Glu Ser Ile His
    130                 135                 140

Lys Ser Ser Ser Cys Asp Ile Thr Ile Asn Gly Ser Cys Val Thr Cys
145                 150                 155                 160

Val Asn Leu Glu Thr Asp Pro Thr Lys Ile Asn Pro His Tyr Leu His
                165                 170                 175

Pro Lys Asp Lys Tyr Leu Tyr His Asn Ser Glu Tyr Gly Met Arg Gly
            180                 185                 190

Ser Tyr Gly Val Thr Phe Ile Asp Glu Leu Asn Gln Cys Leu Leu Asp
        195                 200                 205

Ile Lys Glu Leu Ser Tyr Asp Ile Cys Tyr Arg Glu
    210                 215                 220
```

<210> 98

<211> 284
<212> PRT
<213> Vaccinia virus

<400> 98
Met Asp Leu Ser Arg Ile Asn Thr Trp Lys Ser Lys Gln Leu Lys Ser
1   5   10   15

Phe Leu Ser Ser Lys Asp Ala Phe Lys Ala Asp Ile Asn Gly His Ser
            20   25   30

Ala Leu Tyr Tyr Ala Ile Ala Asp Asn Asn Val Arg Leu Val Cys Thr
        35   40   45

Leu Leu Asn Ala Gly Ala Leu Lys Asn Leu Leu Glu Asn Glu Phe Pro
    50   55   60

Leu His Gln Ala Ala Thr Leu Glu Asp Thr Lys Ile Val Lys Ile Leu
65   70   75   80

Leu Phe Ser Gly Leu Asp Asp Ser Gln Phe Asp Asp Lys Gly Asn Thr
                85   90   95

Ala Leu Tyr Tyr Ala Val Asp Ser Gly Asn Met Gln Thr Val Lys Leu
            100   105   110

Phe Val Lys Lys Asn Trp Arg Leu Met Phe Tyr Gly Lys Thr Gly Trp
        115   120   125

Lys Thr Ser Phe Tyr His Ala Val Met Leu Asn Asp Val Ser Ile Val
    130   135   140

Ser Tyr Phe Leu Ser Glu Ile Pro Ser Thr Phe Asp Leu Ala Ile Leu
145   150   155   160

Leu Ser Cys Ile His Ile Thr Ile Lys Asn Gly His Val Asp Met Met
                165   170   175

Ile Leu Leu Leu Asp Tyr Met Thr Ser Thr Asn Thr Asn Asn Ser Leu

```
            180                 185                 190

Leu Phe Ile Pro Asp Ile Lys Leu Ala Ile Asp Asn Lys Asp Ile Glu
        195                 200                 205

Met Leu Gln Ala Leu Phe Lys Tyr Asp Ile Asn Ile Tyr Ser Ala Asn
    210                 215                 220

Leu Glu Asn Val Leu Leu Asp Asp Ala Glu Ile Ala Lys Met Ile Ile
225                 230                 235                 240

Glu Lys His Val Glu Tyr Lys Ser Asp Ser Tyr Thr Lys Asp Leu Asp
                245                 250                 255

Ile Val Lys Asn Asn Lys Leu Asp Glu Ile Ile Ser Lys Asn Lys Glu
            260                 265                 270

Leu Lys Leu Met Tyr Val Asn Cys Val Lys Lys Asn
        275                 280


<210> 99
<211> 309
<212> PRT
<213> Vaccinia virus

<400> 99
Ile Glu Leu Leu Lys Thr Met Asp Leu Arg Lys Arg Asp Leu Gly Pro
1               5                   10                  15

Ala Phe Thr Glu Leu Ile Ser Gly Leu Ala Lys Leu Lys Thr Ser Lys
            20                  25                  30

Tyr Thr Tyr Thr Asp Leu Thr Tyr Gln Ser Phe Val Asp Asn Thr Val
        35                  40                  45

Cys Ile Lys Pro Ser Tyr Tyr Gln Gln Tyr His Arg Phe Gly Leu Tyr
    50                  55                  60

Arg Leu Asn Phe Arg Arg Asp Ala Val Asn Lys Ile Asn Ser Ile Val
```

```
65                  70                  75                  80

Glu Arg Arg Ser Gly Met Ser Asn Val Val Asp Ser Asn Met Leu Asp
                85                  90                  95

Asn Asn Thr Leu Trp Ala Ile Ile Asn Thr Ile Tyr Phe Lys Gly Ile
            100                 105                 110

Trp Gln Tyr Pro Phe Asp Ile Thr Lys Thr Arg Asn Ala Ser Phe Thr
        115                 120                 125

Asn Lys Tyr Gly Thr Lys Thr Val Pro Met Met Asn Val Val Thr Lys
    130                 135                 140

Leu Gln Gly Asn Thr Ile Thr Ile Asp Asp Glu Glu Tyr Asp Met Val
145                 150                 155                 160

Arg Leu Pro Tyr Lys Asp Ala Asn Ile Ser Met Tyr Leu Ala Ile Gly
                165                 170                 175

Asp Asn Met Thr His Phe Thr Asp Ser Ile Thr Ala Ala Lys Leu Asp
            180                 185                 190

Tyr Trp Ser Ser Gln Leu Gly Asn Lys Val Tyr Asn Leu Lys Leu Pro
        195                 200                 205

Lys Phe Ser Ile Glu Asn Lys Arg Asp Ile Lys Ser Ile Ala Glu Met
    210                 215                 220

Met Ala Pro Ser Met Phe Asn Pro Asp Asn Ala Ser Phe Lys His Met
225                 230                 235                 240

Thr Arg Asp Pro Leu Tyr Ile Tyr Lys Met Phe Gln Asn Ala Lys Ile
                245                 250                 255

Asp Val Asp Glu Gln Gly Thr Val Ala Glu Ala Ser Thr Ile Met Val
            260                 265                 270
```

Ala Thr Ala Arg Ser Ser Pro Glu Lys Leu Glu Phe Asn Thr Pro Phe
        275   280   285

Val Phe Ile Ile Arg His Asp Ile Thr Gly Phe Ile Leu Phe Met Gly
    290   295   300

Lys Val Glu Ser Pro
305

<210> 100
<211> 88
<212> PRT
<213> Vaccinia virus

<400> 100
Met Leu Ala Phe Cys Tyr Ser Leu Pro Asn Ala Gly Asp Val Ile Lys
1   5   10   15

Gly Arg Val Tyr Glu Asn Asp Tyr Ala Leu Tyr Ile Tyr Leu Phe Asp
            20   25   30

Tyr Pro His Ser Glu Ala Ile Leu Ala Glu Ser Val Lys Met His Met
        35   40   45

Asp Arg Tyr Val Glu Tyr Arg Asp Lys Leu Val Gly Lys Thr Val Lys
    50   55   60

Val Lys Val Ile Arg Val Asp Tyr Thr Lys Gly Tyr Ile Asp Val Asn
65   70   75   80

Tyr Lys Arg Met Cys Arg His Gln
                85

<210> 101
<211> 424
<212> PRT
<213> Vaccinia virus

<400> 101
Met Asn Pro Asp Asn Thr Ile Ala Val Ile Thr Glu Thr Ile Pro Ile

```
1               5                   10                  15

Gly Met Gln Phe Asp Lys Val Tyr Leu Ser Thr Phe Asn Met Trp Arg
            20                  25                  30

Glu Ile Leu Ser Asn Thr Thr Lys Thr Leu Asp Ile Ser Ser Phe Tyr
        35                  40                  45

Trp Ser Leu Ser Asp Glu Val Gly Thr Asn Phe Gly Thr Ile Ile Leu
    50                  55                  60

Asn Glu Ile Val Gln Leu Pro Lys Arg Gly Val Arg Val Arg Val Ala
65                  70                  75                  80

Val Asn Lys Ser Asn Lys Pro Leu Lys Asp Val Glu Arg Leu Gln Met
                85                  90                  95

Ala Gly Val Glu Val Arg Tyr Ile Asp Ile Thr Asn Ile Leu Gly Gly
            100                 105                 110

Val Leu His Thr Lys Phe Trp Ile Ser Asp Asn Thr His Ile Tyr Leu
        115                 120                 125

Gly Ser Ala Asn Met Asp Trp Arg Ser Leu Thr Gln Val Lys Glu Leu
    130                 135                 140

Gly Ile Ala Ile Phe Asn Asn Arg Asn Leu Ala Ala Asp Leu Thr Gln
145                 150                 155                 160

Ile Phe Glu Val Tyr Trp Tyr Leu Gly Val Asn Asn Leu Pro Tyr Asn
                165                 170                 175

Trp Lys Asn Phe Tyr Pro Ser Tyr Tyr Asn Thr Asp His Pro Leu Ser
            180                 185                 190

Ile Asn Val Ser Gly Val Pro His Ser Val Phe Ile Ala Ser Ala Pro
        195                 200                 205
```

```
Gln Gln Leu Cys Thr Met Glu Arg Thr Asn Asp Leu Thr Ala Leu Leu
    210                 215                 220

Ser Cys Ile Arg Asn Ala Ser Lys Phe Val Tyr Val Ser Val Met Asn
225                 230                 235                 240

Phe Ile Pro Ile Ile Tyr Ser Lys Ala Gly Lys Ile Leu Phe Trp Pro
                245                 250                 255

Tyr Ile Glu Asp Glu Leu Arg Arg Ser Ala Ile Asp Arg Gln Val Ser
            260                 265                 270

Val Lys Leu Leu Ile Ser Cys Trp Gln Arg Ser Ser Phe Ile Met Arg
        275                 280                 285

Asn Phe Leu Arg Ser Ile Ala Met Leu Lys Ser Lys Asn Ile Asn Ile
    290                 295                 300

Glu Val Lys Leu Phe Ile Val Pro Asp Ala Asp Pro Pro Ile Pro Tyr
305                 310                 315                 320

Ser Arg Val Asn His Ala Lys Tyr Met Val Thr Asp Lys Thr Ala Tyr
                325                 330                 335

Ile Gly Thr Ser Asn Trp Thr Gly Asn Tyr Phe Thr Asp Thr Cys Gly
            340                 345                 350

Ala Ser Ile Asn Ile Thr Pro Asp Asp Gly Leu Gly Leu Arg Gln Gln
        355                 360                 365

Leu Glu Asp Ile Phe Met Arg Asp Trp Asn Ser Lys Tyr Ser Tyr Glu
    370                 375                 380

Leu Tyr Asp Thr Ser Pro Thr Lys Arg Cys Lys Leu Leu Lys Asn Met
385                 390                 395                 400

Lys Gln Cys Thr Asn Asp Ile Tyr Cys Asp Glu Ile Gln Pro Glu Lys
```

405 410 415

Glu Ile Pro Glu Tyr Ser Leu Glu
420

<210> 102
<211> 175
<212> PRT
<213> Vaccinia virus

<400> 102
Met Gly His Ser Met Gly Ala Thr Ile Ser Ile Leu Ala Ser Tyr Asp
1 5 10 15

Asn Pro Asn Leu Phe Thr Ala Met Ile Leu Met Ser Pro Leu Val Asn
20 25 30

Ala Asp Ala Val Ser Arg Leu Asn Leu Leu Ala Ala Lys Leu Met Gly
35 40 45

Thr Ile Thr Pro Asn Ala Pro Val Gly Lys Leu Cys Pro Glu Ser Val
50 55 60

Ser Arg Asp Met Asp Lys Val Tyr Lys Tyr Gln Tyr Asp Pro Leu Ile
65 70 75 80

Asn His Glu Lys Ile Lys Ala Gly Phe Ala Ser Gln Val Leu Lys Ala
85 90 95

Thr Asn Lys Val Arg Lys Ile Ile Ser Lys Ile Asn Thr Pro Pro Thr
100 105 110

Leu Ile Leu Gln Gly Thr Asn Asn Lys Ile Ser Asp Val Leu Gly Ala
115 120 125

Tyr Tyr Phe Met Gln His Ala Asn Cys Asn Arg Glu Ile Lys Ile Tyr
130 135 140

Glu Gly Ala Lys His His Leu His Lys Glu Thr Asp Glu Val Lys Lys

145 150 155 160

Ser Val Met Lys Glu Ile Glu Thr Trp Ile Phe Asn Arg Val Lys
165 170 175

<210> 103
<211> 81
<212> PRT
<213> Vaccinia virus

<400> 103
Met Ser Ala Asn Cys Met Phe Asn Leu Asp Asn Asp Tyr Ile Tyr Trp
1 5 10 15

Lys Pro Ile Thr Tyr Pro Lys Ala Leu Val Phe Ile Ser His Gly Ala
20 25 30

Gly Lys His Ser Gly Arg Tyr Asp Glu Leu Ala Glu Asn Ile Ser Ser
35 40 45

Leu Gly Ile Leu Val Phe Ser His Asp His Ile Gly His Gly Arg Ser
50 55 60

Asn Gly Glu Lys Met Met Ile Asp Asp Phe Gly Thr Ala Arg Gly Asn
65 70 75 80

Tyr

<210> 104
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 104
Met Ala Thr Lys Leu Asp Tyr Glu Asp Ala Val Phe Tyr Phe Val Asp
1 5 10 15

Asp Asp Lys Ile Cys Ser Arg Asp Ser Ile Ile Asp Leu Ile Asp Glu
20 25 30

```
Tyr Ile Thr Trp Arg Asn His Val Ile Val Phe Asn Lys Asp Ile Thr
        35                  40                  45

Ser Cys Gly Arg Leu Tyr Lys Glu Leu Met Lys Phe Asp Asp Val Ala
    50                  55                  60

Ile Arg Tyr Tyr Gly Ile Asp Lys Ile Asn Glu Ile Val Glu Ala Met
65                  70                  75                  80

Ser Glu Gly Asp His Tyr Ile Asn Phe Thr Lys Val His Asp Gln Glu
                85                  90                  95

Ser Leu Phe Ala Thr Ile Gly Ile Cys Ala Lys Ile Thr Glu His Trp
            100                 105                 110

Gly Tyr Lys Lys Ile Ser Glu Ser Arg Phe Gln Ser Leu Gly Asn Ile
        115                 120                 125

Thr Asp Leu Met Thr Asp Asp Asn Ile Asn Ile Leu Ile Leu Phe Leu
    130                 135                 140

Glu Lys Lys Leu Asn
145


<210> 105
<211> 226
<212> PRT
<213> Vaccinia virus

<400> 105
Met Leu Ser Met Phe Met Cys Asn Asn Ile Val Asp Tyr Val Asp Asp
1               5                   10                  15

Ile Asp Asn Gly Ile Val Gln Asp Ile Glu Asp Glu Ala Ser Asn Asn
            20                  25                  30

Val Asp His Asp Tyr Val Tyr Pro Leu Pro Glu Asn Met Val Tyr Arg
        35                  40                  45
```

```
Phe Asp Lys Ser Thr Asn Ile Leu Asp Tyr Leu Ser Thr Glu Arg Asp
    50                  55                  60

His Val Met Met Ala Val Arg Tyr Tyr Met Ser Lys Gln Arg Leu Asp
65                  70                  75                  80

Asp Leu Tyr Arg Gln Leu Pro Thr Lys Thr Arg Ser Tyr Ile Asp Ile
                85                  90                  95

Ile Asn Ile Tyr Cys Asp Lys Val Ser Asn Asp Tyr Asn Arg Asp Met
            100                 105                 110

Asn Ile Met Tyr Asp Met Ala Ser Thr Lys Ser Phe Thr Val Tyr Asp
        115                 120                 125

Ile Asn Asn Glu Val Asn Thr Ile Leu Met Asp Asn Lys Gly Leu Gly
    130                 135                 140

Val Arg Leu Ala Thr Ile Ser Phe Ile Thr Glu Leu Gly Arg Arg Cys
145                 150                 155                 160

Met Asn Pro Val Lys Thr Ile Lys Met Phe Thr Leu Leu Ser His Thr
                165                 170                 175

Ile Cys Asp Asp Cys Phe Val Asp Tyr Ile Thr Asp Ile Ser Pro Pro
            180                 185                 190

Asp Asn Thr Ile Pro Asn Thr Ser Thr Arg Glu Tyr Leu Lys Leu Ile
        195                 200                 205

Gly Ile Thr Ala Ile Met Phe Ala Thr Tyr Lys Thr Leu Lys Tyr Met
    210                 215                 220

Ile Gly
225
```

<210> 106

<211> 147
<212> PRT
<213> Vaccinia virus

<400> 106
Met Phe Asn Met Asn Ile Asn Ser Pro Val Arg Phe Val Lys Glu Thr
1   5   10   15

Asn Arg Ala Lys Ser Pro Thr Arg Gln Ser Pro Gly Ala Ala Gly Tyr
            20   25   30

Asp Leu Tyr Ser Ala Tyr Asp Tyr Thr Ile Pro Pro Gly Glu Arg Gln
        35   40   45

Leu Ile Lys Thr Asp Ile Ser Met Ser Met Pro Lys Phe Cys Tyr Gly
    50   55   60

Arg Ile Ala Pro Arg Ser Gly Leu Ser Leu Lys Gly Ile Asp Ile Gly
65   70   75   80

Gly Gly Val Ile Asp Glu Asp Tyr Arg Gly Asn Ile Gly Val Ile Leu
                85   90   95

Ile Asn Asn Gly Lys Cys Thr Phe Asn Val Asn Thr Gly Asp Arg Ile
            100   105   110

Ala Gln Leu Ile Tyr Gln Arg Ile Tyr Tyr Pro Glu Leu Glu Glu Val
        115   120   125

Gln Ser Leu Asp Ser Thr Asn Arg Gly Asp Gln Gly Phe Gly Ser Thr
    130   135   140

Gly Leu Arg
145

<210> 107
<211> 480
<212> PRT
<213> Vaccinia virus

<400> 107
Met Pro Ile Phe Val Asn Thr Val Tyr Cys Lys Asn Ile Leu Ala Leu
1   5   10   15

Ser Met Thr Lys Lys Phe Lys Thr Ile Ile Asp Ala Ile Gly Gly Asn
            20   25   30

Ile Ile Val Asn Ser Thr Ile Leu Lys Lys Leu Ser Pro Tyr Phe Arg
        35   40   45

Thr His Leu Arg Gln Lys Tyr Thr Lys Asn Lys Asp Pro Val Thr Arg
    50   55   60

Val Cys Leu Asp Leu Asp Ile His Ser Leu Thr Ser Ile Val Ile Tyr
65   70   75   80

Ser Tyr Thr Gly Lys Val Tyr Ile Asp Ser His Asn Val Val Asn Leu
                85   90   95

Leu Arg Ala Ser Ile Leu Thr Ser Val Glu Phe Ile Ile Tyr Thr Cys
            100   105   110

Ile Asn Phe Ile Leu Arg Asp Phe Arg Lys Glu Tyr Cys Val Glu Cys
        115   120   125

Tyr Met Met Gly Ile Glu Tyr Gly Leu Ser Asn Leu Leu Cys His Thr
    130   135   140

Lys Asn Phe Ile Ala Lys His Phe Leu Glu Leu Glu Asp Asp Ile Ile
145   150   155   160

Asp Asn Phe Asp Tyr Leu Ser Ile Lys Leu Ile Leu Glu Ser Asp Glu
                165   170   175

Leu Asn Val Pro Asp Glu Asp Tyr Val Val Asp Phe Val Ile Lys Trp
            180   185   190

Tyr Ile Lys Arg Arg Asn Lys Leu Gly Asn Leu Leu Leu Leu Ile Lys

```
        195                 200                 205

Asn Val Ile Arg Ser Asn Tyr Leu Ser Pro Arg Gly Ile Asn Asn Val
    210                 215                 220

Lys Trp Ile Leu Asp Cys Thr Lys Ile Phe His Cys Asp Lys Gln Pro
225                 230                 235                 240

Arg Lys Ser Tyr Lys Tyr Pro Phe Ile Glu Tyr Pro Met Asn Met Asp
                245                 250                 255

Gln Ile Ile Asp Ile Phe His Met Cys Thr Ser Thr His Val Gly Glu
            260                 265                 270

Val Val Tyr Leu Ile Gly Gly Trp Met Asn Asn Glu Ile His Asn Asn
        275                 280                 285

Ala Ile Ala Val Asn Tyr Ile Ser Asn Asn Trp Ile Pro Ile Pro Pro
    290                 295                 300

Met Asn Ser Pro Arg Leu Tyr Ala Ser Gly Ile Pro Ala Asn Asn Lys
305                 310                 315                 320

Leu Tyr Val Val Gly Gly Leu Pro Asn Pro Thr Ser Val Glu Arg Trp
                325                 330                 335

Phe His Gly Asp Ala Ala Trp Val Asn Met Pro Ser Leu Leu Lys Pro
            340                 345                 350

Arg Cys Asn Pro Ala Val Ala Ser Ile Asn Asn Val Ile Tyr Val Met
        355                 360                 365

Gly Gly His Ser Glu Thr Asp Thr Thr Thr Glu Tyr Leu Leu Pro Asn
    370                 375                 380

His Asp Gln Trp Gln Phe Gly Pro Ser Thr Tyr Tyr Pro His Tyr Lys
385                 390                 395                 400
```

Ser Cys Ala Leu Val Phe Gly Arg Arg Leu Phe Leu Val Gly Arg Asn
405 410 415

Ala Glu Phe Tyr Cys Glu Ser Ser Asn Thr Trp Thr Leu Ile Asp Asp
420 425 430

Pro Ile Tyr Pro Arg Asp Asn Pro Glu Leu Ile Ile Val Asp Asn Lys
435 440 445

Leu Leu Leu Ile Gly Gly Phe Tyr Arg Glu Ser Tyr Ile Asp Thr Ile
450 455 460

Glu Val Tyr Asn His His Thr Tyr Ser Trp Asn Ile Trp Asp Gly Lys
465 470 475 480

<210> 108
<211> 222
<212> PRT
<213> Vaccinia virus

<400> 108
Met Asn His Cys Leu Leu Ala Ile Ser Ala Val Tyr Phe Lys Ala Lys
1 5 10 15

Trp Leu Thr Pro Phe Glu Lys Glu Phe Thr Ser Asp Tyr Pro Phe Tyr
20 25 30

Val Ser Pro Thr Glu Met Val Asp Val Ser Met Met Ser Met Tyr Gly
35 40 45

Glu Leu Phe Asn His Ala Ser Val Lys Glu Ser Phe Gly Asn Phe Ser
50 55 60

Ile Ile Glu Leu Pro Tyr Val Gly Asp Thr Ser Met Met Val Ile Leu
65 70 75 80

Pro Asp Lys Ile Asp Gly Leu Glu Ser Ile Glu Gln Asn Leu Thr Asp
85 90 95

```
Thr Asn Phe Lys Lys Trp Cys Asn Ser Leu Asp Ala Met Phe Ile Asp
            100                 105                 110


Val His Ile Pro Lys Phe Lys Val Thr Gly Ser Tyr Asn Leu Val Asp
        115                 120                 125


Thr Leu Val Lys Ser Gly Leu Thr Glu Val Phe Gly Ser Thr Gly Asp
    130                 135                 140


Tyr Ser Asn Met Cys Asn Leu Asp Val Ser Val Asp Ala Met Ile His
145                 150                 155                 160


Lys Thr Tyr Ile Asp Val Asn Glu Glu Tyr Thr Glu Ala Ala Ala Ala
                165                 170                 175


Thr Cys Ala Leu Val Ser Asp Cys Ala Ser Thr Ile Thr Asn Glu Phe
            180                 185                 190


Cys Val Asp His Pro Phe Ile Tyr Val Ile Arg His Val Asp Gly Lys
        195                 200                 205


Ile Leu Phe Val Gly Arg Tyr Cys Ser Pro Thr Thr Asn Cys
    210                 215                 220


<210> 109
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 109
Met Thr Ala Asn Phe Ser Thr His Val Phe Ser Pro Gln His Cys Gly
1               5                   10                  15


Cys Asp Arg Leu Thr Ser Ile Asp Asp Val Lys Gln Cys Leu Thr Glu
            20                  25                  30


Tyr Ile Tyr Trp Ser Ser Tyr Ala Tyr Arg Asn Arg Gln Cys Ala Gly
        35                  40                  45
```

```
Gln Leu Tyr Ser Thr Leu Leu Ser Phe Arg Asp Asp Ala Glu Leu Val
    50                  55                  60

Phe Ile Asp Ile Arg Glu Leu Val Lys Asn Met Pro Trp Asp Asp Val
65                  70                  75                  80

Lys Asp Cys Thr Glu Ile Ile Arg Cys Tyr Ile Pro Asp Glu Gln Lys
                85                  90                  95

Thr Ile Arg Glu Ile Ser Ala Ile Ile Gly Leu Cys Ala Tyr Ala Ala
            100                 105                 110

Thr Tyr Trp Gly Gly Glu Asp His Pro Thr Ser Asn Ser Leu Asn Ala
        115                 120                 125

Leu Phe Val Met Leu Glu Met Leu Asn Tyr Val Asp Tyr Asn Ile Ile
    130                 135                 140

Phe Arg Arg Met Asn
145
```

<210> 110
<211> 91
<212> PRT
<213> Vaccinia virus

<400> 110

```
Met Tyr Asn Ser Ser Ile His Thr Pro Glu Tyr Asp Val Ile Ile His
1               5                   10                  15

Val Ile Glu His Leu Lys His His Lys Gln Cys Val Gln Thr Val Thr
            20                  25                  30

Ser Gly Met Val Phe Thr Ser Pro Val Ser Ser Ser Ile Cys Thr Lys
        35                  40                  45

Ser Asp Asp Gly Arg Asn Leu Ser Asp Gly Phe Leu Leu Ile Arg Tyr
    50                  55                  60
```

Ile Thr Thr Asp Asp Phe Cys Thr Ile Phe Asp Ile Ile Pro Arg His
65 70 75 80

Ile Phe Tyr Gln Leu Ala Asn Val Asp Glu His
85 90

<210> 111
<211> 30
<212> PRT
<213> Vaccinia virus

<400> 111
Met Ser Ile Leu Pro Val Ile Phe Leu Pro Ile Phe Phe Tyr Ser Ser
1 5 10 15

Phe Val Gln Thr Phe Asn Ala Ser Glu Cys Ile Asp Lys Gly
20 25 30

<210> 112
<211> 75
<212> PRT
<213> Vaccinia virus

<400> 112
Met Val Ile Ile Pro Gly Val Arg Cys Leu Ser Leu Leu Phe Leu Arg
1 5 10 15

Arg Arg Cys Pro Leu His Ile Ile Ser Ala Phe Thr Leu Leu Ala Ile
20 25 30

Asn Ala Leu Ile Leu Gly His Thr Ile Ser Pro Val Asp Leu Ser Phe
35 40 45

Thr Ile Cys Gly Tyr Glu Ile Lys Ser Ile Phe Asp Ser Glu Thr Asp
50 55 60

Thr Ile Val Lys Phe Asn Asp Ile Met Ser Gln
65 70 75

<210> 113

<211> 340
<212> PRT
<213> Vaccinia virus

<400> 113
Met Ser Arg Lys Phe Met Gln Val Tyr Glu Tyr Asp Arg Glu Gln Tyr
1   5   10   15

Leu Asp Glu Phe Ile Glu Asp Arg Tyr Asn Asp Ser Phe Ile Thr Ser
            20   25   30

Pro Glu Tyr Tyr Ser Ala Glu Lys Tyr Met Cys Arg Tyr Thr Thr Leu
        35   40   45

Asn His Asn Cys Val Asn Val Arg Arg Cys Ala Leu Asp Ser Lys Leu
    50   55   60

Leu His Asp Ile Ile Thr Asn Cys Lys Ile Tyr Asn Asn Ile Glu Leu
65   70   75   80

Val Arg Ala Thr Lys Phe Val Tyr Tyr Leu Asp Leu Ile Lys Cys Asn
                85   90   95

Trp Val Ser Lys Val Gly Asp Ser Val Leu Tyr Pro Val Ile Phe Ile
            100   105   110

Thr His Thr Ser Thr Arg Asn Leu Asp Lys Val Ser Val Lys Thr Tyr
        115   120   125

Lys Gly Val Lys Val Lys Lys Leu Asn Arg Cys Ala Asp His Ala Ile
    130   135   140

Val Ile Asn Pro Phe Val Lys Phe Lys Leu Thr Leu Pro Asn Lys Thr
145   150   155   160

Ser His Ala Lys Val Leu Val Thr Phe Cys Lys Leu Arg Thr Asp Ile
                165   170   175

Thr Pro Val Glu Ala Pro Leu Pro Gly Asn Val Leu Val Tyr Thr Phe

```
            180                 185                 190

Pro Asp Ile Asn Lys Arg Ile Pro Gly Tyr Ile His Val Asn Ile Glu
        195                 200                 205

Gly Cys Ile Asp Gly Met Ile Tyr Ile Asn Ser Ser Lys Phe Ala Cys
    210                 215                 220

Val Leu Lys Leu His Arg Ser Met Tyr Arg Ile Pro Pro Phe Pro Ile
225                 230                 235                 240

Asp Ile Cys Ser Cys Cys Ser Gln Tyr Thr Asn Asp Asp Ile Glu Ile
                245                 250                 255

Pro Ile His Asp Leu Ile Lys Asp Val Ala Ile Phe Lys Asn Lys Glu
            260                 265                 270

Thr Val Tyr Tyr Leu Lys Leu Asn Asn Lys Thr Ile Ala Arg Phe Thr
        275                 280                 285

Tyr Phe Asn Asn Ile Asp Thr Ala Ile Thr Gln Glu His Glu Tyr Val
    290                 295                 300

Lys Ile Ala Leu Gly Ile Val Cys Lys Leu Met Ile Asn Asn Met His
305                 310                 315                 320

Ser Ile Val Gly Val Asn His Ser Asn Thr Phe Val Asn Cys Leu Leu
                325                 330                 335

Glu Asp Asn Val
            340
```

<210> 114
<211> 574
<212> PRT
<213> Vaccinia virus

<400> 114
Met Ser Arg Arg Leu Ile Tyr Val Leu Asn Ile Asn Arg Lys Ser Thr

```
1               5                   10                  15

His Lys Ile Gln Glu Asn Glu Ile Tyr Thr Tyr Phe Ser His Cys Asn
            20                  25                  30

Ile Asp His Thr Ser Thr Glu Leu Asp Phe Val Val Lys Asn Tyr Asp
        35                  40                  45

Leu Asn Arg Arg Gln His Val Thr Gly Tyr Thr Ala Leu His Cys Tyr
    50                  55                  60

Leu Tyr Asn Asn Tyr Phe Thr Asn Asp Val Leu Lys Ile Leu Leu Asn
65                  70                  75                  80

His Asp Val Asn Val Thr Met Lys Thr Ser Ser Gly Arg Met Pro Val
                85                  90                  95

Tyr Ile Leu Leu Thr Arg Cys Cys Asn Ile Ser His Asp Val Val Ile
            100                 105                 110

Asp Met Ile Asp Lys Asp Lys Asn His Leu Ser His Arg Asp Tyr Ser
        115                 120                 125

Asn Leu Leu Leu Glu Tyr Ile Lys Ser Arg Tyr Met Leu Leu Lys Glu
    130                 135                 140

Glu Asp Ile Asp Glu Asn Ile Val Ser Thr Leu Leu Asp Lys Gly Ile
145                 150                 155                 160

Asp Pro Asn Phe Lys Gln Asp Gly Tyr Thr Ala Leu His Tyr Tyr Tyr
                165                 170                 175

Leu Cys Leu Ala His Val Tyr Lys Pro Gly Glu Cys Arg Lys Pro Ile
            180                 185                 190

Thr Ile Lys Lys Ala Lys Arg Ile Ile Ser Leu Phe Ile Gln His Gly
        195                 200                 205
```

```
Ala Asn Leu Asn Ala Leu Asp Asn Cys Gly Asn Thr Pro Phe His Leu
    210                 215                 220

Tyr Leu Ser Ile Glu Met Cys Asn Asn Ile His Met Thr Lys Met Leu
225                 230                 235                 240

Leu Thr Phe Asn Pro Asn Phe Lys Ile Cys Asn Asn His Gly Leu Thr
                245                 250                 255

Pro Ile Leu Cys Tyr Ile Thr Ser Asp Tyr Ile Gln His Asp Ile Leu
            260                 265                 270

Val Met Leu Ile His His Tyr Glu Thr Asn Val Gly Glu Met Pro Ile
        275                 280                 285

Asp Glu Arg Arg Met Ile Val Phe Glu Phe Ile Lys Thr Tyr Ser Thr
    290                 295                 300

Arg Pro Ala Asp Ser Ile Thr Tyr Leu Met Asn Arg Phe Lys Asn Ile
305                 310                 315                 320

Asn Ile Tyr Thr Arg Tyr Glu Gly Lys Thr Leu Leu His Val Ala Cys
                325                 330                 335

Glu Tyr Asn Asn Thr Gln Val Ile Asp Tyr Leu Ile Arg Ile Asn Gly
            340                 345                 350

Asp Ile Asn Ala Leu Thr Asp Asn Asn Lys His Ala Thr Gln Leu Ile
        355                 360                 365

Ile Asp Asn Lys Glu Asn Ser Pro Tyr Thr Ile Asn Cys Leu Leu Tyr
    370                 375                 380

Ile Leu Arg Tyr Ile Val Asp Lys Asn Val Ile Arg Ser Leu Val Asp
385                 390                 395                 400

Gln Leu Pro Ser Leu Pro Ile Phe Asp Ile Lys Ser Phe Glu Lys Phe
```

```
                405                 410                 415

Ile Ser Tyr Cys Ile Leu Leu Asp Asp Thr Phe Tyr Asp Arg His Val
            420                 425                 430

Lys Asn Arg Asp Ser Lys Thr Tyr Arg Tyr Ala Phe Ser Lys Tyr Met
        435                 440                 445

Ser Phe Asp Lys Tyr Asp Gly Ile Ile Thr Lys Cys His Asp Glu Thr
    450                 455                 460

Met Leu Leu Lys Leu Ser Thr Val Leu Asp Thr Thr Leu Tyr Ala Val
465                 470                 475                 480

Leu Arg Cys His Asn Ser Arg Lys Leu Arg Arg Tyr Leu Thr Glu Leu
                485                 490                 495

Lys Lys Tyr Asn Asn Asp Lys Ser Phe Lys Ile Tyr Ser Asn Ile Met
            500                 505                 510

Asn Glu Arg Tyr Leu Asn Val Tyr Tyr Lys Asp Met Tyr Val Ser Lys
        515                 520                 525

Val Tyr Asp Lys Leu Phe Pro Val Phe Thr Asp Lys Asn Cys Leu Leu
    530                 535                 540

Thr Leu Leu Pro Ser Glu Ile Ile Tyr Glu Ile Leu Tyr Met Leu Thr
545                 550                 555                 560

Ile Asn Asp Leu Tyr Asn Ile Ser Tyr Pro Pro Thr Lys Val
                565                 570


<210> 115
<211> 353
<212> PRT
<213> Vaccinia virus

<400> 115
Met Thr Met Lys Met Met Val His Ile Tyr Phe Val Ser Leu Ser Leu
```

```
1               5                   10                  15

Leu Leu Leu Leu Phe His Ser Tyr Ala Ile Asp Ile Glu Asn Glu Ile
            20                  25                  30

Thr Glu Phe Phe Asn Lys Met Arg Asp Thr Leu Pro Ala Lys Asp Ser
        35                  40                  45

Lys Trp Leu Asn Pro Ala Cys Met Phe Gly Gly Thr Met Asn Asp Met
    50                  55                  60

Ala Thr Leu Gly Glu Pro Phe Ser Ala Lys Cys Pro Pro Ile Glu Asp
65                  70                  75                  80

Ser Leu Leu Ser His Arg Tyr Lys Asp Tyr Val Val Lys Trp Glu Arg
                85                  90                  95

Leu Glu Lys Asn Arg Arg Arg Gln Val Ser Asn Lys Arg Val Lys His
            100                 105                 110

Gly Asp Leu Trp Ile Ala Asn Tyr Thr Ser Lys Phe Ser Asn Arg Arg
        115                 120                 125

Tyr Leu Cys Thr Val Thr Thr Lys Asn Gly Asp Cys Val Gln Gly Ile
    130                 135                 140

Val Arg Ser His Ile Lys Lys Pro Pro Ser Cys Ile Pro Lys Thr Tyr
145                 150                 155                 160

Glu Leu Gly Thr His Asp Lys Tyr Gly Ile Asp Leu Tyr Cys Gly Ile
                165                 170                 175

Leu Tyr Ala Lys His Tyr Asn Asn Ile Thr Trp Tyr Lys Asp Asn Lys
            180                 185                 190

Glu Ile Asn Ile Asp Asp Ile Lys Tyr Ser Gln Thr Gly Lys Glu Leu
        195                 200                 205
```

```
Ile Ile His Asn Pro Glu Leu Glu Asp Ser Gly Arg Tyr Asp Cys Tyr
    210                 215                 220

Val His Tyr Asp Asp Val Arg Ile Lys Asn Asp Ile Val Val Ser Arg
225                 230                 235                 240

Cys Lys Ile Leu Thr Val Ile Pro Ser Gln Asp His Arg Phe Lys Leu
                245                 250                 255

Ile Leu Asp Pro Lys Ile Asn Val Thr Ile Gly Glu Pro Ala Asn Ile
            260                 265                 270

Thr Cys Thr Ala Val Ser Thr Ser Leu Leu Ile Asp Asp Val Leu Ile
        275                 280                 285

Glu Trp Glu Asn Pro Ser Gly Trp Leu Ile Gly Phe Asp Phe Asp Val
    290                 295                 300

Tyr Ser Val Leu Thr Ser Arg Gly Gly Ile Thr Glu Ala Thr Leu Tyr
305                 310                 315                 320

Phe Glu Asn Val Thr Glu Glu Tyr Ile Gly Asn Thr Tyr Lys Cys Arg
                325                 330                 335

Gly His Asn Tyr Tyr Phe Glu Lys Thr Leu Thr Thr Thr Val Val Leu
            340                 345                 350

Glu
```

<210> 116
<211> 127
<212> PRT
<213> Vaccinia virus

<400> 116

```
Met Asp Glu Asp Thr Arg Leu Ser Arg Tyr Leu Tyr Leu Thr Asp Arg
1               5                   10                  15
```

```
Glu His Ile Asn Val Asp Ser Ile Lys Gln Leu Cys Lys Ile Ser Asp
            20                  25                  30

Pro Asn Ala Cys Tyr Arg Cys Gly Cys Thr Ala Leu His Glu Tyr Phe
        35                  40                  45

Tyr Asn Tyr Arg Ser Val Asn Gly Lys Tyr Lys Tyr Arg Tyr Asn Gly
    50                  55                  60

Tyr Tyr Gln Tyr Tyr Ser Ser Ser Asp Tyr Glu Asn Tyr Asn Glu Tyr
65                  70                  75                  80

Tyr Tyr Asp Asp Tyr Asp Arg Thr Gly Met Asn Ser Glu Ser Asp Ser
                85                  90                  95

Glu Ser Asp Asn Ile Ser Ile Lys Thr Glu Tyr Glu Asn Glu Tyr Glu
            100                 105                 110

Phe Tyr Asp Glu Thr Gln Asp Gln Ser Thr Gln His Asn Asp Leu
        115                 120                 125
```

<210> 117
<211> 91
<212> PRT
<213> Vaccinia virus

<400> 117

```
Met Ser Leu Glu Ser Phe Ile Ile Thr Thr Phe Asn Asn Asn Ser Ser
1               5                   10                  15

Thr Asn Ile Asp Asn Met Cys His Leu Tyr Val Lys Val Cys Pro Ser
            20                  25                  30

Ser Leu Leu Phe Arg Leu Phe Val Glu Cys Cys Asp Ile Asn Lys Leu
        35                  40                  45

Val Glu Gly Thr Thr Pro Leu His Cys Tyr Leu Met Asn Glu Gly Phe
    50                  55                  60
```

```
Glu Ser Ser Val Leu Lys Asn Leu Leu Lys Glu Tyr Val Met Asn Thr
65                  70                  75                  80


Phe Asn Val His Asp Ile His Tyr Thr Asn Ile
                85                  90


<210> 118
<211> 181
<212> PRT
<213> Vaccinia virus

<400> 118
Met Ile Ser Leu Ser Phe Leu Ile His Asn Pro Leu Lys Lys Trp Lys
1               5                   10                  15


Leu Lys Pro Ser Ile Ser Ile Asn Gly Tyr Arg Ser Thr Phe Thr Met
            20                  25                  30


Ala Phe Pro Cys Ala Gln Phe Arg Pro Cys His Cys His Ala Thr Lys
        35                  40                  45


Asp Ser Leu Asn Thr Val Ala Asp Val Arg His Cys Leu Thr Glu Tyr
    50                  55                  60


Ile Leu Trp Val Ser His Arg Trp Thr His Arg Glu Ser Ala Gly Ser
65                  70                  75                  80


Leu Tyr Arg Leu Leu Ile Ser Phe Arg Thr Asp Ala Thr Glu Leu Phe
                85                  90                  95


Gly Gly Glu Leu Lys Asp Ser Leu Pro Trp Asp Asn Ile Asp Asn Cys
            100                 105                 110


Val Glu Ile Ile Lys Cys Phe Ile Arg Asn Asp Ser Met Lys Thr Ala
        115                 120                 125


Glu Glu Leu Arg Ala Ile Ile Gly Leu Cys Thr Gln Ser Ala Ile Val
    130                 135                 140
```

```
Ser Gly Arg Val Phe Asn Asp Lys Tyr Ile Asp Ile Leu Leu Met Leu
145                 150                 155                 160


Arg Lys Ile Leu Asn Glu Asn Asp Tyr Leu Thr Leu Leu Asp His Ile
                165                 170                 175


Arg Thr Ala Lys Tyr
            180


<210> 119
<211> 386
<212> PRT
<213> Vaccinia virus

<400> 119
Met Ile Ala Phe Ile Ile Phe Arg Glu Ile Gly Ile Ile Ser Thr Arg
1               5                   10                  15


Ile Ala Met Asp Tyr Cys Gly Arg Glu Cys Thr Ile Leu Cys Arg Leu
            20                  25                  30


Leu Asp Glu Asp Val Thr Tyr Lys Lys Ile Lys Leu Glu Ile Glu Thr
        35                  40                  45


Cys His Asn Leu Ser Lys His Ile Asp Arg Arg Gly Asn Asn Ala Leu
    50                  55                  60


His Cys Tyr Val Ser Asn Lys Cys Asp Thr Asp Ile Lys Ile Val Arg
65                  70                  75                  80


Leu Leu Leu Ser Arg Gly Val Glu Arg Leu Cys Arg Asn Asn Glu Gly
                85                  90                  95


Leu Thr Pro Leu Gly Ala Tyr Ser Lys His Arg Tyr Val Lys Ser Gln
            100                 105                 110


Ile Val His Leu Leu Ile Ser Ser Tyr Ser Asn Ser Ser Asn Glu Leu
        115                 120                 125
```

```
Lys Ser Asn Ile Asn Asp Phe Asp Leu Ser Ser Asp Asn Ile Asp Leu
    130                 135                 140

Arg Leu Leu Lys Tyr Leu Ile Val Asp Lys Arg Ile Arg Pro Ser Lys
145                 150                 155                 160

Asn Thr Asn Tyr Ala Ile Asn Gly Leu Gly Leu Val Asp Ile Tyr Val
                165                 170                 175

Thr Thr Pro Asn Pro Arg Pro Glu Val Leu Leu Trp Leu Leu Lys Ser
            180                 185                 190

Glu Cys Tyr Ser Thr Gly Tyr Val Phe Arg Thr Cys Met Tyr Asn Ser
        195                 200                 205

Asp Met Cys Lys Asn Ser Leu His Tyr Tyr Ile Ser Ser His Arg Glu
    210                 215                 220

Ser Gln Ser Leu Ser Lys Asp Val Ile Lys Cys Leu Ile Asn Asn Asn
225                 230                 235                 240

Val Ser Ile His Gly Arg Asp Glu Gly Gly Ser Leu Pro Ile Gln Tyr
                245                 250                 255

Tyr Trp Ser Phe Ser Thr Ile Asp Ile Glu Ile Val Lys Leu Leu Leu
            260                 265                 270

Ile Lys Asp Val Asp Thr Cys Arg Val Tyr Asp Val Ser Pro Ile Leu
        275                 280                 285

Glu Ala Tyr Tyr Leu Asn Lys Arg Phe Arg Val Thr Pro Tyr Asn Val
    290                 295                 300

Asp Met Glu Ile Val Asn Leu Leu Ile Glu Arg Arg His Thr Leu Val
305                 310                 315                 320

Asp Val Met Arg Ser Ile Thr Ser Tyr Asp Ser Arg Glu Tyr Asn His
```

325 330 335

Tyr Ile Ile Asp Asn Ile Leu Lys Arg Phe Arg Gln Gln Asp Glu Ser
340 345 350

Ile Val Gln Ala Met Leu Ile Asn Tyr Leu His Tyr Gly Asp Met Val
355 360 365

Val Arg Cys Met Leu Asp Asn Gly Gln Gln Leu Ser Ser Ala Arg Leu
370 375 380

Leu Cys
385

<210> 120
<211> 150
<212> PRT
<213> Vaccinia virus

<400> 120
Met Tyr Gly Leu Ile Leu Ser Arg Phe Asn Asn Cys Gly Tyr His Cys
1 5 10 15

Tyr Glu Thr Ile Leu Ile Asp Val Phe Asp Ile Leu Ser Lys Tyr Met
20 25 30

Asp Asp Ile Asp Met Ile Asp Asn Glu Asn Lys Thr Leu Leu Tyr Tyr
35 40 45

Ala Val Asp Val Asn Asn Ile Gln Phe Ala Lys Arg Leu Leu Glu Tyr
50 55 60

Gly Ala Ser Val Thr Thr Ser Arg Ser Ile Ile Asn Thr Ala Ile Gln
65 70 75 80

Lys Ser Ser Tyr Gln Arg Glu Asn Lys Thr Arg Ile Val Asp Leu Leu
85 90 95

Leu Ser Tyr His Pro Thr Leu Glu Thr Met Ile Asp Ala Phe Asn Arg

```
            100                 105                 110

Asp Ile Arg Tyr Leu Tyr Pro Glu Pro Leu Phe Ala Cys Ile Arg Tyr
        115                 120                 125

Ala Leu Ile Leu Asp Asp Asp Phe Pro Ser Lys Val Ser Met Ile Ser
    130                 135                 140

Pro Val Ile Ile Arg Asn
145                 150
```

<210> 121
<211> 91
<212> PRT
<213> Vaccinia virus

<400> 121

```
Met Arg Arg Cys Ile His Ile Lys Glu Arg Lys Ile His Met Thr Asn
1               5                   10                  15

Ile Val Asp Arg Asn Val Thr Phe Ile Leu Thr Val Val His Lys Tyr
            20                  25                  30

Val Arg Tyr Val Pro His Thr Val Ala Asn Asp Ala His Asn Leu Val
        35                  40                  45

His Leu Ala His Leu Ile His Phe Ile Ile Tyr Phe Phe Ile Ile Arg
    50                  55                  60

Asp Val Arg Lys Lys Lys Lys Lys Lys Lys Lys Asn Arg Thr Ile Tyr
65                  70                  75                  80

Phe Phe Ser Asn Val Tyr Ala Arg His Ile Lys
                85                  90
```

<210> 122
<211> 259
<212> PRT
<213> Vaccinia virus

<400> 122
Met Ser Arg Ile Asn Ile Thr Lys Lys Ile Tyr Cys Ser Val Phe Leu
1   5   10   15

Phe Leu Phe Leu Phe Leu Ser Tyr Ile Ser Asn Tyr Glu Lys Val Asn
            20   25   30

Asp Glu Met Tyr Glu Met Gly Glu Met Asp Glu Ile Val Ser Ile Val
        35   40   45

Arg Asp Ser Met Trp Tyr Ile Pro Asn Val Phe Met Asp Asp Gly Lys
    50   55   60

Asn Glu Gly His Val Ser Val Asn Asn Val Cys His Met Tyr Phe Thr
65   70   75   80

Phe Phe Asp Val Asp Thr Ser Ser His Leu Phe Lys Leu Val Ile Lys
                85   90   95

His Cys Asp Leu Asn Lys Arg Gly Asn Ser Pro Leu His Cys Tyr Thr
            100   105   110

Met Asn Thr Arg Phe Asn Pro Ser Val Leu Lys Ile Leu Leu His His
        115   120   125

Gly Met Arg Asn Phe Asp Ser Lys Asp Glu Lys Gly His His Tyr Leu
    130   135   140

Ile His Ser Leu Ser Ile Asp Asn Lys Ile Phe Asp Ile Leu Thr Asp
145   150   155   160

Thr Ile Asp Asp Phe Ser Lys Ser Ser Asp Leu Leu Leu Cys Tyr Leu
                165   170   175

Arg Tyr Lys Phe Asn Gly Ser Leu Asn Tyr Tyr Val Leu Tyr Lys Gly
            180   185   190

Ser Asp Pro Asn Cys Ala Asp Glu Asp Glu Leu Thr Ser Leu His Tyr

```
        195                 200                 205

Tyr Cys Lys His Ile Ser Thr Phe Tyr Lys Ser Asn Tyr Tyr Lys Leu
    210                 215                 220

Ser His Thr Lys Met Arg Ala Glu Lys Arg Phe Ile Tyr Ala Ile Ile
225                 230                 235                 240

Asp Tyr Gly Ala Asn Ile Asn Ala Val Thr His Leu Pro Ser Thr Val
                245                 250                 255

Tyr Gln Thr
```

<210> 123
<211> 103
<212> PRT
<213> Vaccinia virus

<400> 123

```
Met Glu Gln Thr Leu Thr Arg Leu His Thr Tyr Leu Gln Gln Tyr Thr
1               5                   10                  15

Lys His Ser Pro Arg Val Val Tyr Ala Leu Leu Ser Arg Gly Tyr Val
            20                  25                  30

Ile Ile Leu Ile Val His Pro Ser Trp Asn Asp Cys Ala Thr Gly His
        35                  40                  45

Ile Leu Ile Met Leu Leu Asn Trp His Glu Gln Lys Glu Glu Gly Gln
    50                  55                  60

His Leu Leu Tyr Leu Phe Ile Lys His Asn Gln Gly Tyr Thr Leu Asn
65                  70                  75                  80

Ile Leu Arg Tyr Leu Leu Asp Arg Phe Asp Ile Gln Lys Asp Glu Tyr
                85                  90                  95

Ile Tyr Arg Leu Ser Lys Leu
```

100

<210> 124
<211> 113
<212> PRT
<213> Vaccinia virus

<400> 124
Met Leu Pro His Thr Ser Asp Thr Thr Ser Thr Phe Arg Leu Lys Thr
1 5 10 15

Val Phe Asp Leu Val Phe Glu Asn Arg Asn Ile Ile Tyr Lys Ala Asp
20 25 30

Val Val Asn Asp Ile Ile His His Arg Leu Lys Val Ser Leu Pro Met
35 40 45

Ile Lys Ser Leu Phe Tyr Lys Met Ser Glu Phe Ser Pro Tyr Asp Asp
50 55 60

Tyr Tyr Val Lys Lys Ile Leu Ala Tyr Cys Leu Leu Arg Asp Glu Ser
65 70 75 80

Phe Ala Glu Leu His Ser Lys Phe Cys Leu Asn Glu Asp Tyr Lys Ser
85 90 95

Val Phe Met Lys Asn Ile Ser Phe Asp Lys Ile Asp Ser Ile Ile Val
100 105 110

Thr

<210> 125
<211> 122
<212> PRT
<213> Vaccinia virus

<400> 125
Met Lys Ser Val Leu Tyr Ser Tyr Ile Leu Phe Leu Ser Cys Ile Ile
1 5 10 15

Ile Asn Gly Arg Asp Ile Ala Pro His Ala Pro Ser Asp Gly Lys Cys
            20   25   30

Lys Asp Asn Glu Tyr Lys Arg His Asn Leu Cys Pro Gly Thr Tyr Ala
        35   40   45

Ser Arg Leu Cys Asp Ser Lys Thr Asn Thr Gln Cys Thr Pro Cys Gly
    50   55   60

Ser Gly Thr Phe Thr Ser Arg Asn Asn His Leu Pro Ala Cys Leu Ser
65   70   75   80

Cys Asn Gly Arg Arg Asp Arg Val Thr Leu Leu Thr Ile Glu Ser Val
                85   90   95

Asn Ala Leu Pro Asp Ile Ile Val Phe Ser Lys Asp His Pro Asp Ala
            100   105   110

Arg His Val Phe Pro Lys Gln Asn Val Glu
        115   120

<210> 126
<211> 244
<212> PRT
<213> Vaccinia virus

<400> 126
Met His Val Pro Ala Ser Leu Gln Gln Ser Ser Ser Ser Ser Ser Ser
1   5   10   15

Cys Thr Glu Glu Glu Asn Lys His His Met Gly Ile Asp Val Ile Ile
            20   25   30

Lys Val Thr Lys Gln Asp Gln Thr Pro Thr Asn Asp Lys Ile Cys Gln
        35   40   45

Ser Val Thr Glu Ile Thr Glu Ser Glu Ser Asp Pro Asp Pro Glu Val
    50   55   60

```
Glu Ser Glu Asp Asp Ser Thr Ser Val Glu Asp Val Asp Pro Pro Thr
65                  70                  75                  80

Thr Tyr Tyr Ser Ile Ile Gly Gly Gly Leu Arg Met Asn Phe Gly Phe
                85                  90                  95

Thr Lys Cys Pro Gln Ile Lys Ser Ile Ser Glu Ser Ala Asp Gly Asn
            100                 105                 110

Thr Val Asn Ala Arg Leu Ser Ser Val Ser Pro Gly Gln Gly Lys Asp
        115                 120                 125

Ser Pro Ala Ile Thr Arg Glu Glu Ala Leu Ala Met Ile Lys Asp Cys
    130                 135                 140

Glu Val Ser Ile Asp Ile Arg Cys Ser Glu Glu Glu Lys Asp Ser Asp
145                 150                 155                 160

Ile Lys Thr His Pro Val Leu Gly Ser Asn Ile Ser His Lys Lys Val
                165                 170                 175

Ser Tyr Glu Asp Ile Ile Gly Ser Thr Ile Val Asp Thr Lys Cys Val
            180                 185                 190

Lys Asn Leu Glu Phe Ser Val Arg Ile Gly Asp Met Cys Lys Glu Ser
        195                 200                 205

Ser Glu Leu Glu Val Lys Asp Gly Phe Lys Tyr Val Asp Gly Ser Ala
    210                 215                 220

Ser Glu Gly Ala Thr Asp Asp Thr Ser Leu Ile Asp Ser Thr Lys Leu
225                 230                 235                 240

Lys Ala Cys Val
```

<210> 127

<211> 345
<212> PRT
<213> Vaccinia virus

<400> 127
Met Asp Ile Phe Arg Glu Ile Ala Ser Ser Met Lys Gly Glu Asn Val
1   5   10   15

Phe Ile Ser Pro Ala Ser Ile Ser Ser Val Leu Thr Ile Leu Tyr Tyr
            20   25   30

Gly Ala Asn Gly Ser Thr Ala Glu Gln Leu Ser Lys Tyr Val Glu Lys
        35   40   45

Glu Glu Asn Met Asp Lys Val Ser Ala Gln Asn Ile Ser Phe Lys Ser
    50   55   60

Ile Asn Lys Val Tyr Gly Arg Tyr Ser Ala Val Phe Lys Asp Ser Phe
65   70   75   80

Leu Arg Lys Ile Gly Asp Lys Phe Gln Thr Val Asp Phe Thr Asp Cys
                85   90   95

Arg Thr Ile Asp Ala Ile Asn Lys Cys Val Asp Ile Phe Thr Glu Gly
            100   105   110

Lys Ile Asn Pro Leu Leu Asp Glu Pro Leu Ser Pro Asp Thr Cys Leu
        115   120   125

Leu Ala Ile Ser Ala Val Tyr Phe Lys Ala Lys Trp Leu Thr Pro Phe
    130   135   140

Glu Lys Glu Phe Thr Ser Asp Tyr Pro Phe Tyr Val Ser Pro Thr Glu
145   150   155   160

Met Val Asp Val Ser Met Met Ser Met Tyr Gly Lys Ala Phe Asn His
                165   170   175

Ala Ser Val Lys Glu Ser Phe Gly Asn Phe Ser Ile Ile Glu Leu Pro

```
            180                 185                 190

Tyr Val Gly Asp Thr Ser Met Met Val Ile Leu Pro Asp Lys Ile Asp
        195                 200                 205

Gly Leu Glu Ser Ile Glu Gln Asn Leu Thr Asp Thr Asn Phe Lys Lys
    210                 215                 220

Trp Cys Asn Ser Leu Glu Ala Thr Phe Ile Asp Val His Ile Pro Lys
225                 230                 235                 240

Phe Lys Val Thr Gly Ser Tyr Asn Leu Val Asp Thr Leu Val Lys Ser
                245                 250                 255

Gly Leu Thr Glu Val Phe Gly Ser Thr Gly Asp Tyr Ser Asn Met Cys
            260                 265                 270

Asn Ser Asp Val Ser Val Asp Ala Met Ile His Lys Thr Tyr Ile Asp
        275                 280                 285

Val Asn Glu Glu Tyr Thr Glu Ala Ala Ala Ala Thr Cys Ala Leu Val
    290                 295                 300

Ser Asp Cys Ala Ser Thr Ile Thr Asn Glu Phe Cys Val Asp His Pro
305                 310                 315                 320

Phe Ile Tyr Val Ile Arg His Val Asp Gly Lys Ile Leu Phe Val Gly
                325                 330                 335

Arg Tyr Cys Ser Pro Thr Thr Asn Cys
            340                 345


<210> 128
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 128
Met Thr Ala Asn Phe Ser Thr His Val Phe Ser Pro Gln His Cys Gly
```

1 5 10 15

Cys Asp Arg Leu Thr Ser Ile Asp Asp Val Arg Gln Cys Leu Thr Glu
20 25 30

Tyr Ile Tyr Trp Ser Ser Tyr Ala Tyr Arg Asn Arg Gln Cys Ala Gly
35 40 45

Gln Leu Tyr Ser Thr Leu Leu Ser Phe Arg Asp Asp Ala Glu Leu Val
50 55 60

Phe Ile Asp Ile Arg Glu Leu Val Lys Asn Met Pro Trp Asp Asp Val
65 70 75 80

Lys Asp Cys Ala Glu Ile Ile Arg Cys Tyr Ile Pro Asp Glu Gln Lys
85 90 95

Thr Ile Arg Glu Ile Ser Ala Ile Ile Gly Leu Cys Ala Tyr Ala Ala
100 105 110

Thr Tyr Trp Gly Gly Glu Asp His Pro Thr Ser Asn Ser Leu Asn Ala
115 120 125

Leu Phe Val Met Leu Glu Met Leu Asn Tyr Val Asp Tyr Asn Ile Ile
130 135 140

Phe Arg Arg Met Asn
145

<210> 129
<211> 326
<212> PRT
<213> Vaccinia virus

<400> 129
Met Ser Ile Leu Pro Val Ile Phe Leu Ser Ile Phe Phe Tyr Ser Ser
1 5 10 15

Phe Val Gln Thr Phe Asn Ala Pro Glu Cys Ile Asp Lys Gly Gln Tyr

```
            20                  25                  30

Phe Ala Ser Phe Met Glu Leu Glu Asn Glu Pro Val Ile Leu Pro Cys
        35                  40                  45

Pro Gln Ile Asn Thr Leu Ser Ser Gly Tyr Asn Ile Leu Asp Ile Leu
    50                  55                  60

Trp Glu Lys Arg Gly Ala Asp Asn Asp Arg Ile Ile Pro Ile Asp Asn
65                  70                  75                  80

Gly Ser Asn Met Leu Ile Leu Asn Pro Thr Gln Ser Asp Ser Gly Ile
                85                  90                  95

Tyr Ile Cys Ile Thr Thr Asn Glu Thr Tyr Cys Asp Met Met Ser Leu
            100                 105                 110

Asn Leu Thr Ile Val Ser Val Ser Glu Ser Asn Ile Asp Leu Ile Ser
        115                 120                 125

Tyr Pro Gln Ile Val Asn Glu Arg Ser Thr Gly Glu Met Val Cys Pro
    130                 135                 140

Asn Ile Asn Ala Phe Ile Ala Ser Asn Val Asn Ala Asp Ile Ile Trp
145                 150                 155                 160

Ser Gly His Arg Arg Leu Arg Asn Lys Arg Leu Lys Gln Arg Thr Pro
                165                 170                 175

Gly Ile Ile Thr Ile Glu Asp Val Arg Lys Asn Asp Ala Gly Tyr Tyr
            180                 185                 190

Thr Cys Val Leu Glu Tyr Ile Tyr Gly Gly Lys Thr Tyr Asn Val Thr
        195                 200                 205

Arg Ile Val Lys Leu Glu Val Arg Asp Lys Ile Ile Pro Ser Thr Met
    210                 215                 220
```

```
Gln Leu Pro Asp Gly Ile Val Thr Ser Ile Gly Ser Asn Leu Thr Ile
225                 230                 235                 240


Ala Cys Arg Val Ser Leu Arg Pro Pro Thr Thr Asp Ala Asp Val Phe
                245                 250                 255


Trp Ile Ser Asn Gly Met Tyr Tyr Glu Glu Asp Asp Gly Asp Gly Asn
            260                 265                 270


Gly Arg Ile Ser Val Ala Asn Lys Ile Tyr Met Thr Asp Lys Arg Arg
        275                 280                 285


Val Ile Thr Ser Arg Leu Asn Ile Asn Pro Val Lys Glu Glu Asp Ala
    290                 295                 300


Thr Thr Phe Thr Cys Met Ala Phe Thr Ile Pro Ser Ile Ser Lys Thr
305                 310                 315                 320


Val Thr Val Ser Ile Thr
                325


<210> 130
<211> 340
<212> PRT
<213> Vaccinia virus

<400> 130
Met Ser Arg Lys Phe Met Gln Val Tyr Glu Tyr Asp Arg Glu Gln Tyr
1               5                   10                  15


Leu Asp Glu Phe Ile Glu Asp Arg Tyr Asn Asp Ser Phe Ile Thr Ser
            20                  25                  30


Pro Glu Tyr Tyr Ser Ala Glu Lys Tyr Met Cys Arg Tyr Thr Thr Leu
        35                  40                  45


Asn His Asn Cys Ile Asn Val Arg Arg Cys Ala Leu Asp Ser Lys Leu
    50                  55                  60
```

```
Leu His Asp Ile Ile Thr Asn Cys Lys Ile Tyr Asn Asn Ile Glu Leu
65                  70                  75                  80

Val Arg Ala Thr Lys Phe Val Tyr Tyr Leu Asp Leu Ile Lys Cys Asn
                85                  90                  95

Trp Val Ser Lys Val Gly Asp Ser Val Leu Tyr Pro Val Ile Phe Ile
            100                 105                 110

Thr His Thr Ser Thr Arg Asn Leu Asp Lys Val Ser Val Lys Thr Tyr
        115                 120                 125

Lys Gly Val Lys Val Lys Lys Leu Asn Arg Cys Ala Asp His Ala Ile
    130                 135                 140

Val Ile Asn Pro Phe Val Lys Phe Lys Leu Thr Leu Pro Asn Lys Thr
145                 150                 155                 160

Ser His Ala Lys Val Leu Val Thr Phe Cys Lys Leu Lys Thr Asp Ile
                165                 170                 175

Thr Pro Val Glu Ala Pro Leu Pro Gly Asn Val Leu Val Tyr Thr Phe
            180                 185                 190

Pro Asp Ile Asn Lys Arg Ile Pro Gly Tyr Ile His Leu Asn Ile Glu
        195                 200                 205

Gly Cys Ile Asp Gly Met Ile Tyr Ile Asn Ser Ser Lys Phe Ala Cys
    210                 215                 220

Val Leu Lys Leu His Arg Ser Met Tyr Arg Ile Pro Pro Phe Pro Ile
225                 230                 235                 240

Asp Ile Cys Ser Cys Cys Ser Gln Tyr Ile Asn Tyr Asp Ile Glu Ile
                245                 250                 255

Pro Ile His Asp Leu Ile Lys Asp Val Ala Ile Phe Lys Asn Lys Glu
```

260 265 270

Thr Val Tyr Tyr Leu Lys Leu Asn Asn Lys Thr Ile Ala Arg Phe Thr
275 280 285

Tyr Phe Asn Asn Ile Asp Thr Ala Ile Thr Gln Glu His Glu Tyr Val
290 295 300

Lys Ile Ala Leu Gly Ile Val Cys Lys Leu Met Ile Asn Asn Met His
305 310 315 320

Ser Ile Val Gly Val Asn His Ser Asn Thr Phe Val Asn Cys Leu Leu
325 330 335

Glu Asp Asn Val
340

<210> 131
<211> 574
<212> PRT
<213> Vaccinia virus

<400> 131
Met Ser Arg Arg Leu Ile Tyr Val Leu Asn Ile Asn Arg Glu Ser Thr
1 5 10 15

His Lys Ile Gln Glu Asn Glu Ile Tyr Thr Tyr Phe Ser His Cys Asn
20 25 30

Ile Asp His Thr Ser Thr Glu Leu Asp Phe Val Val Lys Asn Tyr Asp
35 40 45

Leu Asn Arg Arg Gln Pro Val Thr Gly Tyr Thr Ala Leu His Cys Tyr
50 55 60

Leu Tyr Asn Asn Tyr Phe Thr Asn Asp Val Leu Lys Ile Leu Leu Asn
65 70 75 80

His Gly Val Asp Val Thr Met Lys Thr Ser Ser Gly Arg Met Pro Val

```
                85                  90                  95

Tyr Ile Leu Leu Thr Arg Cys Cys Asn Ile Ser His Asp Val Val Ile
            100                 105                 110

Asp Met Ile Asp Lys Asp Lys Asn His Leu Leu His Arg Asp Tyr Ser
        115                 120                 125

Asn Leu Leu Leu Glu Tyr Ile Lys Ser Arg Tyr Met Leu Leu Lys Glu
    130                 135                 140

Glu Asp Ile Asp Glu Asn Ile Val Ser Thr Leu Leu Asp Lys Gly Ile
145                 150                 155                 160

Asp Pro Asn Phe Lys Gln Asp Gly Tyr Thr Ala Leu His Tyr Tyr Tyr
                165                 170                 175

Leu Cys Leu Ala His Val Tyr Lys Pro Gly Glu Cys Arg Lys Pro Ile
            180                 185                 190

Thr Ile Lys Lys Ala Lys Arg Ile Ile Ser Leu Phe Ile Gln His Gly
        195                 200                 205

Ala Asn Leu Asn Ala Leu Asp Asn Cys Gly Asn Thr Pro Phe His Leu
    210                 215                 220

Tyr Leu Ser Ile Glu Met Cys Asn Asn Ile His Met Thr Lys Met Leu
225                 230                 235                 240

Leu Thr Phe Asn Pro Asn Phe Glu Ile Cys Asn Asn His Gly Leu Thr
                245                 250                 255

Pro Ile Leu Cys Tyr Ile Thr Ser Asp Tyr Ile Gln His Asp Ile Leu
            260                 265                 270

Val Met Leu Ile His His Tyr Glu Thr Asn Val Gly Glu Met Pro Ile
        275                 280                 285
```

```
Asp Glu Arg Arg Ile Ile Val Phe Glu Phe Ile Lys Thr Tyr Ser Thr
    290                 295                 300

Arg Pro Ala Asp Ser Ile Thr Tyr Leu Met Asn Arg Phe Lys Asn Ile
305                 310                 315                 320

Asp Ile Tyr Thr Arg Tyr Glu Gly Lys Thr Leu Leu His Val Ala Cys
                325                 330                 335

Glu Tyr Asn Asn Thr His Val Ile Asp Tyr Leu Ile Arg Ile Asn Gly
            340                 345                 350

Asp Ile Asn Ala Leu Thr Asp Asn Asn Lys His Ala Thr Gln Leu Ile
        355                 360                 365

Ile Asp Asn Lys Glu Asn Ser Pro Tyr Thr Ile Asn Cys Leu Leu Tyr
    370                 375                 380

Ile Leu Arg Tyr Ile Val Asp Lys Asn Val Ile Arg Ser Leu Val Asp
385                 390                 395                 400

Gln Leu Pro Ser Leu Pro Ile Phe Asp Ile Lys Ser Phe Glu Lys Phe
                405                 410                 415

Ile Ser Tyr Cys Ile Leu Leu Asp Asp Thr Phe Tyr Asn Arg His Val
            420                 425                 430

Arg Asn Arg Asp Ser Lys Thr Tyr Arg Tyr Ala Phe Ser Lys Tyr Met
        435                 440                 445

Ser Phe Asp Lys Tyr Asp Gly Ile Ile Thr Lys Cys His Lys Glu Thr
    450                 455                 460

Ile Leu Leu Lys Leu Ser Thr Val Leu Asp Thr Thr Leu Tyr Ala Val
465                 470                 475                 480

Leu Arg Cys His Asn Ser Lys Lys Leu Arg Arg Tyr Leu Thr Glu Leu
```

```
                485                 490                 495

Lys Lys Tyr Asn Asn Asp Lys Ser Phe Lys Ile Tyr Ser Asn Ile Met
            500                 505                 510

Asn Glu Arg Tyr Leu Asn Val Tyr Tyr Lys Asp Met Tyr Val Ser Lys
        515                 520                 525

Val Tyr Asp Lys Leu Phe Pro Val Phe Thr Asp Lys Asn Cys Leu Leu
    530                 535                 540

Thr Leu Leu Pro Ser Glu Ile Ile Tyr Glu Ile Leu Tyr Met Leu Thr
545                 550                 555                 560

Ile Asn Asp Leu Tyr Asn Ile Ser Tyr Pro Pro Thr Lys Val
                565                 570
```

<210> 132
<211> 351
<212> PRT
<213> Vaccinia virus

<400> 132

```
Met Thr Met Lys Met Met Val His Ile Tyr Phe Val Ser Leu Leu Leu
1               5                   10                  15

Leu Leu Phe His Ser Tyr Ala Ile Asp Ile Glu Asn Glu Ile Thr Glu
            20                  25                  30

Phe Phe Asn Lys Met Arg Asp Thr Leu Pro Ala Lys Asp Ser Lys Trp
        35                  40                  45

Leu Asn Pro Ala Cys Met Phe Gly Gly Thr Met Asn Asp Ile Ala Ala
    50                  55                  60

Leu Gly Glu Pro Phe Ser Ala Lys Cys Pro Pro Ile Glu Asp Ser Leu
65                  70                  75                  80

Leu Ser His Arg Tyr Lys Asp Tyr Val Val Lys Trp Glu Arg Leu Glu
```

```
                85                  90                  95

Lys Asn Arg Arg Arg Gln Val Ser Asn Lys Arg Val Lys His Gly Asp
            100                 105                 110

Leu Trp Ile Ala Asn Tyr Thr Ser Lys Phe Ser Asn Arg Arg Tyr Leu
        115                 120                 125

Cys Thr Val Thr Thr Lys Asn Gly Asp Cys Val Gln Gly Ile Val Arg
    130                 135                 140

Ser His Ile Arg Lys Pro Pro Ser Cys Ile Pro Lys Thr Tyr Glu Leu
145                 150                 155                 160

Gly Thr His Asp Lys Tyr Gly Ile Asp Leu Tyr Cys Gly Ile Leu Tyr
                165                 170                 175

Ala Lys His Tyr Asn Asn Ile Thr Trp Tyr Lys Asp Asn Lys Glu Ile
            180                 185                 190

Asn Ile Asp Asp Ile Lys Tyr Ser Gln Thr Gly Lys Glu Leu Ile Ile
        195                 200                 205

His Asn Pro Glu Leu Glu Asp Ser Gly Arg Tyr Asp Cys Tyr Val His
    210                 215                 220

Tyr Asp Asp Val Arg Ile Lys Asn Asp Ile Val Val Ser Arg Cys Lys
225                 230                 235                 240

Ile Leu Thr Val Ile Pro Ser Gln Asp His Arg Phe Lys Leu Ile Leu
                245                 250                 255

Asp Pro Lys Ile Asn Val Thr Ile Gly Glu Pro Ala Asn Ile Thr Cys
            260                 265                 270

Thr Ala Val Ser Thr Ser Leu Leu Ile Asp Asp Val Leu Ile Glu Trp
        275                 280                 285
```

Glu Asn Pro Ser Gly Trp Leu Ile Gly Phe Asp Phe Asp Val Tyr Ser
290 295 300

Val Leu Thr Ser Arg Gly Gly Ile Thr Glu Ala Thr Leu Tyr Phe Glu
305 310 315 320

Asn Val Thr Glu Glu Tyr Ile Gly Asn Thr Tyr Lys Cys Arg Gly His
325 330 335

Asn Tyr Tyr Phe Glu Lys Thr Leu Thr Thr Thr Val Val Leu Glu
340 345 350

<210> 133
<211> 56
<212> PRT
<213> Vaccinia virus

<400> 133
Met His Val Ile Asp Val Asp Val Arg Leu Tyr Met Ser Thr Phe Ile
1 5 10 15

Ile Ile Asp Gln Ser Thr Glu Asn Thr Ser Ile Asp Thr Thr Val Thr
20 25 30

Ile Asn Ile Ile Tyr Leu Ala Ile Met Lys Ile Ile Met Asn Ile Ile
35 40 45

Met Met Ile Met Ile Glu Leu Val
50 55

<210> 134
<211> 53
<212> PRT
<213> Vaccinia virus

<400> 134
Met Asn Ser Glu Ser Asp Asn Ile Ser Ile Lys Thr Glu Tyr Glu Phe
1 5 10 15

Tyr Asp Glu Thr Gln Asp Gln Ser Thr Gln Leu Val Gly Tyr Asp Ile

```
            20                  25                  30

Lys Leu Lys Thr Asn Glu Asp Asp Phe Met Ala Met Ile Asp Gln Trp
        35                  40                  45

Val Ser Met Ile Ile
    50
```

<210> 135
<211> 309
<212> PRT
<213> Vaccinia virus

<400> 135

```
Met Glu Met Tyr Pro Arg His Arg Tyr Ser Lys His Ser Val Phe Lys
1               5                   10                  15

Gly Phe Ser Asp Lys Val Arg Lys Asn Asp Leu Asp Met Asn Val Val
            20                  25                  30

Lys Glu Leu Leu Ser Asn Gly Ala Ser Leu Thr Ile Lys Asp Ser Ser
        35                  40                  45

Asn Lys Asp Pro Ile Thr Val Tyr Phe Arg Arg Thr Ile Met Asn Leu
    50                  55                  60

Glu Met Ile Asp Glu Arg Lys Tyr Ile Val His Ser Tyr Leu Lys Asn
65                  70                  75                  80

Tyr Lys Asn Phe Asp Tyr Pro Phe Phe Arg Lys Leu Val Leu Thr Asn
                85                  90                  95

Lys His Cys Leu Asn Asn Tyr Tyr Asn Ile Ser Asp Ser Lys Tyr Gly
            100                 105                 110

Thr Pro Leu His Ile Leu Ala Ser Asn Lys Lys Leu Ile Thr Pro Asn
        115                 120                 125

Tyr Met Lys Leu Leu Val Tyr Asn Gly Asn Asp Ile Asn Ala Arg Gly
```

```
    130                 135                 140

Glu Asp Thr Gln Met Arg Thr Pro Leu His Lys Tyr Leu Cys Lys Phe
145                 150                 155                 160

Val Tyr His Asn Ile Glu Tyr Gly Ile Arg Tyr Tyr Asn Glu Lys Ile
                165                 170                 175

Ile Asp Ala Phe Ile Glu Leu Gly Ala Asp Leu Thr Ile Pro Asn Asp
            180                 185                 190

Asp Gly Met Ile Pro Val Val Tyr Cys Ile His Ser Asn Ala Glu Tyr
        195                 200                 205

Gly Tyr Asn Asn Ile Thr Asn Ile Lys Ile Ile Arg Lys Leu Leu Asn
    210                 215                 220

Leu Ser Arg Arg Ala Ser His Asn Leu Phe Arg Asp Arg Val Met His
225                 230                 235                 240

Asp Tyr Ile Ser Asn Thr Tyr Ile Asp Leu Glu Cys Leu Asp Ile Ile
                245                 250                 255

Arg Ser Leu Asp Gly Phe Asp Ile Asn Gly Tyr Phe Glu Gly Arg Thr
            260                 265                 270

Pro Leu His Cys Ala Ile Gln His Asn Phe Thr Gln Ile Ala Lys Tyr
        275                 280                 285

Leu Leu Asp Arg Gly Ala Asp Ile Val Val Pro Asn Thr Leu Ile Ile
    290                 295                 300

His Gln Tyr Ile Gln
305
```

<210> 136
<211> 134
<212> PRT

<213> Vaccinia virus

<400> 136
Met Glu Glu Asp Thr Asn Ile Ser Asn Lys Val Ile Arg Tyr Asn Thr
1   5   10   15

Val Asn Asn Ile Trp Glu Thr Leu Pro Asn Phe Trp Thr Gly Thr Ile
            20   25   30

Asn Pro Gly Val Val Ser His Lys Asp Asp Ile Tyr Val Val Cys Asp
        35   40   45

Ile Lys Asp Glu Lys Asn Val Lys Thr Cys Ile Phe Arg Tyr Asn Thr
    50   55   60

Asn Thr Tyr Asn Gly Trp Glu Leu Val Thr Thr Thr Glu Ser Arg Leu
65   70   75   80

Ser Ala Leu His Thr Ile Leu Tyr Asn Asn Thr Ile Met Met Leu His
                85   90   95

Cys Tyr Glu Ser Tyr Met Leu Gln Asp Thr Phe Asn Val Tyr Thr Arg
            100   105   110

Glu Trp Asn His Met Cys His Gln His Ser Asn Ser Tyr Ile Met Tyr
        115   120   125

Asn Ile Leu Pro Ile Tyr
    130

<210> 137
<211> 353
<212> PRT
<213> Vaccinia virus

<400> 137
Met Asp Ile Phe Lys Glu Leu Ile Leu Lys His Thr Asp Glu Asn Val
1   5   10   15

Leu Ile Ser Pro Val Ser Ile Leu Ser Thr Leu Ser Ile Leu Asn His

```
            20                  25                  30

Gly Ala Ala Gly Ser Thr Ala Glu Gln Leu Ser Lys Tyr Ile Glu Asn
        35                  40                  45

Met Asn Glu Asn Thr Pro Asp Asp Asn Asn Asp Met Asp Val Asp Ile
    50                  55                  60

Pro Tyr Cys Ala Thr Leu Ala Thr Ala Asn Lys Ile Tyr Gly Ser Asp
65                  70                  75                  80

Ser Ile Glu Phe His Ala Ser Phe Leu Gln Lys Ile Lys Asp Asp Phe
                85                  90                  95

Gln Thr Val Asn Phe Asn Asn Ala Asn Gln Thr Lys Glu Leu Ile Asn
            100                 105                 110

Glu Trp Val Lys Thr Met Thr Asn Gly Lys Ile Asn Ser Leu Leu Thr
        115                 120                 125

Ser Pro Leu Ser Ile Asn Thr Arg Met Thr Val Val Ser Ala Val His
    130                 135                 140

Phe Lys Ala Met Trp Lys Tyr Pro Phe Ser Lys His Leu Thr Tyr Thr
145                 150                 155                 160

Asp Lys Phe Tyr Ile Ser Lys Asn Ile Val Thr Ser Val Asp Met Met
                165                 170                 175

Val Ser Thr Glu Asn Asn Leu Gln Tyr Val His Ile Asn Glu Leu Phe
            180                 185                 190

Gly Gly Phe Ser Ile Ile Asp Ile Pro Tyr Glu Gly Asn Ser Ser Met
        195                 200                 205

Val Ile Ile Leu Pro Asp Asp Ile Glu Gly Ile Tyr Asn Ile Glu Lys
    210                 215                 220
```

```
Asn Ile Thr Asp Glu Lys Phe Lys Lys Trp Cys Gly Met Leu Ser Thr
225                 230                 235                 240


Lys Ser Ile Asp Leu Tyr Met Pro Lys Phe Lys Val Glu Met Thr Glu
                245                 250                 255


Pro Tyr Asn Leu Val Pro Ile Leu Glu Asn Leu Gly Leu Thr Asn Ile
            260                 265                 270


Phe Gly Tyr Tyr Ala Asp Phe Ser Lys Met Cys Asn Glu Thr Ile Thr
        275                 280                 285


Val Glu Lys Phe Leu His Thr Thr Phe Ile Asp Val Asn Glu Glu Tyr
    290                 295                 300


Thr Glu Ala Ser Ala Val Thr Gly Val Phe Met Thr Asn Phe Ser Met
305                 310                 315                 320


Val Tyr Arg Thr Lys Val Tyr Ile Asn His Pro Phe Met Tyr Met Ile
                325                 330                 335


Lys Asp Asn Thr Gly Arg Ile Leu Phe Ile Gly Lys Tyr Cys Tyr Pro
            340                 345                 350


Gln
```

<210> 138
<211> 190
<212> PRT
<213> Vaccinia virus

<400> 138

```
Met Met Ile Tyr Gly Leu Ile Ala Cys Leu Ile Phe Val Thr Ser Ser
1               5                   10                  15


Ile Ala Ser Pro Leu Tyr Ile Pro Val Ile Pro Pro Ile Ser Glu Asp
            20                  25                  30
```

```
Lys Ser Phe Asn Ser Val Glu Val Leu Val Ser Leu Phe Arg Asp Asp
        35                  40                  45

Gln Lys Asp Tyr Thr Val Thr Ser Gln Phe Asn Asn Tyr Thr Ile Asp
    50                  55                  60

Thr Lys Asp Trp Thr Ile Gly Val Leu Ser Thr Pro Asp Gly Leu Asp
65                  70                  75                  80

Ile Pro Leu Thr Asn Ile Thr Tyr Trp Ser Arg Phe Thr Ile Gly Arg
                85                  90                  95

Ala Leu Phe Lys Ser Glu Ser Glu Asp Ile Phe Gln Lys Lys Met Ser
            100                 105                 110

Ile Leu Gly Val Ser Ile Glu Cys Lys Lys Ser Ser Thr Leu Leu Thr
        115                 120                 125

Phe Leu Thr Val Arg Lys Met Thr Arg Val Phe Asn Lys Phe Pro Asp
    130                 135                 140

Met Ala Tyr Tyr Arg Gly Asp Cys Leu Lys Ala Val Tyr Val Thr Met
145                 150                 155                 160

Thr Tyr Lys Asn Thr Lys Thr Gly Glu Thr Asp Tyr Thr Tyr Leu Ser
                165                 170                 175

Asn Gly Gly Leu Pro Ala Tyr Tyr Arg Asn Gly Val Asp Gly
            180                 185                 190
```

<210> 139
<211> 62
<212> PRT
<213> Vaccinia virus

<400> 139

```
Met Lys Leu Phe Thr Gln Asn Asp Arg Tyr Phe Gly Leu Leu Asp Ser
1               5                   10                  15
```

```
Cys Thr His Ile Phe Cys Ile Thr Cys Ile Asn Ile Trp His Lys Thr
            20                  25                  30

Arg Arg Glu Thr Gly Ala Ser Asp Asn Cys Pro Ile Cys Arg Thr Arg
        35                  40                  45

Phe Arg Asn Ile Thr Met Ser Lys Phe Tyr Lys Leu Val Asn
    50                  55                  60
```

<210> 140
<211> 184
<212> PRT
<213> Vaccinia virus

<400> 140

```
Met Glu Phe Asp Pro Ala Lys Ile Asn Thr Ser Ser Ile Asp His Val
1               5                   10                  15

Thr Ile Leu Gln Tyr Ile Asp Glu Pro Asn Asp Ile Arg Leu Thr Val
            20                  25                  30

Cys Ile Ile Arg Asn Ile Asn Asn Ile Thr Tyr Tyr Ile Asn Ile Thr
        35                  40                  45

Lys Ile Asn Thr His Leu Ala Asn Gln Phe Arg Ala Trp Lys Lys Arg
    50                  55                  60

Ile Ala Gly Arg Asp Tyr Met Thr Asn Leu Ser Arg Asp Thr Gly Ile
65                  70                  75                  80

Gln Gln Ser Lys Leu Thr Glu Thr Ile Arg Asn Cys Gln Lys Asn Arg
                85                  90                  95

Asn Ile Tyr Gly Leu Tyr Ile His Tyr Asn Leu Val Ile Asn Val Val
            100                 105                 110

Ile Asp Trp Ile Thr Asp Val Ile Val Gln Ser Ile Leu Arg Gly Leu
        115                 120                 125
```

```
Val Asn Trp Tyr Ile Ala Asn Asn Thr Tyr Thr Pro Asn Thr Pro Asn
    130                 135                 140

Asn Thr Thr Thr Ile Ser Glu Leu Asp Ile Ile Lys Ile Leu Asp Lys
145                 150                 155                 160

Tyr Glu Asp Val Tyr Arg Val Ser Lys Glu Lys Glu Cys Gly Ile Cys
                165                 170                 175

Tyr Glu Val Val Tyr Ser Lys Arg
            180
```

<210> 141
<211> 331
<212> PRT
<213> Vaccinia virus

<400> 141

```
Met Asp Ile Tyr Asp Asp Lys Gly Leu Gln Thr Ile Lys Leu Phe Asn
1               5                   10                  15

Asn Glu Phe Asp Cys Ile Arg Asn Asp Ile Arg Glu Leu Phe Lys His
            20                  25                  30

Val Thr Asp Ser Asp Ser Ile Gln Leu Pro Met Glu Asp Asn Ser Asp
        35                  40                  45

Ile Ile Glu Asn Ile Arg Lys Ile Leu Tyr Arg Arg Leu Lys Asn Val
    50                  55                  60

Glu Cys Val Asp Ile Asp Ser Thr Ile Thr Phe Met Lys Tyr Asp Pro
65                  70                  75                  80

Asn Asp Asp Asn Lys Arg Thr Cys Ser Asn Trp Val Pro Leu Thr Asn
                85                  90                  95

Asn Tyr Met Glu Tyr Cys Leu Val Ile Tyr Leu Glu Thr Pro Ile Cys
            100                 105                 110
```

```
Gly Gly Lys Ile Lys Leu Tyr His Pro Thr Gly Asn Ile Lys Ser Asp
        115                 120                 125

Lys Asp Ile Met Phe Ala Lys Thr Leu Asp Phe Lys Ser Lys Lys Val
    130                 135                 140

Leu Thr Gly Arg Lys Thr Ile Ala Val Leu Asp Ile Ser Val Ser Tyr
145                 150                 155                 160

Asn Arg Ser Met Thr Thr Ile His Tyr Asn Asp Asp Val Asp Ile Asp
                165                 170                 175

Ile His Thr Asp Lys Asn Gly Lys Glu Leu Cys Tyr Cys Tyr Ile Thr
            180                 185                 190

Ile Asp Asp His Tyr Leu Val Asp Val Glu Thr Ile Gly Val Ile Val
        195                 200                 205

Asn Arg Ser Gly Lys Cys Leu Leu Val Asn Asn His Leu Gly Ile Gly
    210                 215                 220

Ile Val Lys Asp Lys Arg Ile Ser Asp Ser Phe Gly Asp Val Cys Met
225                 230                 235                 240

Asp Thr Ile Phe Asp Phe Ser Glu Ala Arg Glu Leu Phe Ser Leu Thr
                245                 250                 255

Asn Asp Asp Asn Arg Asn Ile Ala Trp Asp Thr Asp Lys Leu Asp Asp
            260                 265                 270

Asp Thr Asp Ile Trp Thr Pro Val Thr Glu Asp Asp Tyr Lys Phe Leu
        275                 280                 285

Ser Arg Leu Val Leu Tyr Ala Lys Ser Gln Ser Asp Thr Val Phe Asp
    290                 295                 300

Tyr Tyr Val Leu Thr Gly Asp Thr Glu Pro Pro Thr Val Phe Ile Phe
```

305 310 315 320

Lys Val Thr Arg Phe Tyr Phe Asn Met Pro Lys
325 330

<210> 142
<211> 140
<212> PRT
<213> Vaccinia virus

<400> 142
Met Ser Met Lys Tyr Leu Met Leu Leu Phe Ala Ala Met Ile Ile Arg
1 5 10 15

Ser Phe Ala Asp Ser Gly Asn Ala Ile Glu Thr Thr Ser Pro Glu Ile
20 25 30

Thr Asn Ala Thr Thr Asp Ile Pro Ala Ile Arg Leu Cys Gly Pro Glu
35 40 45

Gly Asp Gly Tyr Cys Leu His Gly Asp Cys Ile His Ala Arg Asp Ile
50 55 60

Asp Gly Met Tyr Cys Arg Cys Ser His Gly Tyr Thr Gly Ile Arg Cys
65 70 75 80

Gln His Val Val Leu Val Asp Tyr Gln Arg Ser Glu Asn Pro Asn Thr
85 90 95

Thr Thr Ser Tyr Ile Pro Ser Pro Gly Ile Met Leu Val Leu Val Gly
100 105 110

Ile Ile Ile Ile Thr Cys Cys Leu Leu Ser Val Tyr Arg Phe Thr Arg
115 120 125

Arg Thr Lys Leu Pro Ile Gln Asp Met Val Val Pro
130 135 140

<210> 143

<211> 112
<212> PRT
<213> Vaccinia virus

<400> 143
Met Asp Glu Ile Val Arg Ile Val Arg Asp Ser Met Trp Tyr Ile Pro
1   5   10   15

Asn Val Phe Met Asp Asp Gly Lys Asn Glu Gly His Val Ser Val Asn
            20   25   30

Asn Val Cys His Met Tyr Phe Thr Phe Phe Asp Val Asp Thr Ser Ser
        35   40   45

His Leu Phe Lys Leu Val Ile Lys His Cys Asp Leu Asn Lys Arg Gly
    50   55   60

Asn Ser Pro Leu His Cys Tyr Thr Met Asn Thr Arg Phe Asn Pro Ser
65   70   75   80

Val Leu Lys Ile Leu Leu His His Gly Met Arg Asn Phe Asp Ser Lys
                85   90   95

Asp Glu Lys Gly His His Tyr Gln Ser Ile Thr Arg Ser Leu Ile Tyr
            100   105   110

<210> 144
<211> 109
<212> PRT
<213> Vaccinia virus

<400> 144
Met Leu Phe Tyr Leu Glu Glu Pro Ile Arg Gly Tyr Val Ile Ile Leu
1   5   10   15

Ile Val His Pro Ser Trp Asn Asp Cys Ala Thr Gly His Ile Leu Ile
            20   25   30

Met Leu Leu Asn Trp His Glu Gln Lys Glu Glu Gly Gln His Leu Leu
        35   40   45

Tyr Leu Phe Ile Lys His Asn Gln Gly Tyr Thr Leu Asn Ile Leu Arg
    50   55   60

Tyr Leu Leu Asp Arg Phe Asp Ile Gln Lys Asp Glu Tyr Tyr Asn Thr
65   70   75   80

Ala Phe Gln Asn Cys Asn Asn Asn Val Ala Ser Tyr Ile Gly Tyr Asp
                85   90   95

Ile Asn Leu Pro Thr Lys Asp Gly Ile Arg Leu Gly Val
            100   105

<210> 145
<211> 64
<212> PRT
<213> Vaccinia virus

<400> 145
Met Leu Pro His Thr Ser Asp Thr Thr Ser Thr Phe Arg Leu Lys Thr
1   5   10   15

Val Phe Asp Leu Val Phe Glu Asn Arg Asn Ile Ile Tyr Lys Ala Asp
            20   25   30

Val Val Asn Asp Ile Ile His His Arg Leu Lys Val Ser Leu Pro Met
        35   40   45

Ile Lys Ser Leu Phe Tyr Lys Met Ser Leu Pro Thr Thr Ile Thr Thr
    50   55   60

<210> 146
<211> 48
<212> PRT
<213> Vaccinia virus

<400> 146
Met Tyr Asp Asp Leu Ile Glu Gln Cys His Leu Ser Met Glu Arg Lys
1   5   10   15

Ser Lys Leu Val Asp Lys Ala Leu Asn Lys Leu Glu Ser Thr Ile Gly

```
            20                  25                  30

Gln Ser Arg Leu Ser Tyr Leu Pro Pro Glu Ile Met Arg Asn Ile Ile
        35                  40                  45


<210> 147
<211> 122
<212> PRT
<213> Vaccinia virus

<400> 147
Met Lys Ser Val Leu Tyr Ser Tyr Ile Leu Phe Leu Ser Cys Ile Ile
1               5                   10                  15


Ile Asn Gly Arg Asp Ile Ala Pro His Ala Pro Ser Asp Gly Lys Cys
            20                  25                  30


Lys Asp Asn Glu Tyr Lys Arg His Asn Leu Cys Pro Gly Thr Tyr Ala
        35                  40                  45


Ser Arg Leu Cys Asp Ser Lys Thr Asn Thr Gln Cys Thr Pro Cys Gly
    50                  55                  60


Ser Gly Thr Phe Thr Ser Arg Asn Asn His Leu Pro Ala Cys Leu Ser
65                  70                  75                  80


Cys Asn Gly Arg Arg Asp Arg Val Thr Arg Leu Thr Ile Glu Ser Val
                85                  90                  95


Asn Ala Leu Pro Asp Ile Ile Val Phe Ser Lys Asp His Pro Asp Ala
            100                 105                 110


Arg His Val Phe Pro Lys Gln Asn Val Glu
        115                 120


<210> 148
<211> 72
<212> PRT
<213> Vaccinia virus
```

<400> 148
Met Asp Ser Leu Arg Pro Val Val Val Val Asn Trp Ile Gln Ile Asn
1   5   10   15

Phe His Ile Asp Ile Val Lys Gly Ile Thr Gly Tyr Gly Phe Ala Phe
            20   25   30

Ile Cys Gly Arg Asp Gly Val Arg Ile Cys Ser Glu Thr Thr Arg Arg
        35   40   45

Thr Asp Asp Val Ser Gly Tyr Ser Val Ser Tyr Ser Thr Phe Cys Leu
    50   55   60

Gly Asn Thr Cys Leu Ala Ser Gly
65   70

<210> 149
<211> 61
<212> PRT
<213> Vaccinia virus

<400> 149
Met Trp Lys Leu Ile Cys Ile Gln Leu Thr Thr Thr Thr Gly Leu Ser
1   5   10   15

Glu Ser Ile Ser Thr Ser Glu Leu Thr Ile Thr Met Asn His Lys Asp
            20   25   30

Cys Asn Pro Val Phe Arg Glu Glu Tyr Phe Ser Val Leu Asn Lys Val
        35   40   45

Ala Thr Ser Gly Phe Phe Thr Gly Glu Arg Cys Ala Leu
    50   55   60

<210> 150
<211> 244
<212> PRT
<213> Vaccinia virus

<400> 150
Met His Val Pro Ala Ser Leu Gln Gln Ser Ser Ser Ser Ser Ser Ser Ser

```
1               5                   10                  15

Cys Thr Glu Glu Glu Asn Lys His His Met Gly Ile Asp Val Ile Ile
            20                  25                  30

Lys Val Thr Lys Gln Asp Gln Thr Pro Thr Asn Asp Lys Ile Cys Gln
        35                  40                  45

Ser Val Thr Glu Ile Thr Glu Ser Glu Ser Asp Pro Asp Pro Glu Val
    50                  55                  60

Glu Ser Glu Asp Asp Ser Thr Ser Val Glu Asp Val Asp Pro Pro Thr
65                  70                  75                  80

Thr Tyr Tyr Ser Ile Ile Gly Gly Gly Leu Arg Met Asn Phe Gly Phe
                85                  90                  95

Thr Lys Cys Pro Gln Ile Lys Ser Ile Ser Glu Ser Ala Asp Gly Asn
            100                 105                 110

Thr Val Asn Ala Arg Leu Ser Ser Val Ser Pro Gly Gln Gly Lys Asp
        115                 120                 125

Ser Pro Ala Ile Thr His Glu Glu Ala Leu Ala Met Ile Lys Asp Cys
    130                 135                 140

Glu Val Ser Ile Asp Ile Arg Cys Ser Glu Glu Glu Lys Asp Ser Asp
145                 150                 155                 160

Ile Lys Thr His Pro Val Leu Gly Ser Asn Ile Ser His Lys Lys Val
                165                 170                 175

Ser Tyr Glu Asp Ile Ile Gly Ser Thr Ile Val Asp Thr Lys Cys Val
            180                 185                 190

Lys Asn Leu Glu Phe Ser Val Arg Ile Gly Asp Met Cys Lys Glu Ser
        195                 200                 205
```

```
Ser Glu Leu Glu Val Lys Asp Gly Phe Lys Tyr Val Asp Gly Ser Ala
    210                 215                 220

Ser Glu Gly Ala Thr Asp Asp Thr Ser Leu Ile Asp Ser Thr Lys Leu
225                 230                 235                 240

Lys Ala Cys Val
```

<210> 151
<211> 222
<212> PRT
<213> Vaccinia virus

<400> 151

```
Met Asn His Cys Leu Leu Ala Ile Ser Ala Val Tyr Phe Lys Ala Lys
1               5                   10                  15

Trp Leu Thr Pro Phe Glu Lys Glu Phe Thr Ser Asp Tyr Pro Phe Tyr
            20                  25                  30

Val Ser Pro Thr Glu Met Val Asp Val Ser Met Met Ser Met Tyr Gly
        35                  40                  45

Lys Ala Phe Asn His Ala Ser Val Lys Glu Ser Phe Gly Asn Phe Ser
    50                  55                  60

Ile Ile Glu Leu Pro Tyr Val Gly Asp Thr Ser Met Met Val Ile Leu
65                  70                  75                  80

Pro Asp Lys Ile Asp Gly Leu Glu Ser Ile Glu Gln Asn Leu Thr Asp
                85                  90                  95

Thr Asn Phe Lys Lys Trp Cys Asp Phe Met Asp Ala Met Phe Ile Asp
            100                 105                 110

Val His Ile Pro Lys Phe Lys Val Thr Gly Ser Tyr Asn Leu Val Asp
        115                 120                 125
```

```
Thr Leu Val Lys Ser Gly Leu Thr Glu Val Phe Gly Ser Thr Gly Asp
    130                 135                 140

Tyr Ser Asn Met Cys Asn Leu Asp Val Ser Val Asp Ala Met Ile His
145                 150                 155                 160

Lys Thr Tyr Ile Asp Val Asn Glu Glu Tyr Thr Glu Ala Ala Ala Ala
                165                 170                 175

Thr Cys Ala Leu Val Ser Asp Cys Ala Ser Thr Ile Thr Asn Glu Phe
            180                 185                 190

Cys Val Asp His Pro Phe Ile Tyr Val Ile Arg His Val Asp Gly Lys
        195                 200                 205

Ile Leu Phe Val Gly Arg Tyr Cys Ser Pro Thr Thr Asn Cys
    210                 215                 220
```

<210> 152
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 152

```
Met Thr Ala Asn Phe Ser Thr His Val Phe Ser Pro Gln His Cys Gly
1               5                   10                  15

Cys Asp Arg Leu Thr Ser Ile Asp Asp Val Lys Gln Cys Leu Thr Glu
            20                  25                  30

Tyr Ile Tyr Trp Ser Ser Tyr Ala Tyr Arg Asn Arg Gln Cys Ala Gly
        35                  40                  45

Gln Leu Tyr Ser Thr Leu Leu Ser Phe Arg Asp Asp Ala Glu Leu Val
    50                  55                  60

Phe Ile Asp Ile Arg Glu Leu Val Lys Asn Met Pro Trp Asp Asp Val
65                  70                  75                  80
```

```
Lys Asp Cys Thr Glu Ile Ile Arg Cys Tyr Ile Pro Asp Glu Gln Lys
                85                  90                  95

Thr Ile Arg Glu Ile Ser Ala Ile Ile Gly Leu Cys Ala Tyr Ala Ala
            100                 105                 110

Thr Tyr Trp Gly Gly Glu Asp His Pro Thr Ser Asn Ser Leu Asn Ala
        115                 120                 125

Leu Phe Val Met Leu Glu Met Leu Asn Tyr Val Asp Tyr Asn Ile Ile
    130                 135                 140

Phe Arg Arg Met Asn
145
```

<210> 153
<211> 91
<212> PRT
<213> Vaccinia virus

<400> 153

```
Met Tyr Asn Ser Ser Ile His Thr Pro Glu Tyr Asp Val Ile Ile His
1               5                   10                  15

Val Ile Glu His Leu Lys His His Lys Gln Cys Val Gln Thr Val Thr
            20                  25                  30

Ser Gly Met Val Phe Thr Ser Pro Val Ser Ser Ser Ile Cys Thr Lys
        35                  40                  45

Ser Asp Asp Gly Arg Asn Leu Ser Asp Gly Phe Leu Leu Ile Arg Tyr
    50                  55                  60

Ile Thr Thr Asp Asp Phe Cys Thr Ile Phe Asp Ile Ile Pro Arg His
65                  70                  75                  80

Ile Phe Tyr Gln Leu Ala Asn Val Asp Glu His
                85                  90
```

<210> 154
<211> 290
<212> PRT
<213> Vaccinia virus

<400> 154
```
Met Glu Leu Glu Asn Glu Pro Val Ile Leu Pro Cys Pro Gln Ile Asn
1               5                  10                  15


Thr Leu Ser Ser Gly Tyr Asn Ile Leu Asp Ile Leu Trp Glu Lys Arg
            20                  25                  30


Gly Ala Asp Asn Asp Arg Ile Ile Pro Ile Asp Asn Gly Ser Asn Met
        35                  40                  45


Leu Ile Leu Asn Pro Thr Gln Ser Asp Ser Gly Ile Tyr Ile Cys Ile
    50                  55                  60


Thr Thr Asn Glu Thr Tyr Cys Asp Met Met Ser Leu Asn Leu Thr Ile
65                  70                  75                  80


Val Ser Val Leu Glu Ser Asn Ile Asp Leu Ile Ser Tyr Pro Gln Ile
                85                  90                  95


Val Asn Glu Arg Ser Thr Gly Glu Met Val Cys Pro Asn Ile Asn Ala
            100                 105                 110


Phe Ile Ala Ser Asn Val Asn Ala Asp Ile Ile Trp Ser Gly His Arg
        115                 120                 125


Arg Leu Arg Asn Lys Arg Leu Lys Gln Arg Thr Pro Gly Ile Ile Thr
    130                 135                 140


Ile Glu Asp Val Arg Lys Asn Asp Ala Gly Tyr Tyr Thr Cys Val Leu
145                 150                 155                 160


Glu Tyr Ile Tyr Arg Gly Lys Thr Tyr Asn Val Thr Arg Ile Val Lys
                165                 170                 175
```

```
Leu Glu Val Arg Asp Lys Ile Ile Pro Ser Thr Met Gln Leu Pro Asp
            180                 185                 190

Gly Ile Val Thr Ser Ile Gly Ser Asn Leu Thr Ile Ala Cys Arg Val
        195                 200                 205

Ser Leu Arg Pro Pro Thr Thr Asp Ala Asp Val Phe Trp Ile Ser Asn
    210                 215                 220

Gly Met Tyr Tyr Glu Glu Asp Asp Gly Asp Gly Asn Gly Arg Ile Ser
225                 230                 235                 240

Val Ala Asn Lys Ile Tyr Met Thr Asp Lys Arg Arg Val Ile Thr Ser
                245                 250                 255

Arg Leu Asn Ile Asn Pro Val Lys Glu Glu Asp Ala Thr Thr Phe Thr
            260                 265                 270

Cys Met Ala Phe Thr Ile Pro Ser Ile Ser Lys Thr Val Thr Val Ser
        275                 280                 285

Ile Thr
    290
```

<210> 155
<211> 75
<212> PRT
<213> Vaccinia virus

<400> 155

```
Met Val Ile Ile Pro Gly Val Arg Cys Leu Ser Leu Leu Phe Leu Arg
1               5                   10                  15

Arg Arg Cys Pro Leu His Ile Ile Ser Ala Phe Thr Leu Leu Ala Ile
            20                  25                  30

Asn Ala Leu Ile Leu Gly His Thr Ile Ser Pro Val Asp Leu Ser Phe
        35                  40                  45
```

Thr Ile Cys Gly Tyr Glu Ile Arg Ser Ile Phe Asp Ser Lys Thr Asp
    50   55   60

Thr Ile Val Lys Phe Asn Asp Ile Met Ser Gln
65   70   75

<210> 156
<211> 340
<212> PRT
<213> Vaccinia virus

<400> 156
Met Ser Arg Lys Phe Met Gln Val Tyr Glu Tyr Asp Arg Glu Gln Tyr
1   5   10   15

Leu Asp Glu Phe Ile Glu Asp Arg Tyr Asn Asp Ser Phe Ile Thr Ser
            20   25   30

Pro Glu Tyr Tyr Ser Ala Glu Lys Tyr Met Cys Arg Tyr Thr Thr Leu
        35   40   45

Asn His Asn Cys Val Asn Val Arg Arg Cys Ala Leu Asp Ser Lys Leu
    50   55   60

Leu His Asp Ile Ile Thr Asn Cys Lys Ile Tyr Asn Asn Ile Glu Leu
65   70   75   80

Val Arg Ala Thr Lys Phe Val Tyr Tyr Leu Asp Leu Ile Lys Cys Asn
                85   90   95

Trp Val Ser Lys Val Gly Asp Ser Val Leu Tyr Pro Val Ile Phe Ile
            100   105   110

Thr His Thr Ser Thr Arg Asn Leu Asp Lys Val Ser Val Lys Thr Tyr
        115   120   125

Lys Gly Val Lys Val Lys Lys Leu Asn Arg Cys Ala Asp His Ala Ile
    130   135   140

```
Val Ile Asn Pro Phe Val Lys Phe Lys Leu Thr Leu Pro Asn Lys Thr
145                 150                 155                 160

Ser His Ala Lys Val Leu Val Thr Phe Cys Lys Leu Arg Thr Asp Ile
                165                 170                 175

Thr Gln Ile Glu Ala Pro Leu Ser Gly Asn Val Leu Val Tyr Thr Phe
            180                 185                 190

Pro Asn Ile Asn Lys Arg Ile Pro Gly Tyr Ile His Val Asn Ile Glu
        195                 200                 205

Gly Cys Ile Asp Gly Met Ile Tyr Ile Asn Ser Ser Lys Phe Ala Cys
    210                 215                 220

Val Leu Lys Leu His Arg Ser Met Tyr Arg Ile Pro Pro Phe Pro Ile
225                 230                 235                 240

Asp Ile Cys Ser Cys Cys Ser Gln Tyr Thr Asn Gly Asp Ile Glu Ile
                245                 250                 255

Pro Ile His Asp Leu Ile Lys Asp Val Ala Ile Phe Lys Asn Lys Glu
            260                 265                 270

Thr Val Tyr Tyr Leu Lys Leu Asn Asn Lys Thr Ile Ala Arg Phe Thr
        275                 280                 285

Tyr Phe Asn Asn Ile Asp Thr Ala Ile Thr Gln Glu His Glu Tyr Val
    290                 295                 300

Lys Ile Ala Leu Gly Ile Val Cys Lys Leu Met Ile Asn Asn Met His
305                 310                 315                 320

Ser Ile Val Gly Val Asn His Ser Asn Thr Phe Val Asn Cys Leu Leu
                325                 330                 335

Glu Asp Asn Val
```

340

<210> 157
<211> 574
<212> PRT
<213> Vaccinia virus

<400> 157
Met Ser Arg Arg Leu Ile Tyr Val Leu Asn Ile Asn Arg Glu Ser Thr
1 5 10 15

His Lys Ile Gln Glu Asn Glu Ile Tyr Thr Tyr Phe Ser His Cys Asn
20 25 30

Ile Asp His Thr Ser Thr Glu Leu Asp Phe Val Val Lys Asn Tyr Asp
35 40 45

Leu Asn Arg Arg His Pro Val Thr Gly Tyr Thr Ala Leu His Cys Tyr
50 55 60

Leu Tyr Asn Asn Tyr Phe Thr Asn Asp Val Leu Lys Ile Leu Leu Asn
65 70 75 80

His Gly Val Asp Val Thr Met Lys Thr Ser Ser Gly Arg Met Pro Val
85 90 95

Tyr Ile Leu Leu Thr Arg Cys Cys Asn Ile Ser His Asp Val Val Ile
100 105 110

Asp Met Ile Asp Lys Asp Lys Asn His Leu Leu His Arg Asp Tyr Ser
115 120 125

Asn Leu Leu Leu Glu Tyr Ile Lys Ser Arg Tyr Met Leu Leu Lys Glu
130 135 140

Glu Asp Ile Asp Glu Asn Ile Val Ser Thr Leu Leu Asp Lys Gly Ile
145 150 155 160

Asp Pro Asn Phe Lys Gln Asp Gly Tyr Thr Ala Leu His Tyr Tyr Tyr

```
                165                 170                 175

Leu Cys Leu Ala His Val Tyr Lys Pro Gly Glu Cys Arg Lys Pro Ile
            180                 185                 190

Thr Ile Lys Lys Ala Lys Arg Ile Ile Ser Leu Phe Ile Gln His Gly
        195                 200                 205

Ala Asn Leu Asn Ala Leu Asp Asn Cys Gly Asn Thr Pro Phe His Leu
    210                 215                 220

Tyr Leu Ser Ile Glu Met Cys Asn Asn Ile His Met Thr Lys Met Leu
225                 230                 235                 240

Leu Thr Phe Asn Pro Asn Phe Lys Ile Cys Asn Asn His Gly Leu Thr
                245                 250                 255

Pro Ile Leu Cys Tyr Ile Thr Ser Asp Tyr Ile Gln His Asp Ile Leu
            260                 265                 270

Val Met Leu Ile His His Tyr Glu Thr Asn Val Gly Glu Met Pro Ile
        275                 280                 285

Asp Glu Arg Arg Ile Ile Val Phe Glu Phe Ile Lys Thr Tyr Ser Thr
    290                 295                 300

Arg Pro Ala Asp Ser Ile Thr Tyr Leu Met Asn Arg Phe Lys Asn Ile
305                 310                 315                 320

Asn Ile Tyr Thr Arg Tyr Glu Gly Lys Thr Leu Leu His Val Ala Cys
                325                 330                 335

Glu Tyr Asn Asn Thr Gln Val Ile Asp Tyr Leu Ile Arg Ile Asn Gly
            340                 345                 350

Asp Ile Asn Ala Leu Thr Asp Asn Asn Lys His Ala Thr Gln Leu Ile
        355                 360                 365
```

```
Ile Asp Asn Lys Glu Asn Ser Pro Tyr Thr Ile Asn Cys Leu Leu Tyr
    370                 375                 380

Ile Leu Arg Tyr Ile Val Asp Lys Asn Val Ile Arg Ser Leu Val Asp
385                 390                 395                 400

Gln Leu Pro Ser Leu Pro Ile Phe Asp Ile Lys Ser Phe Glu Lys Phe
                405                 410                 415

Ile Ser Tyr Cys Ile Leu Leu Asp Asp Thr Phe Tyr Asp Arg His Val
            420                 425                 430

Lys Asn Arg Asn Ser Lys Thr Tyr Arg Tyr Ala Phe Ser Lys Tyr Met
        435                 440                 445

Ser Phe Asp Lys Tyr Asp Gly Ile Ile Thr Lys Cys His Asp Glu Thr
    450                 455                 460

Met Leu Leu Lys Leu Ser Thr Val Leu Asp Thr Thr Leu Tyr Ala Val
465                 470                 475                 480

Leu Arg Cys His Asn Ser Arg Lys Leu Arg Arg Tyr Leu Thr Glu Leu
                485                 490                 495

Lys Lys Tyr Asn Asn Asp Lys Ser Phe Lys Ile Tyr Ser Asn Ile Met
            500                 505                 510

Asn Glu Arg Tyr Leu Asn Val Tyr Tyr Lys Asp Met Tyr Val Ser Lys
        515                 520                 525

Val Tyr Asp Lys Leu Phe Pro Val Phe Thr Asp Lys Asn Cys Leu Leu
    530                 535                 540

Thr Leu Leu Pro Ser Glu Ile Ile Tyr Glu Ile Leu Tyr Met Leu Thr
545                 550                 555                 560

Ile Asn Asp Leu Tyr Asn Ile Ser Tyr Pro Pro Thr Lys Val
```

565 570

<210> 158
<211> 353
<212> PRT
<213> Vaccinia virus

<400> 158
Met Thr Met Lys Met Met Val His Ile Tyr Phe Val Ser Leu Ser Leu
1 5 10 15

Leu Leu Leu Leu Phe His Ser Tyr Ala Ile Asp Ile Glu Asn Glu Ile
20 25 30

Thr Glu Phe Phe Asn Lys Met Arg Asp Thr Leu Pro Ala Lys Asp Ser
35 40 45

Lys Trp Leu Asn Pro Ala Cys Met Phe Gly Gly Thr Met Asn Asp Ile
50 55 60

Ala Ala Leu Gly Glu Pro Phe Ser Ala Lys Cys Pro Pro Ile Glu Asp
65 70 75 80

Ser Leu Leu Ser His Arg Tyr Lys Asp Tyr Val Val Lys Trp Glu Arg
85 90 95

Leu Glu Lys Asn Arg Arg Arg Gln Val Ser Asn Lys Arg Val Lys His
100 105 110

Gly Asp Leu Trp Ile Ala Asn Tyr Thr Ser Lys Phe Ser Asn Arg Arg
115 120 125

Tyr Leu Cys Thr Val Thr Thr Lys Asn Gly Asp Cys Val Gln Gly Ile
130 135 140

Val Arg Ser His Ile Lys Lys Pro Pro Ser Cys Ile Pro Lys Thr Tyr
145 150 155 160

Glu Leu Gly Thr His Asp Lys Tyr Gly Ile Asp Leu Tyr Cys Gly Ile

```
                165                 170                 175

Leu Tyr Ala Lys His Tyr Asn Asn Ile Thr Trp Tyr Lys Asp Asn Lys
            180                 185                 190

Glu Ile Asn Ile Asp Asp Ile Lys Tyr Ser Gln Thr Gly Lys Glu Leu
        195                 200                 205

Ile Ile His Asn Pro Glu Leu Glu Asp Ser Gly Arg Tyr Asp Cys Tyr
    210                 215                 220

Val His Tyr Asp Asp Val Arg Ile Lys Asn Asp Ile Val Val Ser Arg
225                 230                 235                 240

Cys Lys Ile Leu Thr Val Ile Pro Ser Gln Asp His Arg Phe Lys Leu
                245                 250                 255

Ile Leu Asp Pro Lys Ile Asn Val Thr Ile Gly Glu Pro Ala Asn Ile
            260                 265                 270

Thr Cys Thr Ala Val Ser Thr Ser Leu Leu Ile Asp Asp Val Leu Ile
        275                 280                 285

Glu Trp Glu Asn Pro Ser Gly Trp Leu Ile Gly Phe Asp Phe Asp Val
    290                 295                 300

Tyr Ser Val Leu Thr Ser Arg Gly Gly Ile Thr Glu Ala Thr Leu Tyr
305                 310                 315                 320

Phe Glu Asn Val Thr Glu Glu Tyr Ile Gly Asn Thr Tyr Lys Cys Arg
                325                 330                 335

Gly His Asn Tyr Tyr Phe Glu Lys Thr Leu Thr Thr Thr Val Val Leu
            340                 345                 350

Glu
```

<210> 159
<211> 56
<212> PRT
<213> Vaccinia virus

<400> 159
Met His Val Ile Asp Val Asp Val Arg Leu Tyr Met Ser Thr Phe Ile
1   5   10   15

Ile Ile Asp Gln Ser Thr Glu Asn Thr Ser Ile Asp Thr Thr Val Thr
            20   25   30

Ile Asn Ile Ile Tyr Leu Ala Ile Met Lys Ile Ile Met Asn Ile Ile
        35   40   45

Met Met Ile Met Ile Glu Leu Val
    50   55

<210> 160
<211> 271
<212> PRT
<213> Vaccinia virus

<400> 160
Leu Lys Asn Val Glu Cys Val Asp Ile Asp Ser Thr Ile Thr Phe Met
1   5   10   15

Lys Tyr Asp Pro Asn Asp Asp Asn Lys Arg Thr Cys Ser Asn Trp Val
            20   25   30

Pro Leu Thr Asn Asn Tyr Met Glu Tyr Cys Leu Val Ile Tyr Leu Glu
        35   40   45

Thr Pro Ile Cys Gly Gly Lys Ile Lys Leu Tyr His Pro Thr Gly Asn
    50   55   60

Ile Lys Ser Asp Lys Asp Ile Met Phe Ala Lys Thr Leu Asp Phe Lys
65   70   75   80

Ser Thr Lys Val Leu Thr Gly Arg Lys Thr Ile Ala Val Leu Asp Ile

```
                85                  90                  95

Ser Val Ser Tyr Asn Arg Ser Met Thr Thr Ile His Tyr Asn Asp Asp
            100                 105                 110

Val Asp Ile Asp Ile His Thr Asp Lys Asn Gly Lys Glu Leu Cys Tyr
        115                 120                 125

Cys Tyr Ile Thr Ile Asp Asp His Tyr Leu Val Asp Val Glu Thr Ile
    130                 135                 140

Gly Val Ile Val Asn Arg Ser Gly Lys Cys Leu Leu Val Asn Asn His
145                 150                 155                 160

Leu Gly Ile Gly Ile Val Lys Asp Lys Arg Ile Ser Asp Ser Phe Gly
                165                 170                 175

Asp Val Cys Met Asp Thr Ile Phe Asp Phe Ser Glu Ala Arg Glu Leu
            180                 185                 190

Phe Ser Leu Thr Asn Asp Asp Asn Arg Asn Ile Ala Trp Asp Thr Asp
        195                 200                 205

Lys Leu Asp Asp Asp Thr Asp Ile Trp Thr Pro Val Thr Glu Asn Asp
    210                 215                 220

Tyr Lys Phe Leu Ser Arg Leu Val Leu Tyr Ala Lys Ser Gln Ser Asp
225                 230                 235                 240

Thr Val Phe Asp Tyr Tyr Val Leu Thr Gly Asp Thr Glu Pro Pro Thr
                245                 250                 255

Val Phe Ile Phe Lys Val Thr Arg Phe Tyr Phe Asn Met Pro Lys
            260                 265                 270
```

<210> 161
<211> 74
<212> PRT

<213> Vaccinia virus

<400> 161
Met Tyr Cys Arg Cys Ser His Gly Tyr Thr Gly Ile Arg Cys Gln His
1   5   10   15

Val Val Leu Val Asp Tyr Gln Arg Ser Glu Lys Pro Asn Thr Thr Thr
            20   25   30

Ser Tyr Ile Pro Ser Pro Gly Ile Met Leu Val Leu Val Gly Ile Ile
        35   40   45

Ile Ile Thr Cys Cys Leu Leu Ser Val Tyr Arg Phe Thr Arg Arg Thr
    50   55   60

Lys Leu Pro Leu Gln Asp Met Val Val Pro
65   70

<210> 162
<211> 244
<212> PRT
<213> Vaccinia virus

<400> 162
Met His Val Pro Ala Ser Leu Gln Gln Ser Ser Ser Ser Ser Ser Ser
1   5   10   15

Cys Thr Glu Glu Glu Asn Lys His His Met Gly Ile Asp Val Ile Ile
            20   25   30

Lys Val Thr Lys Gln Asp Gln Thr Pro Thr Asn Asp Lys Ile Cys Gln
        35   40   45

Ser Val Thr Glu Ile Thr Glu Ser Glu Ser Asp Pro Asp Pro Glu Val
    50   55   60

Glu Ser Glu Asp Asp Ser Thr Ser Val Glu Asp Val Asp Pro Pro Thr
65   70   75   80

Thr Tyr Tyr Ser Ile Ile Gly Gly Gly Leu Arg Met Asn Phe Gly Phe

```
                85                  90                  95

Thr Lys Cys Pro Gln Ile Lys Ser Ile Ser Glu Ser Ala Asp Gly Asn
            100                 105                 110

Thr Val Asn Ala Arg Leu Ser Ser Val Ser Pro Gly Gln Gly Lys Asp
        115                 120                 125

Ser Pro Ala Ile Thr His Glu Glu Ala Leu Ala Met Ile Lys Asp Cys
    130                 135                 140

Glu Val Ser Ile Asp Ile Arg Cys Ser Glu Glu Glu Lys Asp Ser Asp
145                 150                 155                 160

Ile Lys Thr His Pro Val Leu Gly Ser Asn Ile Ser His Lys Lys Val
                165                 170                 175

Ser Tyr Glu Asp Ile Ile Gly Ser Thr Ile Val Asp Thr Lys Cys Val
            180                 185                 190

Lys Asn Leu Glu Phe Ser Val Arg Ile Gly Asp Met Cys Lys Glu Ser
        195                 200                 205

Ser Glu Leu Glu Val Lys Asp Gly Phe Lys Tyr Val Asp Gly Ser Ala
    210                 215                 220

Ser Glu Gly Ala Thr Asp Asp Thr Ser Leu Ile Asp Ser Thr Lys Leu
225                 230                 235                 240

Lys Ala Cys Val
```

<210> 163
<211> 222
<212> PRT
<213> Vaccinia virus

<400> 163

```
Met Asn His Cys Leu Leu Ala Ile Ser Ala Val Tyr Phe Lys Ala Lys
```

```
1               5                   10                  15

Trp Leu Thr Pro Phe Glu Lys Glu Phe Thr Ser Asp Tyr Pro Phe Tyr
            20                  25                  30

Val Ser Pro Thr Glu Met Val Asp Val Ser Met Met Ser Met Tyr Gly
        35                  40                  45

Lys Ala Phe Asn His Ala Ser Val Lys Glu Ser Phe Gly Asn Phe Ser
    50                  55                  60

Ile Ile Glu Leu Pro Tyr Val Gly Asp Thr Ser Met Met Val Ile Leu
65                  70                  75                  80

Pro Asp Lys Ile Asp Gly Leu Glu Ser Ile Glu Gln Asn Leu Thr Asp
                85                  90                  95

Thr Asn Phe Lys Lys Trp Cys Asp Phe Met Asp Ala Met Phe Ile Asp
            100                 105                 110

Val His Ile Pro Lys Phe Lys Val Thr Gly Ser Tyr Asn Leu Val Asp
        115                 120                 125

Thr Leu Val Lys Ser Gly Leu Thr Glu Val Phe Gly Ser Thr Gly Asp
    130                 135                 140

Tyr Ser Asn Met Cys Asn Leu Asp Val Ser Val Asp Ala Met Ile His
145                 150                 155                 160

Lys Thr Tyr Ile Asp Val Asn Glu Glu Tyr Thr Glu Ala Ala Ala Ala
                165                 170                 175

Thr Cys Ala Leu Val Ser Asp Cys Ala Ser Thr Val Thr Asn Glu Phe
            180                 185                 190

Cys Ala Asp His Pro Phe Ile Tyr Val Ile Arg His Val Asp Gly Lys
        195                 200                 205
```

```
Ile Leu Phe Val Gly Arg Tyr Cys Ser Pro Thr Thr Asn Cys
    210                 215                 220


<210> 164
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 164
Met Thr Ala Asn Phe Ser Thr His Val Phe Ser Pro Gln His Cys Gly
1               5                   10                  15


Cys Asp Arg Leu Thr Ser Ile Asp Asp Val Lys Gln Cys Leu Thr Glu
            20                  25                  30


Tyr Ile Tyr Trp Ser Ser Tyr Ala Tyr Arg Asn Arg Gln Cys Ala Gly
        35                  40                  45


Gln Leu Tyr Ser Thr Leu Leu Ser Phe Arg Asp Asp Ala Glu Leu Val
    50                  55                  60


Phe Ile Asp Ile Arg Glu Leu Val Lys His Met Pro Trp Asp Asp Val
65                  70                  75                  80


Lys Asp Cys Ala Glu Ile Ile Arg Cys Tyr Ile Pro Asp Glu Gln Lys
                85                  90                  95


Thr Ile Arg Glu Ile Ser Ala Ile Ile Gly Leu Cys Ala Tyr Ala Ala
            100                 105                 110


Thr Tyr Trp Gly Gly Glu Asp His Pro Thr Ser Asn Ser Leu Asn Ala
        115                 120                 125


Leu Phe Val Met Leu Glu Met Leu Asn Tyr Val Asp Tyr Asn Ile Ile
    130                 135                 140


Phe Arg Arg Met Asn
145
```

<210> 165
<211> 326
<212> PRT
<213> Vaccinia virus

<400> 165
Met Ser Ile Leu Pro Val Ile Phe Leu Ser Ile Phe Phe Tyr Ser Ser
1   5   10   15

Phe Val Gln Thr Phe Asn Ala Ser Glu Cys Ile Asp Lys Gly Gln Tyr
            20   25   30

Phe Ala Ser Phe Met Glu Leu Glu Asn Glu Pro Val Ile Leu Pro Cys
        35   40   45

Pro Gln Ile Asn Thr Leu Ser Ser Gly Tyr Asn Ile Leu Asp Ile Leu
    50   55   60

Trp Glu Lys Arg Gly Ala Asp Asn Asp Arg Ile Ile Pro Ile Asp Asn
65   70   75   80

Gly Ser Asn Met Leu Ile Leu Asn Pro Thr Gln Ser Asp Ser Gly Ile
                85   90   95

Tyr Ile Cys Ile Thr Thr Asn Glu Thr Tyr Cys Asp Met Met Ser Leu
            100   105   110

Asn Leu Thr Ile Val Ser Val Ser Glu Ser Asn Ile Asp Leu Ile Ser
        115   120   125

Tyr Pro Gln Ile Val Asn Glu Arg Ser Thr Gly Glu Met Val Cys Pro
    130   135   140

Asn Ile Asn Ala Phe Ile Ala Ser Asn Val Asn Ala Asp Ile Ile Trp
145   150   155   160

Ser Gly His Arg Arg Leu Arg Asn Lys Arg Leu Lys Gln Arg Thr Pro
                165   170   175

```
Gly Ile Ile Thr Ile Glu Asp Val Arg Lys Asn Asp Ala Gly Tyr Tyr
            180                 185                 190

Thr Cys Val Leu Glu Tyr Ile Tyr Gly Gly Lys Thr Tyr Asn Val Thr
        195                 200                 205

Arg Ile Val Lys Leu Glu Val Arg Asp Lys Ile Ile Pro Ser Thr Met
    210                 215                 220

Gln Leu Pro Asp Gly Ile Val Thr Ser Ile Gly Ser Asn Leu Thr Ile
225                 230                 235                 240

Ala Cys Arg Val Ser Leu Arg Pro Pro Thr Thr Asp Thr Asp Val Phe
                245                 250                 255

Trp Ile Ser Asn Gly Met Tyr Tyr Glu Glu Asp Asp Gly Asp Gly Asp
            260                 265                 270

Gly Arg Ile Ser Val Ala Asn Lys Ile Tyr Met Thr Asp Lys Arg Arg
        275                 280                 285

Val Ile Thr Ser Arg Leu Asn Ile Asn Pro Val Lys Glu Glu Asp Ala
    290                 295                 300

Thr Thr Phe Thr Cys Met Ala Phe Thr Ile Pro Ser Ile Ser Lys Thr
305                 310                 315                 320

Val Thr Val Ser Ile Thr
                325
```

<210> 166
<211> 340
<212> PRT
<213> Vaccinia virus

<400> 166

```
Met Ser Arg Lys Phe Met Gln Val Tyr Glu Tyr Asp Arg Glu Gln Tyr
1               5                   10                  15
```

```
Leu Asp Glu Phe Ile Glu Asp Arg Tyr Asn Asp Ser Phe Ile Thr Ser
            20                  25                  30

Pro Glu Tyr Tyr Ser Ala Glu Lys Tyr Met Cys Arg Tyr Thr Thr Leu
        35                  40                  45

Asn His Asn Cys Val Asn Val Arg Arg Cys Ala Leu Asp Ser Lys Leu
    50                  55                  60

Leu His Asp Ile Ile Thr Asn Cys Lys Ile Tyr Asn Asn Ile Glu Leu
65                  70                  75                  80

Val Arg Ala Thr Lys Phe Val Tyr Tyr Leu Asp Leu Ile Lys Cys Asn
                85                  90                  95

Trp Val Ser Lys Val Gly Asp Ser Val Leu Tyr Pro Val Ile Phe Ile
            100                 105                 110

Thr His Thr Ser Thr Arg Asn Leu Asp Lys Val Ser Val Lys Thr Tyr
        115                 120                 125

Lys Gly Val Lys Val Lys Lys Leu Asn Arg Cys Ala Asp His Ala Ile
    130                 135                 140

Val Ile Asn Pro Phe Val Lys Phe Lys Leu Thr Leu Pro Asn Lys Thr
145                 150                 155                 160

Ser His Ala Lys Val Leu Val Thr Phe Cys Lys Leu Arg Thr Asp Ile
                165                 170                 175

Thr Gln Ile Glu Ala Pro Leu Ser Gly Asn Val Leu Val Tyr Thr Phe
            180                 185                 190

Pro Asp Ile Asn Lys Arg Ile Pro Gly Tyr Ile His Val Asn Ile Glu
        195                 200                 205

Gly Cys Ile Asp Gly Met Ile Tyr Ile Asn Ser Ser Lys Phe Ala Cys
```

```
    210                 215                 220

Val Leu Lys Leu His Arg Ser Met Tyr Arg Ile Pro Pro Phe Pro Ile
225                 230                 235                 240

Asp Ile Cys Ser Cys Cys Ser Gln Tyr Thr Asn Asp Asp Ile Glu Ile
                245                 250                 255

Pro Ile His Asp Leu Ile Lys Asp Val Ala Ile Phe Lys Asn Lys Glu
            260                 265                 270

Thr Val Tyr Tyr Leu Lys Leu Asn Asn Lys Thr Ile Ala Arg Phe Thr
        275                 280                 285

Tyr Phe Asn Asn Ile Asp Thr Ala Ile Thr Gln Glu His Glu Tyr Val
    290                 295                 300

Lys Ile Ala Leu Gly Ile Val Cys Lys Leu Met Ile Asn Asn Met His
305                 310                 315                 320

Ser Ile Val Gly Val Asn His Ser Asn Thr Phe Val Asn Cys Leu Leu
                325                 330                 335

Glu Asp Asn Val
            340
```

<210> 167
<211> 574
<212> PRT
<213> Vaccinia virus

<400> 167

```
Met Ser Arg Arg Leu Ile Tyr Val Leu Asn Ile Asn Arg Glu Ser Thr
1               5                   10                  15

His Lys Ile Gln Glu Asn Glu Ile Tyr Thr Tyr Phe Ser His Cys Asn
            20                  25                  30

Ile Asp His Thr Ser Thr Glu Leu Asp Phe Val Val Lys Asn Tyr Asp
```

```
        35                  40                  45

Leu Asn Arg Arg Gln Pro Val Thr Gly Tyr Thr Ala Leu His Cys Tyr
    50                  55                  60

Leu Tyr Asn Asn Tyr Phe Thr Asn Asp Val Leu Lys Ile Leu Leu Asn
65                  70                  75                  80

His Gly Val Asp Val Thr Met Lys Thr Ser Ser Gly Arg Met Pro Val
                85                  90                  95

Tyr Ile Leu Leu Thr Arg Cys Cys Asn Ile Ser His Asp Val Val Ile
            100                 105                 110

Asp Met Ile Asp Lys Asp Lys Asn His Leu Ser His Arg Asp Tyr Ser
        115                 120                 125

Asn Leu Leu Leu Glu Tyr Ile Lys Ser Arg Tyr Met Leu Leu Lys Glu
    130                 135                 140

Glu Asp Ile Asp Glu Asn Ile Val Ser Thr Leu Leu Asp Lys Gly Ile
145                 150                 155                 160

Asp Pro Asn Phe Lys Gln Asp Gly Tyr Thr Ala Leu His Tyr Tyr Tyr
                165                 170                 175

Leu Cys Leu Ala His Val Tyr Lys Pro Gly Glu Cys Arg Lys Pro Ile
            180                 185                 190

Thr Ile Lys Lys Ala Lys Arg Ile Ile Ser Leu Phe Ile Gln His Gly
        195                 200                 205

Ala Asn Leu Asn Ala Leu Asp Asn Cys Gly Asn Thr Pro Phe His Leu
    210                 215                 220

Tyr Leu Ser Ile Glu Met Cys Asn Asn Ile His Met Thr Lys Met Leu
225                 230                 235                 240
```

```
Leu Thr Phe Asn Pro Asn Phe Lys Ile Cys Asn Asn His Gly Leu Thr
                245                 250                 255

Pro Ile Leu Cys Tyr Ile Thr Ser Asp Tyr Ile Gln His Asp Ile Leu
            260                 265                 270

Val Met Leu Ile His His Tyr Glu Thr Asn Val Gly Glu Met Pro Ile
        275                 280                 285

Asp Glu Arg Arg Ile Ile Val Phe Glu Phe Ile Lys Thr Tyr Ser Thr
    290                 295                 300

Arg Pro Ala Asp Ser Ile Thr Tyr Leu Met Asn Arg Phe Lys Asn Ile
305                 310                 315                 320

Asn Ile Tyr Thr Arg Tyr Glu Gly Lys Thr Leu Leu His Val Ala Cys
                325                 330                 335

Glu Tyr Asn Asn Thr His Val Ile Asp Tyr Leu Ile Arg Ile Asn Gly
            340                 345                 350

Asp Ile Asn Ala Leu Thr Asp Asn Asn Lys His Ala Ile Gln Leu Ile
        355                 360                 365

Ile Asp Asn Lys Glu Asn Ser Pro Tyr Thr Ile Asp Cys Leu Leu Tyr
    370                 375                 380

Ile Leu Arg Tyr Ile Val Asp Lys Asn Val Ile Arg Ser Leu Val Asp
385                 390                 395                 400

Gln Leu Pro Ser Leu Pro Ile Phe Asp Ile Lys Ser Phe Glu Lys Phe
                405                 410                 415

Ile Ser Tyr Cys Ile Leu Leu Asp Asp Thr Phe Tyr Asn Arg His Val
            420                 425                 430

Arg Asn Arg Asn Ser Lys Thr Tyr Arg Tyr Ala Phe Ser Lys Tyr Met
```

```
        435                 440                 445

Ser Phe Asp Lys Tyr Asp Gly Ile Ile Thr Lys Cys His Asp Glu Thr
    450                 455                 460

Met Leu Leu Lys Leu Ser Thr Val Leu Asp Thr Thr Leu Tyr Ala Val
465                 470                 475                 480

Leu Arg Cys His Asn Ser Lys Lys Leu Arg Arg Tyr Leu Asn Glu Leu
                485                 490                 495

Lys Lys Tyr Asn Asn Asp Lys Ser Phe Lys Ile Tyr Ser Asn Ile Met
            500                 505                 510

Asn Glu Arg Tyr Leu Asn Val Tyr Tyr Lys Asp Met Tyr Val Ser Lys
        515                 520                 525

Val Tyr Asp Lys Leu Phe Pro Val Phe Thr Asp Lys Asn Cys Leu Leu
    530                 535                 540

Thr Leu Leu Pro Ser Glu Ile Ile Tyr Glu Ile Leu Tyr Met Leu Thr
545                 550                 555                 560

Ile Asn Asp Leu Tyr Asn Ile Ser Tyr Pro Pro Thr Lys Val
                565                 570


<210> 168
<211> 265
<212> PRT
<213> Vaccinia virus

<400> 168
Met Thr Met Lys Met Met Val His Ile Tyr Phe Val Ser Leu Ser Leu
1               5                   10                  15

Leu Leu Leu Leu Phe His Ser Tyr Ala Ile Asp Ile Glu Asn Glu Ile
            20                  25                  30

Thr Glu Phe Phe Asn Lys Met Arg Asp Thr Leu Pro Ala Lys Asp Ser
```

```
        35                  40                  45

Lys Trp Leu Asn Pro Ala Cys Met Phe Gly Gly Thr Met Asn Asp Ile
    50                  55                  60

Ala Thr Leu Gly Glu Pro Phe Ser Ala Lys Cys Pro Pro Ile Glu Asp
65                  70                  75                  80

Ser Leu Leu Ser His Arg Tyr Lys Asp Tyr Val Val Lys Trp Glu Arg
                85                  90                  95

Leu Glu Lys Asn Arg Arg Arg Gln Val Ser Asn Lys Arg Val Lys His
            100                 105                 110

Gly Asp Leu Trp Ile Ala Asn Tyr Thr Ser Lys Phe Ser Asn Arg Arg
        115                 120                 125

Tyr Leu Cys Thr Val Thr Thr Lys Asn Gly Asp Cys Val Gln Gly Ile
    130                 135                 140

Val Arg Ser His Ile Arg Lys Pro Pro Ser Cys Ile Pro Lys Thr Tyr
145                 150                 155                 160

Glu Leu Gly Thr His Asp Lys Tyr Gly Ile Asp Leu Tyr Cys Gly Ile
                165                 170                 175

Leu Tyr Ala Lys His Tyr Asn Asn Ile Thr Trp Tyr Lys Asp Asn Lys
            180                 185                 190

Glu Ile Asn Ile Asp Asp Ile Lys Tyr Ser Gln Thr Gly Lys Lys Leu
        195                 200                 205

Ile Ile His Asn Pro Glu Leu Glu Asp Ser Gly Arg Tyr Asp Cys Tyr
    210                 215                 220

Val His Tyr Asp Asp Val Arg Ile Lys Asn Asp Ile Val Val Ser Arg
225                 230                 235                 240
```

Cys Lys Ile Leu Thr Val Ile Pro Ser Gln Asp His Arg Phe Lys Leu
245 250 255

Lys Arg Asn Cys Gly Tyr Ala Ser Asn
260 265

<210> 169
<211> 91
<212> PRT
<213> Vaccinia virus

<400> 169
Met Arg Gln Ile Lys Ile Asn Gly Thr Asp Met Leu Thr Val Met Tyr
1 5 10 15

Met Leu Asn Lys Pro Thr Lys Lys Arg Tyr Val Asn Asn Pro Ile Phe
20 25 30

Thr Asp Trp Ala Asn Lys Gln Tyr Lys Phe Tyr Asn Gln Ile Ile Tyr
35 40 45

Asn Ala Asn Lys Leu Ile Glu Gln Ser Lys Lys Ile Asp Asp Met Ile
50 55 60

Glu Glu Val Ser Ile Asp Asp Asn Arg Leu Ser Thr Leu Pro Leu Glu
65 70 75 80

Ile Arg His Leu Ile Phe Ser Tyr Ala Phe Leu
85 90

<210> 170
<211> 55
<212> PRT
<213> Vaccinia virus

<400> 170
Met Ser Ser Lys Gly Gly Ser Gly Gly Met Trp Ser Val Phe Ile His
1 5 10 15

Gly His Asp Gly Ser Asn Lys Gly Ser Lys Thr Tyr Thr Ser Gly Gly

```
            20                  25                  30

Gly Gly Met Trp Gly Gly Gly Ser Ser Ser Gly Val Asn Gly Gly Val
        35                  40                  45

Lys Ser Gly Thr Gly Lys Ile
    50                  55

<210> 171
<211> 71
<212> PRT
<213> Vaccinia virus

<400> 171
Met Phe Asp Tyr Leu Glu Asn Glu Glu Val Ala Leu Asp Glu Leu Lys
1               5                   10                  15

Gln Met Leu Arg Asp Arg Asp Pro Asn Asp Thr Arg Asn Gln Phe Lys
            20                  25                  30

Asn Asn Ala Leu His Ala Tyr Leu Phe Asn Glu His Cys Asn Asn Val
        35                  40                  45

Glu Val Val Lys Leu Leu Leu Asp Ser Gly Thr Asn Pro Leu Arg Lys
    50                  55                  60

Asn Trp Arg Gln Leu Pro His
65                  70

<210> 172
<211> 83
<212> PRT
<213> Vaccinia virus

<400> 172
Met Leu Lys Leu Lys Asp Ile Ala Met Ala Leu Leu Glu Ala Thr Gly
1               5                   10                  15

Phe Ser Asn Ile Asn Asp Phe Asn Ile Phe Ser Tyr Met Lys Ser Lys
            20                  25                  30
```

Asn Val Asp Val Asp Leu Ile Lys Val Leu Val Glu His Gly Phe Asp
        35   40   45

Leu Ser Val Lys Cys Glu Asn His Arg Ser Val Ile Glu Asn Tyr Val
    50   55   60

Met Thr Met Ile Leu Phe Ile Glu Asn Gly Cys Ser Val Leu Tyr Glu
65   70   75   80

Asp Glu Tyr

<210> 173
<211> 170
<212> PRT
<213> Vaccinia virus

<400> 173
Met Lys Gly Ile Asp Asn Thr Ala Tyr Ser Tyr Ile Asp Asp Leu Thr
1   5   10   15

Cys Cys Thr Arg Gly Ile Met Ala Asp Tyr Leu Asn Ser Asp Tyr Arg
            20   25   30

Tyr Asn Lys Asp Val Asp Leu Val Lys Leu Phe Leu Glu Asn Gly Lys
        35   40   45

Pro His Gly Ile Met Cys Ser Ile Val Pro Leu Trp Arg Asn Asp Lys
    50   55   60

Glu Thr Ile Phe Leu Ile Leu Lys Thr Met Asn Ser Asp Val Leu Gln
65   70   75   80

His Ile Leu Ile Glu Tyr Met Thr Phe Gly Asp Ile Pro Leu Val Glu
                85   90   95

Tyr Gly Thr Val Val Asn Lys Glu Ala Ile His Gly Tyr Phe Arg Asn
            100   105   110

```
Ile Asn Ile Asp Ser Tyr Thr Met Lys Tyr Leu Leu Lys Lys Glu Gly
        115                 120                 125


Arg Cys His Gln Leu Ser Arg Leu Asp Thr Tyr Val Asn Pro Thr Met
    130                 135                 140


Asp Val Ile Ile Ser Thr Leu Ile His Thr Lys Arg Val Phe Val Thr
145                 150                 155                 160


Cys Leu Met Leu Ala Gln Phe Leu Val Leu
                165                 170


<210> 174
<211> 173
<212> PRT
<213> Vaccinia virus

<400> 174
Met Pro Ser Ile Ile Ser Ile Gly His Leu Cys Lys Ser Asn Tyr Gly
1               5                   10                  15


Cys Tyr Asn Phe Tyr Thr Tyr Thr Tyr Lys Lys Gly Leu Cys Asp Met
            20                  25                  30


Ser Tyr Ala Cys Pro Ile Leu Ser Thr Ile Asn Ile Cys Leu Pro Tyr
        35                  40                  45


Leu Lys Asp Ile Asn Met Ile Asp Lys Arg Gly Glu Thr Leu Leu His
    50                  55                  60


Lys Ala Val Arg Tyr Asn Lys Gln Ser Leu Val Ser Leu Leu Leu Glu
65                  70                  75                  80


Ser Gly Ser Asp Val Asn Ile Arg Ser Asn Asn Gly Tyr Thr Cys Ile
                85                  90                  95


Ala Ile Ala Ile Asn Glu Ser Lys Asn Ile Glu Leu Leu Lys Met Leu
            100                 105                 110
```

```
Leu Cys His Lys Pro Thr Leu Asp Tyr Val Ile Asp Ser Leu Arg Glu
        115                 120                 125


Ile Ser Asn Ile Val Asp Asn Asp Tyr Ala Ile Lys Gln Cys Ile Lys
    130                 135                 140


Tyr Ala Met Ile Ile Asp Asp Cys Thr Ser Ser Lys Ile Pro Glu Phe
145                 150                 155                 160


Ile Ser Gln Arg Tyr Asn Asp Tyr Ile Asp Leu Cys Asn
                165                 170


<210> 175
<211> 90
<212> PRT
<213> Vaccinia virus

<400> 175
Met Lys Lys Ile Met Val Gly Gly Asn Thr Met Phe Ser Leu Ile Phe
1               5                   10                  15


Thr Asp His Gly Ala Lys Ile Ile His Arg Tyr Ala Asn Asn Pro Glu
            20                  25                  30


Leu Arg Glu Tyr Tyr Glu Leu Lys Gln Asn Lys Ile Tyr Val Glu Ala
        35                  40                  45


Tyr Asp Ile Ile Ser Asn Ala Ile Val Lys His Asp Arg Ile His Lys
    50                  55                  60


Thr Ile Glu Ser Val Asp Asp Asn Thr Tyr Ile Ser Asn Leu Pro Tyr
65                  70                  75                  80


Thr Ile Lys Tyr Lys Ile Phe Glu Gln Gln
                85                  90


<210> 176
<211> 126
<212> PRT
```

<213> Vaccinia virus

<400> 176
Met Arg Ile Leu Phe Leu Ile Ala Phe Met Tyr Gly Cys Val His Ser
1   5   10   15

Tyr Val Asn Ala Val Glu Thr Lys Cys Ser Asn Leu Asp Ile Val Thr
            20   25   30

Ser Ser Gly Glu Phe His Cys Ser Gly Cys Val Glu His Met Pro Asn
        35   40   45

Phe Ser Tyr Met Tyr Trp Leu Ala Lys Asp Met Arg Ser Asp Glu Asp
    50   55   60

Ala Lys Phe Ile Glu His Leu Gly Glu Gly Ile Lys Glu Asp Glu Thr
65   70   75   80

Val Arg Thr Ile Asp Gly Arg Ile Val Thr Leu Gln Lys Val Leu His
                85   90   95

Val Thr Asp Thr Asn Lys Phe Ala His Tyr Arg Phe Thr Cys Val Leu
            100   105   110

Thr Thr Ile Asp Gly Val Ser Lys Lys Asn Ile Trp Leu Lys
        115   120   125

<210> 177
<211> 62
<212> PRT
<213> Vaccinia virus

<400> 177
Met Lys Leu Phe Thr Gln Asn Asp Arg Tyr Phe Gly Leu Leu Asp Ser
1   5   10   15

Cys Asn His Ile Phe Cys Ile Thr Cys Ile Asn Ile Trp His Lys Thr
            20   25   30

Arg Arg Glu Thr Gly Ala Ser Asp Asn Cys Pro Ile Cys Arg Thr Arg

```
        35                  40                  45


Phe Arg Asn Ile Thr Met Ser Lys Phe Tyr Lys Leu Val Asn
    50                  55                  60


<210> 178
<211> 66
<212> PRT
<213> Vaccinia virus

<400> 178
Met His Tyr Pro Lys Tyr Tyr Ile Asn Ile Thr Lys Ile Asn Pro His
1               5                   10                  15


Leu Ala Asn Gln Phe Arg Ala Trp Lys Lys Arg Ile Ala Gly Arg Asp
            20                  25                  30


Tyr Met Thr Asn Leu Ser Lys Asp Thr Gly Ile Gln Gln Ser Lys Leu
        35                  40                  45


Tyr Val Thr Val Lys Lys Ile Glu Thr Tyr Met Val Tyr Ile Tyr Thr
    50                  55                  60


Thr Ile
65


<210> 179
<211> 331
<212> PRT
<213> Vaccinia virus

<400> 179
Met Asp Ile Tyr Asp Asp Lys Gly Leu Gln Thr Ile Lys Leu Phe Asn
1               5                   10                  15


Asn Glu Phe Asp Cys Ile Arg Asn Asp Ile Arg Glu Leu Phe Lys His
            20                  25                  30


Val Thr Asp Ser Asp Ser Ile Gln Leu Pro Met Glu Asp Asn Ser Asp
        35                  40                  45
```

```
Ile Ile Glu Asn Ile Arg Lys Ile Leu Tyr Arg Arg Leu Lys Asn Val
    50                  55                  60

Glu Cys Val Asp Ile Asp Asn Thr Ile Thr Phe Met Lys Tyr Asp Pro
65                  70                  75                  80

Asn Asp Asp Asn Lys Arg Thr Cys Ser Asn Trp Val Pro Leu Thr Asn
                85                  90                  95

Asn Tyr Met Glu Tyr Cys Leu Val Ile Tyr Leu Glu Thr Pro Ile Cys
            100                 105                 110

Gly Gly Lys Ile Lys Leu Tyr His Pro Thr Gly Asn Ile Lys Ser Asp
        115                 120                 125

Lys Asp Ile Met Phe Ala Lys Thr Leu Asp Phe Lys Ser Lys Lys Val
    130                 135                 140

Leu Thr Gly Arg Lys Thr Ile Ala Val Leu Asp Ile Ser Val Ser Tyr
145                 150                 155                 160

Asn Arg Ser Ile Thr Thr Ile His Tyr Asn Asp Asp Val Asp Ile Asp
                165                 170                 175

Ile His Thr Asp Lys Asn Gly Lys Glu Leu Cys Tyr Cys Tyr Ile Thr
            180                 185                 190

Ile Asp Asp His Tyr Leu Val Asp Val Glu Thr Ile Gly Val Ile Val
        195                 200                 205

Asn Arg Ser Gly Lys Cys Leu Leu Val Asn Asn His Leu Gly Ile Gly
    210                 215                 220

Ile Val Lys Asp Lys Arg Ile Ser Asp Ser Phe Gly Asp Val Cys Met
225                 230                 235                 240

Asp Thr Ile Phe Asp Phe Ser Glu Ala Arg Glu Leu Phe Ser Leu Thr
```

```
                245                 250                 255

Asn Asp Asp Asn Arg Asn Ile Ala Trp Asp Thr Asp Lys Leu Asp Asp
            260                 265                 270

Asp Thr Asp Ile Trp Thr Pro Val Thr Glu Asn Asp Tyr Lys Phe Leu
        275                 280                 285

Ser Arg Leu Val Leu Tyr Ala Lys Ser Gln Ser Asp Thr Val Phe Asp
    290                 295                 300

Tyr Tyr Val Leu Thr Gly Asp Thr Glu Pro Pro Thr Val Phe Ile Phe
305                 310                 315                 320

Lys Val Thr Arg Phe Tyr Phe Asn Met Pro Lys
                325                 330
```

<210> 180
<211> 141
<212> PRT
<213> Vaccinia virus

<400> 180

```
Met Leu Ile Asn Tyr Leu Met Leu Leu Phe Ala Ala Met Ile Ile Arg
1               5                   10                  15

Ser Phe Ala Asp Ser Gly Asn Ala Ile Glu Thr Thr Leu Pro Glu Ile
            20                  25                  30

Thr Asn Ala Thr Thr Asp Ile Pro Ala Ile Arg Leu Cys Gly Pro Glu
        35                  40                  45

Gly Asp Gly Tyr Cys Leu His Gly Asp Cys Ile His Ala Arg Asp Ile
    50                  55                  60

Asp Gly Met Tyr Cys Arg Cys Ser His Gly Tyr Thr Gly Ile Arg Cys
65                  70                  75                  80

Gln His Val Val Leu Val Asp Tyr Gln Arg Ser Glu Lys Pro Asn Thr
```

```
                85                  90                  95

Thr Thr Ser Tyr Ile Pro Ser Pro Gly Ile Met Leu Val Leu Val Gly
            100                 105                 110

Ile Ile Ile Ile Thr Cys Cys Leu Leu Ser Val Tyr Arg Phe Thr Arg
        115                 120                 125

Arg Thr Asn Lys Leu Pro Leu Gln Asp Met Val Val Pro
    130                 135                 140
```

<210> 181
<211> 357
<212> PRT
<213> Vaccinia virus

<400> 181

```
Met Asp Ile Phe Lys Glu Leu Ile Val Lys His Pro Asp Glu Asn Val
1               5                   10                  15

Leu Ile Ser Pro Val Ser Ile Leu Ser Thr Leu Ser Ile Leu Asn His
            20                  25                  30

Gly Ala Ala Gly Ser Thr Ala Glu Gln Leu Ser Lys Tyr Ile Glu Asn
        35                  40                  45

Met Asn Glu Asn Thr Pro Asp Asp Lys Lys Asp Asp Asn Asn Asp Met
    50                  55                  60

Asp Val Asp Ile Pro Tyr Cys Ala Thr Leu Ala Thr Ala Asn Lys Ile
65                  70                  75                  80

Tyr Gly Ser Asp Ser Ile Glu Phe His Ala Ser Phe Leu Gln Lys Ile
                85                  90                  95

Lys Asp Asp Phe Gln Thr Val Asn Phe Asn Asn Ala Asn Gln Thr Lys
            100                 105                 110

Glu Leu Ile Asn Glu Trp Val Lys Thr Met Thr Asn Gly Lys Ile Asn
```

```
        115                 120                 125

Ser Leu Leu Thr Ser Pro Leu Ser Ile Asn Thr Arg Met Thr Val Val
    130                 135                 140

Ser Ala Val His Phe Lys Ala Met Trp Lys Tyr Pro Phe Ser Lys His
145                 150                 155                 160

Leu Thr Tyr Thr Asp Lys Phe Tyr Ile Ser Lys Asn Ile Val Thr Ser
                165                 170                 175

Val Asp Met Met Val Gly Thr Glu Asn Asn Leu Gln Tyr Val His Ile
            180                 185                 190

Asn Glu Leu Phe Gly Gly Phe Ser Ile Ile Asp Ile Pro Tyr Glu Gly
        195                 200                 205

Asn Ser Ser Met Val Ile Ile Leu Pro Asp Asp Ile Glu Gly Ile Tyr
    210                 215                 220

Asn Ile Glu Lys Asn Ile Thr Asp Glu Lys Phe Lys Lys Trp Cys Gly
225                 230                 235                 240

Met Leu Ser Thr Lys Ser Ile Asp Leu Tyr Met Pro Lys Phe Lys Val
                245                 250                 255

Glu Met Thr Glu Pro Tyr Asn Leu Val Pro Ile Leu Glu Asn Leu Gly
            260                 265                 270

Leu Thr Asn Ile Phe Gly Tyr Tyr Ala Asp Phe Ser Lys Met Cys Asn
        275                 280                 285

Glu Thr Ile Thr Val Glu Lys Phe Leu His Thr Thr Phe Ile Asp Val
    290                 295                 300

Asn Glu Glu Tyr Thr Glu Ala Ser Ala Val Thr Gly Val Phe Met Thr
305                 310                 315                 320
```

```
Asn Phe Ala Met Val Tyr Arg Thr Lys Val Tyr Ile Asn His Pro Phe
                325                 330                 335


Met Tyr Met Ile Lys Asp Thr Thr Gly Arg Ile Leu Phe Ile Gly Lys
            340                 345                 350


Tyr Cys Tyr Pro Gln
        355


<210> 182
<211> 190
<212> PRT
<213> Vaccinia virus

<400> 182
Met Met Ile Tyr Gly Leu Ile Ala Cys Leu Ile Phe Val Thr Ser Ser
1               5                   10                  15


Ile Ala Ser Pro Leu Tyr Ile Pro Val Ile Pro Pro Ile Thr Glu Asp
            20                  25                  30


Lys Ser Phe Asn Ser Val Glu Val Leu Val Ser Leu Phe Arg Asp Asp
        35                  40                  45


Gln Lys Asp Tyr Thr Val Thr Ser Gln Phe Asn Asn Tyr Thr Ile Asp
    50                  55                  60


Thr Lys Asp Trp Thr Ile Gly Val Leu Ser Thr Pro Asp Gly Leu Asp
65                  70                  75                  80


Ile Pro Leu Thr Asn Ile Thr Tyr Trp Ser Arg Phe Thr Ile Gly Arg
                85                  90                  95


Ala Leu Phe Lys Ser Glu Ser Glu Asp Ile Phe Gln Lys Lys Met Ser
            100                 105                 110


Ile Leu Gly Val Ser Ile Glu Cys Lys Lys Ser Ser Thr Leu Leu Thr
        115                 120                 125
```

```
Phe Leu Thr Val Arg Lys Met Thr Arg Val Phe Asn Lys Phe Pro Asp
    130                 135                 140


Met Ala Tyr Tyr Arg Gly Asp Cys Leu Lys Ala Val Tyr Val Thr Met
145                 150                 155                 160


Thr Tyr Lys Asn Thr Lys Thr Gly Glu Thr Asp Tyr Thr Tyr Leu Ser
                165                 170                 175


Asn Gly Gly Leu Pro Ala Tyr Tyr Arg Asn Gly Val Asp Gly
            180                 185                 190


<210> 183
<211> 51
<212> PRT
<213> Vaccinia virus

<400> 183
Met Asn Leu Gln Lys Leu Ser Leu Ala Ile Tyr Leu Thr Ala Thr Cys
1               5                   10                  15


Ser Trp Cys Tyr Glu Thr Cys Ile Arg Lys Thr Ala Leu Tyr His Asp
            20                  25                  30


Ile Gln Leu Glu His Val Glu Asp Asn Lys Asp Ser Val Ala Ser Leu
        35                  40                  45


Pro Tyr Lys
    50


<210> 184
<211> 87
<212> PRT
<213> Vaccinia virus

<400> 184
Met Ser Leu Glu Ser Phe Ile Ile Thr Thr Phe Asn Asn Asn Ser Ser
1               5                   10                  15


Thr Asn Ile Asp Asn Met Cys His Leu Tyr Val Lys Val Cys Pro Ser
```

```
            20                  25                  30

Ser Leu Leu Phe Arg Leu Phe Val Glu Cys Cys Asp Ile Asn Lys Leu
        35                  40                  45

Val Glu Gly Thr Thr Pro Leu His Cys Tyr Leu Met Asn Glu Gly Phe
    50                  55                  60

Glu Ser Ser Val Leu Lys Asn Leu Leu Lys Glu Tyr Val Met Thr Ser
65                  70                  75                  80

Ile Thr Gln Ile Phe Asn Ser
                85
```

<210> 185
<211> 181
<212> PRT
<213> Vaccinia virus

<400> 185

```
Met Ile Ser Leu Ser Phe Leu Ile His Asn Pro Leu Lys Lys Trp Lys
1               5                   10                  15

Leu Lys Pro Ser Ile Ser Ile Asn Gly Tyr Arg Ser Thr Phe Thr Met
            20                  25                  30

Ala Phe Pro Cys Ala Gln Phe Arg Pro Cys His Cys His Ala Thr Lys
        35                  40                  45

Asp Ser Leu Asn Thr Val Ala Asp Val Arg His Cys Leu Thr Glu Tyr
    50                  55                  60

Ile Leu Trp Val Ser His Arg Trp Thr His Arg Glu Thr Ala Gly Pro
65                  70                  75                  80

Leu Tyr Arg Leu Leu Ile Ser Phe Arg Thr Asp Ala Thr Glu Leu Phe
                85                  90                  95

Gly Gly Glu Leu Lys Asp Ser Leu Pro Trp Asp Asn Ile Asp Asn Cys
```

```
            100                 105                 110

Val Glu Ile Ile Lys Cys Phe Ile Arg Asn Asp Ser Met Lys Thr Ala
        115                 120                 125

Glu Glu Leu Arg Ala Ile Ile Gly Leu Cys Thr Gln Ser Ala Ile Val
    130                 135                 140

Ser Gly Arg Val Phe Asn Asp Lys Tyr Ile Asp Ile Leu Leu Met Leu
145                 150                 155                 160

Arg Lys Ile Leu Asn Glu Asn Asp Tyr Leu Thr Leu Leu Asp His Ile
                165                 170                 175

Arg Thr Ala Lys Tyr
            180
```

<210> 186
<211> 382
<212> PRT
<213> Vaccinia virus

<400> 186

```
Met Ile Ala Phe Ile Ile Phe Arg Glu Ile Gly Ile Ile Ser Thr Arg
1               5                   10                  15

Ile Ala Met Asp Cys Thr Cys Ile Leu Cys Arg Leu Leu Asp Glu Asp
            20                  25                  30

Val Thr Tyr Lys Lys Ile Lys Leu Glu Ile Glu Thr Cys His Asn Leu
        35                  40                  45

Ser Lys His Ile Asp Arg Arg Gly Asn Asn Ala Leu His Cys Tyr Val
    50                  55                  60

Phe Asn Lys Cys Asp Thr Asp Ile Lys Ile Val Arg Leu Leu Leu Ser
65                  70                  75                  80

Arg Gly Val Glu Arg Leu Cys Arg Asn Asn Glu Gly Leu Thr Pro Leu
```

```
                85                  90                  95

Gly Val Tyr Ser Lys His Arg Tyr Val Lys Ser Gln Ile Val His Leu
            100                 105                 110

Leu Ile Ser Ser Tyr Ser Asn Ser Ser Asn Glu Leu Lys Ser Asn Ile
        115                 120                 125

Asn Asp Phe Asp Leu Ser Ser Asp Asn Ile Asp Leu Arg Leu Leu Lys
    130                 135                 140

Tyr Leu Ile Val Asp Lys Arg Ile Arg Pro Ser Lys Asn Thr Asn Tyr
145                 150                 155                 160

Ala Ile Asn Ser Leu Gly Leu Val Asp Ile Tyr Val Thr Thr Pro Asn
                165                 170                 175

Pro Arg Pro Glu Val Leu Leu Trp Leu Leu Lys Ser Glu Cys Tyr Ser
            180                 185                 190

Thr Gly Tyr Val Phe Arg Thr Cys Met Tyr Asn Ser Asp Met Cys Lys
        195                 200                 205

Asn Ser Leu His Tyr Tyr Ile Ser Ser His Arg Glu Ser Gln Ser Leu
    210                 215                 220

Ser Lys Asp Val Ile Lys Cys Leu Ile Asn Asn Asn Val Ser Ile His
225                 230                 235                 240

Gly Arg Asp Glu Gly Gly Ser Leu Pro Ile Gln Tyr Tyr Trp Ser Phe
                245                 250                 255

Ser Thr Ile Asp Ile Glu Ile Val Lys Leu Leu Leu Ile Lys Asp Val
            260                 265                 270

Asp Thr Cys Arg Val Tyr Asp Val Ser Pro Ile Leu Glu Ala Tyr Tyr
        275                 280                 285
```

```
Leu Asn Lys Arg Phe Arg Val Thr Pro Tyr Asn Val Asp Met Glu Ile
    290                 295                 300

Val Asn Leu Leu Ile Glu Arg Arg His Thr Leu Val Asp Val Met Arg
305                 310                 315                 320

Ser Ile Thr Ser Tyr Asp Ser Arg Glu Tyr Asn His Tyr Ile Ile Asp
                325                 330                 335

Asn Ile Leu Lys Arg Phe Arg Gln Gln Asp Glu Ser Ile Val Gln Ala
            340                 345                 350

Met Leu Ile Asn Tyr Leu His Tyr Gly Asp Met Val Val Arg Cys Met
        355                 360                 365

Leu Asp Asn Gly Gln Gln Leu Ser Ser Ala Arg Leu Leu Cys
    370                 375                 380
```

<210> 187
<211> 198
<212> PRT
<213> Vaccinia virus

<400> 187

```
Met Tyr Gly Leu Ile Leu Ser Arg Phe Asn Asn Cys Gly Tyr His Cys
1               5                   10                  15

Tyr Glu Thr Ile Leu Ile Asp Val Phe Asp Ile Leu Ser Lys Tyr Met
            20                  25                  30

Asp Asn Ile Asp Met Ile Asp Asn Glu Asn Lys Thr Leu Leu Tyr Tyr
        35                  40                  45

Ala Val Asp Val Asn Asn Ile Gln Phe Ala Lys Arg Leu Leu Glu Tyr
    50                  55                  60

Gly Ala Ser Val Thr Thr Ser Arg Ser Ile Ile Asn Thr Ala Ile Gln
65                  70                  75                  80
```

```
Lys Ser Ser Tyr Arg Arg Glu Asn Lys Thr Lys Leu Val Asp Leu Leu
                85                  90                  95

Leu Ser Tyr His Pro Thr Leu Glu Thr Met Ile Asp Ala Phe Asn Arg
            100                 105                 110

Asp Ile Arg Tyr Leu Tyr Pro Glu Pro Leu Phe Ala Cys Ile Arg Tyr
        115                 120                 125

Ala Leu Ile Leu Asp Asp Asp Phe Pro Ser Lys Val Lys Tyr Asp Ile
    130                 135                 140

Ser Gly Arg His Lys Glu Leu Lys Arg Tyr Arg Val Asp Ile Asn Arg
145                 150                 155                 160

Met Lys Asn Ala Tyr Ile Ser Gly Val Ser Met Phe Asp Ile Leu Phe
                165                 170                 175

Lys Arg Ser Lys Arg His Arg Leu Arg Tyr Ala Lys Asn Pro Thr Ser
            180                 185                 190

Asn Gly Thr Lys Lys Asn
        195


<210> 188
<211> 147
<212> PRT
<213> Vaccinia virus

<400> 188
Met Ser Arg Ile Asn Ile Thr Lys Lys Ile Tyr Cys Ser Val Phe Leu
1               5                   10                  15

Phe Leu Phe Leu Ser Tyr Ile Ser Asn Tyr Glu Lys Val Asn Asp Glu
            20                  25                  30

Met Tyr Glu Met Gly Glu Met Asp Glu Ile Val Ser Ile Val Arg Asp
        35                  40                  45
```

```
Ser Met Trp Tyr Ile Pro Asn Val Phe Met Asp Asp Gly Lys Asn Glu
    50                  55                  60

Gly His Val Ser Val Asn Asn Val Cys His Met Tyr Phe Thr Phe Phe
65                  70                  75                  80

Asp Val Asp Thr Ser Ser His Leu Phe Lys Leu Val Ile Lys His Cys
                85                  90                  95

Asp Leu Asn Lys Arg Gly Asn Ser Pro Leu His Cys Tyr Thr Met Asn
            100                 105                 110

Thr Arg Phe Asn Pro Ser Val Leu Lys Ile Leu Leu His His Gly Met
        115                 120                 125

Arg Asn Phe Asp Ser Lys Asp Asp His Tyr Gln Ser Ile Thr Arg Ser
    130                 135                 140

Leu Ile Tyr
145
```

<210> 189
<211> 128
<212> PRT
<213> Vaccinia virus

<400> 189

```
Met Glu Gln Thr Leu Thr Arg Leu His Thr Tyr Leu Gln Gln Tyr Thr
1               5                   10                  15

Lys His Ser Pro Arg Val Val Tyr Ala Leu Leu Ser Arg Gly Tyr Val
            20                  25                  30

Ile Ile Leu Ile Val His Pro Ser Trp Asn Asp Cys Ala Thr Gly His
        35                  40                  45

Ile Leu Ile Met Leu Leu Asn Trp His Glu Gln Lys Glu Glu Gly Gln
    50                  55                  60
```

```
His Leu Leu Tyr Leu Phe Ile Lys His Asn Gln Gly Tyr Thr Leu Asn
65                  70                  75                  80


Ile Leu Arg Tyr Leu Leu Asp Arg Phe Asp Ile Gln Lys Asp Glu Tyr
                85                  90                  95


Tyr Asn Thr Ala Phe Gln Asn Cys Asn Asn Asn Val Ala Ser Tyr Ile
            100                 105                 110


Gly Tyr Asp Ile Asn Leu Pro Thr Lys Asp Gly Ile Arg Leu Gly Val
        115                 120                 125


<210> 190
<211> 111
<212> PRT
<213> Vaccinia virus

<400> 190
Met Leu Pro His Thr Ser Asp Thr Thr Ser Thr Phe Arg Leu Lys Thr
1               5                   10                  15


Val Phe Asp Leu Val Phe Glu Asn Arg Asn Ile Ile Tyr Lys Ala Asp
            20                  25                  30


Val Val Asn Asp Ile Ile His His Arg Leu Lys Val Pro Met Ile Lys
        35                  40                  45


Ser Leu Phe Tyr Lys Met Ser Glu Phe Ser Pro Tyr Asp Asp Tyr Tyr
    50                  55                  60


Val Lys Lys Ile Leu Ala Tyr Cys Leu Leu Arg Asp Glu Ser Phe Ala
65                  70                  75                  80


Glu Leu His Ser Lys Phe Cys Leu Asn Glu Asp Tyr Lys Ser Val Phe
                85                  90                  95


Met Lys Asn Ile Ser Phe Asp Lys Ile Asp Ser Ile Ile Val Thr
            100                 105                 110
```

<210> 191
<211> 94
<212> PRT
<213> Vaccinia virus

<400> 191
Met His His Pro Met Glu Ser Val Lys Thr Thr Asn Thr Asn Ala Ile
1   5   10   15

Ile Cys Val Arg Glu His Thr Leu Pro Asp Tyr Ala Asn Thr Gln Cys
            20   25   30

Thr Pro Cys Gly Ser Gly Thr Phe Thr Ser Arg Asn Asn His Leu Pro
        35   40   45

Ala Cys Leu Ser Cys Asn Gly Arg Arg Asp Arg Val Thr Leu Leu Thr
    50   55   60

Ile Glu Ser Val Asn Ala Leu Pro Asp Ile Ile Val Phe Ser Lys Asp
65   70   75   80

His Pro Asp Ala Arg His Val Phe Pro Lys Gln Asn Val Glu
                85   90

<210> 192
<211> 241
<212> PRT
<213> Vaccinia virus

<400> 192
Met His Val Pro Ala Ser Leu Gln Gln Ser Ser Ser Ser Cys Thr Glu
1   5   10   15

Glu Glu Asn Lys His His Met Gly Ile Asp Val Ile Ile Lys Val Thr
            20   25   30

Lys Gln Asp Gln Thr Pro Thr Asn Asp Lys Ile Cys Gln Ser Val Thr
        35   40   45

Glu Ile Thr Glu Ser Glu Ser Asp Pro Asp Pro Glu Val Glu Ser Glu

```
    50                  55                  60

Asp Asp Ser Thr Ser Val Glu Asp Val Asp Leu Pro Thr Thr Tyr Tyr
65                  70                  75                  80

Ser Ile Ile Gly Gly Gly Leu Arg Met Asn Phe Gly Phe Thr Lys Cys
                85                  90                  95

Pro Gln Ile Lys Ser Ile Ser Glu Ser Ala Asp Gly Asn Thr Val Asn
            100                 105                 110

Ala Arg Leu Ser Ser Val Ser Pro Gly Gln Gly Lys Asp Ser Pro Ala
        115                 120                 125

Ile Thr His Glu Glu Ala Leu Ala Met Ile Lys Asp Cys Glu Val Ser
    130                 135                 140

Ile Asp Ile Arg Cys Ser Glu Glu Glu Lys Asp Ser Asp Ile Lys Thr
145                 150                 155                 160

His Pro Val Leu Gly Ser Asn Ile Ser His Lys Lys Val Ser Tyr Glu
                165                 170                 175

Asp Ile Ile Gly Ser Thr Ile Val Asp Thr Lys Cys Val Lys Asn Leu
            180                 185                 190

Glu Phe Ser Val Arg Ile Gly Asp Met Cys Lys Glu Ser Ser Glu Leu
        195                 200                 205

Glu Val Lys Asp Gly Phe Lys Tyr Val Asp Gly Ser Ala Ser Glu Gly
    210                 215                 220

Ala Thr Asp Asp Thr Ser Leu Ile Asp Ser Thr Lys Leu Lys Ala Cys
225                 230                 235                 240

Val
```

<210> 193
<211> 62
<212> PRT
<213> Vaccinia virus

<400> 193
Met Lys Leu Phe Thr Gln Asn Asp Arg Tyr Phe Gly Leu Leu Asp Ser
1   5   10   15

Cys Asn His Ile Phe Cys Ile Thr Cys Ile Asn Ile Trp His Lys Thr
            20   25   30

Arg Arg Glu Thr Gly Ala Ser Asp Asn Cys Pro Ile Cys Arg Thr Arg
        35   40   45

Phe Arg Asn Ile Thr Met Ser Lys Phe Tyr Lys Leu Val Asn
    50   55   60

<210> 194
<211> 66
<212> PRT
<213> Vaccinia virus

<400> 194
Met His Tyr Pro Lys Tyr Tyr Ile Asn Ile Thr Lys Ile Asn Pro His
1   5   10   15

Leu Ala Asn Gln Phe Arg Ala Trp Lys Lys Arg Ile Ala Gly Arg Asp
            20   25   30

Tyr Met Thr Asn Leu Ser Lys Asp Thr Gly Ile Gln Gln Ser Lys Leu
        35   40   45

Tyr Val Thr Val Lys Lys Ile Glu Thr Tyr Met Val Tyr Ile Tyr Thr
    50   55   60

Thr Ile
65

<210> 195

<211> 331
<212> PRT
<213> Vaccinia virus

<400> 195
Met Asp Ile Tyr Asp Asp Lys Gly Leu Gln Thr Ile Lys Leu Phe Asn
1   5   10   15

Asn Glu Phe Asp Cys Ile Arg Asn Asp Ile Arg Glu Leu Phe Lys His
            20   25   30

Val Thr Asp Ser Asp Ser Ile Gln Leu Pro Met Glu Asp Asn Ser Asp
        35   40   45

Ile Ile Glu Asn Ile Arg Lys Ile Leu Tyr Arg Arg Leu Lys Asn Val
    50   55   60

Glu Cys Val Asp Ile Asp Asn Thr Ile Thr Phe Met Lys Tyr Asp Pro
65   70   75   80

Asn Asp Asp Asn Lys Arg Thr Cys Ser Asn Trp Val Pro Leu Thr Asn
                85   90   95

Asn Tyr Met Glu Tyr Cys Leu Val Ile Tyr Leu Glu Thr Pro Ile Cys
            100   105   110

Gly Gly Lys Ile Lys Leu Tyr His Pro Thr Gly Asn Ile Lys Ser Asp
        115   120   125

Lys Asp Ile Met Phe Ala Lys Thr Leu Asp Phe Lys Ser Lys Lys Val
    130   135   140

Leu Thr Gly Arg Lys Thr Ile Ala Val Leu Asp Ile Ser Val Ser Tyr
145   150   155   160

Asn Arg Ser Ile Thr Thr Ile His Tyr Asn Asp Asp Val Asp Ile Asp
                165   170   175

Ile His Thr Asp Lys Asn Gly Lys Glu Leu Cys Tyr Cys Tyr Ile Thr

```
            180                 185                 190

Ile Asp Asp His Tyr Leu Val Asp Val Glu Thr Ile Gly Val Ile Val
        195                 200                 205

Asn Arg Ser Gly Lys Cys Leu Leu Val Asn Asn His Leu Gly Ile Gly
    210                 215                 220

Ile Val Lys Asp Lys Arg Ile Ser Asp Ser Phe Gly Asp Val Cys Met
225                 230                 235                 240

Asp Thr Ile Phe Asp Phe Ser Glu Ala Arg Glu Leu Phe Ser Leu Thr
                245                 250                 255

Asn Asp Asp Asn Arg Asn Ile Ala Trp Asp Thr Asp Lys Leu Asp Asp
            260                 265                 270

Asp Thr Asp Ile Trp Thr Pro Val Thr Glu Asn Asp Tyr Lys Phe Leu
        275                 280                 285

Ser Arg Leu Val Leu Tyr Ala Lys Ser Gln Ser Asp Thr Val Phe Asp
    290                 295                 300

Tyr Tyr Val Leu Thr Gly Asp Thr Glu Pro Pro Thr Val Phe Ile Phe
305                 310                 315                 320

Lys Val Thr Arg Phe Tyr Phe Asn Met Pro Lys
                325                 330


<210> 196
<211> 141
<212> PRT
<213> Vaccinia virus

<400> 196
Met Leu Ile Asn Tyr Leu Met Leu Leu Phe Ala Ala Met Ile Ile Arg
1               5                   10                  15

Ser Phe Ala Asp Ser Gly Asn Ala Ile Glu Thr Thr Leu Pro Glu Ile
```

```
            20                  25                  30

Thr Asn Ala Thr Thr Asp Ile Pro Ala Ile Arg Leu Cys Gly Pro Glu
        35                  40                  45

Gly Asp Gly Tyr Cys Leu His Gly Asp Cys Ile His Ala Arg Asp Ile
    50                  55                  60

Asp Gly Met Tyr Cys Arg Cys Ser His Gly Tyr Thr Gly Ile Arg Cys
65                  70                  75                  80

Gln His Val Val Leu Val Asp Tyr Gln Arg Ser Glu Lys Pro Asn Thr
                85                  90                  95

Thr Thr Ser Tyr Ile Pro Ser Pro Gly Ile Met Leu Val Leu Val Gly
            100                 105                 110

Ile Ile Ile Ile Thr Cys Cys Leu Leu Ser Val Tyr Arg Phe Thr Arg
        115                 120                 125

Arg Thr Asn Lys Leu Pro Leu Gln Asp Met Val Val Pro
    130                 135                 140
```

<210> 197
<211> 94
<212> PRT
<213> Vaccinia virus

<400> 197

```
Met His His Pro Met Glu Ser Val Lys Thr Thr Asn Thr Asn Ala Ile
1               5                   10                  15

Ile Cys Val Arg Glu His Thr Leu Pro Asp Tyr Ala Asn Thr Gln Cys
            20                  25                  30

Thr Pro Cys Gly Ser Gly Thr Phe Thr Ser Arg Asn Asn His Leu Pro
        35                  40                  45

Ala Cys Leu Ser Cys Asn Gly Arg Arg Asp Arg Val Thr Leu Leu Thr
```

50 55 60

Ile Glu Ser Val Asn Ala Leu Pro Asp Ile Ile Val Phe Ser Lys Asp
65 70 75 80

His Pro Asp Ala Arg His Val Phe Pro Lys Gln Asn Val Glu
85 90

<210> 198
<211> 241
<212> PRT
<213> Vaccinia virus

<400> 198
Met His Val Pro Ala Ser Leu Gln Gln Ser Ser Ser Ser Cys Thr Glu
1 5 10 15

Glu Glu Asn Lys His His Met Gly Ile Asp Val Ile Ile Lys Val Thr
20 25 30

Lys Gln Asp Gln Thr Pro Thr Asn Asp Lys Ile Cys Gln Ser Val Thr
35 40 45

Glu Ile Thr Glu Ser Glu Ser Asp Pro Asp Pro Glu Val Glu Ser Glu
50 55 60

Asp Asp Ser Thr Ser Val Glu Asp Val Asp Leu Pro Thr Thr Tyr Tyr
65 70 75 80

Ser Ile Ile Gly Gly Gly Leu Arg Met Asn Phe Gly Phe Thr Lys Cys
85 90 95

Pro Gln Ile Lys Ser Ile Ser Glu Ser Ala Asp Gly Asn Thr Val Asn
100 105 110

Ala Arg Leu Ser Ser Val Ser Pro Gly Gln Gly Lys Asp Ser Pro Ala
115 120 125

Ile Thr His Glu Glu Ala Leu Ala Met Ile Lys Asp Cys Glu Val Ser

130 135 140

Ile Asp Ile Arg Cys Ser Glu Glu Glu Lys Asp Ser Asp Ile Lys Thr
145 150 155 160

His Pro Val Leu Gly Ser Asn Ile Ser His Lys Lys Val Ser Tyr Glu
165 170 175

Asp Ile Ile Gly Ser Thr Ile Val Asp Thr Lys Cys Val Lys Asn Leu
180 185 190

Glu Phe Ser Val Arg Ile Gly Asp Met Cys Lys Glu Ser Ser Glu Leu
195 200 205

Glu Val Lys Asp Gly Phe Lys Tyr Val Asp Gly Ser Ala Ser Glu Gly
210 215 220

Ala Thr Asp Asp Thr Ser Leu Ile Asp Ser Thr Lys Leu Lys Ala Cys
225 230 235 240

Val

<210> 199
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 199
Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser
1 5 10 15

<210> 200
<211> 149
<212> PRT
<213> Vaccinia virus

<400> 200
Met Thr Ala Asn Phe Ser Thr His Val Phe Ser Pro Gln His Cys Gly
1   5   10   15

Cys Asp Arg Leu Thr Ser Ile Asp Asp Val Lys Gln Cys Leu Thr Glu
            20   25   30

Tyr Ile Tyr Trp Ser Ser Tyr Ala Tyr Arg Asn Arg Gln Cys Ala Gly
        35   40   45

Gln Leu Tyr Ser Thr Leu Leu Ser Phe Arg Asp Asp Ala Glu Leu Val
    50   55   60

Phe Ile Asp Ile Arg Glu Leu Val Lys Asn Met Pro Trp Asp Asp Val
65   70   75   80

Lys Asp Cys Thr Glu Ile Ile Arg Cys Tyr Ile Pro Asp Glu Gln Lys
                85   90   95

Thr Ile Arg Glu Ile Ser Ala Ile Ile Gly Leu Cys Ala Tyr Ala Ala
            100   105   110

Thr Tyr Trp Gly Gly Glu Asp His Pro Thr Ser Asn Ser Leu Asn Ala
        115   120   125

Leu Phe Val Met Leu Glu Met Leu Asn Tyr Val Asp Tyr Asn Ile Ile
    130   135   140

Phe Arg Arg Met Asn
145

<210> 201
<211> 326
<212> PRT
<213> Vaccinia virus

<400> 201
Met Ser Ile Leu Pro Val Ile Phe Leu Pro Ile Phe Phe Tyr Ser Ser
1   5   10   15

```
Phe Val Gln Thr Phe Asn Ala Pro Glu Cys Ile Asp Lys Gly Gln Tyr
            20                  25                  30

Phe Ala Ser Phe Met Glu Leu Glu Asn Glu Pro Val Ile Leu Pro Cys
        35                  40                  45

Pro Gln Ile Asn Thr Leu Ser Ser Gly Tyr Asn Ile Leu Asp Ile Leu
    50                  55                  60

Trp Glu Lys Arg Gly Ala Asp Asn Asp Arg Ile Ile Pro Ile Asp Asn
65                  70                  75                  80

Gly Ser Asn Met Leu Ile Leu Asn Pro Thr Gln Ser Asp Ser Gly Ile
                85                  90                  95

Tyr Ile Cys Ile Thr Thr Asn Glu Thr Tyr Cys Asp Met Met Ser Leu
            100                 105                 110

Asn Leu Thr Ile Val Ser Val Ser Glu Ser Asn Ile Asp Leu Ile Ser
        115                 120                 125

Tyr Pro Gln Ile Val Asn Glu Arg Ser Thr Gly Glu Met Val Cys Pro
    130                 135                 140

Asn Ile Asn Ala Phe Ile Ala Ser Asn Val Asn Ala Asp Ile Ile Trp
145                 150                 155                 160

Ser Gly His Arg Arg Leu Arg Asn Lys Arg Leu Lys Gln Arg Thr Pro
                165                 170                 175

Gly Ile Ile Thr Ile Glu Asp Val Arg Lys Asn Asp Ala Gly Tyr Tyr
            180                 185                 190

Thr Cys Val Leu Glu Tyr Ile Tyr Arg Gly Lys Thr Tyr Asn Val Thr
        195                 200                 205

Arg Ile Val Lys Leu Glu Val Arg Asp Lys Ile Ile Pro Ser Thr Met
```

```
    210                 215                 220

Gln Leu Pro Asp Gly Ile Val Thr Ser Ile Gly Ser Asn Leu Thr Ile
225                 230                 235                 240

Ala Cys Arg Val Ser Leu Arg Pro Pro Thr Thr Asp Ala Asp Val Phe
                245                 250                 255

Trp Ile Ser Asn Gly Met Tyr Tyr Glu Glu Asp Asp Gly Asp Gly Asn
            260                 265                 270

Gly Arg Ile Ser Val Ala Asn Lys Ile Tyr Met Thr Asp Lys Arg Arg
        275                 280                 285

Val Ile Thr Ser Arg Leu Asn Ile Asn Pro Val Lys Glu Glu Asp Ala
    290                 295                 300

Thr Thr Phe Thr Cys Met Ala Phe Thr Ile Pro Ser Ile Ser Lys Thr
305                 310                 315                 320

Val Thr Val Ser Ile Thr
                325


<210> 202
<211> 340
<212> PRT
<213> Vaccinia virus

<400> 202
Met Ser Arg Lys Phe Met Gln Val Tyr Glu Tyr Asp Arg Glu Gln Tyr
1               5                   10                  15

Leu Asp Glu Phe Ile Glu Asp Arg Tyr Asn Asp Ser Phe Ile Thr Ser
            20                  25                  30

Pro Glu Tyr Tyr Ser Ala Glu Lys Tyr Met Cys Arg Tyr Thr Thr Leu
        35                  40                  45

Asn His Asn Cys Ile Asn Val Arg Arg Cys Ala Leu Asp Ser Lys Leu
```

```
    50                  55                  60

Leu His Asp Ile Ile Thr Asn Cys Lys Ile Tyr Asn Asn Ile Glu Leu
65                  70                  75                  80

Val Arg Ala Thr Lys Phe Val Tyr Tyr Leu Asp Leu Ile Lys Cys Asn
                85                  90                  95

Trp Val Ser Lys Val Gly Asp Ser Val Leu Tyr Pro Val Ile Phe Ile
            100                 105                 110

Thr His Thr Ser Thr Arg Asn Leu Asp Lys Val Ser Val Lys Thr Tyr
        115                 120                 125

Lys Gly Val Lys Val Lys Lys Leu Asn Arg Cys Ala Asp His Ala Ile
    130                 135                 140

Val Ile Asn Pro Phe Val Lys Phe Lys Leu Thr Leu Pro Asn Lys Thr
145                 150                 155                 160

Ser His Ala Lys Val Leu Val Thr Phe Cys Lys Leu Arg Thr Asp Ile
                165                 170                 175

Thr Gln Ile Glu Ala Pro Leu Ser Gly Asn Val Leu Val Tyr Thr Phe
            180                 185                 190

Pro Asp Ile Asn Lys Arg Ile Pro Gly Tyr Ile His Val Asn Ile Glu
        195                 200                 205

Gly Cys Ile Asp Gly Met Ile Tyr Ile Asn Ser Ser Lys Phe Ala Cys
    210                 215                 220

Val Leu Lys Leu His Arg Ser Met Tyr Arg Ile Pro Pro Phe Pro Ile
225                 230                 235                 240

Asp Ile Cys Ser Cys Cys Ser Gln Tyr Thr Asn Asp Asp Ile Glu Ile
                245                 250                 255
```

```
Pro Ile His Asp Leu Ile Lys Asp Val Ala Ile Phe Lys Asn Lys Glu
            260                 265                 270

Thr Val Tyr Tyr Leu Lys Leu Asn Asn Lys Thr Ile Ala Arg Phe Thr
        275                 280                 285

Tyr Phe Asn Asn Ile Asp Thr Ala Ile Thr Gln Glu His Glu Tyr Val
    290                 295                 300

Lys Ile Ala Leu Gly Ile Val Cys Lys Leu Met Ile Asn Asn Met His
305                 310                 315                 320

Ser Ile Val Gly Val Asn His Ser Asn Thr Phe Val Asn Cys Leu Leu
                325                 330                 335

Glu Asp Asn Val
            340
```

<210> 203
<211> 167
<212> PRT
<213> Vaccinia virus

<400> 203

```
Met Thr Lys Val Ile Ile Ile Leu Gly Phe Leu Ile Ile Asn Thr Asn
1               5                   10                  15

Ser Leu Ser Met Lys Cys Glu Gln Gly Val Ser Tyr Tyr Asn Ser Gln
            20                  25                  30

Glu Leu Lys Cys Cys Lys Leu Cys Lys Pro Gly Thr Tyr Ser Asp His
        35                  40                  45

Arg Cys Asp Lys Tyr Ser Asp Thr Ile Cys Gly His Cys Pro Ser Asp
    50                  55                  60

Thr Phe Thr Ser Ile Tyr Asn Arg Ser Pro Trp Cys His Ser Cys Arg
65                  70                  75                  80
```

```
Gly Pro Cys Gly Thr Asn Arg Val Glu Val Thr Pro Cys Thr Pro Thr
                85                  90                  95

Thr Asn Arg Ile Cys His Cys Asp Ser Asn Ser Tyr Cys Leu Leu Lys
            100                 105                 110

Ala Ser Asp Gly Asn Cys Val Thr Cys Ala Pro Lys Thr Lys Cys Gly
        115                 120                 125

Arg Gly Tyr Gly Lys Lys Gly Glu Asp Glu Met Gly Asn Thr Ile Cys
    130                 135                 140

Lys Lys Cys Arg Lys Gly Thr Tyr Ser Asp Ile Val Ser Asp Ser Asp
145                 150                 155                 160

Gln Cys Lys Pro Met Thr Arg
                165
```

<210> 204
<211> 237
<212> PRT
<213> Vaccinia virus

<400> 204

```
Met Ala Met Pro Ser Leu Ser Ala Cys Ser Ser Ile Glu Asp Asp Phe
1               5                   10                  15

Asn Tyr Gly Ser Ser Val Ala Ser Ala Ser Val His Ile Arg Met Ala
            20                  25                  30

Phe Leu Arg Lys Val Tyr Gly Ile Leu Cys Leu Gln Phe Leu Leu Thr
        35                  40                  45

Thr Ala Thr Thr Ala Val Phe Leu Tyr Phe Asp Cys Met Arg Thr Phe
    50                  55                  60

Ile Gln Gly Ser Pro Val Leu Ile Leu Ala Ser Met Phe Gly Ser Ile
65                  70                  75                  80
```

```
Gly Leu Ile Phe Ala Leu Thr Leu His Arg His Lys His Pro Leu Asn
                85                  90                  95

Leu Tyr Leu Leu Cys Gly Phe Thr Leu Ser Glu Ser Leu Thr Leu Ala
            100                 105                 110

Ser Val Val Thr Phe Tyr Asp Val His Val Val Met Gln Ala Phe Met
        115                 120                 125

Leu Thr Thr Ala Ala Phe Leu Ala Leu Thr Thr Tyr Thr Leu Gln Ser
    130                 135                 140

Lys Arg Asp Phe Ser Lys Leu Gly Ala Gly Leu Phe Ala Ala Leu Trp
145                 150                 155                 160

Ile Leu Ile Leu Ser Gly Leu Leu Gly Ile Phe Val Gln Asn Glu Thr
                165                 170                 175

Val Lys Leu Val Leu Ser Ala Phe Gly Ala Leu Val Phe Cys Gly Phe
            180                 185                 190

Ile Ile Tyr Asp Thr His Ser Leu Ile His Lys Leu Ser Pro Glu Glu
        195                 200                 205

Tyr Val Leu Ala Ser Ile Asn Leu Tyr Leu Asp Ile Ile Asn Leu Phe
    210                 215                 220

Leu His Leu Leu Gln Leu Leu Glu Val Ser Asn Lys Lys
225                 230                 235


<210> 205
<211> 147
<212> PRT
<213> Vaccinia virus

<400> 205
Met Ala Ser Pro Cys Ala Lys Phe Arg Pro Cys His Cys His Ala Thr
1               5                   10                  15
```

```
Lys Asp Ser Leu Asn Thr Val Ala Asp Val Arg His Cys Leu Thr Glu
            20                  25                  30

Tyr Ile Leu Trp Val Ser His Arg Trp Thr His Arg Glu Ser Ala Gly
        35                  40                  45

Ser Leu Tyr Arg Leu Leu Ile Ser Phe Arg Thr Asp Ala Thr Glu Leu
    50                  55                  60

Phe Gly Gly Glu Leu Lys Asp Ser Leu Pro Trp Asp Asn Cys Val Glu
65                  70                  75                  80

Ile Ile Lys Cys Phe Ile Arg Asn Asp Ser Met Lys Thr Ala Glu Glu
                85                  90                  95

Leu Arg Ala Ile Ile Gly Leu Cys Thr Gln Ser Ala Ile Val Ser Gly
            100                 105                 110

Arg Val Phe Asn Asp Lys Tyr Ile Asp Ile Leu Leu Met Leu Arg Lys
        115                 120                 125

Ile Leu Asn Glu Asn Asp Tyr Leu Thr Leu Leu Asp His Ile Arg Thr
    130                 135                 140

Ala Lys Tyr
145
```

<210> 206
<211> 128
<212> PRT
<213> Vaccinia virus

<400> 206

```
Met Glu Gln Thr Leu Thr Arg Leu His Thr Tyr Leu Gln Gln Tyr Thr
1               5                   10                  15

Lys His Ser Pro Arg Val Val Tyr Ala Leu Leu Ser Arg Gly Tyr Val
            20                  25                  30
```

```
Ile Ile Leu Ile Val His Pro Ser Trp Asn Asp Cys Ala Thr Gly His
        35                  40                  45


Ile Leu Ile Met Leu Leu Asn Trp His Glu Gln Lys Glu Glu Gly Gln
    50                  55                  60


His Leu Leu Tyr Leu Phe Ile Lys His Asn Gln Gly Tyr Thr Leu Asn
65                  70                  75                  80


Ile Leu Arg Tyr Leu Leu Asp Arg Phe Asp Ile Gln Lys Asp Glu Tyr
                85                  90                  95


Tyr Asn Thr Ala Phe Gln Asn Cys Asn Asn Asn Val Ala Ser Tyr Ile
            100                 105                 110


Gly Tyr Asp Ile Asn Leu Pro Thr Lys Asp Gly Ile Arg Leu Gly Val
        115                 120                 125


<210> 207
<211> 64
<212> PRT
<213> Vaccinia virus

<400> 207
Met Leu Pro His Thr Ser Asp Thr Thr Ser Thr Phe Arg Leu Lys Thr
1               5                   10                  15


Val Phe Asp Leu Val Phe Glu Asn Arg Asn Ile Ile Tyr Lys Ala Asp
            20                  25                  30


Val Val Asn Asp Ile Ile His His Arg Leu Lys Val Ser Leu Pro Met
        35                  40                  45


Ile Lys Ser Leu Phe Tyr Lys Met Ser Leu Pro Thr Thr Ile Thr Thr
    50                  55                  60


<210> 208
<211> 258
<212> PRT
```

<213> Vaccinia virus

<400> 208

```
Met Lys Gln Tyr Ile Val Leu Ala Cys Met Cys Leu Ala Ala Ala Ala
1               5                  10                  15


Met Pro Ala Ser Leu Gln Gln Ser Ser Ser Ser Ser Ser Ser Cys Thr
            20                  25                  30


Glu Glu Glu Asn Lys His His Met Gly Ile Asp Val Ile Ile Lys Val
        35                  40                  45


Thr Lys Gln Asp Gln Thr Pro Thr Asn Asp Lys Ile Cys Gln Ser Val
    50                  55                  60


Thr Glu Ile Thr Glu Ser Glu Ser Asp Pro Asp Pro Glu Val Glu Ser
65                  70                  75                  80


Glu Asp Asp Ser Thr Ser Val Glu Asp Val Asp Pro Pro Thr Thr Tyr
                85                  90                  95


Tyr Ser Ile Ile Gly Gly Gly Leu Arg Met Asn Phe Gly Phe Thr Lys
            100                 105                 110


Cys Pro Gln Ile Lys Ser Ile Ser Glu Ser Ala Asp Gly Asn Thr Val
        115                 120                 125


Asn Ala Arg Leu Ser Ser Val Ser Pro Gly Gln Gly Lys Asp Ser Pro
    130                 135                 140


Ala Ile Thr His Glu Glu Ala Leu Ala Met Ile Lys Asp Cys Glu Val
145                 150                 155                 160


Ser Ile Asp Ile Arg Cys Ser Glu Glu Glu Lys Asp Ser Asp Ile Lys
                165                 170                 175


Thr His Pro Val Leu Gly Ser Asn Ile Ser His Lys Lys Val Ser Tyr
            180                 185                 190
```

Glu Asp Ile Ile Gly Ser Thr Ile Val Asp Thr Lys Cys Val Lys Asn
195 200 205

Leu Glu Phe Ser Val Arg Ile Gly Asp Met Cys Lys Glu Ser Ser Glu
210 215 220

Leu Glu Val Lys Asp Gly Phe Lys Tyr Val Asp Gly Ser Ala Ser Glu
225 230 235 240

Gly Ala Thr Asp Asp Thr Ser Leu Ile Asp Ser Thr Lys Leu Lys Ala
245 250 255

Cys Val

<210> 209
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 209
Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys Val Asn
1 5 10 15

<210> 210
<211> 156904
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>
<221> misc_feature
<222> (18348)..(19490)
<223> remaining portion of the C2L gene

<220>
<221> misc_feature
<222> (19491)..(19849)
<223> remaining portion of the F3L gene

<220>
<221> misc_feature
<222> (153421)..(153469)
<223> sequence that replaces a portion of the B8R gene sequence

<220>
<221> misc_feature
<222> (153430)..(153463)
<223> loxP site

<220>
<221> misc_feature
<222> (153470)..(153619)
<223> remaining portion of the B8R gene

<220>
<221> misc_feature
<222> (153514)..(153528)
<223> potential transcription regulatory sequences of the B9R gene

<220>
<221> misc_feature
<222> (153638)..(153667)
<223> potential transcription regulatory sequences of the B9R gene

<220>
<221> misc_feature
<222> (156094)..(156489)
<223> remaining portion of the B14R gene

<220>
<221> misc_feature
<222> (156490)..(156904)
<223> remaining portion of the B29R (ITR) gene

<400> 210
tcagacacac gctttgagtt ttgttgaatc gatgagtgaa gtatcatcgg ttgcaccttc 60

agatgccgat ccgtcgacat acttgaatcc atccttgacc tcaagttcag atgattcctt 120

gcacatgtct ccgatacgaa cgctaaactc tagattcttg acacattttg tatcgacgat 180

cgttgaaccg atgatatctt cgtaactcac tttcttatga gagatgttag acccgagtac 240

tggatgggtc ttgatgtcgc tgtctttctc ttcttcgcta catctgatgt cgatagacac 300

ctcacagtct ttgatcatag ccagagcttc ttcacgagtg atcgcgggag agtccttacc 360

ttgtcctggg gacacgctgg acaatctagc attcactgtg tttccatcag cggattctga 420

gatggattta atctgaggac atttggtgaa tccaaagttc attctcagac ctccaccgat 480

gatggagtaa taagtggtag gaggatctac atcctcgact gatgtggaat catcttctga 540

ttccacctcg ggatctggat ctgactcgga ctctgtaatt tccgttacgg attggcaaat 600

cttatcattg gtcggtgttt ggtcttgctt tgtgactttg ataataacat cgattcccat 660

atgatgtttg ttttcttctt ccgtacacga ggaggaggat gaggatgatt gctgaagact 720

ggcaggcaca tgcatgccag gacgatatat tgtttcataa ttgctattga ttgagtactg 780

ttctttatga ttctacttcc ttaccatgca ataaattaga atatattttc tacttttacg 840

agaaattaat tattgtattt attatttatg ggtgaaaaac ttactataaa aagcgggtgg 900

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tagaagcgct tttaacgacg atggtatata catccgtaga aatatgatta acaagttgta 152700

cggatacgca tctctaacta ctattggcac gatcgctgga ggtgtttgtt attatctgtt 152760

gatgcatcta gttagtttgt ataaataatt atttcaatat actagttaaa attttaagat 152820

tttaaatgta taaaaaacta ataacgtttt tatttgtaat aggtgcatta gcatcctatt 152880

cgaataatga gtacactccg tttaataaac tgagtgtaaa actctatata gatggagtag 152940

ataatataga aaattcatat actgatgata ataatgaatt ggtgttaaat tttaaagagt 153000

acacaatttc tattattaca gagtcatgcg acgtcggatt tgattccata gatatagatg 153060

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ttaaaattgg atctacttat atatttgatc gtcatggaca tagtaataca tattattcaa 153360

aatatgattt ttaaaaattt aaaatatatt atcacttcag tgacagtagt caaataacaa 153420

gctggccgca taacttcgta taatgtatgc tatacgaagt tatgtcgacg atgttcccaa 153480

tttcaaggac aaaatggcca gagttatcaa gagaaaattt aataaacagt ctcaatctta 153540

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cttgactaaa tattcataac taatttttat taatgataca aaaacgaaat aaaactgcat 153660

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atagtccttc tgttcccctc tatcatctac tccatgtcta ttagacgatg tgagaagact 153780

gaagaggaaa catggggatt gaaaataggg ttgtgtataa ttgccaaaga tttctatccc 153840

gaaagaactg attgcagtgt tcatctccca actgcaagtg aaggattgat aactgaaggc 153900

aatggattca gggatatacg aaacaccgat aaattataaa aaaagcaatg tgtccgctgt 153960

ttccgttaat aatactattt tcgtaactgg cggattattc ataaataact ctaatagcac 154020

gatcgtggtt aacaatatgg aaaaacttga catttataaa gacaaacaat ggtcgattat 154080

agaaatgcct atggctaggg tatatcacgg catcgactcg acatttggaa tgttatattt 154140

tgccggaggt ctatccgtta ccgaacaata tggtaattta gagaaaaaca acgagatatc 154200

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tgtggaaaag tatgatggtg catggaagtt agtacatgat cgtctccccg ctataaaggc 154380

attatcaact tctccttatt gattgaaaat gaaaatataa atagttttta tgtatagcag 154440

tattacccta tagttttatt gcttactact aacatggata cagatacaga tacagataca 154500

gatacagata cagatacaga tacagataca gatgttacaa atgtagaaga tatcataaat 154560

gaaatagata gagagaaaga agaaatacta aaaaatgtag aaattgaaaa taataaaaac 154620

attaacaaga atcatccaag tggatatatt agagaagcac tcgttattaa tacaagtagt 154680

aatagtgatt ccattgataa agaagttata gaatgtatca gtcacgatgt aggaatatag 154740

atcatatcta ctaattttta taatcaatac aaaacataaa aaacaactcg ttattacata 154800

gcaggcatgg aatccttcaa gtattgtttt gataacgatg gcaagaaatg gattatcgga 154860

aatactttat attctggtaa ttcaatactc tataaggtca gaaaaaattt cactagttcg 154920

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cgattctata tatctgtatt ggatcctttg actatcgaca actggacacg ggaacgtggt 155040

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gcatgtgtca ctatgataaa cacgttagag tttatacact ctcgaggatt tacccatgga 155220

aaaatagaac cgaggaatat actgattaga aataaacgtc tttcactaat tgactattct 155280

agaactaaca aactatacaa gagtggaaac tcacatatag attacaacga ggacatgata 155340

acttcaggaa atatcaatta tatgtgtgta gacaatcatc ttggagcaac agtttcaaga 155400

cgaggagatt tagaaatgtt gggatattgc atgatagaat ggttcggtgg caaacttcca 155460

tggaaaaacg aaagtagtat aaaagtaata aaacaaaaaa aagaatataa aaaatttata 155520

gctactttct ttgaggactg ttttcctgaa ggaaatgaac ctctggaatt agttagatat 155580

atagaattag tatacacgtt agattattct caaactccta attatgacag actacgtaga 155640

ctgtttatac aagattgaaa ttatattctt tttttataga gtgtggtagt gttacggata 155700

tctaatatta atattagact atctctatcg cgctacacga ccaatatcga ttactatgaa 155760

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caatactgta ttatggagct aatggatcca ctgctgaaca gctatcaaaa tatgtagaaa 155880

cggaggagaa cacggataag gttagcgctc agaatatctc attcaaatcc ataaataaag 155940

tatatgggcg atattctgcc gtgtttaaag atttcttttt gggaaaaatt ggcgataagt 156000

ttcaaactgt tgacttcact gattgtcgca ctatagatgc aatcaacaag tgtgtagata 156060

tctttactga ggggaaaatc aatccactat tggatgaacc attgtctcct agcaattagt 156120

gccgtatact ttaaagcaaa atggttgacg ccattcgaaa aggaatttac cagtgattat 156180

ccctttacg tatcaccaac ggaaatggta gatgtaagta tgatgtctat gtacggcgag 156240

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tatgttggag atactagtat gatggtcatt cttccagaca agattgatgg attagaatcc 156360

atagaacaaa atctaacaga tacaaatttt aagaaatggt gtaactctct ggatgctatg 156420

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ctagtaaaga tccgctgatg gaaacacagt gaatgctaga ttgtccagcg tgtccccagg 156540

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aacgatcgtc gatacaaaat gtgtcaagaa tctagagttt agcgttcgta tcggagacat 156780

gtgcaaggaa tcatctgaac ttgaggtcaa ggatggattc aagtatgtcg acggatcggc 156840

atctgaaggt gcaaccgatg atacttcact catcgattca acaaaactca aagcgtgtgt 156900

ctga 156904

<210> 211
<211> 727
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<220>
<221> MISC_FEATURE
<222> (1)..(20)
<223> Signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (21)..(490)
<223> heavy chain sequence

<220>
<221> MISC_FEATURE
<222> (469)..(491)
<223> T2A sequence

<220>
<221> MISC_FEATURE
<222> (491)..(512)
<223> Signal peptide sequence

<220>
<221> MISC_FEATURE
<222> (513)..(727)
<223> light chain sequence

<400> 211
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1   5   10   15

Gly Ser Thr Gly Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val
            20   25   30

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
        35   40   45

Phe Ser Ser Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
    50   55   60

Leu Glu Trp Val Thr Phe Ile Ser Tyr Asp Gly Asn Asn Lys Tyr Tyr
65   70   75   80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
                85   90   95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
            100   105   110

Ile Tyr Tyr Cys Ala Arg Thr Gly Trp Leu Gly Pro Phe Asp Tyr Trp
        115   120   125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
    130   135   140

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
145   150   155   160

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Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
               165                 170                 175

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
            180                 185                 190

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
        195                 200                 205

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
    210                 215                 220

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser
225                 230                 235                 240

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
               245                 250                 255

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            260                 265                 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        275                 280                 285

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    290                 295                 300

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
305                 310                 315                 320

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
               325                 330                 335

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            340                 345                 350

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
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        355                 360                 365

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
    370                 375                 380

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
385                 390                 395                 400

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                405                 410                 415

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            420                 425                 430

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        435                 440                 445

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    450                 455                 460

Ser Pro Gly Lys Pro Arg Gly Ser Gly Glu Gly Arg Gly Ser Leu Leu
465                 470                 475                 480

Thr Cys Gly Asp Val Glu Glu Asn Pro Gly Pro Lys Leu Met Ala Trp
                485                 490                 495

Thr Pro Gly Ile Phe Met Val Leu Ser Tyr Leu Thr Gly Ser Phe Ser
            500                 505                 510

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
        515                 520                 525

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Ser
    530                 535                 540

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
545                 550                 555                 560
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Ile Tyr Gly Ala Phe Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
                565                 570                 575

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
            580                 585                 590

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
        595                 600                 605

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
    610                 615                 620

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
625                 630                 635                 640

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
                645                 650                 655

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
            660                 665                 670

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
        675                 680                 685

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
    690                 695                 700

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
705                 710                 715                 720

Ser Phe Asn Arg Gly Glu Cys
                725
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<210> 212
<211> 260
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<220>
<221> MISC_FEATURE
<222> (235)..(255)
<223> B7-1 transmembrane domain

<220>
<221> MISC_FEATURE
<222> (235)..(260)
<223> B7-1 cytoplasmic domain

<400> 212
Met Cys Pro Ala Arg Ser Leu Leu Leu Val Ala Thr Leu Val Leu Leu
1 5 10 15

Asp His Leu Ser Leu Ala Arg Asn Leu Pro Val Ala Thr Pro Asp Pro
20 25 30

Gly Met Phe Pro Cys Leu His His Ser Gln Asn Leu Leu Arg Ala Val
35 40 45

Ser Asn Met Leu Gln Lys Ala Arg Gln Thr Leu Glu Phe Tyr Pro Cys
50 55 60

Thr Ser Glu Glu Ile Asp His Glu Asp Ile Thr Lys Asp Lys Thr Ser
65 70 75 80

Thr Val Glu Ala Cys Leu Pro Leu Glu Leu Thr Lys Asn Glu Ser Cys
85 90 95

Leu Asn Ser Arg Glu Thr Ser Phe Ile Thr Asn Gly Ser Cys Leu Ala
100 105 110

Ser Arg Lys Thr Ser Phe Met Met Ala Leu Cys Leu Ser Ser Ile Tyr
115 120 125

Glu Asp Leu Lys Met Tyr Gln Val Glu Phe Lys Thr Met Asn Ala Lys
130 135 140

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Leu Leu Met Asp Pro Lys Arg Gln Ile Phe Leu Asp Gln Asn Met Leu
145                 150                 155                 160


Ala Val Ile Asp Glu Leu Met Gln Ala Leu Asn Phe Asn Ser Glu Thr
                165                 170                 175


Val Pro Gln Lys Ser Ser Leu Glu Glu Pro Asp Phe Tyr Lys Thr Lys
            180                 185                 190


Ile Lys Leu Cys Ile Leu Leu His Ala Phe Arg Ile Arg Ala Val Thr
        195                 200                 205


Ile Asp Arg Val Met Ser Tyr Leu Asn Ala Ser Gly Gly Gly Gly Ser
    210                 215                 220


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Leu Leu Pro Ser Trp Ala
225                 230                 235                 240


Ile Thr Leu Ile Ser Val Asn Gly Ile Phe Val Ile Cys Cys Leu Thr
                245                 250                 255


Tyr Cys Phe Ala
            260


<210> 213
<211> 186
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 213
Met Thr Val Leu Ala Pro Ala Trp Ser Pro Thr Thr Tyr Leu Leu Leu
1               5                   10                  15


Leu Leu Leu Leu Ser Ser Gly Leu Ser Gly Thr Gln Asp Cys Ser Phe
            20                  25                  30
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Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
        35                  40                  45

Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
    50                  55                  60

Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
65                  70                  75                  80

Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
                85                  90                  95

Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
            100                 105                 110

Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
        115                 120                 125

Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
    130                 135                 140

Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
145                 150                 155                 160

Gly Ala Pro Arg Pro Gln Ser Pro Gly Pro Ala Ala Cys Gly Ala Leu
                165                 170                 175

Thr Trp Pro Arg Pro His Pro Ala Glu Pro
            180                 185
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<210> 214
<211> 2184
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polynucleotide

<400> 214
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caggttcagc tagtcgaatc gggtggagga gtcgtgcagc cgggacgttc cttacgttta 120

tcttgcgcag cgtctggttt tactttctcg tcctacacta tgcattgggt tcgtcaggct 180

ccgggaaagg gattggagtg ggtaacattt ataagttacg acggtaataa taaatactat 240

gcagacagtg tgaagggacg tttcactata tctcgagata atagtaagaa cactttgtat 300

ttgcagatga attcattgag agcggaagat acagcaattt actactgcgc cagaaccgga 360

tggttgggtc cctttgacta ttggggacag ggtactcttg ttacggtgtc ttctgcttca 420

acaaagggtc cctctgtctt cccgcttgcg ccctcatcaa aatcgacgtc gggtggaacc 480

gctgccttgg gatgcttggt taaggactat ttccccgaac ctgtcaccgt gtcttggaat 540

tccggtgctc taacgtctgg tgtgcacact ttccctgccg ttttacaaag ttccggacta 600

tattcacttt cgtccgtagt aactgttcca agttcgtccc ttggaacaca gacctatata 660

tgcaacgtaa accacaaacc ctccaatacc aaagtcgata aaagagttga gcctaaatcc 720

tgcgacaaaa cacacacctg cccaccttgc ccggcccctg aacttcttgg aggaccatct 780

gtattccttt tcccaccgaa gcctaaggac accttgatga tatccagaac tcccgaagtc 840

acgtgcgtag tagtcgatgt gagtcacgaa gatccggaag tcaagtttaa ctggtatgta 900

gacggagtag aggttcataa cgccaagacc aagccaagag aagaacaata taactcgact 960

tacagagtcg tgtctgtatt aaccgtcttg catcaggact ggttaaacgg taaagagtac 1020

aagtgcaagg tctccaataa agccctacct gcccccatcg aaaaaaccat atccaaggct 1080

aagggtcagc ctagagaacc tcaagtttac acattaccgc ccagtagaga tgaacttacg 1140

aagaatcaag tgagtctaac ctgccttgtt aaaggattct accccagtga catagcggtg 1200

gagtgggagt ccaacggtca acccgagaac aattataaga cgacaccgcc cgttcttgac 1260

agtgacggat cgttctttct atactctaag ttgactgtgg ataaatcccg atggcagcag 1320

ggaaacgtat tctcttgctc agtgatgcat gaggcgttgc acaatcatta cacccaaaag 1380

tctttgtcgc taagtccagg taaaccgcgg ggcagcggag agggcagagg aagcctgctg 1440

acttgtggcg atgtggaaga gaaccctggc cctaagctta tggcttggac accaggaatc 1500

ttcatggtac ttagttactt gacaggatct ttctcggaaa tagtcttaac tcagtcaccg 1560

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atctacggtg cgttttcgag agcgactggt atcccggata gattttctgg atcgggttct 1740

ggtactgatt tcactttaac gatttcgaga ctagagcccg aagattttgc tgtgtattat 1800

tgccagcaat atggatctag tccgtggacg ttcggtcagg gtaccaaggt cgagataaaa 1860

agaactgtgg ccgcaccctc cgtgtttatc tttccccctt ccgacgaaca gctaaagtcg 1920

ggtactgcat cggtggtatg tttacttaac aacttttacc cacgagaggc caaggtacaa 1980

tggaaggtgg ataacgcctt acaatcagga aactcacaag agtccgtcac cgagcaagat 2040

tccaaggaca gtacatactc gttatcctcg acattaacat tgagtaaggc ggattatgag 2100

aagcataagg tttacgcatg cgaagtgacg caccaaggac tttcatcccc cgtcaccaag 2160

tctttcaatc gtggtgagtg ctga 2184

<210> 215
<211> 783
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polynucleotide

<220>
<221> misc_feature
<222> (703)..(765)
<223> B7-1 transmembrane domain

<220>
<221> misc_feature
<222> (703)..(780)
<223> B7-1 cytoplasmic domain

<400> 215
atgtgtcccg cgcgatcgtt attgttagtt gcgacgttgg tcctacttga ccatctatca 60

ctagcgcgta atttgcccgt tgccacacca gatcccggaa tgtttccttg cttacatcat 120

agtcagaact tacttcgtgc agtctccaac atgttacaga aagcccgaca gaccttagag 180

ttctatccct gtacttccga agagatagat cacgaggaca taacgaaaga caaaacatcg 240

accgttgaag cgtgcttacc cttagaacta accaaaaatg aaagttgtct aaactctaga 300

gaaacgagtt ttatcaccaa tggaagttgc ttggcgtcta gaaaaacatc atttatgatg 360

gccttgtgtc tttcctccat atacgaggac ttgaagatgt atcaggtcga gttcaagaca 420

atgaacgcga aattgcttat ggaccccaaa cgacagatat ttttggacca aaacatgtta 480

gctgttatag acgaattgat gcaggcgcta aacttcaatt cggaaactgt gccacagaag 540

tcatccttag aggagcccga tttttacaag acaaaaatca agttatgcat tcttcttcac 600

gcgtttagaa ttcgtgccgt tacgattgat agagtaatgt cgtacttgaa tgcgtcgggt 660

ggaggaggtt ccggaggagg aggatccgga ggaggtggat ccttacttcc ttcgtgggct 720

ataacattaa tctccgttaa tggtatcttc gtgatttgct gtctaacata ctgctttgca 780

tga 783

<210> 216
<211> 561
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polynucleotide

<400> 216
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tctagtggtt tatcaggaac gcaagactgc tcattccaac attcaccgat cagttccgac 120

tttgcagtta agattcgaga actatcagac tacctattgc aagactatcc ggtgacggta 180

gcatcgaatc ttcaagacga agagctttgt ggtggactat ggcgtcttgt acttgcccaa 240

agatggatgg agcgactaaa aaccgttgcc ggttcaaaga tgcagggttt actagagcgt 300

gtgaatacgg aaattcattt tgttacgaaa tgtgcgttcc aacccccacc cagttgcttg 360

cgtttcgtgc agactaatat ctctcgttta ctacaagaaa catccgagca actagtggcg 420

ctaaagccct ggataacacg tcaaaacttt agtcgttgct tggagttaca gtgccaaccc 480

ggtgccccac gacctcaaag tcctggtcca gcggcttgcg gagcccttac ctggcctcga 540

ccgcatccgg ccgaaccatg a 561

<210> 217
<211> 470
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 217
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Thr Phe Ile Ser Tyr Asp Gly Asn Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Thr Gly Trp Leu Gly Pro Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

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Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
```

```
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445

Pro Arg Gly Ser Gly Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp
    450                 455                 460

Val Glu Glu Asn Pro Gly
465                 470


<210> 218
<211> 215
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      polypeptide

<400> 218
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
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1               5                   10                  15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Ser
            20                  25                  30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45

Ile Tyr Gly Ala Phe Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
            100                 105                 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
        115                 120                 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
    130                 135                 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
            180                 185                 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
        195                 200                 205
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Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 219
<211> 512
<212> PRT
<213> Vaccinia virus

<400> 219
Met Glu Ser Val Ile Phe Ser Ile Asn Gly Glu Ile Ile Gln Val Asn
1 5 10 15

Lys Glu Ile Ile Thr Ala Ser Pro Tyr Asn Phe Phe Lys Arg Ile Gln
20 25 30

Asp His His Leu Lys Asp Glu Ala Ile Ile Leu Asn Gly Ile Asn Tyr
35 40 45

His Ala Phe Glu Ser Leu Leu Asp Tyr Ile Arg Trp Lys Lys Ile Asn
50 55 60

Ile Thr Ile Asn Asn Val Glu Met Ile Leu Val Ala Ala Ile Ile Ile
65 70 75 80

Asp Val Pro Pro Val Val Asp Leu Cys Val Lys Thr Met Ile His Asn
85 90 95

Ile Asn Ser Thr Asn Cys Ile Arg Met Phe Asn Phe Ser Lys Arg Tyr
100 105 110

Gly Ile Lys Lys Leu Tyr Asn Ala Ser Met Ser Glu Ile Ile Asn Asn
115 120 125

Ile Thr Ala Val Thr Ser Asp Pro Glu Phe Gly Lys Leu Ser Lys Asp
130 135 140

Glu Leu Thr Thr Ile Leu Ser His Glu Asn Val Asn Val Asn His Glu
145 150 155 160

```
Asp Val Thr Ala Met Ile Leu Leu Lys Trp Ile His Lys Asn Pro Asn
                165                 170                 175

Asp Val Asp Ile Ile Asn Ile Leu His Pro Lys Phe Met Thr Asn Thr
            180                 185                 190

Met Arg Asn Ala Ile Ser Leu Leu Gly Leu Thr Ile Ser Lys Ser Thr
        195                 200                 205

Lys Pro Val Thr Arg Asn Gly Ile Lys His Asn Ile Val Val Ile Lys
    210                 215                 220

Asn Ser Asp Tyr Ile Ser Thr Ile Thr His Tyr Ser Pro Arg Thr Glu
225                 230                 235                 240

Tyr Trp Thr Ile Val Gly Asn Thr Asp Arg Gln Phe Tyr Asn Ala Asn
                245                 250                 255

Val Leu His Asn Cys Leu Tyr Ile Ile Gly Gly Met Ile Asn Asn Arg
            260                 265                 270

His Val Tyr Ser Val Ser Arg Val Asp Leu Glu Thr Lys Lys Trp Lys
        275                 280                 285

Thr Val Thr Asn Met Ser Ser Leu Lys Ser Glu Val Ser Thr Cys Val
    290                 295                 300

Asn Asp Gly Lys Leu Tyr Val Ile Gly Gly Leu Glu Phe Ser Ile Ser
305                 310                 315                 320

Thr Gly Val Ala Glu Tyr Leu Lys His Gly Thr Ser Lys Trp Ile Arg
                325                 330                 335

Leu Pro Asn Leu Ile Thr Pro Arg Tyr Ser Gly Ala Ser Val Phe Val
            340                 345                 350

Asn Asp Asp Ile Tyr Val Met Gly Gly Val Tyr Thr Thr Tyr Glu Lys
```

```
        355                 360                 365

Tyr Val Val Leu Asn Asp Val Glu Cys Phe Thr Lys Asn Arg Trp Ile
    370                 375                 380

Lys Lys Ser Pro Met Pro Arg His His Ser Ile Val Tyr Ala Val Glu
385                 390                 395                 400

Tyr Asp Gly Asp Ile Tyr Val Ile Thr Gly Ile Thr His Glu Thr Arg
                405                 410                 415

Asn Tyr Leu Tyr Lys Tyr Ile Val Lys Glu Asp Lys Trp Ile Glu Leu
            420                 425                 430

Tyr Met Tyr Phe Asn His Val Gly Lys Met Phe Val Cys Ser Cys Gly
        435                 440                 445

Asp Tyr Ile Leu Ile Ile Ala Asp Ala Lys Tyr Glu Tyr Tyr Pro Lys
    450                 455                 460

Ser Asn Thr Trp Asn Leu Phe Asp Met Ser Thr Arg Asn Ile Glu Tyr
465                 470                 475                 480

Tyr Asp Met Phe Thr Lys Asp Glu Thr Pro Lys Cys Asn Val Thr His
                485                 490                 495

Lys Ser Leu Pro Ser Phe Leu Ser Asn Cys Glu Lys Gln Phe Leu Gln
            500                 505                 510


<210> 220
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 220
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser
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1 5 10 15

<210> 221
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 221
Cys Thr Ala Cys Arg Trp Lys Lys Ala Cys Gln Arg
1 5 10

<210> 222
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 222
Val Leu Asp Gly Leu Asp Val Leu Leu
1 5

<210> 223
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 223
Ser Leu Tyr Ser Phe Pro Glu Pro Glu Ala
1 5 10

<210> 224
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 224
Ala Leu Tyr Val Asp Ser Leu Phe Phe Leu
1 5 10

<210> 225
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 225
Ser Leu Leu Gln His Leu Ile Gly Leu
1 5

<210> 226
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 226
Leu Tyr Val Asp Ser Leu Phe Phe Leu
1 5

<210> 227
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 227
Thr Ser Glu Lys Arg Pro Phe Met Cys Ala Tyr
1 5 10

<210> 228
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 228
Cys Met Thr Trp Asn Gln Met Asn Leu
1 5

<210> 229
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 229
Leu Ser His Leu Gln Met His Ser Arg Lys His
1 5 10

<210> 230
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 230
Lys Arg Tyr Phe Lys Leu Ser His Leu Gln Met His Ser Arg Lys His
1 5 10 15

<210> 231
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 231
Cys Tyr Met Glu Ala Val Ala Leu
1 5

<210> 232
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 232
Ser Leu Leu Phe Leu Leu Phe Ser Leu
1 5

<210> 233
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 233
Val Leu Pro Leu Thr Val Ala Glu Val
1 5

<210> 234
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 234
Ala Leu Gln Gly Gly Gly Pro Pro Tyr
1 5

<210> 235

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 235
Leu Tyr Pro Lys Ala Arg Leu Ala Phe
1 5

<210> 236
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 236
Ala Phe Leu Pro Trp His Arg Leu Phe
1 5

<210> 237
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 237
Ser Leu Leu Met Trp Ile Thr Gln Cys
1 5

<210> 238
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 238
Leu Ala Met Pro Phe Ala Thr Pro Met
1   5

<210> 239
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 239
Ala Arg Gly Pro Glu Ser Arg Leu Leu
1   5

<210> 240
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 240
Met Leu Met Ala Gln Glu Ala Leu Ala Phe Leu
1   5   10

<210> 241
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 241
Tyr Leu Ala Met Pro Phe Ala Thr Pro Met Glu
1   5   10

<210> 242
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 242
Ala Ser Gly Pro Gly Gly Gly Ala Pro Arg
1 5 10

<210> 243
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 243
Leu Ala Ala Gln Glu Arg Arg Val Pro Arg
1 5 10

<210> 244
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 244
Thr Val Ser Gly Asn Ile Leu Thr Ile Arg
1 5 10

<210> 245
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 245
Ala Pro Arg Gly Pro His Gly Gly Ala Ala Ser Gly Leu

1 5 10

<210> 246
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 246
Met Pro Phe Ala Thr Pro Met Glu Ala Glu Leu
1 5 10

<210> 247
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 247
Lys Glu Phe Thr Val Ser Gly Asn Ile Leu Thr Ile
1 5 10

<210> 248
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 248
Met Pro Phe Ala Thr Pro Met Glu Ala
1 5

<210> 249
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 249
Phe Ala Thr Pro Met Glu Ala Glu Leu
1 5

<210> 250
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 250
Phe Ala Thr Pro Met Glu Ala Glu Leu Ala Arg
1 5 10

<210> 251
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 251
Ser Leu Leu Met Trp Ile Thr Gln Cys Phe Leu Pro Val Phe
1 5 10

<210> 252
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 252
Leu Leu Glu Phe Tyr Leu Ala Met Pro Phe Ala Thr Pro Met Glu Ala
1 5 10 15

Glu Leu Ala Arg Arg Ser Leu Ala Gln
20 25

<210> 253
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 253
Glu Phe Tyr Leu Ala Met Pro Phe Ala Thr Pro Met
1 5 10

<210> 254
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 254
Pro Gly Val Leu Leu Lys Glu Phe Thr Val Ser Gly Asn Ile Leu Thr
1 5 10 15

Ile Arg Leu Thr Ala Ala Asp His Arg
20 25

<210> 255
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 255
Arg Leu Leu Glu Phe Tyr Leu Ala Met Pro Phe Ala
1 5 10

<210> 256
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 256
Gln Gly Ala Met Leu Ala Ala Gln Glu Arg Arg Val Pro Arg Ala Ala
1 5 10 15

Glu Val Pro Arg
20

<210> 257
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 257
Pro Phe Ala Thr Pro Met Glu Ala Glu Leu Ala Arg Arg
1 5 10

<210> 258
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 258
Pro Gly Val Leu Leu Lys Glu Phe Thr Val Ser Gly Asn Ile Leu Thr
1 5 10 15

Ile Arg Leu Thr
20

<210> 259
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 259
Val Leu Leu Lys Glu Phe Thr Val Ser Gly
1 5 10

<210> 260
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 260
Ala Ala Asp His Arg Gln Leu Gln Leu Ser Ile Ser Ser Cys Leu Gln
1 5 10 15

Gln Leu

<210> 261
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 261
Leu Lys Glu Phe Thr Val Ser Gly Asn Ile Leu Thr Ile Arg Leu
1 5 10 15

<210> 262
<211> 11
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 262
Lys Glu Phe Thr Val Ser Gly Asn Ile Leu Thr
1 5 10

<210> 263
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 263
Leu Leu Glu Phe Tyr Leu Ala Met Pro Phe Ala Thr Pro Met
1 5 10

<210> 264
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 264
Ala Gly Ala Thr Gly Gly Arg Gly Pro Arg Gly Ala Gly Ala
1 5 10

<210> 265
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 265
Thr Tyr Tyr Arg Pro Gly Val Asn Leu Ser Leu Ser Cys

1 5 10

<210> 266
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 266
Glu Ile Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn
1 5 10

<210> 267
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 267
Tyr Ala Cys Phe Val Ser Asn Leu Ala Thr Gly Arg Asn Asn Ser
1 5 10 15

<210> 268
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 268
Leu Trp Trp Val Asn Asn Gln Ser Leu Pro Val Ser Pro
1 5 10

<210> 269
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 269
Asn Ser Ile Val Lys Ser Ile Thr Val Ser Ala Ser Gly
1 5 10

<210> 270
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 270
Lys Thr Trp Gly Gln Tyr Trp Gln Val
1 5

<210> 271
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 271
Ala Met Leu Gly Thr His Thr Met Glu Val
1 5 10

<210> 272
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 272
Ile Thr Asp Gln Val Pro Phe Ser Val
1 5

<210> 273
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 273
Tyr Leu Glu Pro Gly Pro Val Thr Ala
1 5

<210> 274
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 274
Leu Leu Asp Gly Thr Ala Thr Leu Arg Leu
1 5 10

<210> 275
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 275
Val Leu Tyr Arg Tyr Gly Ser Phe Ser Val
1 5 10

<210> 276
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 276
Ser Leu Ala Asp Thr Asn Ser Leu Ala Val
1 5 10

<210> 277
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 277
Arg Leu Met Lys Gln Asp Phe Ser Val
1 5

<210> 278
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 278
Arg Leu Pro Arg Ile Phe Cys Ser Cys
1 5

<210> 279
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 279
Leu Ile Tyr Arg Arg Arg Leu Met Lys
1 5

<210> 280

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 280
Ala Leu Leu Ala Val Gly Ala Thr Lys
1 5

<210> 281
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 281
Ile Ala Leu Asn Phe Pro Gly Ser Gln Lys
1 5 10

<210> 282
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 282
Arg Ser Tyr Val Pro Leu Ala His Arg
1 5

<210> 283
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 283
Val Val Pro Cys Glu Pro Pro Glu Val
1   5

<210> 284
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 284
His Leu Tyr Gln Gly Cys Gln Val Val
1   5

<210> 285
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 285
Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys
1   5   10

<210> 286
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 286
Pro Leu Gln Pro Glu Gln Leu Gln Val
1   5

<210> 287
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 287
Thr Leu Glu Glu Ile Thr Gly Tyr Leu
1 5

<210> 288
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 288
Ala Leu Ile His His Asn Thr His Leu
1 5

<210> 289
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 289
Pro Leu Thr Ser Ile Ile Ser Ala Val
1 5

<210> 290
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 290
Val Leu Arg Glu Asn Thr Ser Pro Lys

1 5

<210> 291
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 291
Thr Tyr Leu Pro Thr Asn Ala Ser Leu
1 5

<210> 292
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 292
Arg Tyr Gln Leu Asp Pro Lys Phe Ile
1 5

<210> 293
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 293
Ile Leu Phe Thr Ile Asn Phe Thr Ile
1 5

<210> 294
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 294
Val Leu Phe Thr Ile Asn Phe Thr Ile
1 5

<210> 295
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 295
Thr Leu Asn Phe Thr Ile Thr Asn Leu
1 5

<210> 296
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 296
Val Leu Gln Gly Leu Leu Lys Pro Leu
1 5

<210> 297
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 297
Val Leu Gln Gly Leu Leu Arg Pro Val
1 5

<210> 298
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 298
Arg Leu Asp Pro Lys Ser Pro Gly Val
1 5

<210> 299
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 299
Gln Leu Tyr Trp Glu Leu Ser Lys Leu
1 5

<210> 300
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 300
Lys Leu Thr Arg Gly Ile Val Glu Leu
1 5

<210> 301
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 301
Gln Leu Thr Asn Gly Ile Thr Glu Leu
1 5

<210> 302
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 302
Gln Leu Thr His Asn Ile Thr Glu Leu
1 5

<210> 303
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 303
Thr Leu Asp Arg Asn Ser Leu Tyr Val
1 5

<210> 304
<211> 9
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 304
Phe Leu Leu Ser Leu Ala Leu Met Leu
1 5

<210> 305

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 305
Asn Leu Gly Pro Trp Ile Gln Gln Val
1 5

<210> 306
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 306
Ile Leu Asp Ser Ser Glu Glu Asp Lys
1 5

<210> 307
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 307
Tyr Leu Pro Lys Ser Trp Thr Ile Gln Val
1 5 10

<210> 308
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 308
Trp Ile His Glu Gln Met Glu Arg Asp Leu Lys Thr
1   5   10

<210> 309
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 309
Leu Leu Ala Asn Ala Tyr Ile Tyr Val
1   5

<210> 310
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 310
Tyr Leu Leu Cys Lys Ala Phe Gly Ala
1   5

<210> 311
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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      peptide

<400> 311
Lys Leu Ser Pro Tyr Val His Tyr Thr
1   5

<210> 312
<211> 20
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 312
Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly
1 5 10 15

Val Thr Ser Ala
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<210> 313
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 313
Ser Thr Ala Pro Pro Val His Asn Val
1 5

<210> 314
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 314
Leu Leu Leu Leu Thr Val Leu Thr Val
1 5

<210> 315
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 315
Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr
1 5 10

<210> 316
<211> 9
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 316
Met Leu Ala Val Ile Ser Cys Ala Val
1 5

<210> 317
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 317
Arg Gln Lys Arg Ile Leu Val Asn Leu
1 5

<210> 318
<211> 9
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<213> Artificial Sequence

<220>
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<400> 318
Asn Tyr Asn Asn Phe Tyr Arg Phe Leu
1 5

<210> 319

<211> 10
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 319
Glu Tyr Ser Lys Glu Cys Leu Lys Glu Phe
1 5 10

<210> 320
<211> 9
<212> PRT
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<220>
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peptide

<400> 320
Glu Tyr Leu Ser Leu Ser Asp Lys Ile
1 5

<210> 321
<211> 9
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 321
Glu Leu Val Arg Arg Ile Leu Ser Arg
1 5

<210> 322
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 322
Ala Pro Arg Gly Val Arg Met Ala Val
1   5

<210> 323
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 323
Cys Leu Ser Arg Arg Pro Trp Lys Arg Ser Trp Ser Ala Gly Ser Cys
1   5   10   15

Pro Gly Met Pro His Leu
            20

<210> 324
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 324
Ile Leu Ser Arg Asp Ala Ala Pro Leu Pro Arg Pro Gly
1   5   10

<210> 325
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 325
Glu Val Asp Pro Ala Ser Asn Thr Tyr
1   5

<210> 326
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 326
Gly Val Tyr Asp Gly Arg Glu His Thr Val
1 5 10

<210> 327
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 327
Asn Tyr Lys Arg Cys Phe Pro Val Ile
1 5

<210> 328
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 328
Ser Glu Ser Leu Lys Met Ile Phe
1 5

<210> 329
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 329
Ile Asn Lys Thr Ser Gly Pro Lys Arg Gly Lys His Ala Trp Thr His
1 5 10 15

Arg Leu Arg Glu
20

<210> 330
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 330
Tyr Phe Ser Lys Lys Glu Trp Glu Lys Met Lys Ser Ser Glu Lys Ile
1 5 10 15

Val Tyr Val Tyr
20

<210> 331
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 331
Met Lys Leu Asn Tyr Glu Val Met Thr Lys Leu Gly Phe Lys Val Thr
1 5 10 15

Leu Pro Pro Phe
20

<210> 332
<211> 20
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 332
Lys His Ala Trp Thr His Arg Leu Arg Glu Arg Lys Gln Leu Val Val
1 5 10 15

Tyr Glu Glu Ile
20

<210> 333
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 333
Leu Gly Phe Lys Val Thr Leu Pro Pro Phe Met Arg Ser Lys Arg Ala
1 5 10 15

Ala Asp Phe His
20

<210> 334
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 334
Lys Ser Ser Glu Lys Ile Val Tyr Val Tyr Met Lys Leu Asn Tyr Glu
1 5 10 15

Val Met Thr Lys
20

<210> 335
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 335
Ser Leu Gly Trp Leu Phe Leu Leu Leu
1 5

<210> 336
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 336
Leu Ser Arg Leu Ser Asn Arg Leu Leu
1 5

<210> 337
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 337
Thr Met Asn Gly Ser Lys Ser Pro Val
1 5

<210> 338
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 338
Pro Leu Leu Glu Asn Val Ile Ser Lys
1 5

<210> 339
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 339
Ser Leu Ser Lys Ile Leu Asp Thr Val
1 5

<210> 340
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 340
Ala Ala Arg Ala Val Phe Leu Ala Leu
1 5

<210> 341
<211> 9
<212> PRT
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<220>
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<400> 341
Glu Ala Asp Pro Thr Gly His Ser Tyr
1 5

<210> 342

<211> 9
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<220>
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peptide

<400> 342
Lys Val Leu Glu Tyr Val Ile Lys Val
1 5

<210> 343
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 343
Ser Leu Phe Arg Ala Val Ile Thr Lys
1 5

<210> 344
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 344
Glu Val Tyr Asp Gly Arg Glu His Ser Ala
1 5 10

<210> 345
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 345
Arg Val Arg Phe Phe Phe Pro Ser Leu
1   5

<210> 346
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 346
Arg Glu Pro Val Thr Lys Ala Glu Met Leu
1   5   10

<210> 347
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 347
Lys Glu Ala Asp Pro Thr Gly His Ser Tyr
1   5   10

<210> 348
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 348
Asp Pro Ala Arg Tyr Glu Phe Leu Trp
1   5

<210> 349
<211> 11
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<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 349
Ile Thr Lys Lys Val Ala Asp Leu Val Gly Phe
1 5 10

<210> 350
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 350
Ser Ala Phe Pro Thr Thr Ile Asn Phe
1 5

<210> 351
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 351
Ser Ala Tyr Gly Glu Pro Arg Lys Leu
1 5

<210> 352
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 352
Thr Ser Cys Ile Leu Glu Ser Leu Phe Arg Ala Val Ile Thr Lys

1 5 10 15

<210> 353
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 353
Pro Arg Ala Leu Ala Glu Thr Ser Tyr Val Lys Val Leu Glu Tyr
1 5 10 15

<210> 354
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 354
Phe Leu Leu Leu Lys Tyr Arg Ala Arg Glu Pro Val Thr Lys Ala Glu
1 5 10 15

<210> 355
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
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<400> 355
Glu Tyr Val Ile Lys Val Ser Ala Arg Val Arg Phe
1 5 10

<210> 356
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 356
Tyr Leu Gln Leu Val Phe Gly Ile Glu Val
1 5 10

<210> 357
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 357
Glu Tyr Leu Gln Leu Val Phe Gly Ile
1 5

<210> 358
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 358
Glu Gly Asp Cys Ala Pro Glu Glu Lys
1 5

<210> 359
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 359
Leu Leu Lys Tyr Arg Ala Arg Glu Pro Val Thr Lys Ala Glu
1 5 10

<210> 360
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 360
Lys Ala Ser Glu Lys Ile Phe Tyr Val
1 5

<210> 361
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 361
Glu Lys Ile Gln Lys Ala Phe Asp Asp Ile Ala Lys Tyr Phe Ser Lys
1 5 10 15

<210> 362
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 362
Phe Gly Arg Leu Gln Gly Ile Ser Pro Lys Ile
1 5 10

<210> 363
<211> 18
<212> PRT
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<220>
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peptide

<400> 363
Trp Glu Lys Met Lys Ala Ser Glu Lys Ile Phe Tyr Val Tyr Met Lys
1 5 10 15

Arg Lys

<210> 364
<211> 15
<212> PRT
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<220>
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peptide

<400> 364
Lys Ile Phe Tyr Val Tyr Met Lys Arg Lys Tyr Glu Ala Met Thr
1 5 10 15

<210> 365
<211> 14
<212> PRT
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<220>
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peptide

<400> 365
Lys Ile Phe Tyr Val Tyr Met Lys Arg Lys Tyr Glu Ala Met
1 5 10

<210> 366
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 366
Cys Glu Phe His Ala Cys Trp Pro Ala Phe Thr Val Leu Gly Glu

1 5 10 15

<210> 367
<211> 9
<212> PRT
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<220>
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<400> 367
Lys Phe Leu Asp Ala Leu Ile Ser Leu
1 5

<210> 368
<211> 10
<212> PRT
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<220>
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<400> 368
Ala Leu Gly Gly His Pro Leu Leu Gly Val
1 5 10

<210> 369
<211> 9
<212> PRT
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<220>
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<400> 369
Leu Pro Arg Trp Pro Pro Pro Gln Leu
1 5

<210> 370
<211> 9
<212> PRT
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<220>
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peptide

<400> 370
Ile Leu Ala Lys Phe Leu His Trp Leu
1 5

<210> 371
<211> 9
<212> PRT
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<220>
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peptide

<400> 371
Arg Leu Val Asp Asp Phe Leu Leu Val
1 5

<210> 372
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 372
Arg Pro Gly Leu Leu Gly Ala Ser Val Leu Gly Leu Asp Asp Ile
1 5 10 15

<210> 373
<211> 15
<212> PRT
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<220>
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peptide

<400> 373
Leu Thr Asp Leu Gln Pro Tyr Met Arg Gln Phe Val Ala His Leu
1 5 10 15

<210> 374
<211> 9
<212> PRT
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<220>
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peptide

<400> 374
Val Val Val Gly Ala Val Gly Val Gly
1 5

<210> 375
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 375
His Leu Ser Thr Ala Phe Ala Arg Val
1 5

<210> 376
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 376
Lys Ile Phe Gly Ser Leu Ala Phe Leu
1 5

<210> 377
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 377
Ile Ile Ser Ala Val Val Gly Ile Leu
1 5

<210> 378
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 378
Ala Leu Cys Arg Trp Gly Leu Leu Leu
1 5

<210> 379
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 379
Ile Leu His Asn Gly Ala Tyr Ser Leu
1 5

<210> 380
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 380
Arg Leu Leu Gln Glu Thr Glu Leu Val
1 5

<210> 381

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 381
Val Val Lys Gly Val Val Phe Gly Ile
1 5

<210> 382
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 382
Tyr Met Ile Met Val Lys Cys Trp Met Ile
1 5 10

<210> 383
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 383
Ser Leu Leu Ser Gly Asp Trp Val Leu
1 5

<210> 384
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 384
Gly Leu Gln Leu Gly Val Gln Ala Val
1 5

<210> 385
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 385
Pro Leu Thr Glu Tyr Ile Gln Pro Val
1 5

<210> 386
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 386
Ser Pro Arg Trp Trp Pro Thr Cys Leu
1 5

<210> 387
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 387
Gly Val Ala Leu Gln Thr Met Lys Gln
1 5

<210> 388
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 388
Phe Met Asn Lys Phe Ile Tyr Glu Ile
1 5

<210> 389
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 389
Gln Leu Ala Val Ser Val Ile Leu Arg Val
1 5 10

<210> 390
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 390
Leu Pro Ala Val Val Gly Leu Ser Pro Gly Glu Gln Glu Tyr
1 5 10

<210> 391
<211> 9
<212> PRT
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<220>
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peptide

<400> 391
Asn Tyr Ala Arg Thr Glu Asp Phe Phe

1 5

<210> 392
<211> 9
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<400> 392
Phe Leu Ile Ile Trp Gln Asn Thr Met
1 5

<210> 393
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<220>
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<400> 393
Thr Leu Tyr Gln Asp Asp Thr Leu Thr Leu Gln Ala Ala Gly
1 5 10

<210> 394
<211> 10
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<220>
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<400> 394
Ser Leu Tyr Lys Phe Ser Pro Phe Pro Leu
1 5 10

<210> 395
<211> 9
<212> PRT
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<220>
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peptide

<400> 395
Lys Glu Leu Glu Gly Ile Leu Leu Leu
1 5

<210> 396
<211> 9
<212> PRT
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<220>
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peptide

<400> 396
Arg Leu Ser Ser Cys Val Pro Val Ala
1 5

<210> 397
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 397
Val Leu Leu Gln Ala Gly Ser Leu His Ala
1 5 10

<210> 398
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 398
Leu Leu Asn Ala Phe Thr Val Thr Val
1 5

<210> 399
<211> 8
<212> PRT
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<220>
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peptide

<400> 399
Val Leu Phe Tyr Leu Gly Gln Tyr
1 5

<210> 400
<211> 10
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<220>
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peptide

<400> 400
Phe Ile Ala Ser Asn Gly Val Lys Leu Val
1 5 10

<210> 401
<211> 9
<212> PRT
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<220>
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peptide

<400> 401
Glu Thr Val Ser Glu Gln Ser Asn Val
1 5

<210> 402
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 402
Phe Leu Asp Glu Phe Met Glu Gly Val
1 5

<210> 403
<211> 8
<212> PRT
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<220>
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<400> 403
Gln Gln Ile Thr Lys Thr Glu Val
1 5

<210> 404
<211> 8
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<400> 404
Tyr Arg Pro Arg Pro Arg Arg Tyr
1 5

<210> 405
<211> 9
<212> PRT
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<220>
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<400> 405
Ala Leu Lys Asp Val Glu Glu Arg Val
1 5

<210> 406

<211> 9
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 406
Ile Ser Gly Gly Pro Arg Ile Ser Tyr
1 5

<210> 407
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 407
Arg Gln Lys Lys Ile Arg Ile Gln Leu
1 5

<210> 408
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 408
His Leu Gly Ser Arg Gln Lys Lys Ile Arg Ile Gln Leu Arg Ser Gln
1 5 10 15

<210> 409
<211> 17
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 409
Cys Ala Thr Trp Lys Val Ile Cys Lys Ser Cys Ile Ser Gln Thr Pro
1 5 10 15

Gly

<210> 410
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 410
Phe Leu Gly Tyr Leu Ile Leu Gly Val
1 5

<210> 411
<211> 9
<212> PRT
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<220>
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<400> 411
Met Ile Ala Val Phe Leu Pro Ile Val
1 5

<210> 412
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 412
His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys
1 5 10 15

<210> 413
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 413
Phe Leu Phe Leu Leu Phe Phe Trp Leu
1 5

<210> 414
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 414
Thr Leu Met Ser Ala Met Thr Asn Leu
1 5

<210> 415
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 415
Ala Leu Asp Val Tyr Asn Gly Leu Leu
1 5

<210> 416
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 416
Phe Leu Thr Pro Lys Lys Leu Gln Cys Val
1 5 10

<210> 417
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 417
Val Ile Ser Asn Asp Val Cys Ala Gln Val
1 5 10

<210> 418
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 418
Tyr Tyr Trp Pro Arg Pro Arg Arg Tyr
1 5

<210> 419
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 419
Asn Thr Tyr Ala Ser Pro Arg Phe Lys
1 5

<210> 420

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 420
Ser Leu Phe Glu Gly Ile Asp Ile Tyr Thr
1 5 10

<210> 421
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 421
Ala Leu Ser Val Met Gly Val Tyr Val
1 5

<210> 422
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 422
Gly Leu Gln Leu Gly Val Gln Ala
1 5

<210> 423
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 423
Tyr Ser Val Tyr Phe Asn Leu Pro Ala Asp Thr Ile Tyr Thr Asn
1   5   10   15

<210> 424
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 424
Glu Asp Leu Thr Val Lys Ile Gly Asp Phe Gly Leu Ala Thr Glu Lys
1   5   10   15

Ser Arg Trp Ser Gly Ser His Gln Phe Glu Gln Leu Ser
            20   25

<210> 425
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 425
Ser Tyr Leu Asp Ser Gly Ile His Phe
1   5

<210> 426
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 426
Phe Ser Trp Ala Met Asp Leu Asp Pro Lys Gly Ala
1   5   10

<210> 427
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 427
Ala Cys Asp Pro His Ser Gly His Phe Val
1 5 10

<210> 428
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 428
Cys Ile Leu Gly Lys Leu Phe Thr Lys
1 5

<210> 429
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 429
Ala Val Cys Pro Trp Thr Trp Leu Arg
1 5

<210> 430
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 430
Ile Leu Asp Lys Val Leu Val His Leu
1 5

<210> 431
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 431
Gly Leu Phe Gly Asp Ile Tyr Leu Ala
1 5

<210> 432
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 432
Met Ile Phe Glu Lys His Gly Phe Arg Arg Thr Thr Pro Pro
1 5 10

<210> 433
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 433
Ser Leu Ala Asp Glu Ala Glu Val Tyr Leu
1 5 10

<210> 434

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 434
Thr Leu Asp Trp Leu Leu Gln Thr Pro Lys
1 5 10

<210> 435
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 435
Ile Leu Asn Ala Met Ile Ala Lys Ile
1 5

<210> 436
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 436
Trp Arg Arg Ala Pro Ala Pro Gly Ala
1 5

<210> 437
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 437
Pro Val Thr Trp Arg Arg Ala Pro Ala
1   5

<210> 438
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 438
Phe Leu Glu Gly Asn Glu Val Gly Lys Thr Tyr
1   5   10

<210> 439
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 439
Lys Thr Leu Thr Ser Val Phe Gln Lys
1   5

<210> 440
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 440
Glu Glu Lys Leu Ile Val Val Leu Phe
1   5

<210> 441
<211> 11
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 441
Ser Glu Leu Phe Arg Ser Gly Leu Asp Ser Tyr
1 5 10

<210> 442
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 442
Phe Arg Ser Gly Leu Asp Ser Tyr Val
1 5

<210> 443
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 443
Glu Ala Phe Ile Gln Pro Ile Thr Arg
1 5

<210> 444
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 444
Arg Val Ile Lys Asn Ser Ile Arg Leu Thr Leu

1 5 10

<210> 445
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 445
Lys Ile Asn Lys Asn Pro Lys Tyr Lys
1 5

<210> 446
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 446
Tyr Thr Asp Phe His Cys Gln Tyr Val
1 5

<210> 447
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 447
Leu Leu Leu Asp Asp Leu Leu Val Ser Ile
1 5 10

<210> 448
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 448
Pro Tyr Tyr Phe Ala Ala Glu Leu Pro Pro Arg Asn Leu Pro Glu Pro
1 5 10 15

<210> 449
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 449
Ile Leu Asp Thr Ala Gly Arg Glu Glu Tyr
1 5 10

<210> 450
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 450
Arg Pro His Val Pro Glu Ser Ala Phe
1 5

<210> 451
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 451
Lys Ile Phe Ser Glu Val Thr Leu Lys
1 5

<210> 452
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 452
Ser His Glu Thr Val Ile Ile Glu Leu
1 5

<210> 453
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 453
Gly Glu Leu Ile Gly Ile Leu Asn Ala Ala Lys Val Pro Ala Asp
1 5 10 15

<210> 454
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 454
Leu Tyr Ser Ala Cys Phe Trp Trp Leu
1 5

<210> 455
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 455
Val Leu His Trp Asp Pro Glu Thr Val
1 5

<210> 456
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 456
Met Ser Leu Gln Arg Gln Phe Leu Arg
1 5

<210> 457
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 457
Ile Ser Pro Asn Ser Val Phe Ser Gln Trp Arg Val Val Cys Asp Ser
1 5 10 15

Leu Glu Asp Tyr
20

<210> 458
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 458
Ser Leu Pro Tyr Trp Asn Phe Ala Thr Gly

1 5 10

<210> 459
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 459
Ser Gln Trp Arg Val Val Cys Asp Ser Leu Glu Asp Tyr Asp Thr
1 5 10 15

<210> 460
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 460
Ser Val Tyr Asp Phe Phe Val Trp Leu
1 5

<210> 461
<211> 9
<212> PRT
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<220>
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<400> 461
Thr Leu Asp Ser Gln Val Met Ser Leu
1 5

<210> 462
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 462
Leu Leu Gly Pro Gly Arg Pro Tyr Arg
1 5

<210> 463
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 463
Ala Asn Asp Pro Ile Phe Val Val Leu
1 5

<210> 464
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 464
Gln Cys Thr Glu Val Arg Ala Asp Thr Arg Pro Trp Ser Gly Pro
1 5 10 15

<210> 465
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 465
Ala Leu Pro Tyr Trp Asn Phe Ala Thr Gly
1 5 10

<210> 466
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 466
Lys Cys Asp Ile Cys Thr Asp Glu Tyr
1 5

<210> 467
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 467
Ser Ser Asp Tyr Val Ile Pro Ile Gly Thr Tyr
1 5 10

<210> 468
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 468
Met Leu Leu Ala Val Leu Tyr Cys Leu
1 5

<210> 469
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 469
Cys Leu Leu Trp Ser Phe Gln Thr Ser Ala
1 5 10

<210> 470
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 470
Tyr Met Asp Gly Thr Met Ser Gln Val
1 5

<210> 471
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 471
Ile Tyr Met Asp Gly Thr Ala Asp Phe Ser Phe
1 5 10

<210> 472
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 472
Gln Cys Ser Gly Asn Phe Met Gly Phe
1 5

<210> 473

<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 473
Thr Pro Arg Leu Pro Ser Ser Ala Asp Val Glu Phe
1 5 10

<210> 474
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 474
Leu Pro Ser Ser Ala Asp Val Glu Phe
1 5

<210> 475
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 475
Leu His His Ala Phe Val Asp Ser Ile Phe
1 5 10

<210> 476
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 476
Ser Glu Ile Trp Arg Asp Ile Asp Phe
1   5

<210> 477
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 477
Gln Asn Ile Leu Leu Ser Asn Ala Pro Leu Gly Pro Gln Phe Pro
1   5   10   15

<210> 478
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 478
Ser Tyr Leu Gln Asp Ser Asp Pro Asp Ser Phe Gln Asp
1   5   10

<210> 479
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 479
Phe Leu Leu His His Ala Phe Val Asp Ser Ile Phe Glu Gln Trp Leu
1   5   10   15

Gln Arg His Arg Pro
            20

<210> 480
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 480
Tyr Thr Thr Ala Glu Glu Ala Ala Gly Ile Gly Ile Leu Thr Val Ile
1 5 10 15

Leu Gly Val Leu Leu Leu Ile Gly Cys Trp Tyr Cys Arg Arg
20 25 30

<210> 481
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 481
Ala Leu Asn Phe Pro Gly Ser Gln Lys
1 5

<210> 482
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 482
Val Tyr Phe Phe Leu Pro Asp His Leu
1 5

<210> 483
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 483
Arg Thr Lys Gln Leu Tyr Pro Glu Trp
1 5

<210> 484
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 484
His Thr Met Glu Val Thr Val Tyr His Arg
1 5 10

<210> 485
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 485
Ser Ser Pro Gly Cys Gln Pro Pro Ala
1 5

<210> 486
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 486
Val Pro Leu Asp Cys Val Leu Tyr Arg Tyr

1 5 10

<210> 487
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 487
Leu Pro His Ser Ser Ser His Trp Leu
1 5

<210> 488
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 488
Ser Asn Asp Gly Pro Thr Leu Ile
1 5

<210> 489
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 489
Gly Arg Ala Met Leu Gly Thr His Thr Met Glu Val Thr Val Tyr
1 5 10 15

<210> 490
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 490
Trp Asn Arg Gln Leu Tyr Pro Glu Trp Thr Glu Ala Gln Arg Leu Asp
1 5 10 15

<210> 491
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 491
Thr Thr Glu Trp Val Glu Thr Thr Ala Arg Glu Leu Pro Ile Pro Glu
1 5 10 15

Pro Glu

<210> 492
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 492
Thr Gly Arg Ala Met Leu Gly Thr His Thr Met Glu Val Thr Val Tyr
1 5 10 15

His

<210> 493
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 493
Val Leu Pro Asp Val Phe Ile Arg Cys Val
1 5 10

<210> 494
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 494
Arg Tyr Cys Asn Leu Glu Gly Pro Pro Ile
1 5 10

<210> 495
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 495
Lys Trp Thr Glu Pro Tyr Cys Val Ile Ala Ala Val Lys Ile Phe Pro
1 5 10 15

Arg Phe Phe Met Val Ala Lys Gln
20

<210> 496
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 496
Lys Cys Cys Lys Ile Arg Tyr Cys Asn Leu Glu Gly Pro Pro Ile Asn
1   5   10   15

Ser Ser Val Phe
            20

<210> 497
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 497
Gly Leu Tyr Asp Gly Met Glu His Leu
1   5

<210> 498
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 498
Phe Leu Trp Gly Pro Arg Ala Leu Val
1   5

<210> 499
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 499
Val Arg Ile Gly His Leu Tyr Ile Leu
1   5

<210> 500
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 500
Arg Glu Pro Phe Thr Lys Ala Glu Met Leu Gly Ser Val Ile Arg
1 5 10 15

<210> 501
<211> 14
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 501
Ala Glu Leu Val His Phe Leu Leu Leu Lys Tyr Arg Ala Arg
1 5 10

<210> 502
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 502
Leu Leu Phe Gly Leu Ala Leu Ile Glu Val
1 5 10

<210> 503
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 503
Ser Glu Ser Ile Lys Lys Lys Val Leu
1 5

<210> 504
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 504
Ala Ser Ser Thr Leu Tyr Leu Val Phe
1 5

<210> 505
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 505
Ser Ser Thr Leu Tyr Leu Val Phe Ser Pro Ser Ser Phe Ser Thr
1 5 10 15

<210> 506
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 506
Gln Gly Gln His Phe Leu Gln Lys Val
1 5

<210> 507

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 507
Glu Val Ile Ser Cys Lys Leu Ile Lys Arg
1 5 10

<210> 508
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 508
Phe Pro Ser Asp Ser Trp Cys Tyr Phe
1 5

<210> 509
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 509
Leu Tyr Ala Thr Val Ile His Asp Ile
1 5

<210> 510
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 510
Ser Ser Lys Ala Leu Gln Arg Pro Val
1 5

<210> 511
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 511
Gly Phe Lys Gln Ser Ser Lys Ala Leu
1 5

<210> 512
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 512
Ala Thr Gly Phe Lys Gln Ser Ser Lys Ala Leu Gln Arg Pro Val Ala
1 5 10 15

Ser

<210> 513
<211> 16
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 513
Thr Met Lys Gln Ile Cys Lys Lys Glu Ile Arg Arg Leu His Gln Tyr
1 5 10 15

<210> 514
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 514
Lys Ile Leu Asp Ala Val Val Ala Gln Lys
1 5 10

<210> 515
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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peptide

<400> 515
Arg Ile Ala Glu Cys Ile Leu Gly Met
1 5

<210> 516
<211> 15
<212> PRT
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<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 516
Ile Gly Arg Ile Ala Glu Cys Ile Leu Gly Met Asn Pro Ser Arg
1 5 10 15

<210> 517
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 517
Tyr Val Asp Phe Arg Glu Tyr Glu Tyr Tyr
1 5 10

<210> 518
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 518
Phe Leu Asp Arg Phe Leu Ser Cys Met
1 5

<210> 519
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 519
Ser Leu Ile Ala Ala Ala Ala Phe Cys Leu Ala
1 5 10

<210> 520
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 520
Val Val Met Ser Trp Ala Pro Pro Val
1 5

<210> 521

<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 521
Asn Ser Asn His Val Ala Ser Gly Ala Gly Glu Ala Ala Ile Glu Thr
1 5 10 15

Gln Ser Ser Ser Ser Glu Glu Ile Val
20 25

<210> 522
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 522
Ile Leu Phe Gly Ile Ser Leu Arg Glu Val
1 5 10

<210> 523
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 523
Lys Val Val Glu Phe Leu Ala Met Leu
1 5

<210> 524
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 524
Ser Ser Ala Leu Leu Ser Ile Phe Gln Ser Ser Pro Glu
1 5 10

<210> 525
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 525
Ser Phe Ser Tyr Thr Leu Leu Ser Leu
1 5

<210> 526
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 526
Val Ser Ser Phe Phe Ser Tyr Thr Leu
1 5

<210> 527
<211> 93
<212> PRT
<213> Vaccinia virus

<400> 527
Met His His Pro Met Glu Ser Val Lys Thr Thr Asn Thr Asn Ala Ile
1 5 10 15

Ile Cys Val Arg Glu His Thr Leu Pro Asp Tyr Ala Asn Thr Gln Cys
20 25 30

```
Thr Pro Cys Gly Ser Gly Thr Phe Thr Ser Arg Asn Asn His Leu Pro
        35                  40                  45


Ala Cys Leu Ser Cys Asn Gly Arg Arg Asp Arg Val Thr Leu Leu Thr
    50                  55                  60


Ile Glu Ser Val Asn Ala Leu Pro Asp Ile Ile Val Phe Ser Lys Asp
65                  70                  75                  80


His Pro Asp Ala Arg His Val Phe Pro Lys Gln Asn Val
                85                  90


<210> 528
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 528
Lys Pro Leu Phe Arg Arg Met Ser Ser Leu Glu Leu Val Ile Ala
1               5                   10                  15


<210> 529
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 529
Met Val Lys Ile Ser Gly Gly Pro Arg
1               5


<210> 530
<211> 9
<212> PRT
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 530
Glu Val Asp Pro Ile Gly His Val Tyr
1 5

<210> 531
<211> 244
<212> PRT
<213> Vaccinia virus

<400> 531
Met His Val Pro Ala Ser Leu Gln Gln Ser Ser Ser Ser Ser Ser Ser
1 5 10 15

Cys Thr Glu Glu Glu Asn Lys His His Met Gly Ile Asp Val Ile Ile
20 25 30

Lys Val Thr Lys Gln Asp Gln Thr Pro Thr Asn Asp Lys Ile Cys Gln
35 40 45

Ser Val Thr Glu Ile Thr Glu Ser Glu Ser Asp Pro Asp Pro Glu Val
50 55 60

Glu Ser Glu Asp Asp Ser Thr Ser Val Glu Asp Val Asp Pro Pro Thr
65 70 75 80

Thr Tyr Tyr Ser Ile Ile Gly Gly Gly Leu Arg Met Asn Phe Gly Phe
85 90 95

Thr Lys Cys Pro Gln Ile Lys Ser Ile Ser Glu Ser Ala Asp Gly Asn
100 105 110

Thr Val Asn Ala Arg Leu Ser Ser Val Ser Pro Gly Gln Gly Lys Asp
115 120 125

Ser Pro Ala Ile Thr His Glu Glu Ala Leu Ala Met Ile Lys Asp Cys
130 135 140

Glu Val Ser Ile Asp Ile Arg Cys Ser Glu Glu Glu Lys Asp Ser Asp
145 150 155 160

Ile Lys Thr His Pro Val Leu Gly Ser Asn Ile Ser His Lys Lys Val
165 170 175

Ser Tyr Glu Asp Ile Ile Gly Ser Thr Ile Val Asp Thr Lys Cys Val
180 185 190

Lys Asn Leu Glu Phe Ser Val Arg Ile Gly Asp Met Cys Lys Glu Ser
195 200 205

Ser Glu Leu Glu Val Lys Asp Gly Phe Lys Tyr Val Asp Gly Ser Ala
210 215 220

Ser Glu Gly Ala Thr Asp Asp Thr Ser Leu Ile Asp Ser Thr Lys Leu
225 230 235 240

Lys Ala Cys Val

<210> 532
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 532
Glu Val Asp Pro Ile Gly His Leu Tyr
1 5

<210> 533
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic

peptide

<400> 533
Lys Val Ala Glu Leu Val His Phe Leu
1 5

<210> 534
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 534
Thr Phe Pro Asp Leu Glu Ser Glu Phe
1 5

<210> 535
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 535
Val Ala Glu Leu Val His Phe Leu Leu
1 5

<210> 536
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 536
Met Glu Val Asp Pro Ile Gly His Leu Tyr
1 5 10

<210> 537

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 537
Ala Glu Leu Val His Phe Leu Leu Leu
1 5

<210> 538
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 538
Trp Gln Tyr Phe Phe Pro Val Ile Phe
1 5

<210> 539
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 539
Lys Lys Leu Leu Thr Gln His Phe Val Gln Glu Asn Tyr Leu Glu Tyr
1 5 10 15

<210> 540
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 540
Arg Lys Val Ala Glu Leu Val His Phe Leu Leu Leu Lys Tyr Arg
1   5   10   15

<210> 541
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 541
Ala Cys Tyr Glu Phe Leu Trp Gly Pro Arg Ala Leu Val Glu Thr Ser
1   5   10   15

<210> 542
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 542
Val Ile Phe Ser Lys Ala Ser Ser Ser Leu Gln Leu
1   5   10

<210> 543
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 543
Val Phe Gly Ile Glu Leu Met Glu Val Asp Pro Ile Gly His Leu
1   5   10   15

<210> 544
<211> 15
<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 544
Gly Asp Asn Gln Ile Met Pro Lys Ala Gly Leu Leu Ile Ile Val
1 5 10 15

<210> 545
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 545
Thr Ser Tyr Val Lys Val Leu His His Met Val Lys Ile Ser Gly
1 5 10 15

<210> 546
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 546
Arg Lys Val Ala Glu Leu Val His Phe Leu Leu Leu Lys Tyr Arg Ala
1 5 10 15

<210> 547
<211> 309
<212> PRT
<213> Vaccinia virus

<400> 547
Ile Glu Leu Leu Lys Thr Met Asp Leu Arg Lys Arg Asp Leu Gly Pro
1 5 10 15

Ala Phe Thr Glu Leu Ile Ser Gly Leu Ala Lys Leu Lys Thr Ser Lys

```
            20                  25                  30

Tyr Thr Tyr Thr Asp Leu Thr Tyr Gln Ser Phe Val Asp Asn Thr Val
        35                  40                  45

Cys Ile Lys Pro Ser Tyr Tyr Gln Gln Tyr His Arg Phe Gly Leu Tyr
    50                  55                  60

Arg Leu Asn Phe Arg Arg Asp Ala Val Asn Lys Ile Asn Ser Ile Val
65                  70                  75                  80

Glu Arg Arg Ser Gly Met Ser Asn Val Val Asp Ser Asn Met Leu Asp
                85                  90                  95

Asn Asn Thr Leu Trp Ala Ile Ile Asn Thr Ile Tyr Phe Lys Gly Ile
            100                 105                 110

Trp Gln Tyr Pro Phe Asp Ile Thr Lys Thr Arg Asn Ala Ser Phe Thr
        115                 120                 125

Asn Lys Tyr Gly Thr Lys Thr Val Pro Met Met Asn Val Val Thr Lys
    130                 135                 140

Leu Gln Gly Asn Thr Ile Thr Ile Asp Asp Glu Glu Tyr Asp Met Val
145                 150                 155                 160

Arg Leu Pro Tyr Lys Asp Ala Asn Ile Ser Met Tyr Leu Ala Ile Gly
                165                 170                 175

Asp Asn Met Thr His Phe Thr Asp Ser Ile Thr Ala Ala Lys Leu Asp
            180                 185                 190

Tyr Trp Ser Ser Gln Leu Gly Asn Lys Val Tyr Asn Leu Lys Leu Pro
        195                 200                 205

Lys Phe Ser Ile Glu Asn Lys Arg Asp Ile Lys Ser Ile Ala Glu Met
    210                 215                 220
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```
Met Ala Pro Ser Met Phe Asn Pro Asp Asn Ala Ser Phe Lys His Met
225                 230                 235                 240


Thr Arg Asp Pro Leu Tyr Ile Tyr Lys Met Phe Gln Asn Ala Lys Ile
                245                 250                 255


Asp Val Asp Glu Gln Gly Thr Val Ala Glu Ala Ser Thr Ile Met Val
            260                 265                 270


Ala Thr Ala Arg Ser Ser Pro Glu Lys Leu Glu Phe Asn Thr Pro Phe
        275                 280                 285


Val Phe Ile Ile Arg His Asp Ile Thr Gly Phe Ile Leu Phe Met Gly
    290                 295                 300


Lys Val Glu Ser Pro
305
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<210> 548
<211> 222
<212> PRT
<213> Vaccinia virus

<400> 548

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Met Asn His Cys Leu Leu Ala Ile Ser Ala Val Tyr Phe Lys Ala Lys
1               5                   10                  15


Trp Leu Thr Pro Phe Glu Lys Glu Phe Thr Ser Asp Tyr Pro Phe Tyr
            20                  25                  30


Val Ser Pro Thr Glu Met Val Asp Val Ser Met Met Ser Met Tyr Gly
        35                  40                  45


Lys Ala Phe Asn His Ala Ser Val Lys Glu Ser Phe Gly Asn Phe Ser
    50                  55                  60


Ile Ile Glu Leu Pro Tyr Val Gly Asp Thr Ser Met Met Val Ile Leu
65                  70                  75                  80
```

```
Pro Asp Lys Ile Asp Gly Leu Glu Ser Ile Glu Gln Asn Leu Thr Asp
                85                  90                  95

Thr Asn Phe Lys Lys Trp Cys Asp Phe Met Asp Ala Met Phe Ile Asp
            100                 105                 110

Val His Ile Pro Lys Phe Lys Val Thr Gly Ser Tyr Asn Leu Val Asp
        115                 120                 125

Thr Leu Val Lys Ser Gly Leu Thr Glu Val Phe Gly Ser Thr Gly Asp
    130                 135                 140

Tyr Ser Asn Met Cys Asn Leu Asp Val Ser Val Asp Ala Met Ile His
145                 150                 155                 160

Lys Thr Tyr Ile Asp Val Asn Glu Glu Tyr Thr Glu Ala Ala Ala Ala
                165                 170                 175

Thr Cys Ala Leu Val Ser Asp Cys Ala Ser Thr Val Thr Asn Glu Phe
            180                 185                 190

Cys Ala Asp His Pro Phe Ile Tyr Val Ile Arg His Val Asp Gly Lys
        195                 200                 205

Ile Leu Phe Val Gly Arg Tyr Cys Ser Pro Thr Thr Asn Cys
    210                 215                 220


<210> 549
<211> 289
<212> PRT
<213> Vaccinia virus

<400> 549
Met Glu Leu Glu Asn Glu Pro Val Ile Leu Pro Cys Pro Gln Ile Asn
1               5                   10                  15

Thr Leu Ser Ser Gly Tyr Asn Ile Leu Asp Ile Leu Trp Glu Lys Arg
            20                  25                  30
```

```
Gly Ala Asp Asn Asp Arg Ile Ile Pro Ile Asp Asn Gly Ser Asn Met
        35                  40                  45

Leu Ile Leu Asn Pro Thr Gln Ser Asp Ser Gly Ile Tyr Ile Cys Ile
    50                  55                  60

Thr Thr Asn Glu Thr Tyr Cys Asp Met Met Ser Leu Asn Leu Thr Ile
65                  70                  75                  80

Val Ser Val Leu Glu Ser Asn Ile Asp Leu Ile Ser Tyr Pro Gln Ile
                85                  90                  95

Val Asn Glu Arg Ser Thr Gly Glu Met Val Cys Pro Asn Ile Asn Ala
            100                 105                 110

Phe Ile Ala Ser Asn Val Asn Ala Asp Ile Ile Trp Ser Gly His Arg
        115                 120                 125

Arg Leu Arg Asn Lys Arg Leu Lys Gln Arg Thr Pro Gly Ile Ile Thr
    130                 135                 140

Ile Glu Asp Val Arg Lys Asn Asp Ala Gly Tyr Tyr Thr Cys Val Leu
145                 150                 155                 160

Glu Tyr Ile Tyr Arg Gly Lys Thr Tyr Asn Val Thr Arg Ile Val Lys
                165                 170                 175

Leu Glu Val Arg Asp Lys Ile Ile Pro Ser Thr Met Gln Leu Pro Asp
            180                 185                 190

Gly Ile Val Thr Ser Ile Gly Ser Asn Leu Thr Ile Ala Cys Arg Val
        195                 200                 205

Ser Leu Arg Pro Pro Thr Thr Asp Ala Asp Val Phe Trp Ile Ser Asn
    210                 215                 220

Gly Met Tyr Tyr Glu Glu Asp Asp Gly Asp Gly Asn Gly Arg Ile Ser
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225 230 235 240

Val Ala Asn Lys Ile Tyr Met Thr Asp Lys Arg Arg Val Ile Thr Ser
245 250 255

Arg Leu Asn Ile Asn Pro Val Lys Glu Glu Asp Ala Thr Thr Phe Thr
260 265 270

Cys Met Ala Phe Thr Ile Pro Ser Ile Ser Lys Thr Val Thr Val Ser
275 280 285

Ile

<210> 550
<211> 827
<212> DNA
<213> Vaccinia virus

<400> 550
acaacaccat gagatatatt ataattctcg cagttttgtt cattaatagt atacacgcta 60

aaataactag ttataagttt gaatccgtca attttgattc caaaattgaa tggactgggg 120

atggtctata caatatatcc cttaaaaatt atggcatcaa gacgtggcaa acaatgtata 180

caaatgtacc agaaggaaca tacgacatat ccgcatttcc aaagaatgat ttcgtatctt 240

tctgggttaa atttgaacaa ggcgattata aagtggaaga gtattgtacg ggactatgcg 300

tcgaagtaaa aattggacca ccgactgtaa cattgactga atacgacgac catatcaatt 360

tgtacatcga gcatccgtat gctactagag gtagcaaaaa gattcctatt tacaaacgcg 420

gtgacatgtg tgatatctac ttgttgtata cggctaactt cacattcgga gattctgaag 480

aaccagtaac atatgatatc gatgactacg attgcacgtc tacaggttgc agcatagact 540

ttgccacaac agaaaaagtg tgcgtgacag cacagggagc cacagaaggg tttctcgaaa 600

aaattactcc atggagttcg gaagtatgtc tgacacctaa aaagaatgta tatacatgtg 660

caattagatc caaagaagat gttcccaatt tcaaggacaa aatggccaga gttatcaaga 720

gaaaatttaa taaacagtct caatcttatt taactaaatt tctcggtagc acatcaaatg 780

atgttaccac ttttcttagc atgcttaact tgactaaata ttcataa 827

<210> 551
<211> 15
<212> DNA
<213> Vaccinia virus

<400> 551
aaaatttaat aaaca 15

<210> 552
<211> 150
<212> DNA
<213> Vaccinia virus

<400> 552
gatgttccca atttcaagga caaaatggcc agagttatca agagaaaatt taataaacag 60

tctcaatctt atttaactaa atttctcggt agcacatcaa atgatgttac cacttttctt 120

agcatgctta acttgactaa atattcataa 150

<210> 553
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 553
taaaaaatga aaataaatac aaaggttctt 30

<210> 554
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 554
aaattgaaag cgagaaataa tcataaat 28

<210> 555
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 555
aaaattgaaa tttta 15

<210> 556
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 556
ttttattttt ttttttgga atataaata 29

<210> 557
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 557
aaaattgaaa ttttattttt ttttttgga atataaata 39

<210> 558
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 558
aaaattgaaa aaata 15

<210> 559
<211> 50
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 559
ttttattttt ttttttgga atataaatat ccggtaaaat tgaaaaaata 50

<210> 560
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<220>
<221> modified_base
<222> (3)..(3)
<223> a, c, t, g, unknown or other

<220>
<221> modified_base
<222> (10)..(10)
<223> a, c, t, g, unknown or other

<220>
<221> modified_base
<222> (18)..(21)
<223> a, c, t, g, unknown or other

<400> 560
ttnttttttn ttttttnnn ntataaat 28

<210> 561
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 561
ttgtattttc ttttgttggc atataaat 28

<210> 562
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 562
tttattgtaa gctttttcca ttttaaat 28

<210> 563
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 563
tcattttgtt tttttctatg ctataaat 28

<210> 564
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 564
taaaaattta aaatatatta tcacttcagt 30

<210> 565
<211> 30

<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 565
aaaaaactga tattatataa atattttagt 30

<210> 566
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<220>
<221> modified_base
<222> (1)..(2)
<223> a, c, t, g, unknown or other

<220>
<221> modified_base
<222> (7)..(7)
<223> a, c, t, g, unknown or other

<220>
<221> modified_base
<222> (14)..(14)
<223> a, c, t, g, unknown or other

<220>
<221> modified_base
<222> (18)..(30)
<223> a, c, t, g, unknown or other

<400> 566
nnaaaantga aaanatannn nnnnnnnnnn 30

<210> 567
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 567
aaaaaaatga taaagtaggt tcagttttat 30

<210> 568
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 568
taaaaagtga aaaacaatat tatttttatc 30

<210> 569
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
oligonucleotide

<400> 569
aaaattaaaa aataacttaa tttattattg 30

<210> 570
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 570
Gly Ser Gly Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp Val Glu
1 5 10 15

Glu Asn Pro Gly Pro
20

<210> 571
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 571
Pro Arg Gly Ser Gly Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp
1 5 10 15

Val Glu Glu Asn Pro Gly Pro
20

<210> 572
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 572
Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp Val Glu Glu Asn Pro
1 5 10 15

Gly Pro

<210> 573
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 573
Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1 5 10 15

Glu Glu Asn Pro Gly Pro
            20

<210> 574
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 574
Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn
1   5   10   15

Pro Gly Pro

<210> 575
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 575
Gly Ser Gly Gln Cys Thr Asn Tyr Ala Leu Leu Lys Leu Ala Gly Asp
1   5   10   15

Val Glu Ser Asn Pro Gly Pro
            20

<210> 576
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 576
Gln Cys Thr Asn Tyr Ala Leu Leu Lys Leu Ala Gly Asp Val Glu Ser
1   5   10   15

Asn Pro Gly Pro
            20

<210> 577
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 577
Gly Ser Gly Val Lys Gln Thr Leu Asn Phe Asp Leu Leu Lys Leu Ala
1   5   10   15

Gly Asp Val Glu Ser Asn Pro Gly Pro
            20   25

<210> 578
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
      peptide

<400> 578
Val Lys Gln Thr Leu Asn Phe Asp Leu Leu Lys Leu Ala Gly Asp Val
1   5   10   15

Glu Ser Asn Pro Gly Pro
            20

<210> 579
<211> 846
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polynucleotide

<400> 579
atggagacag atactctatt gctatgggtt ttgttattat gggtgccggg ttccacggga 60

attcgtcgtg ctgacattgt tttaacacag tctccaggta ccctatcatt gtcccctggt 120

gagcgtgcca cgcttagttg cagagcctct cagtctgtgg gatcaagtta tttagcttgg 180

tatcaacaaa aacctggaca agcacctcgt ttgttaatat atggtgcatt cagtagagca 240

actggaattc ctgatcgatt ctcaggatct ggatctggaa cagacttcac acttaccatc 300

tcacgtcttg aacccgagga ctttgcggtc tactactgcc agcagtatgg ttcgtcgcct 360

tggactttcg gacaaggaac caaagttgaa atcaagcgag gaggaggtgg atcgggtggt 420

ggaggatccg gtggaggtgg aagtgaagcg aagctagtcg aatctggagg tggtgtagtg 480

cagcctggac gttcgcttcg actatcctgt gctgcttcag gatttacctt ttcatcttac 540

acgatgcact gggtgcgtca agcgcctggt aaaggactag agtgggtcac gtttatctca 600

tacgacggta ataacaagta ttatgctgat tccgtaaagg gacgtttcac catatcgcgt 660

gacaattcta agaatacctt gtatcttcaa atgaatagtc ttagagctga agacactgcc 720

atttactatt gtgcacgaac gggatggctt ggacctttg attattgggg tcagggtact 780

ttggtcaccg tctccacagc gaagacaaca cctccctcag tctatccact tgctccgcgt 840

agttaa 846

<210> 580
<211> 281
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 580
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

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Gly Ser Thr Gly Ile Arg Arg Ala Asp Ile Val Leu Thr Gln Ser Pro
            20                  25                  30

Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
        35                  40                  45

Ala Ser Gln Ser Val Gly Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys
    50                  55                  60

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Phe Ser Arg Ala
65                  70                  75                  80

Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                85                  90                  95

Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
            100                 105                 110

Cys Gln Gln Tyr Gly Ser Ser Pro Trp Thr Phe Gly Gln Gly Thr Lys
        115                 120                 125

Val Glu Ile Lys Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Glu Ala Lys Leu Val Glu Ser Gly Gly Gly Val Val
145                 150                 155                 160

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
                165                 170                 175

Phe Ser Ser Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
            180                 185                 190

Leu Glu Trp Val Thr Phe Ile Ser Tyr Asp Gly Asn Asn Lys Tyr Tyr
        195                 200                 205

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
```

```
    210                 215                 220

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
225                 230                 235                 240

Ile Tyr Tyr Cys Ala Arg Thr Gly Trp Leu Gly Pro Phe Asp Tyr Trp
                245                 250                 255

Gly Gln Gly Thr Leu Val Thr Val Ser Thr Ala Lys Thr Thr Pro Pro
            260                 265                 270

Ser Val Tyr Pro Leu Ala Pro Arg Ser
        275                 280
```

<210> 581
<211> 855
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polynucleotide

<400> 581

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atggaaaccg atactttgct tctatgggtc cttttgctat gggtgcccgg atcaaccgga       60

ataagacgtg ctgatatcgt tatgacccag accacgctat cattaccagt tagtctaggt      120

gaccaggcca gtatcagttg ccgttcatct cagtccattg tacactcaaa cggaaacacc      180

tacttggagt ggtatcttca gaaacctggt caatctccca agcttctaat ttacaaagtg      240

tctaaccgat tttctggtgt gccggatcga ttttcgggtt ctggtagtgg aacggatttc      300

acgctaaaaa tatcccgagt cgaagctgaa gacctaggag tatattattg ctttcaagga      360

tctcacgtcc cgtacacctt tggtggagga accaagcttg aaataaagcg aggaggtgga      420

ggatcaggag gaggtggttc gggtggtggt ggttccgagg cgaagttaca ggagtcggga      480

cccgtattag tgaagcctgg tgcgagtgtc aaaatgagtt gcaaagccag tggttacacc      540

ttcacagact attacatgaa ctgggtgaag cagtctcacg gaaaatcttt agagtggata      600

ggagtaatta acccgtacaa tggtgatacg agttacaacc agaagttcaa aggtaaggcg      660
```

accttgacgg tcgataaatc ctctagtact gcgtacatgg aactaaactc tttaacctct 720

gaggattctg ccgtatatta ttgtgccaga tattatggtt cgtggttcgc atattgggga 780

cagggaactt taattacggt ctcgacagcc aaaacgactc ccccctcagt ttatcccctt 840

gctcctagaa gttaa 855

<210> 582
<211> 284
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 582
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

Gly Ser Thr Gly Ile Arg Arg Ala Asp Ile Val Met Thr Gln Thr Thr
20 25 30

Leu Ser Leu Pro Val Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg
35 40 45

Ser Ser Gln Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu Trp
50 55 60

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val
65 70 75 80

Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
85 90 95

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu
100 105 110

Gly Val Tyr Tyr Cys Phe Gln Gly Ser His Val Pro Tyr Thr Phe Gly
115 120 125

```
Gly Gly Thr Lys Leu Glu Ile Lys Arg Gly Gly Gly Gly Ser Gly Gly
    130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Glu Ala Lys Leu Gln Glu Ser Gly
145                 150                 155                 160

Pro Val Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala
                165                 170                 175

Ser Gly Tyr Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Lys Gln Ser
            180                 185                 190

His Gly Lys Ser Leu Glu Trp Ile Gly Val Ile Asn Pro Tyr Asn Gly
        195                 200                 205

Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val
    210                 215                 220

Asp Lys Ser Ser Ser Thr Ala Tyr Met Glu Leu Asn Ser Leu Thr Ser
225                 230                 235                 240

Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Tyr Tyr Gly Ser Trp Phe
                245                 250                 255

Ala Tyr Trp Gly Gln Gly Thr Leu Ile Thr Val Ser Thr Ala Lys Thr
            260                 265                 270

Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Arg Ser
        275                 280
```

<210> 583
<211> 1734
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>
<221> misc_feature
<222> (1654)..(1716)
<223> B7-1 transmembrane domain

<220>
<221> misc_feature
<222> (1654)..(1731)
<223> B7-1 cytoplasmic domain

<400> 583
atgtgtcacc agcagttggt catctcttgg ttttccctgg tttttctggc atctcccctc 60

gtggccatat gggaactgaa gaaagatgtt tatgtcgtag aattggattg gtatccggat 120

gcccctggag aaatggtggt cctcacctgt gacacccctg aagaagatgg tatcacctgg 180

accttggacc agagcagtga ggtcttaggc tctggcaaaa ccctgaccat ccaagtcaaa 240

gagtttggag atgctggcca gtacacctgt cacaaaggag gcgaggttct aagccattcg 300

ctcctgctgc ttcacaaaaa ggaagatgga atttggtcca ctgatatttt aaaggaccag 360

aaagaaccca aaaataagac ctttctaaga tgcgaggcca agaattattc tggacgtttc 420

acctgctggt ggctgacgac aatcagtact gatttgacat tcagtgtcaa aagcagcaga 480

ggctcttctg acccccaagg ggtgacgtgc ggagctgcta cactctctgc agagagagtc 540

agaggggaca acaaggagta tgagtactca gtggagtgcc aggaggacag tgcctgccca 600

gctgctgagg agagtctgcc cattgaggtc atggtggatg ccgttcacaa gctcaagtat 660

gaaaactaca ccagcagctt cttcatcagg gacatcatca aacctgaccc acccaagaac 720

ttgcagctga agccattaaa gaattctcgg caggtggagg tcagctggga gtaccctgac 780

acctggagta ctccacattc ctacttctcc ctgacattct gcgttcaggt ccagggcaag 840

agcaagagag aaaagaaaga tagagtcttc acggacaaga cctcagccac ggtcatctgc 900

cgcaaaaatg ccagcattag cgtgcgggcc caggaccgct actatagctc atcttggagc 960

gaatgggcat ctgtgccctg cagtgttcct ggagtagggg tacctggggt gggcgccaga 1020

aacctccccg tggccactcc agacccagga atgttcccat gccttcacca ctcccaaaac 1080

ctgctgaggg ccgtcagcaa catgctccag aaggccagac aaactctaga attttaccct 1140

tgcacttctg aagagattga tcatgaagat atcacaaaag ataaaaccag cacagtggag 1200

gcctgtttac cattggaatt aaccaagaat gagagttgcc taaattccag agagacctct 1260

ttcataacta atgggagttg cctggcctcc agaaagacct cttttatgat ggccctgtgc 1320

cttagtagta tttatgaaga cttgaagatg taccaggtgg agttcaagac catgaatgca 1380

aagctgctga tggaccctaa gaggcagatc tttctagatc aaaacatgct ggcagttatt 1440

gatgagctga tgcaggccct gaatttcaac agtgagactg tgccacaaaa atcctccctt 1500

gaagaaccgg atttttataa aactaaaatc aagctctgca tacttcttca tgctttcaga 1560

attcgggcag tgactattga tagagtgatg agctatctga atgcttccgg aggaggtgga 1620

tcgggtggtg gaggatctgg tggaggtgga agtctgctcc catcctgggc cattacctta 1680

atctcagtaa atggaatttt tgtgatatgc tgcctgacct actgctttgc ctaa 1734

<210> 584
<211> 577
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<220>
<221> MISC_FEATURE
<222> (552)..(572)
<223> B7-1 transmembrane domain

<220>
<221> MISC_FEATURE
<222> (552)..(577)
<223> B7-1 cytoplasmic domain

<400> 584
Met Cys His Gln Gln Leu Val Ile Ser Trp Phe Ser Leu Val Phe Leu
1 5 10 15

Ala Ser Pro Leu Val Ala Ile Trp Glu Leu Lys Lys Asp Val Tyr Val
20 25 30

```
Val Glu Leu Asp Trp Tyr Pro Asp Ala Pro Gly Glu Met Val Val Leu
        35                  40                  45

Thr Cys Asp Thr Pro Glu Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln
    50                  55                  60

Ser Ser Glu Val Leu Gly Ser Gly Lys Thr Leu Thr Ile Gln Val Lys
65                  70                  75                  80

Glu Phe Gly Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly Glu Val
                85                  90                  95

Leu Ser His Ser Leu Leu Leu Leu His Lys Lys Glu Asp Gly Ile Trp
            100                 105                 110

Ser Thr Asp Ile Leu Lys Asp Gln Lys Glu Pro Lys Asn Lys Thr Phe
        115                 120                 125

Leu Arg Cys Glu Ala Lys Asn Tyr Ser Gly Arg Phe Thr Cys Trp Trp
    130                 135                 140

Leu Thr Thr Ile Ser Thr Asp Leu Thr Phe Ser Val Lys Ser Ser Arg
145                 150                 155                 160

Gly Ser Ser Asp Pro Gln Gly Val Thr Cys Gly Ala Ala Thr Leu Ser
                165                 170                 175

Ala Glu Arg Val Arg Gly Asp Asn Lys Glu Tyr Glu Tyr Ser Val Glu
            180                 185                 190

Cys Gln Glu Asp Ser Ala Cys Pro Ala Ala Glu Glu Ser Leu Pro Ile
        195                 200                 205

Glu Val Met Val Asp Ala Val His Lys Leu Lys Tyr Glu Asn Tyr Thr
    210                 215                 220

Ser Ser Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn
```

```
225                 230                 235                 240

Leu Gln Leu Lys Pro Leu Lys Asn Ser Arg Gln Val Glu Val Ser Trp
                245                 250                 255

Glu Tyr Pro Asp Thr Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Thr
            260                 265                 270

Phe Cys Val Gln Val Gln Gly Lys Ser Lys Arg Glu Lys Lys Asp Arg
        275                 280                 285

Val Phe Thr Asp Lys Thr Ser Ala Thr Val Ile Cys Arg Lys Asn Ala
    290                 295                 300

Ser Ile Ser Val Arg Ala Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser
305                 310                 315                 320

Glu Trp Ala Ser Val Pro Cys Ser Val Pro Gly Val Gly Val Pro Gly
                325                 330                 335

Val Gly Ala Arg Asn Leu Pro Val Ala Thr Pro Asp Pro Gly Met Phe
            340                 345                 350

Pro Cys Leu His His Ser Gln Asn Leu Leu Arg Ala Val Ser Asn Met
        355                 360                 365

Leu Gln Lys Ala Arg Gln Thr Leu Glu Phe Tyr Pro Cys Thr Ser Glu
    370                 375                 380

Glu Ile Asp His Glu Asp Ile Thr Lys Asp Lys Thr Ser Thr Val Glu
385                 390                 395                 400

Ala Cys Leu Pro Leu Glu Leu Thr Lys Asn Glu Ser Cys Leu Asn Ser
                405                 410                 415

Arg Glu Thr Ser Phe Ile Thr Asn Gly Ser Cys Leu Ala Ser Arg Lys
            420                 425                 430
```

```
Thr Ser Phe Met Met Ala Leu Cys Leu Ser Ser Ile Tyr Glu Asp Leu
        435                 440                 445

Lys Met Tyr Gln Val Glu Phe Lys Thr Met Asn Ala Lys Leu Leu Met
    450                 455                 460

Asp Pro Lys Arg Gln Ile Phe Leu Asp Gln Asn Met Leu Ala Val Ile
465                 470                 475                 480

Asp Glu Leu Met Gln Ala Leu Asn Phe Asn Ser Glu Thr Val Pro Gln
                485                 490                 495

Lys Ser Ser Leu Glu Glu Pro Asp Phe Tyr Lys Thr Lys Ile Lys Leu
            500                 505                 510

Cys Ile Leu Leu His Ala Phe Arg Ile Arg Ala Val Thr Ile Asp Arg
        515                 520                 525

Val Met Ser Tyr Leu Asn Ala Ser Gly Gly Gly Gly Ser Gly Gly Gly
    530                 535                 540

Gly Ser Gly Gly Gly Gly Ser Leu Leu Pro Ser Trp Ala Ile Thr Leu
545                 550                 555                 560

Ile Ser Val Asn Gly Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe
                565                 570                 575

Ala
```

<210> 585
<211> 774
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>
<221> misc_feature
<222> (691)..(771)
<223> transmembrane and cytoplasmic domain

<400> 585
atgtgtcagt ctcgatacct tcttttccta gcaaccttag cgttattgaa tcatctttca 60

ttagcgcgtg tcattccggt ctccggtccc gcccgttgcc tttcgcaaag tcgtaacttg 120

cttaagacta cggatgatat ggtcaaaact gctagagaaa agttaaaaca ctactcgtgt 180

acggctgaag acatagacca cgaagacatc acgcgagatc aaacaagtac cctaaagact 240

tgcttaccgc tagagcttca taaaaacgag agttgcctag cgacccgaga gacatcttca 300

acaaccagag gatcttgtct acccccctcag aagacttctc taatgatgac cttgtgcctt 360

ggtagtatat atgaagattt aaagatgtac cagactgaat ttcaggcaat caatgcggca 420

ttacaaaacc acaaccatca gcagataata ttagataaag gaatgcttgt agccattgac 480

gaacttatgc agtctctaaa ccacaacggt gagacacttc gtcagaaacc tccggttggt 540

gaggcagatc cttaccgtgt gaaaatgaag ttgtgcattc tattgcatgc attttcgacg 600

cgtgtggtca ccatcaacag agtcatgggt tatctaagtt ctgctggtgg aggtggaagt 660

ggaggtggag gaagtggtgg aggaggaagt accttagtgt tgtttggagc aggtttcggt 720

gcagtcataa cggttgtcgt tatcgtggtg atcataaaat gtttctgcaa gtga 774

<210> 586
<211> 257
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<220>
<221> MISC_FEATURE
<222> (231)..(257)
<223> transmembrane and cytoplasmic domain

<400> 586

```
Met Cys Gln Ser Arg Tyr Leu Leu Phe Leu Ala Thr Leu Ala Leu Leu
1               5                  10                  15

Asn His Leu Ser Leu Ala Arg Val Ile Pro Val Ser Gly Pro Ala Arg
            20                  25                  30

Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp Asp Met Val
        35                  40                  45

Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr Ala Glu Asp
    50                  55                  60

Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr Leu Lys Thr
65                  70                  75                  80

Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu Ala Thr Arg
                85                  90                  95

Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro Gln Lys Thr
            100                 105                 110

Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu Asp Leu Lys
        115                 120                 125

Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu Gln Asn His
    130                 135                 140

Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val Ala Ile Asp
145                 150                 155                 160

Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu Thr Leu Arg Gln Lys
                165                 170                 175

Pro Pro Val Gly Glu Ala Asp Pro Tyr Arg Val Lys Met Lys Leu Cys
            180                 185                 190

Ile Leu Leu His Ala Phe Ser Thr Arg Val Val Thr Ile Asn Arg Val
        195                 200                 205
```

Met Gly Tyr Leu Ser Ser Ala Gly Gly Gly Gly Ser Gly Gly Gly Gly
210 215 220

Ser Gly Gly Gly Gly Ser Thr Leu Val Leu Phe Gly Ala Gly Phe Gly
225 230 235 240

Ala Val Ile Thr Val Val Val Ile Val Val Ile Ile Lys Cys Phe Cys
245 250 255

Lys

<210> 587
<211> 1743
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>
<221> misc_feature
<222> (1660)..(1740)
<223> transmembrane and cytoplasmic domain

<400> 587
atgtgccccc aaaagttgac catctcatgg ttcgcaattg tactactagt gagtcccttg 60

atggcaatgt gggagcttga aaaggacgtc tatgtggtgg aggttgactg gacgcccgat 120

gcgccaggag aaacagtgaa tctaacttgc gacacacctg aagaggatga cataacgtgg 180

acatctgatc aaagacatgg tgtgataggt tctggtaaga cacttacgat taccgtcaag 240

gaatttttgg acgctggaca atacacttgt cacaaaggag gtgaaacact atcgcattca 300

cacctacttt tacacaagaa ggaaaatggt atttggagta cggagatcct aaagaatttt 360

aaaaataaga ccttttaaa gtgcgaagca ccaaattatt ccggacgatt tacatgttca 420

tggttagttc aacgaaatat ggatttaaaa ttcaatatca agtcaagttc tagttccccg 480

gattcccgag cggttacttg cggtatggcc agtttgagtg ccgagaaagt cacactagac 540

cagcgagatt atgagaaata ttccgtttcc tgccaggagg acgtaacttg tccgactgcc 600

gaggagactt tgccgataga gcttgcctta gaggcccgac agcagaataa gtacgagaat 660

tactctacct ctttttttcat ccgagacatc atcaaacctg acccaccaaa gaatttgcaa 720

atgaaaccct taaaaaactc acaggtggag gtgtcctggg aatatcctga ctcttggtct 780

acccccccatt cttacttttc ccttaagttc ttcgttagaa tacaacgtaa aaaagagaag 840

atgaaagaaa cggaagaagg ttgcaaccag aaaggagcat ttctagttga aaagacctct 900

acggaagtcc agtgtaaagg tggaaatgtg tgtgtgcaag cccaggaccg atattacaac 960

agttcgtgtt cgaagtgggc ttgcgtgccg tgtcgtgtcc gatctgtacc aggagtcgga 1020

gttcctggag taggtcgtgt aataccggta tccggaccag ctcgttgctt atctcaatcg 1080

cgaaacctac ttaaaacaac cgatgacatg gtgaagacag cgagagaaaa gcttaaacat 1140

tattcctgta ccgccgaaga catcgatcat gaggatatca cgagagacca gacctcgaca 1200

cttaagacat gcttgccact agaacttcat aaaaatgagt cttgcttagc aacgcgagaa 1260

acgtcgtcta cgacgcgtgg ttcatgtttg ccgccccaaa agacatcctt gatgatgacg 1320

ttgtgtcttg gatccatcta tgaggattta aaaatgtacc agacagaatt tcaggctatc 1380

aatgcagctc tacagaatca taatcaccag cagattatct tagacaaggg aatgttagta 1440

gcaatcgatg agcttatgca atccttgaat cataacggag aaacattacg acaaaagcct 1500

ccggtcggtg aagcggatcc atatcgtgtg aagatgaaat tatgtatatt gttgcacgcc 1560

tttagtacgc gtgtggtcac cataaaccga gtaatgggat acttgtcctc ggcgggaggt 1620

ggtggttctg gtggaggtgg atcaggtggt ggtggttcaa ccttggttct ttttggtgcg 1680

ggtttcggtg ccgtgattac tgtcgtcgtc atagtcgtca ttattaaatg tttttgtaag 1740

taa 1743

<210> 588
<211> 580
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<220>
<221> MISC_FEATURE
<222> (554)..(580)
<223> transmembrane and cytoplasmic domain

<400> 588
Met Cys Pro Gln Lys Leu Thr Ile Ser Trp Phe Ala Ile Val Leu Leu
1 5 10 15

Val Ser Pro Leu Met Ala Met Trp Glu Leu Glu Lys Asp Val Tyr Val
20 25 30

Val Glu Val Asp Trp Thr Pro Asp Ala Pro Gly Glu Thr Val Asn Leu
35 40 45

Thr Cys Asp Thr Pro Glu Glu Asp Asp Ile Thr Trp Thr Ser Asp Gln
50 55 60

Arg His Gly Val Ile Gly Ser Gly Lys Thr Leu Thr Ile Thr Val Lys
65 70 75 80

Glu Phe Leu Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly Glu Thr
85 90 95

Leu Ser His Ser His Leu Leu Leu His Lys Lys Glu Asn Gly Ile Trp
100 105 110

Ser Thr Glu Ile Leu Lys Asn Phe Lys Asn Lys Thr Phe Leu Lys Cys
115 120 125

Glu Ala Pro Asn Tyr Ser Gly Arg Phe Thr Cys Ser Trp Leu Val Gln
130 135 140

Arg Asn Met Asp Leu Lys Phe Asn Ile Lys Ser Ser Ser Ser Ser Pro
145 150 155 160

```
Asp Ser Arg Ala Val Thr Cys Gly Met Ala Ser Leu Ser Ala Glu Lys
                165                 170                 175

Val Thr Leu Asp Gln Arg Asp Tyr Glu Lys Tyr Ser Val Ser Cys Gln
            180                 185                 190

Glu Asp Val Thr Cys Pro Thr Ala Glu Glu Thr Leu Pro Ile Glu Leu
        195                 200                 205

Ala Leu Glu Ala Arg Gln Gln Asn Lys Tyr Glu Asn Tyr Ser Thr Ser
    210                 215                 220

Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn Leu Gln
225                 230                 235                 240

Met Lys Pro Leu Lys Asn Ser Gln Val Glu Val Ser Trp Glu Tyr Pro
                245                 250                 255

Asp Ser Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Lys Phe Phe Val
            260                 265                 270

Arg Ile Gln Arg Lys Lys Glu Lys Met Lys Glu Thr Glu Glu Gly Cys
        275                 280                 285

Asn Gln Lys Gly Ala Phe Leu Val Glu Lys Thr Ser Thr Glu Val Gln
    290                 295                 300

Cys Lys Gly Gly Asn Val Cys Val Gln Ala Gln Asp Arg Tyr Tyr Asn
305                 310                 315                 320

Ser Ser Cys Ser Lys Trp Ala Cys Val Pro Cys Arg Val Arg Ser Val
                325                 330                 335

Pro Gly Val Gly Val Pro Gly Val Gly Arg Val Ile Pro Val Ser Gly
            340                 345                 350

Pro Ala Arg Cys Leu Ser Gln Ser Arg Asn Leu Leu Lys Thr Thr Asp
```

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        355                 360                 365

Asp Met Val Lys Thr Ala Arg Glu Lys Leu Lys His Tyr Ser Cys Thr
    370                 375                 380

Ala Glu Asp Ile Asp His Glu Asp Ile Thr Arg Asp Gln Thr Ser Thr
385                 390                 395                 400

Leu Lys Thr Cys Leu Pro Leu Glu Leu His Lys Asn Glu Ser Cys Leu
                405                 410                 415

Ala Thr Arg Glu Thr Ser Ser Thr Thr Arg Gly Ser Cys Leu Pro Pro
            420                 425                 430

Gln Lys Thr Ser Leu Met Met Thr Leu Cys Leu Gly Ser Ile Tyr Glu
        435                 440                 445

Asp Leu Lys Met Tyr Gln Thr Glu Phe Gln Ala Ile Asn Ala Ala Leu
    450                 455                 460

Gln Asn His Asn His Gln Gln Ile Ile Leu Asp Lys Gly Met Leu Val
465                 470                 475                 480

Ala Ile Asp Glu Leu Met Gln Ser Leu Asn His Asn Gly Glu Thr Leu
                485                 490                 495

Arg Gln Lys Pro Pro Val Gly Glu Ala Asp Pro Tyr Arg Val Lys Met
            500                 505                 510

Lys Leu Cys Ile Leu Leu His Ala Phe Ser Thr Arg Val Val Thr Ile
        515                 520                 525

Asn Arg Val Met Gly Tyr Leu Ser Ser Ala Gly Gly Gly Gly Ser Gly
    530                 535                 540

Gly Gly Gly Ser Gly Gly Gly Gly Ser Thr Leu Val Leu Phe Gly Ala
545                 550                 555                 560
```

Gly Phe Gly Ala Val Ile Thr Val Val Val Ile Val Val Ile Ile Lys
565 570 575

Cys Phe Cys Lys
580

<210> 589
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 589
Pro Arg Gly Ser Gly
1 5

<210> 590
<211> 191737
<212> DNA
<213> Vaccinia virus

<400> 590
gtaaaattaa attaattata aaattatgta tatgatttac taactttagt tagataagtt 60

agtaatacat aaattttagt atattaatat tatattttaa atatttattt agtgtctaga 120

aaaaaatgtg tgaccaacga ccgtaggaaa ctctagaggg taagaaaaat caatcgcttt 180

atagagacca tcagaaagag gtttaatatt tttgtgagac catcgaagga gaaagagata 240

aaacttttt acgactccat cagaaagagg tttaatattt ttgtgagacc atcgaaggag 300

aaagagataa aacttttta cgactccatc agaaagaggt ttaatatttt tgtgagacca 360

tcgaaggaga aagagataaa actttttac gactccatca gaaagaggtt taatattttt 420

gtgagaaagg agaaagagat aaaacttttt tacgactcca tcagaaagag gtttaatatt 480

tttgtgagac catcgaagga gaaagagata aaacttttt acgactccat cagaaagagg 540

tttaatattt ttgtgagacc atcgaaggag aaagagataa aacttttta cgactccatc 600

agaaagaggt ttaatatttt tgtgagacca tcgaaggaga aagagataaa actttttac 660

gactccatca gaaagaggtt taatattttt gtgagaccat cgaaggagac tccatcagaa 720

agaggtttaa tatttttgtg agaaaggaga aagagataaa actttttac gactccatca 780

gaaagaggtt taatattttt gtgagaaagg agaaagagat aaaacttttt tacgactcca 840

tcagaaagag gtttaatatt tttgtgagac catcgaagga gaaagagata aaacttttt 900

acgactccat cagaaagagg tttaatattt ttgtgagacc atcgaaggag aaagagataa 960

aacttttta cgactccatc agaaagaggt ttaatatttt tgtgagacca tcgaagagag 1020

aaagagataa aacttttta cgactccatc agaaagaggt ttaatatttt tgtgagacca 1080

tcgaagagag aaagagataa aacttttta cgactccatc agaaagaggt ttaatatttt 1140

tgtgagacca tcgaagagag aaagagataa aacttttta cgactccatc agaaagaggt 1200

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gaagaagatg ctacaacgtt tacgtgtatg gcgtttacta ttcctagcat cagcaaaaca 960

gttactgtta gtataacgtg a 981

<210> 595
<211> 1023
<212> DNA
<213> Vaccinia virus

<400> 595
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gttagggcga caaaatttgt ttattatctg gatctgataa aatgtaattg ggtatctaag 300

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ttaataaagg atgtggcaat ttttaaaaat aaggagacgg tatattatct aaaattaaat 840

aataaaacta tagctagatt tacgtacttt aataatatag atactgcaat tacacaagaa 900

cacgagtatg tcaaaatagc tctaggtata gtctgcaagt taatgattaa taatatgcat 960

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<210> 596
<211> 1725
<212> DNA
<213> Vaccinia virus

<400> 596
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ctacactgct atttgtataa taattacttt acaaacgatg tactgaagat attattaaat 240

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actagatgtt gtaatatttc acatgatgta gtgatagata tgatagacaa agataaaaac 360

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gatcctaact ttaaacaaga cggatataca gcgttacatt attattattt gtgtctcgca 540

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atttctttgt ttatacaaca tggagctaat ctaaacgcgt tagataattg tggtaataca 660

ccattccatt tgtatcttag tattgaaatg tgtaataata ttcatatgac taaaatgctg 720

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tatataactt ccgactacat acaacacgat attcttgtta tgttaataca tcactatgaa 840

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caacttccat ctctacctat cttcgatata aaatcatttg agaaattcat atcctactgt 1260

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aattgtctac taacattact accttcagaa attatatacg aaatattata catgctgaca 1680

attaacgatc tttataatat atcgtatcca cctaccaaag tatag 1725

<210> 597
<211> 1062
<212> DNA
<213> Vaccinia virus

<400> 597
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agtcttttat cgcacagata taaagactat gtggttaaat gggagaggct agaaaagaat 300

agacggcgac aggtttctaa taaacgtgtt aaacatggtg atttatggat agccaactat 360

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gttcagggta tagttagatc tcatattaaa aaacctcctt catgcattcc aaaaacatat 480

gaactaggta ctcatgataa gtatggcata gacttatact gtggaattct ttacgcaaaa 540

cattataata atataacttg gtataaagat aataaggaaa ttaatatcga cgacattaag 600

tattcacaaa cgggaaagga attaattatt cataatccag agttagaaga tagcggaaga 660

tacgactgtt acgttcatta cgacgacgtt agaatcaaga atgatatcgt agtatcaaga 720

tgtaaaatac ttacggttat accgtcacaa gaccacaggt ttaaactaat actagatccg 780

aaaatcaacg taacgatagg agaacctgcc aatataacat gcactgctgt gtcaacgtca 840

ttattgattg acgatgtact gattgaatgg gaaaatccat ccggatggct tataggattc 900

gattttgatg tatactctgt tttaactagt agaggcggta tcaccgaggc gaccttgtac 960

tttgaaaatg ttactgaaga atatataggt aatacatata aatgtcgtgg acacaactat 1020

tattttgaaa aaacccttac aactacagta gtattggagt aa 1062

<210> 598
<211> 384
<212> DNA
<213> Vaccinia virus

<400> 598
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tgtacggctt tacatgagta cttttataat tatagatcag tcaacggaaa atacaagtat 180

agatacaacg gttactatca atattattca tctagcgatt atgaaaatta taatgaatat 240

tattatgatg attatgatag aactggtatg aacagcgaga gcgatagtga gagtgataat 300

atatcaatca aaacagaata tgagaatgaa tatgaattct atgatgaaac acaagatcaa 360

agtacacaac acaatgactt ataa 384

<210> 599
<211> 276
<212> DNA
<213> Vaccinia virus

<400> 599
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gaatgctgtg atataaacaa actagtagaa ggtacgactc cgttacactg ttatctaatg 180

aatgaaggat ttgaatcatc tgttttaaaa aacctattaa aggagtatgt catgaatacg 240

tttaatgttc atgacatcca ttacacaaat atttaa 276

<210> 600
<211> 546
<212> DNA
<213> Vaccinia virus

<400> 600
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aaggattcac ttccgtggga caatatcgac aattgcgtgg agatcattaa atgtttcatc 360

agaaatgact ccatgaaaac cgccgaagaa cttcgtgcaa tcattggact ttgtactcaa 420

tcagctatcg tctctggaag agtcttcaac gataagtata tcgacatact acttatgctg 480

cgaaagattc tgaacgagaa cgactatctc accctcttgg atcatatccg cactgctaaa 540

tactaa 546

<210> 601
<211> 1161
<212> DNA
<213> Vaccinia virus

<400> 601
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aaaataaaac tagagattga aacgtgtcac aacttatcaa aacatataga tagacgagga 180

aacaatgcgc tacattgtta cgtctccaat aaatgcgata cagacattaa gattgttcga 240

ctgttactct ctcgcggagt cgagagactt tgtagaaaca acgaaggatt aactccgcta 300

ggagcataca gtaagcatag atacgtaaaa tctcagattg tgcatctact gatatccagc 360

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aatatcgact tacgtctgct aaaataccta attgtggata aacggatacg tccgtccaag 480

aatacgaatt atgcaatcaa tggtctcgga ttggtggata tatacgtaac gacgcctaat 540

ccgagaccag aagtattgct atggcttctt aaatcagaat gttacagcac cggttacgta 600

tttcgtacct gtatgtacaa cagtgatatg tgtaagaact ctcttcatta ctatatatcg 660

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gtttccatcc atggcagaga cgaaggagga tctttaccca tccaatacta ctggtctttc 780

tcaaccatag atatagagat tgttaaatta ttattaataa aggatgtgga cacgtgtaga 840

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ccatataatg tagacatgga aatcgttaat cttcttattg agagacgtca tactcttgtc 960

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aacattctaa agagatttag acaacaggat gaatccatcg tacaagccat gttgataaac 1080

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tctgcacgac tactttgtta a 1161

<210> 602
<211> 453
<212> DNA
<213> Vaccinia virus

<400> 602
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gagaataaaa ctctactata ttacgcggtc gatgtcaata atatacaatt tgcaaagcgg 180

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cccactctag agactatgat tgacgcattt aatagagata tacgctatct atatcctgaa 360

ccattattcg cctgtatcag atacgcctta atcctagatg atgattttcc ttctaaagta 420

agtatgatat cgccggtcat cataaggaac taa 453

<210> 603
<211> 780
<212> DNA
<213> Vaccinia virus

<400> 603
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gatgaactca cttctcttca ttactactgt aaacacatat ccacgttcta caaaagcaat 660

tattacaagt taagtcacac taagatgcga gccgagaagc gattcatcta cgcgataata 720

gattatggag caaacattaa cgcggttaca cacttacctt caacagtata ccaaacatag 780

<210> 604
<211> 312
<212> DNA
<213> Vaccinia virus

<400> 604
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tggaacgatt gtgcaacagg tcatattctc ataatgttac tcaattggca cgaacaaaag 180

gaagaaggac aacatctact ttatctattc ataaaacata atcaaggata cactctcaat 240

atactacggt atctactaga taggttcgac attcagaaag acgaatacat ataccgcctt 300

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<210> 605
<211> 342
<212> DNA
<213> Vaccinia virus

<400> 605
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agactgaaag tatctctacc tatgattaaa tcgttgttct acaagatgtc agaattctct 180

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ttcgcggaac tacatagtaa attctgttta aacgaggact ataaaagtgt atttatgaaa 300

aatatatcat tcgataagat agattccatc atcgtgacat aa 342

<210> 606
<211> 369
<212> DNA
<213> Vaccinia virus

<400> 606
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aatttgtgtc cgggaacata cgcttccaga ttatgcgata gcaagactaa cacacaatgt 180

acgccgtgtg gttcgggtac cttcacatct cgcaataatc atttacccgc ttgtctaagt 240

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gatattattg tcttctcaaa ggatcatccg gatgcaaggc atgtgtttcc caaacaaaat 360

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<210> 607
<211> 735
<212> DNA
<213> Vaccinia virus

<400> 607
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gacggatcgg catctgaagg tgcaaccgat gatacttcac tcatcgattc aacaaaactc 720

aaagcgtgtg tctga 735

<210> 608
<211> 675
<212> DNA
<213> Vaccinia virus

<400> 608
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<210> 609
<211> 1539
<212> DNA
<213> Vaccinia virus

<400> 609

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attatattga atggtataaa ctatcacgcg tttgaatcgc tattagacta tatgcgctgg 180

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atcaacattt tacatcccaa gtttatgact aatactatgc gcaatgctat atcattgttg 600

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<210> 610
<211> 681
<212> DNA
<213> Vaccinia virus

<400> 610
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acggaacggg accatgtaat gatggctgtt cgatactata tgagtaaaca acgtttagac 240

gacttgtata gacagttgcc cacaaagact agatcatata tagatattat caacatatat 300

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acaaaatcat ttacagttta tgacataaat aacgaagtta atactatact aatggataac 420

aaggggttgg gtgtaagatt ggcgacaatt tcatttataa ccgaattggg tagacgatgt 480

atgaatccag taaaaactat aaaaatgttt actctactat cgcatactat atgcgatgat 540

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ctcaaataca tgataggata a 681

<210> 611
<211> 444
<212> DNA
<213> Vaccinia virus

<400> 611
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<210> 612
<211> 1443
<212> DNA
<213> Vaccinia virus

<400> 612
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ccagttacaa gggtttgtct agaccttgac attcacagtt taacttctat agttatttac 240

tcgtatactg gaaaggtata tatagatagt cataacgtcg tcaatttatt acgtgcttct 300

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agaaaggaat attgtgtcga gtgttacatg atgggtatag aatacggact atccaatctc 420

ttatgtcata ctaaaaactt tattgccaaa cacttttgg aactggaaga tgacatcata 480

gacaattttg attatctatc tatgaaactt attctagaaa gcgatgaact aaatgttcca 540

gatgaggatt atgtagttga ttttgtcatt aagtggtata taaagcgaag aaataaatta 600

ggaaatctgc tactccttat caaaaatgta atcaggtcaa attatctttc tcccagaggt 660

ataaataatg taaaatggat actagactgt accaaaatat ttcattgtga taaacaacca 720

cgcaaatcat acaagtatcc attcatagag tatcctatga acatggatca aattatagat 780

atattccata tgtgtacaag tactcatgtt ggagaagtag tatatctcat cggtggatgg 840

atgaacaatg aaatacataa caatgctata gctgtaaatt atatatcaaa caattggatt 900

ccaattcctc cgatgaatag ccccagactg tatgctacgg ggatacccgc taacaataaa 960

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<210> 613
<211> 855
<212> DNA
<213> Vaccinia virus

<400> 613
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aataacgtgc gtctagtatg tacgttgttg aacgctggag cattgaaaaa tcttctagag 180

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gctatagata ataaagacat tgagatgtta caggctctgt tcaaatacga cattaatatc 660

tactctgtta atctggaaaa tgtactattg gatgatgccg aaataactaa gatgattata 720

gaaaagcatg ttgaatacaa gtctgactcc tatacaaaag atctcgatat cgtcaagaat 780

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<211> 1110
<212> DNA
<213> Vaccinia virus

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ccgtttggtt attcgttttc tatgtttatg tcgctattgc ctgcatcagg taatactaga 180

atagaattat tgaagactat ggatttgaga aaaagagatc tgggtccagc atttacagaa 240

ttaatatcag gattagctaa gctgaaaaca tctaaatata cgtacactga tctaacttat 300

caaagtttcg tagataatac tgtgtgcatt aaaccgttgt attatcaaca atatcataga 360

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tgggcaatca ttaatactat atattttaaa ggtacatggc aatatccgtt tgatatcact 540

aaaacacgca atgctagttt tactaataag tacggtacga aaacggttcc catgatgaac 600

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cgccttccgt ataaggatgc taatattagt atgtacctgg caataggtga taatatgacc 720

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atagccgaaa tgatggctcc tagtatgttt aatccagata atgcgtcgtt taaacatatg 900

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caaggaactg tagcagaggc atctactatc atggtagcta cggcgagatc atctcctgaa 1020

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<210> 615
<211> 267
<212> DNA
<213> Vaccinia virus

<400> 615
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gcagagagtg ttaagatgca tatggataga tatgttgaat atagggataa actggtaggg 180

aaaactgtaa aagttaaagt gattagagtt gattatacaa aaggatatat agatgtcaat 240

tacaaaagga tgtgtagaca tcaataa 267

<210> 616
<211> 1275
<212> DNA
<213> Vaccinia virus

<400> 616
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acactagata tatcatcttt ttattggagt ttatcggatg aagtgggtac gaatttcggc 180

acgataatat taaacgagat tgtacaatta cccaaaagag gagtacgagt tagagtagcc 240

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gtacgataca tagatattac aaatatccta ggaggagttc ttcatacaaa attttggata 360

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tacagctatg aattgtacga tactagtcct actaaaaggt gtaaactatt aaaaaatatg 1200

aaacaatgta caaatgatat atactgcgat gagatacaac cggaaaaaga aattcctgaa 1260

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<210> 617
<211> 411
<212> DNA
<213> Vaccinia virus

<400> 617
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attctaatgt ctcctctagt taatgcagat gctgtttcaa gactgaatct gctagctgcc 120

aaacttatgg gaaccatcac accaaatgcg ccagtcggaa agctatgtcc agaatcagta 180

tctagagata tggataaagt ttataaatac caatacgacc cattaatcaa tcatgaaaaa 240

attaaggctg gatttgctag tcaggtcttg aaggctacca acaaggttag aaaaataatt 300

tccaagatta acacccccg actctcatac tccagggaac aaacaatgag attagtgatg 360

tttcaggtgc atattatttc atgcaacatg caaattgtaa tagagaaata a 411

<210> 618
<211> 246
<212> DNA
<213> Vaccinia virus

<400> 618
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gaactagctg aaaacatatc atcgttagga attttagtat tctcacatga tcatattgga 180

catggaagaa gtaatggtga aaaaatgatg attgatgact ttggtacagc acgtggtaac 240

tattaa 246

<210> 619
<211> 450
<212> DNA
<213> Vaccinia virus

<400> 619
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atagtgttta acaaagatat taccagttgt ggaagactgt acaaggaatt gatgaagttc 180

gatgatgtcg ctatacggta ctatggtatt gataaaatta atgagattgt cgaagctatg 240

agcgaaggag accactacat caattttaca aaagtccatg atcaggaaag tttattcgct 300

accataggaa tatgtgctaa aatcactgaa cattggggat acaaaaagat ttcagaatct 360

agattccaat cattgggaaa cattacagat ctgatgaccg acgataatat aaacatcttg 420

atacttttc tagaaaaaaa attgaattga 450

<210> 620
<211> 1419
<212> DNA
<213> Vaccinia virus

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aaatataata gtaaaaattt agatgtattt aggaatatgc tacaagctat cgaaccttct 180

ggaaataatt atcacattct acatgcgtat tgtggaatta aaggactaga tgaacgattt 240

gtcgaagaac ttcttcatag aggatactct ccaaatgaga cggatgatga tggaaattat 300

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acagatgatg aagtcataga gagaataaat ttattggtac agtatggagc caagattaac 480

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gtatgctcta aaacagtcaa gaatgtagac attatagatc ttttacttcc atcaacggat 780

gttaataaac aaaacaaatt cggagatagt cctcttacac ttcttattaa gacattgagc 840

ccagcgcatc ttattaacaa attgctatcg actagcaatg ttattacgga tcaaacagtt 900

aatatttgta tcttttatga tagagatgat gttctagaaa ttattaatga taaaggaaag 960

caatatgatt ctaccgattt taagatggct gttgaagtgg gatccataag atgcgtcaaa 1020

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atgttacata atcctacttc tgagaccatg tatctaacta tgaaagctat agaaaaagat 1260

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gaaggagtat cttacgaagt attcgatgat tatttttaa 1419

<210> 621
<211> 663
<212> DNA
<213> Vaccinia virus

<400> 621
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aagaatacta tatgtcctcc tcgacaagat taccggtatt ggtactttgc cgccgaactc 120

actattggtg taaattacga cattaattct actattattg gtgagtgtca tatgagtgaa 180

agctatatcg acagaaatgc taacatagtg ttgactggat acggactaga aataaacatg 240

accatcatgg atacggatca gagatttgtg gcagcggctg agggtgttgg taaagataat 300

aaactatctg ttctgttgtt taccactcag cggctagata aagttcatca taatattagt 360

gtgacaataa catgtatgga aatgaattgt ggaaccacaa aatacgatag cgatcttccg 420

gaatcaattc ataaatcatc atcgtgtgat ataactataa atggatcatg tgtgacatgt 480

gttaacttag agactgatcc aacaaagatt aatccccatt acctacaccc caaggataaa 540

tatctttatc ataattctga gtatggcatg cgtggtagtt atggcgtgac atttatagat 600

gaactaaacc agtgccttct tgacataaaa gaactaagtt atgatatttg ttatagagag 660

taa 663

<210> 622
<211> 354
<212> DNA
<213> Vaccinia virus

<400> 622
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acattgatta agaacatgag aatgacgctg tccgacggtc cattgctaga tagattgaat 180

caaccagtta ataatataga agacgctaag cgaatgatcg ctattagtgc caaagtggct 240

agagacattg gtgaacgttc agaaattaga tgggaagagt cattcaccat actctttagg 300

atgattgaaa catattttga tgatctaatg attgatctat atggtgaaaa ataa 354

<210> 623
<211> 528
<212> DNA
<213> Vaccinia virus

<400> 623
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acaattttac ccgaaggtag tagcatggat ccaaatatca tggattgtat aaacagacac 120

atcaatatgt gtatacaacg cacctatagt tctagtataa ttgccatttt gaatagattc 180

ctaacaatga acaaggatga actaaacaat acacagtgtc atataattaa agaatttatg 240

acatacgaac aaatggcgat tgaccattat ggagaatatg taaacgctat tctatatcaa 300

attcgtaaaa gacctaatca acatcacacc attgatctgt ttaaaaaaat aaaaagaacc 360

ccgtatgaca cttttaaagt ggatcccgta gaattcgtaa aaaaagttat cggatttgta 420

tctatcttga acaaatataa accggtttat agttacgtcc tgtacgagaa cgtcctgtac 480

gatgagttca aatgtttcat taactacgtg gaaactaagt atttctaa 528

<210> 624
<211> 157529
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polynucleotide

<220>
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<222> (18347)..(19489)
<223> remaining portion of the C2L gene

<220>
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<222> (19490)..(19848)
<223> remaining portion of the F3L gene

<220>
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<222> (153418)..(154094)
<223> sequence that is deleted and replaced in SEQ ID NO: 210

<220>
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<222> (154095)..(154244)
<223> portion of the B8R gene that remains in SEQ ID NO: 210

<220>
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<222> (154139)..(154153)
<223> sequence that is deleted and replaced in SEQ ID NO: 210

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<222> (154139)..(154153)
<223> potential transcription regulatory sequences of the B9R gene

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<222> (154263)..(154292)
<223> potential transcription regulatory sequences of the B9R gene

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<223> remaining portion of the B29R (ITR) gene

<400> 624
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cgtggatatg tgtttacagt agtaatgaag agaagtgagt tcatcctcgt cggcgcaatt 3000

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aataactagc ttaaacagat gagacgatgt atccacatca aagaacgtaa aatacatatg 3360

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Leu Trp Glu Lys Arg Gly Ala Asp Asn Asp Arg Ile Ile Pro Ile Asp
35 40 45

Asn Gly Ser Asn Met Leu Ile Leu Asn Pro Thr Gln Ser Asp Ser Gly
50 55 60

Ile Tyr Ile Cys Ile Thr Thr Asn Glu Thr Tyr Cys Asp Met Met Ser
65 70 75 80

Leu Asn Leu Thr Ile Val Ser Val Ser Glu Ser Asn Ile Asp Phe Ile
85 90 95

Ser Tyr Pro Gln Ile Val Asn Glu Arg Ser Thr Gly Glu Met Val Cys
100 105 110

Pro Asn Ile Asn Ala Phe Ile Ala Ser Asn Val Asn Ala Asp Ile Ile
115 120 125

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Trp Ser Gly His Arg Arg Leu Arg Asn Lys Arg Leu Lys Gln Arg Thr
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Pro Gly Ile Ile Thr Ile Glu Asp Val Arg Lys Asn Asp Ala Gly Tyr
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Tyr Thr Cys Val Leu Glu Tyr Ile Tyr Gly Gly Lys Thr Tyr Asn Val
                165                 170                 175

Thr Arg Ile Val Lys Leu Glu Val Arg Asp Lys Ile Ile His Pro Thr
            180                 185                 190

Met Gln Leu Pro Glu Gly Val Val Thr Ser Ile Gly Ser Asn Leu Thr
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Ile Ala Cys Arg Val Ser Leu Arg Pro Pro Thr Thr Asp Ala Asp Val
    210                 215                 220

Phe Trp Ile Ser Asn Gly Met Tyr Tyr Glu Glu Asp Asp Gly Asp Gly
225                 230                 235                 240

Asp Gly Arg Ile Ser Val Ala Asn Lys Ile Tyr Met Thr Asp Lys Arg
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Arg Val Ile Thr Ser Arg Leu Asn Ile Asn Pro Val Lys Glu Glu Asp
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Leu Val Leu Arg Thr Gln Ser Ile Ile Leu His Thr Ile Asn Asn Ala
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Ser Ile Lys Asn Arg
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