CLAIMS

1. A cytomegalovirus (CMV) vector comprising:

(a) a first nucleic acid sequence that encodes at least one heterologous antigen; and

(b) a second nucleic acid sequence comprising a first microRNA recognition element (MRE) operably linked to a CMV gene that is essential or augmenting for CMV growth, wherein the MRE silences expression in the presence of a microRNA that is expressed by a cell of endothelial lineage.

2. A cytomegalovirus (CMV) vector comprising:

(a) a first nucleic acid sequence that encodes at least one heterologous antigen; and

(b) a second nucleic acid sequence comprising a first microRNA recognition element (MRE) operably linked to a CMV gene that is essential or augmenting for CMV growth, wherein the MRE silences expression in the presence of a microRNA that is expressed by a cell of endothelial lineage;

wherein the vector does not express an active UL128 protein or ortholog thereof; does not express an active UL130 protein or ortholog thereof; does not express an active UL146 or ortholog thereof; and does not express an active 147 protein or ortholog thereof.

3. The CMV vector of claim 1 or claim 2, wherein the MRE silences expression in the presence of one or more of miR-126-3p, miR-130a, miR-210, miR-221/222, miR-378, miR-296, and miR-328.

4. The CMV vector of claim 3, wherein the MRE silences expression in the presence of miR-126-3p.

5. The CMV vector of claim 4, wherein the MRE silences the expression of UL122 (IE2) and UL79 in the presence of miR-126-3p.

6. A cytomegalovirus (CMV) vector comprising:

(a) a first nucleic acid sequence that encodes at least one heterologous antigen;

(b) a second nucleic acid sequence comprising a first microRNA recognition element (MRE) operably linked to a CMV gene that is essential or augmenting for CMV growth, wherein the MRE silences expression in the presence of a microRNA that is expressed by a cell of endothelial lineage; and

(c) a third nucleic acid sequence comprising a second MRE operably linked to a CMV gene that is essential or augmenting for CMV growth, wherein the MRE silences expression in the presence of a microRNA that is expressed by a cell of myeloid lineage.

7. A cytomegalovirus (CMV) vector comprising:

(a) a first nucleic acid sequence that encodes at least one heterologous antigen;

(b) a second nucleic acid sequence comprising a first microRNA recognition element (MRE) operably linked to a CMV gene that is essential or augmenting for CMV growth, wherein the MRE silences expression in the presence of a microRNA that is expressed by a cell of endothelial lineage; and

(c) a third nucleic acid sequence comprising a second MRE operably linked to a CMV gene that is essential or augmenting for CMV growth, wherein the MRE silences expression in the presence of a microRNA that is expressed by a cell of myeloid lineage;

wherein the vector does not express an active UL128 protein or ortholog thereof; does not express an active UL130 protein or ortholog thereof; does not express an active UL146 protein or ortholog thereof; and does not express an active UL147 protein or ortholog thereof.

8. The CMV vector of claim 6 or claim 7, wherein the second nucleic acid sequence comprises an MRE that silences expression in the presence of miR-126-3p, miR-130a, miR-210, miR-221/222, miR-378, miR-296, and miR-328.

9. The CMV vector of claim 8, wherein the second nucleic acid sequence comprises an MRE that silences expression in the presence of miR-126-3p.

10. The CMV vector of claim 8, wherein the MRE silences the expression of UL122 (IE2) and UL79 in the presence of miR-126-3p.

11. The CMV vector of claims 7-10, wherein the third nucleic acid sequence comprises an MRE that silences expression in the presence of one or more of miR-142-3p, miR-223, miR-27a, miR-652, miR-155, miR146a, miR-132, miR-21, and miR-125.

12. The CMV vector of claim 11, wherein the third nucleic acid sequence comprises an MRE that silences expression in the presence of miR-142-3p.

13. The CMV vector of any one of claims 1-12, wherein the at least one heterologous antigen comprises a pathogen-specific antigen, a tumor antigen, a tissue-specific antigen, or a host self-antigen.

14. The CMV vector of claim 13, wherein the host self-antigen is an antigen derived from the variable region of a T cell receptor (TCR) or an antigen derived from the variable region of a B cell receptor.

15. The CMV vector of claim 13, wherein the pathogen-specific antigen is derived from a pathogen selected from the group consisting of: human immunodeficiency virus, simian immunodeficiency virus, herpes simplex virus type 1, herpes simplex virus type 2, hepatitis B virus, hepatitis C virus, papillomavirus, Plasmodium parasites, and *Mycobacterium tuberculosis*.

16. The CMV vector of claim 13, wherein the tumor antigen is related to a cancer selected from the group consisting of: acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, non-Hodgkin's lymphoma, multiple myeloma, malignant melanoma, breast cancer, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer, colon cancer, renal cell carcinoma (RCC), and germ cell tumors.

17. The CMV vector of claims 1-16, wherein the CMV vector does not express an active UL82 (pp71) protein, or an ortholog thereof.

18. The CMV vector of any one of claims 1-17, wherein the CMV vector does not express an active US11 protein, or an ortholog thereof.

19. The CMV vector of any one of claims 1-18, wherein the CMV vector does not express an active UL82 (pp71) protein or an active US11 protein, or orthologs thereof.

20. The CMV vector of any one of claims 1-19, wherein the CMV vector is a human CMV vector (HCMV), a cynomolgus CMV (CyCMV) vector, or a rhesus CMV (RhCMV) vector.

21. A human cytomegalovirus (HCMV) vector comprising a nucleic acid sequence that encodes at least one heterologous antigen, wherein the vector: does not express an active UL128 protein or ortholog thereof; does not express an active UL130 protein or ortholog thereof; does not express an active UL146 protein or ortholog thereof; and does not express an active UL147 protein or ortholog thereof.

22. Use of the CMV or HCMV vector of any one of claims 1 to 21 in the manufacture of a medicament for generating an immune response in a subject to the at least one heterologous antigen.

23. A method of generating CD8+ T cells that recognize MHC-E-peptide complexes, the method comprising:

(1) the CMV or HCMV vector of any one of claims 1-21 to be administered to a subject in an amount effective to generate a set of CD8+ T cells that recognize MHC-E/peptide complexes;

(2) identifying a first CD8+ TCR from the set of CD8+ T cells, wherein the first CD8+ TCR recognizes a MHC-E/heterologous antigen-derived peptide complex;

(3) one or more CD8+ T cells to be isolated from the subject; and

(4) transfecting the one or more CD8+ cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3α and CDR3β of the first CD8+ TCR, thereby generating one or more transfected CD8+ T cells that recognize a MHC-E/heterologous antigen-derived peptide complex.

24. A method of generating CD8+ T cells that recognize MHC-E-peptide complexes, the method comprising:

(1) the CMV vector of any one of claims 1-21 to be administered to a first subject in an amount effective to generate a set of CD8+ T cells that recognize MHC-E/peptide complexes;

(2) identifying a first CD8+ TCR from the set of CD8+ T cells, wherein the first CD8+ TCR recognizes a MHC-E/heterologous antigen-derived peptide complex;

(3) one or more CD8+T cells to be isolated from a second subject; and

(4) transfecting the one or more CD8+T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3α and CDR3β of the first CD8+ TCR, thereby generating one or more transfected CD8+ T cells that recognize a MHC-E/heterologous antigen-derived peptide complex.

25. A CD8+T cell generated by the method of claim 23 or claim 24.

26. Use of the CD8+ T cell of claim 25 in the manufacture of a medicament for treating cancer, a pathogenic infection or an autoimmune disease or disorder.