CLAIMS

What is claimed is:

1. A fusion protein comprising or consisting of Ag85A–ESAT-6–Rv3407–Rv2626c–Ra12–TbH9–Ra35–RpfD.

2. A fusion protein encoded by a nucleic acid comprising a sequence having
90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the nucleic acid sequence according to SEQ ID NO:41.

3. The fusion protein of claim 1 or 2, further comprising a poly-His tag.

4. The fusion protein of claim 3, wherein
(i) the poly-His tag comprises or consists of two to six His residues;
(ii) the poly-His tag is located at the N-terminus of the fusion protein; and/or
(iii) the poly-His tag is inserted after the initial Met residue.

5. The fusion protein of any one of claims 1 to 4, further comprising a HA tag.

6. The fusion protein of claim 5, wherein the HA tag is located at the C-terminus of the fusion protein.

7. The fusion protein of any one of claims 1 to 6, wherein the fusion protein further comprises one or more linkers connecting one or more of Ag85A, ESAT-6, Rv3407, Rv2626c, RpfA, RpfD, Ra12, TbH9, and Ra35, wherein each of the one or more linkers comprises or consists of one or more amino acid residues.

8. A nucleic acid molecule encoding the fusion protein according to any one of claims 1 to 7.

9. A vector comprising the nucleic acid molecule of claim 8.

10. The vector of claim 9, further comprising a promoter, wherein a promoter is operably linked to the nucleic acid molecule encoding the fusion protein.

11. The vector of claim 9, wherein the vector is a cytomegalovirus (CMV) vector.

12. The vector of claim 11, wherein the vector is a RhCMV vector, a HCMV vector, or a recombinant HCMV vector.

13. The vector of claim 11 or 12, wherein the promoter is operably linked to the nucleic acid molecule encoding the fusion protein and the promoter is a UL78 promoter, or an ortholog thereof.

14. The vector of claim 13, wherein the nucleic acid molecule encoding the fusion protein replaces all or part of UL78.

15. A recombinant HCMV vector comprising a TR3 backbone and a nucleic acid sequence encoding a heterologous antigen according to SEQ ID NO: 42, wherein:

(a) the vector does not express UL128 or UL130, or orthologs thereof;

(b) the vector comprises a nucleic acid sequence encoding UL146, UL147, UL18, and UL82 or orthologs thereof; and

(c) the heterologous antigen replaces all or part of UL78 and is operably linked to the UL78 promoter.

16. The recombinant HCMV vector of claim 15, wherein the recombinant HCMV vector comprises a nucleic acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the nucleic acid sequence according to SEQ ID NO:44.

17. The vector of any one of claims 12 to 16, wherein the RhCMV or HCMV vector (i) comprises a nucleic acid sequence encoding UL146 and a nucleic acid sequence encoding UL147, or orthologs thereof; and (ii) does not express UL128 or UL130, or orthologs thereof.

18. The vector of any one of claims 15 to 17, wherein the vector does not express a UL128 protein or a UL130 protein, resulting from the presence of one or more mutations in the nucleic acid sequences encoding UL128 and UL130.

19. The vector of claim 18, wherein the mutation in the nucleic acid sequences encoding UL128 and UL130 is a point mutation, frameshift mutation, truncation mutation, or deletion of all of the nucleic acid sequences encoding the viral protein.

20. The vector of any one of claims 11 to 19, wherein the vector is a HCMV vector comprising a TR3 backbone.

21. The vector of any one of claims 11 to 20, wherein the vector further comprises a nucleic acid sequence encoding a microRNA (miRNA) recognition element (MRE), wherein the MRE contains a target site for a miRNA expressed in endothelial cells and/or a miRNA expressed in myeloid cells.

22. A pharmaceutical or immunogenic composition comprising (i) (a) the fusion protein of any one of claims 1 to 7, (b) the nucleic acid of claim 8, or (c) the vector of any one of claims 9 to 21; and (ii) a pharmaceutically acceptable carrier.

23. Use of the fusion protein, nucleic acid, vector, or composition of any one of claims 1 to 22 in the manufacture of a medicament for generating an immune response in a subject.

24. Use of the fusion protein, nucleic acid, vector, or composition of any one of claims 1 to 22 in the manufacture of a medicament for treating or preventing tuberculosis in a subject.

25. Use of the fusion protein, nucleic acid, vector, or composition of any one of claims 1 to 22 in the manufacture of a medicament for treating or preventing tuberculosis in a subject, wherein the subject is CMV positive.

26. The use of claim 24 or 25, wherein the tuberculosis is a latent, pulmonary, and/or recurrent tuberculosis infection.

27. The use of any one of claims 23 to 26, wherein the vector is a CMV vector and the medicament is to be administered in an amount effective to elicit a CD4+ T cell response to a Mtb antigen, wherein at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the CD4+ T cells elicited by the recombinant HCMV vector are restricted by MHC-II or an ortholog thereof.

28. The use of any one of claims 23 to 27, wherein the vector is a CMV vector and the medicament is to be administered in an amount effective to elicit a CD8+ T cell response to a Mtb antigen, wherein at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-Ia or an ortholog thereof.

29. A method of generating CD4+ T cells that recognize MHC-II/peptide complexes, the method comprising:

(a) identifying a first CD4+ TCR from a set of CD4+ T cells, wherein the set of CD4+ T cells are isolated from a first subject that has been administered the CMV vector of any one of claims 11 to 21, and wherein the first CD4+ TCR recognizes a MHC-II/fusion protein-derived peptide complex;

(b) isolating one or more CD4+ T cells from a second subject; and

(c) transfecting the one or more CD4+ T cells isolated from the second subject with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD4+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD4+ TCR, wherein the second CD4+ TCR comprises CDR3α and CDR3β of the first CD4+ TCR, thereby generating one or more TCR-transgenic CD4+ T cells that recognize MHC-II/peptide complexes.

30. A method of generating CD8+ T cells that recognize MHC-Ia/peptide complexes, the method comprising:

(a) identifying a first CD8+ TCR from a set of CD8+ T cells, wherein the set of CD8+ T cells are isolated from a first subject that has been administered the CMV vector of any one of claims 11 to 21, and wherein the first CD8+ TCR recognizes a MHC-Ia/fusion protein-derived peptide complex;

(b) isolating one or more CD8+ T cells from a second subject; and

(c) transfecting the one or more CD8+ T cells isolated from the second subject 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 TCR-transgenic CD8+ T cells that recognize MHC-Ia/peptide complexes.

31. A CD4+ T cell generated by the method of claim 29.

32. Use of the CD4+ T cell of claim 31 in the manufacture of a medicament for treating or preventing a disease in a subject.

33. A CD8+ T cell generated by the method of claim 30.

34. Use of the CD8+ T cell of claim 33 in the manufacture of a medicament for treating or preventing a disease in a subject.