What is claimed is:

CLAIMS

1. A human cytomegalovirus (hCMV) immunogenic composition comprising (a) a messenger ribonucleic acid (mRNA) polynucleotide comprising an open reading frame encoding a hCMV gH polypeptide; (b) a mRNA polynucleotide comprising an open reading frame encoding a hCMV gL polypeptide; (c) a mRNA polynucleotide comprising an open reading frame encoding a hCMV UL128 polypeptide; (d) a mRNA polynucleotide comprising an open reading frame encoding a hCMV UL130 polypeptide; (e) a mRNA polynucleotide comprising an open reading frame encoding a hCMV UL131A polypeptide; and (f) a mRNA polynucleotide comprising an open reading frame encoding a hCMV gB polypeptide, wherein:

the molar ratio of (a):(f) within the immunogenic composition is about 1:1;

the molar ratio of (b):(c):(d):(e) within the immunogenic composition is about 1:1:1:1; and

the molar ratio of each of (a) and (f) to any one of (b), (c), (d) or (e) within the immunogenic composition is about 1.5:1 to 2:1.

2. The hCMV immunogenic composition of claim 1, wherein the molar ratio of (a):(b):(c):(d):(e):(f) is about 2:1:1:1:1:2.

3. The hCMV immunogenic composition of claim 1, wherein the hCMV immunogenic composition is maintained as a liquid formulation until use in administration to patients.

4. The hCMV immunogenic composition of claim 1, wherein the hCMV immunogenic composition is maintained as a lyophilized formulation until use in administration to patients.

5. The hCMV immunogenic composition of claim 1, wherein the hCMV immunogenic composition is stable for at least three months when stored at a temperature of greater than 0 °C and less than or equal to 10 °C.

6. The hCMV immunogenic composition of claim 5, wherein the hCMV immunogenic composition is stable for at least twelve to eighteen months when stored at a temperature of greater than 0 °C and less than or equal to 10 °C.

7. The hCMV immunogenic composition of claim 1, wherein the hCMV immunogenic composition is stable for at least three months when stored at a temperature of about 5 °C.

8. The hCMV immunogenic composition of claim 1, wherein the hCMV immunogenic composition has increased stability relative to an hCMV immunogenic composition in which (a)-(f) are present in approximately equivalent masses.

9. The hCMV immunogenic composition of claim 8, wherein the hCMV immunogenic composition has increased stability when stored for at least three months, or at least twenty-four months, at a temperature of greater than 0 °C and less than or equal to 10 °C relative to an hCMV immunogenic composition in which (a)-(f) are present in approximately equivalent masses.

10. The hCMV immunogenic composition of claim 1, wherein the hCMV immunogenic composition has:

(i) increased pentamer expression relative to an hCMV immunogenic composition in which (a)-(f) are present in approximately equivalent masses;

(ii) increased pentamer antibody levels relative to an hCMV immunogenic composition in which (a)-(f) are present in approximately equivalent masses;

(iii) increased gB expression relative to an hCMV immunogenic composition in which (a)-(f) are present in approximately equivalent masses; and/or

(iv) increased gB antibody levels relative to an hCMV immunogenic composition in which (a)-(f) are present in approximately equivalent masses.

11. The hCMV immunogenic composition of claim 1, wherein the mRNA polynucleotides of (a)-(f) are formulated in at least one lipid nanoparticle in an amount sufficient to induce an antigen-specific immune response to hCMV or a hCMV antigen in a subject.

12. The hCMV immunogenic composition of claim 1, wherein the mRNA polynucleotides of (a)-(f) are formulated in at least one lipid nanoparticle and lyophilized in an amount sufficient to induce an antigen-specific immune response to hCMV or a hCMV antigen in a subject.

13. The hCMV immunogenic composition of claim 1, wherein at least one of the mRNA polynucleotides of (a)-(f) comprises a chemical modification.

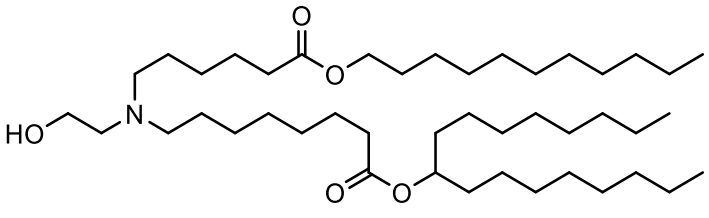
14. The hCMV immunogenic composition of claim 13, wherein at least 80% of the uracil in the open reading frame of mRNA polynucleotides (a)-(f) have a chemical modification selected from N1-methyl-pseudouridine or N1-ethyl-pseudouridine.

15. The hCMV immunogenic composition of claim 14, wherein the chemical modification is in the carbon-5 position of the uracil.

16. The hCMV immunogenic composition of claim 1, wherein at least one of the mRNA polynucleotides of (a)-(f) further comprises at least one 5' terminal cap, and wherein the 5' terminal cap is 7mG(5')ppp(5')N1mpNp.

17. The hCMV immunogenic composition of claim 11, wherein the lipid nanoparticle comprises a mixture of lipids comprising: an ionizable amino lipid; cholesterol; 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC); and 1,2 dimyristoyl-sn-glycerol, methoxypolyethyleneglycol (DMG-PEG).

18. The hCMV immunogenic composition of claim 17, wherein the ionizable amino lipid comprises Compound I:



(Compound I)

19. The hCMV immunogenic composition of claim 17, wherein the lipid nanoparticle comprises a mixture of lipids comprising 20-60 mol% ionizable amino lipid, 25-55 mol% cholesterol, 5-25 mol% DSPC, and 0.5-15 mol% DMG-PEG.

20. The hCMV immunogenic composition of claim 19, wherein the lipid nanoparticle comprises a mixture of lipids comprising 45- 55 mol% ionizable amino lipid, 35-40 mol% cholesterol, 5-15 mol% DSPC, and 1-2 mol% DMG-PEG.

21. The hCMV immunogenic composition of claim 1, wherein the molar ratio of mRNAs (a):(b):(c):(d):(e):(f) is about 2:1:1:1:1:2 and results in 10% less lipid administered to patients compared to when an equal mass of mRNAs (a):(b):(c):(d):(e):(f) is administered.

22. The hCMV immunogenic composition of claim 1, wherein the mRNA encoding hCMV gH protein comprises a nucleotide sequence having at least 90% identity to the nucleotide sequence of sequence of SEQ ID NO: 5, the mRNA encoding hCMV gL protein comprises a nucleotide sequence having at least 90% identity to the nucleotide sequence of sequence of SEQ ID NO: 6, the mRNA encoding hCMV UL128 protein comprises a nucleotide sequence having at least 90% identity to the nucleotide sequence of sequence of SEQ ID NO: 2, the mRNA encoding hCMV UL130 protein comprises a nucleotide sequence having at least 90% identity to the nucleotide sequence of sequence of SEQ ID NO: 3, the mRNA encoding hCMV UL131A protein comprises a nucleotide sequence having at least 90% identity to the nucleotide sequence of sequence of SEQ ID NO: 4, and/or the mRNA encoding hCMV gB protein comprises a nucleotide sequence having at least 90% identity to the nucleotide sequence of sequence of SEQ ID NO: 1.

23. The hCMV immunogenic composition of claim 22, wherein the mRNA encoding hCMV gH protein comprises the nucleotide sequence of sequence of SEQ ID NO: 5, the mRNA encoding hCMV gL protein comprises the nucleotide sequence of sequence of SEQ ID NO: 6, the mRNA encoding hCMV UL128 protein comprises the nucleotide sequence of sequence of SEQ ID NO: 2, the mRNA encoding hCMV UL130 protein comprises the nucleotide sequence of sequence of SEQ ID NO: 3, the mRNA encoding hCMV UL131A protein comprises the nucleotide sequence of sequence of SEQ ID NO: 4, and/or the mRNA encoding hCMV gB protein comprises the nucleotide sequence of sequence of SEQ ID NO: 1.

24. The hCMV immunogenic composition of claim 1, wherein the open reading frame encoding the hCMV gH polypeptide comprises a sequence having at least 90% identity to the sequence of SEQ ID NO: 11, the open reading frame encoding the hCMV gL polypeptide comprises a sequence having at least 90% identity to the sequence of SEQ ID NO: 12, the open reading frame encoding the hCMV UL128 polypeptide comprises a sequence having at least 90% identity to the sequence of SEQ ID NO: 8, the open reading frame encoding the hCMV UL130 polypeptide comprises a sequence having at least 90% identity to the sequence of SEQ ID NO: 9, the open reading frame encoding the hCMV UL131A polypeptide comprises a sequence having at least 90% identity to the of sequence of SEQ ID NO: 10, and/or the open reading frame encoding the hCMV gB polypeptide comprises a sequence having at least 90% identity to the sequence of SEQ ID NO: 7.

25. The hCMV immunogenic composition of claim 24, wherein the open reading frame encoding the hCMV gH polypeptide comprises SEQ ID NO: 11, the open reading frame encoding the hCMV gL polypeptide comprises SEQ ID NO: 12, the open reading frame encoding the hCMV UL128 polypeptide comprises SEQ ID NO: 8, the open reading frame encoding the hCMV UL130 polypeptide comprises SEQ ID NO: 9, the open reading frame encoding the hCMV UL131A polypeptide comprises SEQ ID NO: 10, and/or the open reading frame encoding the hCMV gB polypeptide comprises the sequence of SEQ ID NO: 7.

26. The hCMV immunogenic composition of claim 1, wherein each of the mRNA polynucleotides of (a)-(f) further comprises a polyA tail.

27. The hCMV immunogenic composition of claim 26, wherein the polyA tail is 100 nucleotides in length.

28. The hCMV immunogenic composition of claim 1, wherein the hCMV gH polypeptide comprises an amino acid sequence having at least 90% identity to the amino acid sequence of SEQ ID NO: 19, the hCMV gL polypeptide comprises an amino acid sequence having at least 90% identity to the amino acid sequence of SEQ ID NO: 20, the hCMV UL128 polypeptide comprises an amino acid sequence having at least 90% identity to the amino acid sequence of SEQ ID NO: 16, the hCMV UL130 polypeptide comprises an amino acid sequence having at least 90% identity to the amino acid sequence of SEQ ID NO: 17, the hCMV UL131A polypeptide comprises an amino acid sequence having at least 90% identity to the amino acid

sequence of SEQ ID NO: 18, and/or the hCMV gB polypeptide comprises an amino acid sequence having at least 90% identity to the amino acid sequence of SEQ ID NO: 15.