CLAIMS:

1. A process for producing an isolated HCMV membrane protein complex comprising gH, gL and at least one additional HCMV glycoprotein, wherein said process comprises recombinant expression of said gH, gL and at least one more HCMV glycoprotein.
2. A process for expressing an HCMV membrane protein complex comprising gH, gL and at least one more HCMV glycoprotein by:
   - introducing one or more recombinant nucleic acid molecules which encode gH, gL and at least one more HCMV glycoprotein into an expression system;
   - expressing said one or more nucleic acids in said expression system; and
   - purifying said membrane protein complex.
3. The process of claim 2, which comprises the step of transfecting mammalian cells with a first nucleic acid construct which encodes a fragment of gH that lacks the transmembrane domain, a second nucleic acid construct which encodes the gL protein; and a third nucleic acid construct which encodes at least one more HCMV glycoprotein.
4. The process of any preceding claim, wherein the HCMV membrane protein complex consists of gH, gL and gO.
5. The process of any preceding claim, wherein the HCMV membrane protein complex consists of gH, gL, pUL128, pUL130 and pUL131A.
6. The process of claim 5, wherein said:
   - pUL128 comprises or consists of any one of the sequences recited in SEQ ID NOs: 13, 14, 15 or 33;
   - pUL130 comprises or consists of any one of the sequences recited in SEQ ID NOs: 16, 17 or 34; and/or
   - pUL131A comprises or consists of any one of the sequences recited in SEQ ID NOs: 18, 19, 20 or 35.
7. The process of any preceding claim, wherein the HCMV membrane protein complex has a purity of >85%, >86%, >87%, >88%, >89%, >90%, >91%, >92%, >93%, >94% or >95% by mass.
8. The process of any preceding claim, wherein one or more of gH, gL, gO, pUL128, pUL130 and pUL131A in said HCMV membrane protein complex:
   - have a mammalian glycosylation pattern; and/or
   - do not contain an insect cell pattern of glycosylation.
9. A purified HCMV membrane protein complex comprising gH, gL and at least one more HCMV glycoprotein.

10. An HCMV membrane protein complex comprising gH, gL and at least one more HCMV glycoprotein, wherein said complex is produced by the process of any preceding claim.
11. An immunogenic composition comprising the isolated HCMV membrane complex of claim 9 or claim 10.
12. The immunogenic composition of claims11, wherein said composition is a vaccine.
13. The immunogenic composition of claim 11, wherein said composition comprises an adjuvant.
14. The immunogenic composition of claim 12, wherein said adjuvant is an oil-in-water emulsion or an aluminium salt.
15. An immunogenic composition comprising:
    - a self-replicating RNA molecule that encodes an HCMV membrane protein complex; and
    - the HCMV membrane protein complex of claim 9 or claim 10.
16. A kit comprising:
    - a priming composition comprising a self-replicating RNA molecule that encodes an HCMV membrane protein complex; and
    - a boosting composition comprising the HCMV membrane protein complex of claim 9 or claim 10.
17. A recombinant nucleic acid molecule which encodes gL, gH that lacks a transmembrane domain, and at least one additional HCMV glycoprotein, wherein said recombinant nucleic acid:

    (a) is not a self-replicating RNA molecule;

    (b) is not an alphavirus replicon;

    (c) does not encode any alphavirus nonstructural proteins, such as NSP1, NSP2, NSP3 and NSP4;

    (d) does not contain: an Internal Ribosomal Entry Site (IRES), such as EMCV or EV71; and/or

    (e) does not contain a viral 2A site, such as FMDV.
18. The recombinant nucleic acid molecule of claim 17, wherein said recombinant nucleic acid molecule encodes:
    - gL, gH that lacks a transmembrane domain, pUL128, pUL130 and pUL131A; or
    - gL, gH that lacks a transmembrane domain and gO.
19. A plurality of recombinant nucleic acids, wherein said plurality of recombinant nucleic acids encode gL, gH that lacks a transmembrane domain, and at least one additional HCMV glycoprotein, wherein one or more or all of said plurality of recombinant nucleic acids:

(a) is not a self-replicating RNA molecule;

(b) is not an alphavirus replicon;

(c) does not encode any alphavirus nonstructural proteins, such as NSP1, NSP2, NSP3 and NSP4;

(d) does not contain: an Internal Ribosomal Entry Site (IRES), such as EMCV or EV71; and/or

(e) does not contain a viral 2A site, such as FMDV.

20. The plurality of recombinant nucleic acids of claim 19 comprising:

- a first construct encoding gH that lacks a transmembrane domain and gL; and
- a second construct encoding one additional HCMV glycoprotein.

21. The plurality of recombinant nucleic acids of claim 20, wherein said second construct encodes:

- pUL128, pUL130 and pUL131A; or
- gO.

22. The plurality of recombinant nucleic acids of claim 21 comprising:

- a first recombinant nucleic acid molecule which encodes gL;
- a second recombinant nucleic acid molecule which encodes a fragment of gH that lacks a transmembrane domain; and
- one or more third recombinant nucleic acid molecules which encode one or more additional HCMV proteins.

23. A cell comprising gH, gL and at least one additional HCMV glycoprotein, wherein said cell does not:

(a) contain the HCMV genome;

(b) produce HCMV virions;

(c) contain self-replicating RNA molecules encoding said gH, gL and at least one additional HCMV glycoprotein; and/or

(d) contain alphavirus replicons.

24. A process for producing an isolated or a purified HCMV membrane protein complex comprising gH, gL and at least one additional HCMV glycoprotein, wherein said process involves growing the cell of claim 23 in growth medium.

25. The process of claim 24, wherein said HCMV membrane protein complex is secreted into said growth medium.

26. The process of claim 25, wherein said HCMV membrane protein complex accumulates to a concentration of >0.8 mg, >0.85 mg, >0.88mg, >0.9 mg, >0.95 mg, >1mg, >1.5mg, >2mg, >2.5mg, >3mg, >3.5mg, >4mg, >4.5mg, >5mg of complex per litre of growth medium.

27. An RNA prime-protein boost regimen comprising:

- performing one or more priming immunization(s) with RNA that encodes one or more of the protein components of an HCMV membrane protein complex, wherein said HCMV membrane protein complex comprises gH, gL and at least one additional HCMV glycoprotein;
- performing one or more boosting immunization(s) later with a purified HCMV membrane protein complex, wherein said purified HCMV membrane protein complex comprises gH, gL and at least one additional HCMV glycoprotein.

Claims

1. A composition comprising purified human Cytomegalovirus (HCMV) pentameric complex comprising: HCMV gH, HCMV gL, HCMV pUL128, HCMV pUL130, and HCMV pUL131A, wherein the purity of said pentamer is at least 80% of the total proteinaceous mass in said composition.
2. The composition of claim 1, wherein said gH comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 4, 6, 29 and 30.
3. The composition of claim 1 or 2, wherein said gH comprises the whole of the gH ectodomain.
4. The composition of claim 1 or 2, wherein said gH comprises a truncated form of the gH ectodomain.
5. The composition of any one of claims 1-4, wherein said gH lacks a transmembrane domain.
6. The composition of any one of claims 1-5, wherein said gL comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 7 and 31.
7. The composition of any one of claims 1-6, wherein said gL lacks N-terminal signal sequence.
8. The composition of any one of claims 1-7, wherein said pUL128 comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 15 and 33.
9. The composition of any one of claims 1-8, wherein said pUL130 comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 16, 17 and 34.
10. The composition of any one of claims 1-9, wherein said of pUL130 lacks N-terminal signal sequence.
11. The composition of any one of claims 1-10, wherein said pUL131A comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 18 and 35.
12. The composition of any one of claims 1-11, wherein said pUL131A lacks N-terminal signal sequence.
13. The composition of any one of claims 1-12, wherein the pH is between 6 and 8.
14. The composition of claim 13, wherein the pH is between 6.5 and 7.5.

15. The composition of claim 13 or 14, wherein the pH is maintained by a buffer selected from the group consisting of Tris buffer, citrate buffer, phosphate buffer and histidine buffer.

16. The composition of any one of claims 1-15, further comprising sodium chloride.

17. A combination of:

(a) (i) a recombinant nucleic acid construct encoding HCMV gH and HCMV gL, wherein said gH lacks a transmembrane domain; and (ii) a recombinant nucleic acid construct encoding HCMV pUL128, HCMV pUL130, and HCMV pUL131A; or

(b) (i) a first recombinant nucleic acid construct encoding HCMV gL; (ii) a second recombinant nucleic acid construct encoding HCMV gH, wherein said gH lacks a transmembrane domain; and (iii) a third recombinant nucleic acid construct encoding HCMV pUL128, HCMV pUL130, and HCMV pUL131A.

18. A recombinant nucleic acid construct encoding HCMV gH, HCMV gL, HCMV pUL128, HCMV pUL130, and HCMV pUL131A, wherein said gH lacks a transmembrane domain.

19. The combination of the recombinant nucleic acid constructs of claim 17, or the recombinant nucleic acid construct of claim 18, wherein said gH comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 4, 6, 29 and 30.

20. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any of claims 17-19, wherein said gH comprises the ectodomain of the gH.

21. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-20, wherein said nucleic acid construct encoding HCMV gH comprises a sequence that is at least 89% identical to SEQ ID NO: 24.

22. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-21, wherein said gL, comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 7 and 31.

23. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-22, wherein said gL lacks N-terminal signal sequence.

24. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-23, wherein said nucleic acid construct encoding HCMV gL comprise a sequence that is at least 89% identical to SEQ ID NO: 25.

25. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-24, wherein said pUL128, comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 15 and 33.

26. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-25, wherein said nucleic acid construct encoding HCMV UL128 comprise a sequence that is at least 74% identical to SEQ ID NO: 26.

27. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-26, wherein said pUL130, comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 16, 17, and 34.

28. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-27, wherein said pUL130 lacks N-terminal signal sequence.

29. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-28, wherein said nucleic acid construct encoding HCMV UL130 comprise a sequence that is at least 74% identical to SEQ ID NO: 27.

30. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-29, wherein said pUL131A, comprises a sequence that is at least 80% identical to any one of SEQ ID NOs: 18, and 35.

31. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-30, wherein said pUL131A lacks N-terminal signal sequence.

32. The combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-31, wherein said nucleic acid construct encoding HCMV UL131A comprise a sequence that is at least 74% identical to SEQ ID NO: 28.

33. A host cell comprising the combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-32.

34. The host cell of claim 33, wherein said host cell is a mammalian host cell.

35. The host cell of claim 33 or 34, wherein said host cell is a HEK293 cell.

36. A cell culture for producing HCMV pentameric complex, comprising any one of host cell of claims 33-35 and a growth medium, wherein the amount of said pentameric complex is at a level of more than 0.4 mg per litre of growth medium.

37. The composition of any one of claims 1-16, which is immunogenic and further comprises an adjuvant.

38. The composition of any one of claims 1-16 and 37, for use in raising an antibody.

39. The use of claim 38, wherein said antibody is a neutralizing antibody.

40. A process for producing an HCMV pentameric complex as defined in any one of claims 1-16, wherein said process comprises recombinant expression of HCMV gH, HCMV gL, HCMV pUL128, HCMV pUL130, and HCMV pUL131A.

41. A process for expressing an HCMV pentameric complex comprising:

introducing the combination of the recombinant nucleic acid constructs or the recombinant nucleic acid construct according to any one of claims 17-32 into an expression system;

expressing said nucleic acid constructs in said expression system; and

purifying said HCMV pentameric complex.

42. The process of claim 41, which comprises the step of transfecting cells with the combination of nucleic acid constructs or the recombinant nucleic acid construct of any one of claims 17-32.

43. The process of claim 42, wherein the cells are mammalian cells.

44. The process of claim 43, wherein the cells are HEK293 cells.

45. The process of any one of claims 40-44, wherein the HCMV membrane protein complex has a purity of at least 80% of the total proteinaceous mass.

46. A process for producing an isolated or purified HCMV pentameric complex according to any one of claims 1-16, wherein said process involves growing the host cell of any one of claims 33-35 in growth medium.

47. The process of claim 46 wherein said HCMV pentameric complex is secreted into said growth medium.

48. The process of claim 47 wherein said HCMV complex accumulates to a concentration of more than 0.4mg of complex per litre of growth medium.

49. The process of any one of claims 40-48, wherein the HCMV membrane protein complex has a purity of >95% by mass.

50. The process of claim 49, wherein purity is determined by gel electrophoresis.