Claims

1. An isolated ~~binding member~~antibody molecule for human cytomegalovirus (hCMV) gB protein, which binds hCMV gB protein at a region within residues 121 to 132 and 344 to 438, the residue numbering being defined according to the full length gB strain AD169 amino acid sequence SEQ ID No: 239,

said isolated ~~binding member~~ antibody molecule comprising a set of CDRs: HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein the set of CDRs has 22 or fewer amino acid alterations from a set of CDRs in which:

HCDR1 has amino acid sequence SEQ ID No: 3;

HCDR2 has amino acid sequence SEQ ID No: 4;

HCDR3 has amino acid sequence SEQ ID No: 5;

LCDR1 has amino acid sequence SEQ ID No: 93;

LCDR2 has amino acid sequence SEQ ID No: 94; and

LCDR3 has amino acid sequence SEQ ID No: 95,

and wherein the ~~binding member~~ antibody molecule has a K_D of not more than ~~50nM~~ 0.5nM as defined by surface plasmon resonance.

~~2. The isolated binding member for hCMV gB protein of claim 1, which binds hCMV gB protein with a K_D of not more than 1nM as defined by surface plasmon resonance.~~

~~3. The isolated binding member according to claim 2, wherein the K_D is not more than 0.5nM.~~

42. The isolated ~~binding member~~ antibody molecule according to claim ~~2~~ 1 ~~or claim 3~~, wherein the K_D is not more than 0.1nM.

53. The isolated ~~binding member~~ antibody molecule according to any of the preceding claims, wherein the binding member does not bind to antigenic domain 1 (AD-1) or antigenic domain 2 (AD-2) of hCMV gB protein.

64. The isolated ~~binding member~~ antibody molecule according to any of the preceding claims, wherein the concentration of ~~binding member~~ antibody molecule required for 50% neutralisation of a clinical isolate of hCMV is 10µg/ml or less in a neutralisation assay for neutralisation of hCMV infection of human foreskin fibroblasts.

75. The isolated ~~binding member~~ antibody molecule according to claim ~~64~~, comprising an HCDR1 wherein:
Kabat residue 31 is Asp or Gly;
Kabat residue 32 is His, Phe or Tyr;
Kabat residue 33 is Tyr;
Kabat residue 34 is Met, Ile or Leu; and
Kabat residue 35 is Val or Asn.

86. The isolated ~~binding member~~ antibody molecule according to claim ~~75~~, wherein HCDR1 is SEQ ID No: 3.

97. The isolated ~~binding member~~ antibody molecule according to any of claims ~~6-4~~ to ~~86~~, comprising an HCDR2 wherein:
Kabat residue 50 is Trp, Ser or Cys;
Kabat residue 53 is Gln, Asn or His;
Kabat residue 54 is Ser or Thr;
Kabat residue 58 is Gly, Lys, Asn or His;
Kabat residue 60 is Gly or Ala; and
Kabat residue 64 is Gln or Arg.

108. The isolated ~~binding member~~ antibody molecule according to claim ~~97~~, wherein HCDR2 has amino acid sequence SEQ ID No: 4.

~~11~~9. The isolated ~~binding member~~ antibody molecule according to any of the preceding claims, comprising an HCDR3 wherein:
Kabat residue 99 is Thr or Ala;
Kabat residue 100 is Val or Met;
Kabat residue 100A is Ser or Thr
Kabat residue 100B is Asn or Thr;
Kabat residue 100C is Ser or Phe;
Kabat residue 100E is Leu, Met or Ala;
Kabat residue 100F is Ser or Gly;
Kabat residue 100K is His or Tyr;
Kabat residue 100L is Asn, Ser or Asp;
Kabat residue 100M is Arg, Val or Ile;
Kabat residue 100N is Leu or Met;
Kabat residue 101 is Asp or Gly; and
Kabat residue 102 is Ala, Val or Ile.

~~12~~10. The isolated ~~binding member~~ antibody molecule according to claim ~~11~~9, wherein HCDR3 has amino acid sequence SEQ ID No: 5.

~~13~~11. The isolated ~~binding member~~ antibody molecule according to any of claims ~~7~~5 to ~~12~~10, wherein Kabat residue 26 in LCDR1 is Ser or Asn or where Kabat residue 27 in LCDR1 is Ser or Arg.

~~14~~12. The isolated ~~binding member~~ antibody molecule according to claim ~~13~~11, wherein LCDR1 is SEQ ID No: 93.

~~15~~13. The isolated ~~binding member~~ antibody molecule according to any of claims ~~7~~5 to ~~14~~12, wherein Kabat residue 56 in LCDR2 is Ser or Pro.

~~16~~14. The isolated ~~binding member~~ antibody molecule according to claim ~~15~~13, wherein LCDR2 is SEQ ID No: 94.

~~17~~15. The isolated ~~binding member~~ antibody molecule according to any of the preceding claims, comprising an LCDR3 wherein:
Kabat residue 89 is Gly or Ala;
Kabat residue 91 is Pro or Trp;
Kabat residue 93 is Arg or Ser;
Kabat residue 94 is Ser or Asp;
Kabat residue 95a is Ser, Gly or Ala;
Kabat residue 96 is Val or Tyr; and
Kabat residue 97 is Ile or Val.

~~18~~16. The isolated ~~binding member~~ antibody molecule according to claim ~~17~~15, comprising an LCDR3 having amino acid sequence SEQ ID No: 95.

~~19~~17. The isolated ~~binding member~~ antibody molecule according to any of the preceding claims, comprising a set of CDRs: HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3, wherein:
HCDR1 is SEQ ID NO: 3;
HCDR2 is SEQ ID NO: 4;
HCDR3 is SEQ ID NO: 5;
LCDR1 is SEQ ID NO: 93;
LCDR2 is SEQ ID NO: 94; and
LCDR3 is SEQ ID NO: 95.

~~20~~18. The isolated ~~binding member~~ antibody molecule according to any of the preceding claims, wherein the ~~binding member~~ antibody molecule comprises an antibody molecule or functional fragment thereof comprising an antibody V_H domain, and wherein the V_H domain has the V_H domain amino acid sequence shown in SEQ ID No: 2.

~~21~~19. The isolated ~~binding member~~ antibody molecule according to any of the preceding claims, wherein the ~~binding member~~ antibody molecule comprises an antibody molecule or functional fragment thereof comprising an antibody V_L domain wherein the V_L domain has the V_L domain amino acid sequence shown in SEQ ID No: 92.

~~22~~20. An isolated antibody molecule comprising a heavy chain comprising amino acid sequence SEQ ID No: 2 and a light chain comprising amino acid sequence SEQ ID No: 92.

~~23~~21. An isolated antibody molecule that binds hCMV gB protein, wherein the antibody molecule comprises a V_H domain amino acid sequence at least 90% identical to SEQ ID No: 2 and a V_L domain amino acid sequence at least 90% identical to SEQ ID No: 92.

~~24~~22. An ~~binding member or~~isolated antibody molecule that competes for binding to hCMV gB protein with an ~~binding member or~~ isolated antibody molecule of any of the preceeding claims.

23. The isolated antibody molecule of claim 22, wherein the antibody molecule binds hCMV gB protein at a region within residues 121 to 132 and 344 to 438, the residue numbering being defined according to the full length gB strain AD169 amino acid sequence SEQ ID: 239.

~~25~~24. An isolated antibody molecule according to claim ~~22~~ 20 or ~~23~~21, wherein the antibody molecule is an IgG.

~~26~~25. An isolated V_H domain of an antibody molecule according to any of claims ~~20~~ 18 or ~~22~~ 20 to ~~25~~24.

~~27~~26. An isolated V_L domain of an antibody molecule according to any of claims ~~21~~ 19 to ~~25~~24.

~~28~~27. A composition comprising an isolated ~~binding member according to any of claims 1 to 21, or an~~ antibody molecule according to any of claims ~~22~~ 1 to ~~25~~24, and a pharmaceutically acceptable excipient.

~~29~~28. A composition comprising an isolated ~~binding member according to any of claims 1 to 21, or an~~ antibody molecule according to any of claims ~~22~~ 1 to ~~25~~24, for use in a method of treatment of the human or animal body by therapy.

~~30~~29. The composition according to claim ~~29~~ 28 for use in treating a disorder associated with hCMV.

~~31~~30. A composition comprising an isolated ~~binding member according to any of claims 1 to 21, or an~~ antibody molecule according to any of claims ~~22~~ 1 to ~~25~~24, for use in the treatment of a disorder associated with hCMV in an individual.

~~32~~31. The composition according to claim ~~30~~ 29 or the composition for use according to claim ~~31~~30, wherein the disorder is a hCMV infection.

~~33~~32. The composition according to any one of claims ~~29~~ 28 to ~~32~~31, further comprising an isolated binding member or antibody molecule that binds hCMV gB, gH, gL, UL128, UL130 and/or UL131A protein.

~~34~~33. The composition according to any one of claims ~~29~~ 28 to ~~33~~32, ~~for treating a disorder associated with hCMV in an individual,~~ wherein the individual has a compromised immune system.

~~35~~34. The composition according to claim ~~34~~33, wherein the individual is a pregnant woman, a newborn, a transplant recipient or an individual infected with HIV.

~~36~~35. An isolated nucleic acid molecule comprising a nucleotide sequence encoding an antibody molecule ~~binding member~~ according to any of claims 1 to ~~21~~24, a V_H domain according to claim ~~26~~25, or a V_L domain according to claim ~~27~~26, ~~or an antibody molecule according to any of claims 22 to 25~~.

~~37~~36. A host cell *in vitro* transfected or transduced with a nucleic acid molecule according to claim ~~36~~35.

~~38~~37. A method of producing ~~a binding member,~~ an antibody molecule or an antibody V_H or V_L domain, comprising culturing a host cell according to claim ~~37~~ 36 under conditions for production of the ~~binding member,~~ antibody molecule or antibody V_H or V_L domain.

~~39~~38. The method according to claim ~~38~~37, further comprising isolating and/or purifying the ~~binding member,~~ antibody molecule, V_H domain or V_L domain.

~~40~~39. The method according to claim ~~38~~37 or claim ~~39~~38, further comprising formulating the ~~binding member,~~ antibody molecule, V_H domain or V_L domain into a composition comprising at least one additional component.

~~41~~40. A method of neutralising hCMV in a sample, comprising administering to said sample ~~a binding member according to any of claims 1 to 21, or an~~the antibody molecule according to any of claims ~~22~~1 to ~~25~~24, in an amount sufficient to reduce hCMV infectivity by at least 50% at a concentration of from about 0.1 to about 5.0 µg/ml.

~~42~~41. A composition comprising an isolated ~~binding member according to any of claims 1 to 21, or an~~ antibody molecule according to any of claims ~~22~~1 to ~~25~~24, for use in neutralising hCMV in a subject, wherein the ~~binding member or~~ antibody molecule is present in the composition in an amount sufficient to reduce hCMV infectivity by at least 50% at a concentration of from about 0.1 to about 5.0 µg/ml.