

CLAIMS

1. A method for identifying a candidate therapeutic for treating or preventing a disease caused by a human cytomegalovirus (HCMV) infection comprising contacting a HCMV having a glycoprotein B (gB) polypeptide which comprises a druggable region with a compound, wherein binding of said compound indicates a candidate therapeutic.
2. A method for identifying a candidate therapeutic for treating or preventing a disease caused by HCMV infection, comprising contacting a HCMV gB polypeptide comprising a druggable region with a compound, wherein the modulation of the function or activity of said gB polypeptide indicates a candidate therapeutic.
3. The method of claim 2, wherein said modulation of the activity of said gB polypeptide involves precluding the binding of domain V to the domain V binding groove in the postfusion conformation.
4. A method for identifying a candidate therapeutic for treating or preventing a disease caused by infection with HCMV having a gB polypeptide, comprising contacting the gB polypeptide comprising a druggable region with a compound, wherein the inhibition of fusion of said virus indicates a candidate therapeutic.
5. A method for identifying a candidate therapeutic for a disease caused by infection with HCMV having a gB polypeptide, comprising contacting the gB polypeptide comprising a druggable region with a compound, wherein the inhibition of viral infectivity of said virus indicates a candidate therapeutic.
6. A method for identifying a candidate therapeutic for a disease caused by infection with HCMV having a gB polypeptide, comprising contacting the gB polypeptide comprising a druggable region with a compound, wherein the reduction of at least one symptom of said disease in a subject indicates a candidate therapeutic.
7. The method of any one of claims 1-6, wherein said compound is selected from the following classes of compounds: proteins, peptides, polypeptides, peptidomimetics, antibodies, nucleic acids, and small molecules.

8. The method of claim 7, wherein binding is determined using an *in vitro* assay.
9. The method of claim 7, wherein binding is determined using an *in vivo* assay.
10. The method of claim 7, wherein the druggable region comprises at least one residue from residues K130-A135, D216-W233, R258-K260, A267-V273, R327-D329, W349-E350, V480-K518 or N676-Y690 of SEQ ID NO: 1.
11. The method of claim 10, wherein the residue of the druggable region is in a postfusion conformation.
12. The method of any one of claims 1-11, wherein the compound is a peptide comprising residues (Towne strain) of SEQ ID NO:1 selected from the group consisting of M648-K700 (SEQ ID NO: 260), M648-V697 (SEQ ID NO: 261), S647-V697 (SEQ ID NO: 262), S647-V663 (SEQ ID NO: 263), I653-V697 (SEQ ID NO: 264), I653-Q692 (SEQ ID NO: 265), I653-L680 (SEQ ID NO: 266), I653-S675 (SEQ ID NO: 267), I653-Y667 (SEQ ID NO: 268), R662-V697 (SEQ ID NO: 269), R662-Q692 (SEQ ID NO: 270), R662-L680 (SEQ ID NO: 271), R662-S675 (SEQ ID NO: 272), L664-F678 (SEQ ID NO: 273), S668-V697 (SEQ ID NO: 274), S668-Q692 (SEQ ID NO: 275), S668-V677 (SEQ ID NO: 276), D679-V697 (SEQ ID NO: 277), L680-V697 (SEQ ID NO: 278), L680-Q692 (SEQ ID NO: 279), and R693-K700 (SEQ ID NO: 280).
13. The method of any one of claims 1-11, wherein said compound is in a library of compounds.
14. The method of claim 13, wherein said library is generated using combinatorial synthetic methods.
15. A candidate therapeutic, wherein -said candidate therapeutic is a modulator of HCMV acitivity which interacts with domain V region of glycoprotein B (gB) of HCMV.
16. A candidate therapeutic, wherein said candidate therapeutic is a modulator of HCMV acitivity which precludes the movement of domain V of glycoprotein B (gB) of HCMV.

17. A candidate therapeutic, wherein said candidate therapeutic is a modulator of HCMV activity which precludes completion of the conformational change by interacting with at least one residue from the domain V residues at the trimer interface formed by any subunit in the postfusion trimer.
18. A candidate therapeutic, wherein the candidate therapeutic is an inhibitor of HCMV activity comprising a polypeptide sequence with at least 80% homology to SEQ ID NO: 1.
19. The candidate therapeutic of any one of claims 15-18, wherein the candidate inhibitor is a peptide comprising residues of SEQ ID NO:1 (Towne strain) selected from the group consisting of M648-K700 (SEQ ID NO: 260), M648-V697 (SEQ ID NO: 261), S647-V697 (SEQ ID NO: 262), S647-V663 (SEQ ID NO: 263), I653-V697 (SEQ ID NO: 264), I653-Q692 (SEQ ID NO: 265), I653-L680 (SEQ ID NO: 266), I653-S675 (SEQ ID NO: 267), I653-Y667 (SEQ ID NO: 268), R662-V697 (SEQ ID NO: 269), R662-Q692 (SEQ ID NO: 270), R662-L680 (SEQ ID NO: 271), R662-S675 (SEQ ID NO: 272), L664-F678 (SEQ ID NO: 273), S668-V697 (SEQ ID NO: 274), S668-Q692 (SEQ ID NO: 275), S668-V677 (SEQ ID NO: 276), D679-V697 (SEQ ID NO: 277), L680-V697 (SEQ ID NO: 278), L680-Q692 (SEQ ID NO: 279), and R693-K700 (SEQ ID NO: 280).
20. The candidate therapeutic of any one of claims 15-19, wherein the candidate therapeutic is a nucleic acid.
21. A pharmaceutical composition comprising a candidate therapeutic of any one of claims 15-20.
22. ~~A method of treating a subject having a disease or disorder associated with HCMV infection comprising administering to said subject~~Use of a pharmaceutical composition of claim 21, in the manufacture of a medicament for treating a disease or disorder associated with HCMV infection.
23. ~~A method of preventing a disease or disorder associated with HCMV infection in a subject comprising administering to said subject~~Use of a pharmaceutical composition of claim 21, in the manufacture of a medicament for preventing a disease or disorder associated with HCMV infection.

24. A kit for treating or preventing a disease or disorder associated with HCMV infection, comprising a pharmaceutical composition of claim 21 and optionally instructions for use.
25. A druggable region of HCMV gB comprising residues K130-A135, D216-W233, R258-K260, A267-V273, R327-D329, W349-E350, V480-K518 and N676-Y690 of SEQ ID NO: 1.
26. The druggable region of of HCMV gB of claim 25, wherein the residues of the druggable region are in a postfusion conformation.
27. A pharmaceutical composition of claim 21, for use in therapy.