[0006] Only a few cases have been documented where HIV-1 has been cleared from an individual with a pre-existing infection. Until an effective therapy is developed, the estimated 35 million individuals living with HIV-1 will remain on antiviral drugs to suppress a viral reservoir that has resisted all efforts at eradication.

[0007] A cure for AIDS has been elusive, but recent work suggests that stringent immunological control can clear HIV over time. Specifically, it was found that rhesus macaques (RM) vaccinated with cytomegalovirus (CMV)-based vectors expressing simian immunodeficiency virus (SIV) antigens were initially infected, but SIV was undetectable by several stringent criteria one to two years after infection. This result is even more remarkable in light of the fact that the highly virulent SIVmac239 strain used in these studies has thwarted all previous vaccine attempts. These results have expanded the current paradigm from one focused on a preventative HIV vaccine to one in which an immunotherapy for HIV/AIDS will eventually become an essential part of the fight against this pandemic. Thus, in addition to a preventative vaccine, there remains a need for an effective therapy to treat individuals living with HIV-1. Specifically, there remains a need to design, manufacture, and test prophylactic and therapeutic HIV vaccines in preparation for clinical testing.

SUMMARY

[0008] In one aspect, the present invention refers to an HIV-1 vaccine comprising one or more carriers encoding one or more population episensus antigens, wherein the carrier is a viral vector comprising a cytomegalovirus (CMV) backbone, wherein: i. the CMV backbone lacks the UL130-128 gene region, ii. the CMV backbone lacks the UL82 gene encoding the tegument protein pp71, or iii. the CMV backbone lacks the UL130-128 gene region and the UL82 gene encoding the tegument protein pp71; and wherein the population episensus antigen comprises the amino acid sequence selected from the group of SEQ ID NOs: 691, 697-755, 766, 767, 778, and 779. In one aspect, the present invention refers to a vaccine of the present invention for use in protecting a subject from an HIV-1 infection or for use in treating HIV-1 in a subject in need thereof. In one aspect, the present invention refers to a vaccine of the present invention for use in inducing an effector memory T cell response. In one aspect, the present invention refers to a vaccine for use in inducing an effector memory T cell response comprising one or more carriers encoding one or more antigens, wherein the carrier is a viral vector comprising a cytomegalovirus (CMV) backbone, wherein: i. the CMV backbone lacks the UL130-128 gene region, ii. the CMV backbone lacks the UL82 gene encoding the tegument protein pp71, or iii. the CMV backbone lacks the UL130-128 gene region and the UL82 gene encoding the tegument protein pp71; and wherein the antigen comprises the amino acid sequence selected from the group of SEQ ID NOs: 691-712 and 717-789. In one aspect, the present invention refers to a polypeptide comprising one or more HIV-1 antigens, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: SEQ ID NOs: 691-712 and SEQ ID NOs: 717-789. Provided herein are HIV/SIV polypeptides comprising one or more EpiGraph antigen sequences comprising amino acid sequences corresponding to HIV/SIV Gag, Nef, Pol, Env, including full-length sequences, portions thereof, or any combination thereof. Also provided herein are HIV/SIV polypeptides comprising one or more population episensus antigen sequences comprising amino acid sequences corresponding to HIV/SIV Gag, Nef, Pol, Env, or a combination thereof. Also provided herein are one or more carriers comprising HIV/SIV polypeptides comprising one or more population episensus antigen sequences. Further provided herein are HIV/SIV polypeptides comprising one or more tailored antigen sequences comprising amino acid sequences corresponding to HIV/SIV Gag, Nef, Pol, Env, or a combination thereof. The HIV/SIV polypeptides of the present disclosure can comprise one or more HIV-1 tailored antigens, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: SEQ ID NOs: 692-696 and SEQ ID NOs: 754-789. Also provided herein are one or more carriers comprising HIV/SIV polypeptides comprising one or more tailored antigen

sequences. EpiGraph antigen sequences having SEQ ID NOs: 691-789 are provided herein.

[0009] Provided herein are HIV-1 vaccines comprising one or more carriers and one or more population episensus antigens. Also provided herein are HIV-1 vaccines comprising a vector capable of expressing a population episensus antigen and one or more tailored antigens.

[0010] In some examples, the HIV-1 population episensus antigen comprises epitopes from Gag, Pol, Nef, Env, Tat, Rev, Vpr, Vif, or Vpu. In some examples, the HIV-1 population episensus antigen is a fusion antigen comprising two or more HIV-1 population episensus antigens. In some examples, the HIV-1 population episensus antigen is central to the HIV-1 B clade epidemic in the United States. In some examples, the HIV-1 population episensus antigen is central to the HIV-1 C clade epidemic in South Africa. In some examples, the HIV-1 population episensus antigen is central to the HIV-1 2-clade regional epidemic in Thailand. In some examples, the HIV-1 population episensus antigen is central to the HIV-1 M-group global set.

[0011] In some examples, the HIV-1 population episensus antigen comprises epitopes from Gag. In some examples, the HIV-1 population episensus antigen comprises epitopes from a conserved region of HIV-1. In some examples, the HIV-1 population episensus antigen comprises epitopes from a conserved region of Gag, Pol, or Nef. In some examples, the epitopes from the conserved region of Gag are epitopes from the p24 capsid protein of Gag.

[0012] In some examples, the HIV-1 tailored antigen comprises epitopes from Gag, Pol, Nef, Env, Tat, Rev, Vpr, Vif, or Vpu. In some examples, the HIV-1 tailored antigen is central to the HIV-1 M-group global set. In some examples, the HIV-1 tailored antigen is central to the HIV-1 C clade epidemic in South Africa. In some examples, the HIV-1 tailored antigen is central to the HIV-1 B clade epidemic in the United States.

[0013] Further provided are methods of preventing or treating HIV-1 infection in a subject comprising administering an effective amount of the described HIV-1 vaccines to the subject in need thereof. Further provided are methods of designing and producing an HIV-1 vaccine for a subject comprising sequencing HIV-1 viruses in an individual, selecting vaccine antigens designed to optimally cover the diversity within a geographic

WHAT IS CLAIMED IS:

1. An HIV-1 vaccine comprising one or more carriers encoding one or more population episensus antigens, wherein the carrier is a viral vector comprising a cytomegalovirus (CMV) backbone, wherein:

    i. the CMV backbone lacks the UL130-128 gene region,

    ii. the CMV backbone lacks the UL82 gene encoding the tegument protein pp71, or

    iii. the CMV backbone lacks the UL130-128 gene region and the UL82 gene encoding the tegument protein pp71; and

    wherein the population episensus antigen comprises the amino acid sequence selected from the group of SEQ ID NOs: 691, 697-755, 766, 767, 778, and 779.

2. The vaccine of claim 1, wherein: the amino acid sequence of the population episensus antigen comprises the amino acid sequence of SEQ ID NO: 697, SEQ ID NO: 698, SEQ ID NO: 699, SEQ ID NO: 700, SEQ ID NO: 718, SEQ ID NO: 720, SEQ ID NO: 730, SEQ ID NO: 732, SEQ ID NO: 742, or SEQ ID NO: 744.

3. The vaccine of claim 1, wherein: the amino acid sequence of the population episensus antigen comprises the amino acid sequence of SEQ ID NO: 719, SEQ ID NO: 721, SEQ ID NO: 731, SEQ ID NO: 733, SEQ ID NO: 743, or SEQ ID NO: 745.

4. The vaccine of claim 1, wherein the population episensus antigen is a fusion antigen comprising two or more population episensus antigens.

5. The vaccine of claim 4, wherein:

    i. the fusion antigen comprises the amino acid sequence of SEQ ID NO: 701, SEQ ID NO: 702, SEQ ID NO: 705, or SEQ ID NO: 707; or

    ii. the fusion antigen comprises the amino acid sequence of SEQ ID NO: 706 or SEQ ID NO: 708.

6. The vaccine of claim 1, wherein:

i. the population episensus antigen comprises the amino acid sequence of SEQ ID NO: 722, SEQ ID NO: 724, SEQ ID NO: 734, SEQ ID NO: 736, SEQ ID NO: 746, or SEQ ID NO: 748; or

ii. the population episensus antigen comprises the amino acid sequence of SEQ ID NO: 723, SEQ ID NO: 725, SEQ ID NO: 735, SEQ ID NO: 737, SEQ ID NO: 747, or SEQ ID NO: 749.

7. The vaccine of claim 1, wherein:

i. the population episensus antigen comprises the amino acid sequence of SEQ ID NO: 703, SEQ ID NO: 704, SEQ ID NO: 709, SEQ ID NO: 711, SEQ ID NO: 717, SEQ ID NO: 726, SEQ ID NO: 728, SEQ ID NO: 738, SEQ ID NO: 740, SEQ ID NO: 750, or SEQ ID NO: 752; or

ii. the population episensus antigen comprises the amino acid sequence of SEQ ID NO: 710, SEQ ID NO: 712, SEQ ID NO: 727, SEQ ID NO: 729, SEQ ID NO: 739, SEQ ID NO: 741, SEQ ID NO: 751, or SEQ ID NO: 753.

8. The vaccine of any one of claims 1-7, wherein the vaccine is a prophylactic vaccine or a therapeutic vaccine.

9. The vaccine of any one of claims 1-8, wherein the viral vector carrier further encodes one or more tailored antigens.

10. The vaccine of claim 9, wherein: i. the population episensus antigen comprises a Gag epitope;

ii. the population episensus antigen comprises a Gag epitope, wherein the amino acid sequence of the population episensus antigen comprises the amino acid sequence of SEQ ID NO:691; or

iii. the population episensus antigen comprises the amino acid sequence of an inactivated Gag protein, wherein the amino acid sequence of the inactivated Gag protein was inactivated by eliminating a myristoylation sequence in the N-terminus of the Gag protein.

11. The vaccine of claim 9 or claim 10, wherein:

i. the tailored antigen comprises Gag epitopes;

ii. the tailored antigen comprises Gag epitopes, wherein the amino acid sequence of the tailored antigen comprises the amino acid sequence of: SEQ ID NO: 692, SEQ ID NO: 693, SEQ ID NO: 694, SEQ ID NO: 695, or SEQ ID NO: 696;

iii. the vaccine comprises a first tailored antigen and a second tailored antigen, wherein the first tailored antigen and the second tailored antigen comprise two of the amino acid sequences of: SEQ ID NO: 692, SEQ ID NO: 693, SEQ ID NO: 694, SEQ ID NO: 695, and SEQ ID NO: 696; or

iv. the vaccine comprises a first tailored antigen, a second tailored antigen, and a third tailored antigen, wherein the first tailored antigen, the second tailored antigen, and the third tailored antigen comprise three of the amino acid sequences of: SEQ ID NO: 692, SEQ ID NO: 693, SEQ ID NO: 694, SEQ ID NO: 695, and SEQ ID NO: 696; or

v. the tailored antigen comprises the amino acid sequence of an inactivated Gag protein, wherein the amino acid sequence of the inactivated Gag protein was inactivated by eliminating a myristoylation sequence in the N-terminus of the Gag protein.

12. The vaccine of any one of claims 9-11, wherein:

i. the population episensus antigen comprises an amino acid sequence selected from the group consisting of:SEQ ID NOs: 754-755, 766-767, and 778 - 779;

ii. the population episensus antigen comprises an amino acid sequence selected from the group consisting of: SEQ ID NOs: 754-755, 766-767, and 778-779 and the tailored antigen comprises an amino acid sequence selected from the group consisting of: SEQ ID NOs: 756-765, 768-777, and 780-789;

iii. the vaccine comprises a first tailored antigen and a second tailored antigen, wherein the population episensus antigen comprises an amino acid sequence selected from the group consisting of: SEQ ID NOs: 754-755, 766-767, and 778-779, and wherein the first tailored antigen and the second tailored antigen comprise two of the amino acid sequences selected from the group consisting of: SEQ ID NOs: 756-765, 768-777, and 780-789; or

iv. the vaccine comprises a first tailored antigen, a second tailored antigen, and a third tailored antigen, wherein the population episensus antigen comprises an amino acid sequence selected from the group consisting of: SEQ ID NOs:

754-755, 766-767, and 778-779, and wherein the first tailored antigen, the second tailored antigen, and the third tailored antigen comprise three of the amino acid sequences selected from the group consisting of: SEQ ID NOs: 756-765, 768-777, and 780-789.

13. The vaccine of any one of claims 7-10, further comprising:

i. a HCMV vector comprising a HCMV backbone and a tailored antigen selected to be a best match natural HIV-1 strain; or

ii. a HCMV vector comprising a HCMV backbone and a tailored antigen selected to be a best match different HIV-1 strain.

14. The vaccine of any one of claims 1-8 for use in protecting a subject from an HIV-1 infection or for use in treating HIV-1 in a subject in need thereof.

15. The vaccine of any one of claims 9-13 for use in treating HIV-1 in a subject in need thereof.

16. The vaccine of any of claims 1-13 for use in inducing an effector memory T cell response.

17. A vaccine for use in inducing an effector memory T cell response comprising one or more carriers encoding one or more antigens, wherein the carrier is a viral vector comprising a cytomegalovirus (CMV) backbone, wherein:

i. the CMV backbone lacks the UL130-128 gene region,

ii. the CMV backbone lacks the UL82 gene encoding the tegument protein pp71, or

iii. the CMV backbone lacks the UL130-128 gene region and the UL82 gene encoding the tegument protein pp71; and

wherein the antigen comprises the amino acid sequence selected from the group of SEQ ID NOs: 691-712 and 717-789.

18. A polypeptide comprising one or more HIV-1 antigens, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: SEQ ID NOs: 691-712 and SEQ ID NOs: 717-789.