is not intended to identify key features of the claimed subject matter, nor is it intended to be used as an aid in determining the scope of the claimed subject matter.

[0013] In one aspect, disclosed herein is a composition comprising a plurality of one or more viral vectors, wherein each of the one or more viral vectors includes a sequence encoding an HSV-2-specific meganuclease.

[0013a] In another aspect, also disclosed herein is a pharmaceutical composition, comprising the composition disclosed herein, and a pharmaceutically acceptable carrier or excipient.

[0013b] In another aspect, also disclosed herein is a use of the composition disclosed herein in the manufacture of a medicament for reducing or eliminating latent HSV-2 or HSV-2 reactivation in a subject, wherein the composition is to be administered to a HSV-2-infected cell in the subject.

[0013c] In another aspect, also disclosed herein is a use of the composition disclosed herein in the manufacture of a medicament for reducing or eliminating latent HSV-2 or HSV-2 reactivation in a subject.

[0013d] In another aspect, also disclosed herein is a use of the pharmaceutical composition disclosed herein in the manufacture of a medicament for reducing or eliminating latent HSV-2 or HSV-2 reactivation in a subject.

[0014] Also disclosed herein is a method of reducing or eliminating latent HSV-2 or HSV-2 reactivation in a cell, comprising administering to a cell a plurality of one or more viral vectors including a sequence encoding an HSV-2-specific meganuclease.

[0015] Additionally disclosed herein is a method of reducing or eliminating latent HSV-2 or HSV-2 reactivation in a subject, comprising administering to the subject a plurality of one or more viral vectors including a sequence encoding an HSV-2-specific meganuclease.

DESCRIPTION OF THE DRAWINGS

[0016] The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

[0017] FIG. 1 shows the series of libraries designed for engineering the thermostabilized I-OnuI meganuclease toward the OnuHSV2a DNA target sequence. The desired final OnuHSV2a target sequence is aligned to the wildtype I-OnuI sequence, and a

series of libraries is designed to make small changes to the meganuclease in a step-wise manner, starting at the center of the target sequence (nearest the enzyme active site) and moving progressively outward. Positions in the DNA target sequences which differ from the wildtype I-OnuI recognition sequence are depicted as lower-case letters. The structure of the I-OnuI meganuclease is shown above the target sequence alignment, with the mismatched positions of the bound DNA target shown red in color drawings or black in black and white drawings, and the corresponding positions of incorporated amino acid sidechain variation designated as the spheres.

[0018] FIG. 2 shows the series of libraries designed for engineering the thermostabilized I-OnuI meganuclease toward the OnuHSV2b DNA target sequence. The desired final OnuHSV2b target sequence is aligned to the wildtype I-OnuI sequence, and a series of libraries is designed to make small changes to the meganuclease in a step-wise manner, starting at the center of the target sequence (nearest the enzyme active site) and

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A composition comprising a plurality of one or more viral vectors, wherein each of the one or more viral vectors includes a sequence encoding an HSV-2-specific meganuclease.

2. The composition of Claim 1, wherein the one or more viral vectors is a self-complementary adeno-associated virus (scAAV), a single-stranded adeno-associated virus (ssAAV), or a combination thereof.

3. The composition of Claim 2, wherein the ssAAV is ssAAV9, ssAAV-Dj/8, ssAAV-rh10, ssAAV8, ssAAV1, another serotype adeno-associated virus, or a combination thereof.

4. The composition of Claim 2, wherein the scAAV is scAAV9, scAAV-Dj/8, scAAV-rh10, scAAV8, scAAV1, another serotype adeno-associated virus, or a combination thereof.

5. The composition of Claim 1, wherein the sequence encoding the HSV-2-specific meganuclease is configured to encode an HSV-2-specific meganuclease which targets one or more HSV-2 genes essential for replication.

6. The composition of Claim 1, wherein the sequence encoding the HSV-2-specific meganuclease is configured to encode an HSV-2-specific meganuclease which induces one or more DNA double strand breaks.

7. The composition of Claim 1, wherein the HSV-2-specific meganuclease is configured to induce one or more DNA double strand breaks.

8. The composition of Claim 1, wherein the HSV-2-specific meganuclease is configured to induce two DNA double strand breaks.

9. The composition of Claim 1, wherein the HSV-2-specific meganuclease is configured to target one or more HSV-2 genes essential for replication.

10. The composition of Claim 1, wherein the HSV-2-specific meganuclease comprises a sequence as set forth in SEQ ID NOs: 1-6.

11. The composition of Claim 1, wherein the HSV-2-specific meganuclease comprises SEQ ID NO: 1 or 2.

12. The composition of Claims 1, wherein the HSV-2-specific meganuclease comprises a sequence as set forth in SEQ ID NOs: 7-12.

13. The composition of Claim 1, wherein the HSV-2-specific meganuclease is configured to target one or more sequences as set forth in SEQ ID NOs: 13 and 14.

14. The composition of Claim 1, wherein the one or more viral vectors further includes a regulatory sequence.

15. The composition of Claim 14, wherein the regulatory sequence comprises a sequence as set forth in SEQ ID NO: 42.

16. The composition of Claim 1, wherein the plurality of one or more viral vectors comprises one to three scAAVs, wherein each scAAV is a different serotype, and wherein each scAAV includes a sequence, which is the same or different, encoding an HSV-2-specific meganuclease.

17. A pharmaceutical composition, comprising the composition of any one of Claims 1-16, and a pharmaceutically acceptable carrier or excipient.

18. Use of the composition of any one of Claims 1-16 in the manufacture of a medicament for reducing or eliminating latent HSV-2 or HSV-2 reactivation in a subject, wherein the composition is to be administered to a HSV-2-infected cell in the subject.

19. Use of the composition of any one of Claims 1-16 in the manufacture of a medicament for reducing or eliminating latent HSV-2 or HSV-2 reactivation in a subject.

20. Use of the pharmaceutical composition of Claim 17 in the manufacture of a medicament for reducing or eliminating latent HSV-2 or HSV-2 reactivation in a subject.