The development of next-generation vaccines to treat or prevent viral infection must elicit an increased breadth of cellular immunity in order to allow for successful vaccination outcomes. The need for such vaccines is particularly urgent for the treatment or prevention of HIV-1.

SUMMARY ~~OF THE INVENTION~~

In ~~a first aspect~~ one embodiment, the ~~invention~~ disclosure features a vaccine for treating or reducing the risk of a viral infection in a mammal, such as a human, that includes at least two distinct optimized viral polypeptides (e.g., 2, 3, 4, 5, or more distinct optimized viral polypeptides), wherein the optimized viral polypeptides correspond to the same viral gene product. In one embodiment, the viral infection is caused by a retrovirus, reovirus, picornavirus, togavirus, orthomyxovirus, paramyxovirus, calicivirus, arenavirus, flavivirus, filovirus, bunyavirus, coronavirus, astrovirus, adenovirus, papillomavirus, parvovirus, herpesvirus, hepadnavirus, poxvirus, or polyomavirus. In other embodiments, the retrovirus is human immunodeficiency virus type 1 (HIV-1), and the viral gene products include Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, or Vpu. In a further embodiment, the vaccine includes no more than two optimized viral polypeptides corresponding to one of the Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, or Vpu viral gene products. In another embodiment, the vaccine does not include optimized viral polypeptides corresponding to Gag and Nef. In yet another embodiment, the vaccine includes at least two distinct optimized viral polypeptides (e.g., 2, 3, 4, 5, or more distinct optimized viral polypeptides) for a first viral gene product selected from Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu and one or more distinct optimized viral polypeptides (e.g., 2, 3, 4, 5, or more distinct optimized viral polypeptides) for a second viral gene product different from the first viral gene product selected from Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu.

In one aspect, there is provided a vaccine comprising an optimized viral polypeptide having the amino acid sequence set forth in SEQ ID NO:9.

In ~~a second aspect~~ one embodiment, the ~~invention~~ disclosure features a vaccine for treating or reducing the risk of human immunodeficiency virus type 1 (HIV-1) infection in a mammal, such as a human, that includes an optimized viral polypeptide that has at least seven contiguous amino acids (e.g., at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 50, 100, 150, 175, 200, 250, 300, 350, 400, 450, 500 or more contiguous amino acids in length) having at least 85% amino acid sequence identity to any one of the sequences set forth in SEQ ID NOS:1-29. In one embodiment, the

optimized viral polypeptide has at least seven contiguous amino acids (e.g., at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 50, 100, 150, 175, 200, 250, 300, 350, 400, 450, 500 or more contiguous amino acids in length) having amino acid sequence identity to any one of the sequences set forth in SEQ ID NOS:1-29. In another embodiment, the optimized viral polypeptide has the amino acid sequence of any one of the sequences set forth in SEQ NOS:1-29. In a further embodiment, the vaccine includes at least two optimized viral polypeptides selected from any one or more of groups a)-k): a) SEQ ID NOS:1 and 2; b) SEQ ID NOS:3, 4, and 5; c) SEQ ID NOS:6 and 7; d) SEQ ID NOS:8-12; e) SEQ ID NOS:13, 14, and 15; f) SEQ ID NOS:16, 17, and 18; g) SEQ ID NOS:19 and 20; h) SEQ ID NOS:21, 22, and 23; i) SEQ ID NOS:24 and 25; j) SEQ ID NOS:26 and 27; k) and SEQ ID NOS:21-22. In another embodiment, the vaccine can include a pair of optimized viral polypeptides selected from any one of groups a)-k) above and one or more different optimized viral polypeptides from the same or a different group a)-k). In other embodiments, the vaccine can include at least three or four or more optimized viral polypeptides from one or more of groups a)-k).

In ~~a third aspect~~one embodiment, the ~~invention~~ disclosure features a vaccine for treating or reducing the risk of a viral infection in a mammal, such as a human, that includes at least two pairs of distinct optimized viral polypeptides, wherein each pair of optimized viral polypeptides corresponds to the same viral gene product, and wherein no more than two optimized viral polypeptides incorporated in the vaccine correspond to the same viral gene product. In one embodiment, the vaccine includes at least three pairs of distinct optimized viral polypeptides. In another embodiment, the vaccine includes at least four pairs of distinct optimized viral polypeptides. In one embodiment, the viral infection is caused by a retrovirus, reovirus, picornavirus, togavirus, orthomyxovirus, paramyxovirus, calicivirus, arenavirus, flavivirus, filovirus, bunyavirus, coronavirus, astrovirus, adenovirus, papillomavirus, parvovirus, herpesvirus, hepadnavirus, poxvirus, or polyomavirus. In other embodiments, the retrovirus is human immunodeficiency virus type 1 (HIV-1), and the viral gene products include Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, or Vpu. In a further embodiment, the vaccine includes no more than two optimized viral polypeptides corresponding to one of the Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, or Vpu viral gene products. In another embodiment, the vaccine does not include optimized viral polypeptides corresponding to Gag and Nef. In a further embodiment, the vaccine

includes at least three pairs of distinct optimized viral polypeptides corresponding to any three of the Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, or Vpu viral gene products. In another embodiment, the vaccine includes at least four pairs of distinct optimized viral polypeptides corresponding to any four of the Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, or Vpu viral gene products.

In one embodiment ~~of any of the first three aspects~~ of the ~~invention~~disclosure, the vaccine elicits a cellular immune response against a viral gene product. In another embodiment, the vaccine elicits a cellular immune response against HIV-1. In a further embodiment, the nucleotide sequence of at least one distinct optimized viral polypeptide is encoded by a nucleic acid or vector. In one embodiment, the vector is a recombinant adenovirus, such as adenovirus serotype 26 (Ad26), adenovirus serotype 34 (Ad34), adenovirus serotype 35 (Ad35), adenovirus serotype 48 (Ad48), or adenovirus serotype 5 HVR48 (Ad5HVR48). In a further embodiment, the vaccine is in combination with a pharmaceutically acceptable carrier, excipient, or diluent.

In one aspect, there is provided a vaccine formulated for delivery in a viral vector, wherein said vaccine comprises a nucleic acid molecule encoding a polypeptide as described herein, and said vector is selected from the group consisting of adenovirus serotype 26(Ad26), adenovirus serotype 34 (Ad34), adenovirus serotype 35 (Ad35), adenovirus serotype 48 (Ad48) or adenovirus serotype 5 HVR48 (Ad5HVR48), poxvirus, modified vaccinia virus Ankara (MVA).

In ~~a fourth aspect~~one embodiment, the ~~invention~~ disclosure features a nucleic acid that includes the nucleotide sequence of an optimized viral polypeptide that has at least seven contiguous amino acids (e.g., at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 50, 100, 150, 175, 200, 250, 300, 350, 400, 450, 500 or more contiguous amino acids in length) having at least 85% amino acid sequence identity to any one of the amino acid sequences set forth in SEQ ID NOS:1-29. In one embodiment, the optimized viral polypeptide has at least seven contiguous amino acids (e.g., at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 50, 100, 150, 175, 200, 250, 300, 350, 400, 450, 500 or more contiguous amino acids in length) having sequence identity to any one of the amino acid sequences set forth in SEQ ID NOS:1-29. In another embodiment, the optimized viral polypeptide has any one of the amino acid sequences set forth in SEQ ID NOS:1-29. In a further embodiment, the nucleic acid includes a vector. In one embodiment, the vector is a recombinant adenovirus, such as adenovirus serotype 26 (Ad26), adenovirus serotype 34 (Ad34), adenovirus serotype 35 (Ad35), adenovirus serotype 48 (Ad48), or adenovirus serotype 5 HVR48 (Ad5HVR48).

In ~~a fifth aspect~~one embodiment, the ~~invention~~ disclosure features an optimized viral polypeptide that has at least seven contiguous amino acids (e.g., at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 50, 100, 150, 175, 200, 250, 300,

350, 400, 450, 500 or more contiguous amino acids in length) having at least 85% amino acid sequence identity to any one of the amino acid sequences set forth in SEQ ID NOS:1-29. In one embodiment, the optimized viral polypeptide has at least seven contiguous amino acids (e.g., at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 50, 100, 150, 175, 200, 250, 300, 350, 400, 450, 500 or more contiguous amino acids in length) having sequence identity to any one of the amino acid sequences set forth in SEQ ID NOS:1-29. In another embodiment, the optimized viral polypeptide has any one of the amino acid sequences set forth in SEQ ID NOS:1-29.

In one aspect, there is provided the use of a vaccine as described herein in the manufacture of a medicament for treating or reducing the risk of a viral infection in a mammal, wherein said medicament comprises a pharmaceutically aceptable carrier, excipient, or diluent

In ~~a sixth aspect~~one embodiment, the ~~invention~~ disclosure features a method for treating or reducing the risk of a viral infection in a mammal, such as a human, by administering a vaccine or nucleic acid of the ~~invention~~disclosure. In one embodiment, the viral infection is caused by a retrovirus, reovirus, picornavirus, togavirus, orthomyxovirus, paramyxovirus, calicivirus, arenavirus, flavivirus, filovirus, bunyavirus, coronavirus, astrovirus, adenovirus, papillomavirus, parvovirus, herpesvirus, hepadnavirus, poxvirus, or polyomavirus. In further embodiments, the retrovirus is human immunodeficiency virus type 1 (HIV-1), and the viral gene products include Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, or Vpu. In one embodiment, the vaccine or nucleic acid elicits a cellular immune response against a viral gene product.

In one aspect, there is provided a method of manufacturing a vaccine for treating or reducing the risk of an HIV-1 infection in a human, said method comprising synthesizing a vaccine as described herein.

In ~~a seventh aspect~~one embodiment, the ~~invention~~ disclosure features a method of manufacturing a vaccine for treating or reducing the risk of a viral infection in a mammal, such as a human, by synthesizing a vaccine of the ~~invention~~disclosure.

In ~~an eighth aspect~~one embodiment, the ~~invention~~ disclosure features a method of manufacturing a vaccine for treating or reducing the risk of a viral infection in a mammal, such as a human, by contacting a nucleic acid of the ~~invention~~ disclosure with a cell and isolating a optimized viral polypeptide.

In one embodiment ~~of the seventh or eighth aspects~~ of the ~~invention~~disclosure, the optimized viral polypeptide elicits a cellular immune response when administered to a mammal. The cellular immune response can be against a viral gene product. In another embodiment, the viral infection is caused by a retrovirus, reovirus, picornavirus, togavirus, orthomyxovirus, paramyxovirus, calicivirus, arenavirus, flavivirus, filovirus, bunyavirus, coronavirus, astrovirus, adenovirus, papillomavirus, parvovirus, herpesvirus, hepadnavirus, poxvirus, or polyomavirus. In further

embodiments, the retrovirus is human immunodeficiency virus type 1 (HIV-1), and the viral gene products include Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, or Vpu.

In one aspect, there is provided a kit comprising:

a) a vaccine as described herein;

b) a pharmaceutically acceptable carrier, excipient, or diluent;

c) instructions for the use thereof, and, optionally,

d) an adjuvant.

In ~~a ninth aspect~~one embodiment, the ~~invention~~ disclosure features a kit that includes a vaccine of the ~~invention~~disclosure, a pharmaceutically acceptable carrier, excipient, or diluent, and instructions for the use thereof. In one embodiment, the kit also includes an adjuvant.

In ~~a final aspect~~one embodiment, the ~~invention~~ disclosure features a kit that includes a nucleic acid of the ~~invention~~disclosure, a pharmaceutically acceptable carrier, excipient, or diluent, and instructions for the use thereof. In one embodiment, the kit also includes an adjuvant.

In an embodiment ~~of all aspects~~ of the ~~invention~~disclosure, the optimized viral polypeptide is encoded by a nucleic acid sequence that is optimized for expression in humans (e.g., any one of SEQ ID NOS:5, 10, 11, 12, 15, 18, and 23).

Definitions

By "optimized viral polypeptide" or "computationally-optimized viral polypeptide" is meant an immunogenic polypeptide that is not a naturally-occurring viral peptide, polypeptide, or protein. Optimized viral polypeptide sequences are initially generated by modifying the amino acid sequence of one or more naturally-occurring viral gene products (e.g., peptides, polypeptides, and proteins) to increase the breadth, intensity, depth, or longevity of the antiviral immune response (e.g., cellular or humoral immune responses) generated upon immunization (e.g., when incorporated into a vaccine of the invention) of a mammal (e.g., a human). Thus, the optimized viral polypeptide may correspond to a "parent" viral gene sequence; alternatively, the optimized viral polypeptide may not correspond to a specific "parent" viral gene sequence but may correspond to analogous sequences from various strains or quasispecies of a virus. Modifications to the viral gene sequence that can be included in an optimized viral polypeptide include amino acid additions, substitutions, and deletions. In one embodiment of the invention, the optimized viral polypeptide is the composite or merged amino acid sequence of two or more naturally-occurring viral gene products (e.g., natural or clinical viral isolates) in which each potential epitope (e.g., each contiguous or overlapping amino acid sequence of 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 or more amino acids in length) is analyzed and modified to improve the immunogenicity of the resulting optimized viral polypeptide. Optimized viral

CLAIMS

1. A vaccine comprising an optimized viral polypeptide having the amino acid sequence set forth in SEQ ID NO:9.

2. The vaccine according to claim 1, wherein said vaccine further comprises:
a) at least two distinct optimized gag polypeptides selected from any one or more of the groups: (i) SEQ ID NOs:3 and 4, (ii) SEQ ID NOs:3 and 15, and (iii) SEQ ID NOs:4 and 15; or
b) at least two distinct optimized pol polypeptides selected from any one or more of the groups: (i) SEQ ID NOs:12 and 13, (ii) SEQ ID NOs:12 and 14, and (iii) SEQ ID NOs:13 and 14.

3. The vaccine according to claim 2, wherein said at least two optimized gag viral polypeptides comprise an amino acid sequence having the sequences set forth in each of SEQ ID NO:3 and 4.

4. The vaccine according to claim 2, wherein said at least two optimized pol viral polypeptides comprise an amino acid sequence having the sequences set forth in each of SEQ ID NO:12 and 13.

5. The vaccine according to claim 3 or 4, further comprising an optimized env viral polypeptide having the sequence set forth in SEQ ID NO:10.

6. The vaccine according to claim 1, wherein said vaccine comprises:
a) at least two distinct optimized gag polypeptides selected from any one or more of the groups: (i) SEQ ID NOs:3 and 4, (ii) SEQ ID NOs:3 and 15, and (iii) SEQ ID NOs:4 and 15;
b) at least two distinct optimized pol polypeptides selected from any one or more of the groups: (i) SEQ ID NOs:12 and 13, (ii) SEQ ID NOs:12 and 14, and (iii) SEQ ID NOs:13 and 14; and
c) a distinct optimized env polypeptide selected from one or more of: (i) SEQ ID NO:10 and (ii) SEQ ID NO:11.

7. A vaccine formulated for delivery in a viral vector, wherein said vaccine comprises a nucleic acid molecule encoding the polypeptides of any one of claims 1 to 6, and said vector is selected from the group consisting of adenovirus serotype 26 (Ad26), adenovirus serotype 34 (Ad34), adenovirus serotype 35 (Ad35), adenovirus serotype 48 (Ad48), or adenovirus serotype 5 HVR48 (Ad5HVR48), poxvirus, modified vaccinia virus Ankara (MVA).

8. The vaccine of claim 7, wherein said vector is an adenovirus serotype 26 (Ad26).

9. The vaccine of claim 7, wherein said vector is a modified vaccinia virus Ankara (MVA).

10. The vaccine of any one of claims 1 to 9, wherein said vaccine further comprises a pharmaceutically acceptable carrier, excipient, or diluent.

11. Use of the vaccine of any one of claims 1 to 10 in the manufacture of a medicament for treating or reducing the risk of a viral infection in a mammal, wherein said medicament comprises a pharmaceutically acceptable carrier, excipient, or diluent.

12. The use of claim 11, wherein said mammal is a human.

13. The use of claim 11 or 12, wherein said viral infection is a human immunodeficiency virus type 1 (HIV-1) infection.

14. A method of manufacturing a vaccine for treating or reducing the risk of an HIV-1 infection in a human, said method comprising synthesizing the vaccine of any one of claims 1 to 10.

15. A kit comprising:
a) the vaccine of any one of claims 1-9;
b) a pharmaceutically acceptable carrier, excipient, or diluent;
c) instructions for the use thereof; and, optionally,
d) an adjuvant.

CLAIMS

1. A vaccine for treating or reducing the risk of a viral infection in a mammal comprising at least two distinct optimized viral polypeptides, wherein said optimized viral polypeptides correspond to the same viral gene product.

2. The vaccine of claim 1, wherein said mammal is a human.

3. The vaccine of claim 1, wherein said vaccine elicits a cellular immune response against said viral gene product.

4. The vaccine of claim 1, wherein said viral infection is caused by a retrovirus, reovirus, picornavirus, togavirus, orthomyxovirus, paramyxovirus, calicivirus, arenavirus, flavivirus, filovirus, bunyavirus, coronavirus, astrovirus, adenovirus, papillomavirus, parvovirus, herpesvirus, hepadnavirus, poxvirus, or polyomavirus.

5. The vaccine of claim 4, wherein said retrovirus is human immunodeficiency virus type 1 (HIV-1).

6. The vaccine of claim 5, wherein said viral gene product is selected from the group consisting of Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu.

7. The vaccine of claim 6, wherein said vaccine comprises no more than two optimized viral polypeptides corresponding to one of the viral gene products selected from the group consisting of Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu.

8. The vaccine of claims 5 or 6, wherein said vaccine does not comprise optimized viral polypeptides corresponding to Gag and Nef.

9. A vaccine for treating or reducing the risk of human immunodeficiency virus type 1 (HIV-1) infection in a mammal comprising an optimized viral polypeptide comprising at least seven contiguous amino acids having at least 85% amino acid sequence identity to any one of the sequences set forth in SEQ ID NOS:1-29.

10. The vaccine of claim 9, wherein said optimized viral polypeptide comprises at least seven contiguous amino acids having amino acid sequence identity to any one of the sequences set forth in SEQ ID NOS:1-29.

11. The vaccine of claim 9, wherein said optimized viral polypeptide comprises the amino acid sequence of any one of the sequences set forth in SEQ NOS:1-29.

12. The vaccine of claim 9, wherein said mammal is a human.

13. The vaccine of claim 9, wherein said vaccine elicits a cellular immune response against HIV-1.

14. The vaccine of claim 9, wherein said vaccine comprises at least two said optimized viral polypeptides.

15. The vaccine of claim 14, wherein said at least two said optimized viral polypeptides comprise:

a) SEQ ID NOS:1 and 2;
b) SEQ ID NOS:3 and 4;
c) SEQ ID NOS:5 and 6;
d) SEQ ID NOS:7 and 8;
e) SEQ ID NOS:9 and 10;
f) SEQ ID NOS:10 and 11;
g) SEQ ID NOS:9 and 11;
h) SEQ ID NOS:12 and 13;
i) SEQ ID NOS:13 and 14;
j) SEQ ID NOS:12 and 14;
k) SEQ ID NOS:3 and 15;
l) SEQ ID NOS:4 and 15;
m) SEQ ID NOS:16 and 17;
n) SEQ ID NOS:17 and 18;
o) SEQ ID NOS:16 and 18;
p) SEQ ID NOS:19 and 20;

q) SEQ ID NOS:21 and 22;

r) SEQ ID NOS:22 and 23;

s) SEQ ID NOS:21 and 23;

t) SEQ ID NOS:24 and 25;

u) SEQ ID NOS:26 and 27; or

v) SEQ ID NOS:28 and 29.

16. The vaccine of claim 9, wherein said vaccine comprises at least three said optimized viral polypeptides.

17. The vaccine of claim 9, wherein said vaccine comprises at least four said optimized viral polypeptides.

18. A vaccine for treating or reducing the risk of a viral infection in a mammal comprising at least two pairs of distinct optimized viral polypeptides, wherein each pair of said optimized viral polypeptides corresponds to the same viral gene product, and wherein no more than two optimized viral polypeptides incorporated in the vaccine correspond to the same viral gene product.

19. The vaccine of claim 18, wherein said mammal is a human.

20. The vaccine of claim 18, wherein said vaccine elicits a cellular immune response against said viral gene product.

21. The vaccine of claim 18, comprising at least three pairs of distinct optimized viral polypeptides.

22. The vaccine of claim 18, comprising at least four pairs of distinct optimized viral polypeptides.

23. The vaccine of claim 18, wherein said viral infection is caused by a retrovirus, reovirus, picornavirus, togavirus, orthomyxovirus, paramyxovirus, calicivirus,

arenavirus, flavivirus, filovirus, bunyavirus, coronavirus, astrovirus, adenovirus, papillomavirus, parvovirus, herpesvirus, hepadnavirus, poxvirus, or polyomavirus.

24. The vaccine of claim 23, wherein said retrovirus is human immunodeficiency virus type 1 (HIV-1).

25. The vaccine of claim 24, wherein said at least two pairs of distinct optimized viral polypeptides correspond to any two of the viral gene products selected from the group consisting of Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu.

26. The vaccine of claim 25, wherein said at least two viral gene products are not Gag and Nef.

27. The vaccine of claim 25, comprising at least three pairs of distinct optimized viral polypeptides corresponding to any three of the viral gene products selected from the group consisting of Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu.

28. The vaccine of claim 18, comprising at least four pairs of distinct optimized viral polypeptides corresponding to any four of the viral gene products selected from the group consisting of Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu.

29. The vaccine of claim 24, wherein said vaccine elicits a cellular immune response against HIV-1.

30. The vaccine of claims 1, 9, or 18, wherein the nucleotide sequence of at least one distinct optimized viral polypeptide is encoded by a nucleic acid or vector.

31. The vaccine of claim 30, wherein said vector is a recombinant adenovirus.

32. The vaccine of claim 31, wherein said recombinant adenovirus is adenovirus serotype 26 (Ad26), adenovirus serotype 34 (Ad34), adenovirus serotype 35 (Ad35), adenovirus serotype 48 (Ad48), or adenovirus serotype 5 HVR48 (Ad5HVR48).

33. The vaccine of claims 1, 9, or 18, in further combination with a pharmaceutically acceptable carrier, excipient, or diluent.

34. A nucleic acid comprising the nucleotide sequence of a optimized viral polypeptide comprising at least seven contiguous amino acids having at least 85% amino acid sequence identity to any one of the amino acid sequences set forth in SEQ ID NOS:1-29.

35. The nucleic acid of claim 34, wherein said optimized viral polypeptide comprises at least seven contiguous amino acids having sequence identity to any one of the amino acid sequences set forth in SEQ ID NOS:1-29.

36. The nucleic acid of claim 34, wherein said optimized viral polypeptide comprises any one of the amino acid sequences set forth in SEQ ID NOS:1-29.

37. The nucleic acid of claim 34, further comprising a vector.

38. The nucleic acid of claim 37, wherein said vector is a recombinant adenovirus.

39. The nucleic acid of claim 38, wherein said recombinant adenovirus is adenovirus serotype 26 (Ad26), adenovirus serotype 34 (Ad34), adenovirus serotype 35 (Ad35), adenovirus serotype 48 (Ad48), or adenovirus serotype 5 HVR48 (Ad5HVR48).

40. A optimized viral polypeptide comprising at least seven contiguous amino acids having at least 85% amino acid sequence identity to any one of the amino acid sequences set forth in SEQ ID NOS:1-29.

41. The optimized viral polypeptide of claim 40, wherein said optimized viral polypeptide comprises at least seven contiguous amino acids having sequence identity to any one of the amino acid sequences set forth in SEQ ID NOS:1-29.

42. The optimized viral polypeptide of claim 40, wherein said optimized viral polypeptide comprises any one of the amino acid sequences set forth in SEQ ID NOS:1-29.

43. A method for treating or reducing the risk of a viral infection in a mammal comprising administering to said mammal the vaccine of claim 1, 9, or 18, or the nucleic acid of claim 37.

44. The method of claim 43, wherein said mammal is a human.

45. The method of claim 43, wherein said vaccine or nucleic acid elicits a cellular immune response against said viral gene product.

46. The method of claim 43, wherein said viral infection is caused by a retrovirus, reovirus, picornavirus, togavirus, orthomyxovirus, paramyxovirus, calicivirus, arenavirus, flavivirus, filovirus, bunyavirus, coronavirus, astrovirus, adenovirus, papillomavirus, parvovirus, herpesvirus, hepadnavirus, poxvirus, or polyomavirus.

47. The method of claim 46, wherein said retrovirus is human immunodeficiency virus type 1 (HIV-1).

48. The method of claim 43, wherein said viral gene product is selected from the group consisting of Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu.

49. A method of manufacturing a vaccine for treating or reducing the risk of a viral infection in a mammal, said method comprising synthesizing the vaccine of claims 1, 9, or 18.

50. A method of manufacturing a vaccine for treating or reducing the risk of a viral infection in a mammal, said method comprising the steps of:

a) contacting the nucleic acid of claim 37 with a cell; and

b) isolating said optimized viral polypeptide.

51. The method of claim 49 or 50, wherein said optimized viral polypeptide elicits a cellular immune response when administered to a mammal.

52. The method of claim 49 or 50, wherein said mammal is a human.

53. The method of claim 49 or 50, wherein said vaccine elicits a cellular immune response against said viral gene product.

54. The method of claim 49 or 50, wherein said viral infection is caused by a retrovirus, reovirus, picornavirus, togavirus, orthomyxovirus, paramyxovirus, calicivirus, arenavirus, flavivirus, filovirus, bunyavirus, coronavirus, astrovirus, adenovirus, papillomavirus, parvovirus, herpesvirus, hepadnavirus, poxvirus, or polyomavirus.

55. The method of claim 54, wherein said retrovirus is human immunodeficiency virus type 1 (HIV-1).

56. The method of claim 55, wherein said viral gene product is selected from the group consisting of Gag, Pol, Env, Nef, Tat, Rev, Vif, Vpr, and Vpu.

57. A kit comprising:

a) the vaccine of claims 1, 9, or 18;

b) a pharmaceutically acceptable carrier, excipient, or diluent; and

c) instructions for the use thereof.

58. The kit of claim 57, further comprising an adjuvant.

59. A kit comprising:

a) the nucleic acid of claim 37;

b) a pharmaceutically acceptable carrier, excipient, or diluent; and

c) instructions for the use thereof.

60. The kit of claim 59, further comprising an adjuvant.