

Summary

In one example, the disclosure provides polypeptides comprising an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequence selected from the group consisting of SEQ ID NOS: 1-84, 138-146, and 167-184, wherein X1 is absent or is an amino acid linker, and wherein residues in parentheses are optional and may be present or some or all of the optional residues may be absent. In one aspect, the present disclosure provides a polypeptide comprising an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequence selected from the group consisting of SEQ ID NOS: 1-84, 138-146, and 167-184, wherein X1 is absent or is an amino acid linker, and wherein residues in parentheses are optional and may be present or some or all of the optional residues may be absent. In various specific examples, the polypeptides comprise the amino acid sequence selected from the group consisting of SEQ ID NOS: 1-12 and 142-151, comprise the amino acid sequence selected from the group consisting of SEQ ID NOS: 1-8, or comprise the amino acid sequence selected from the group consisting of SEQ ID NOS: 1 or 5. In another example, the disclosure provides nanoparticles comprising a plurality of such polypeptides. In one aspect, the present disclosure provides a nanoparticle comprising a plurality of any one of the polypeptides disclosed herein.

In another example, the disclosure provides nanoparticles, comprising:

- (a) a plurality of first assemblies, each first assembly comprising a plurality of identical first proteins; and,
- (b) a plurality of second assemblies, each second assembly comprising a plurality of second proteins;

wherein the amino acid sequence of the first protein differs from the sequence of the second protein; wherein the plurality of first assemblies non-covalently interact with the plurality of second assemblies to form the nanoparticle; and wherein the nanoparticle displays on its surface an immunogenic portion of a SARS-CoV-2 antigen or a variant or homolog thereof, present in the at least one second protein.

In one aspect, the present disclosure provides a nanoparticle, comprising: (a) a plurality of first assemblies, each first assembly comprising a plurality of identical first proteins; and, (b) a plurality of second assemblies, each second assembly comprising a plurality of second proteins;

wherein the amino acid sequence of the first protein differs from the sequence of the second protein;

wherein the plurality of first assemblies non-covalently interact with the plurality of second assemblies to form the nanoparticle; and

wherein the nanoparticle displays on its surface an immunogenic portion of a SARS-CoV-2 antigen or a variant or homolog thereof, present in the at least one second protein.

In one example, the second proteins comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequence selected from the group consisting of SEQ ID NOS: 85-124 or 185-193, or consisting of SEQ ID NOS: 85-88, wherein X1 for at least one second protein comprises an immunogenic portion of a SARS-CoV-2 antigen or a variant or homolog thereof, X2 is absent or an amino acid linker, and residues in parentheses are optional. In another example, X1 in at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprises an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to a Spike (S) protein extracellular domain (ECD) amino acid sequence, an S1 subunit amino acid sequence, an S2 subunit amino acid sequence, an S1 receptor binding domain (RBD) amino acid sequence, and/or an N-terminal

domain (NTD) amino acid sequence, from SARS-CoV-2, or a variant or homolog thereof. In a further example, X1 in at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprises an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NO:125-137. In a further example, the first protein comprises an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or some or all of the optional residues may be absent.

In various other examples, the disclosure provides compositions comprising a plurality of nanoparticles disclosed herein, nucleic acid molecules, such as mRNA, encoding the polypeptide disclosed herein, expression vectors comprising the nucleic acid molecules disclosed herein operatively linked to a suitable control sequence, cells comprising the polypeptide, the nanoparticle, the composition, the nucleic acid, and/or the expression vector disclosed herein, and pharmaceutical compositions, kits, and vaccines comprising the polypeptide, the nanoparticle, the composition, the nucleic acid, the expression vector, and/or the cell disclosed herein.

In one aspect, the present disclosure provides a composition, comprising a plurality of any one of the nanoparticles disclosed herein.

In one aspect, the present disclosure provides a nucleic acid molecule encoding any one of the polypeptides disclosed herein, preferably encoding the amino acid sequence of SEQ ID NO:1-12.

In one aspect, the present disclosure provides an expression vector comprising the nucleic acid molecule disclosed herein operatively linked to a suitable control sequence.

In one aspect, the present disclosure provides a cell comprising any one of the polypeptide, the nanoparticle, the composition, the nucleic acid, and/or the expression vector disclosed herein.

In one aspect, the present disclosure provides a pharmaceutical composition comprising (a) any one of the polypeptide, the nanoparticle, the composition, the nucleic acid, the expression vector, and/or the cell disclosed herein; and (b) a pharmaceutically acceptable carrier.

In one aspect, the present disclosure provides a vaccine comprising any one of the polypeptide, the nanoparticle, the composition, the nucleic acid, and/or the composition disclosed herein.

In one aspect, the present disclosure provides a kit, comprising:

- (a) a nucleic acid encoding any one of the polypeptide disclosed herein, preferably wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1 or 5; and
- (b) a nucleic acid encoding first protein comprising an amino acid sequence at least at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or absent, preferably wherein the first protein comprises the amino acid sequence of SEQ ID NO:155.

In one aspect, the present disclosure provides a kit, comprising:

(a) an expression vector comprising a nucleic acid encoding any one of the polypeptide disclosed herein operatively linked to a suitable control sequence, preferably wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1 or 5; and

5 (b) an expression vector comprising a nucleic acid encoding first protein comprising an amino acid sequence at least at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or absent, wherein the nucleic acid is operatively linked to a suitable control
10 sequence, preferably wherein the first protein comprises the amino acid sequence of SEQ ID NO:155.

In one aspect, the present disclosure provides a kit, comprising:

(a) a cell comprising an expression vector, wherein the expression vector comprises a nucleic acid encoding any one of the polypeptide disclosed herein operatively
15 linked to a suitable control sequence, preferably wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1 or 5; and

(b) a cell comprising an expression vector, wherein the expression vector comprises a nucleic acid encoding first protein comprising an amino acid sequence at least at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%
20 identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or absent, wherein the nucleic acid is operatively linked to a suitable control sequence, preferably wherein the first protein comprises the amino acid sequence of SEQ ID NO:155.

In another example, the disclosure provides methods to treat or limit development of a
25 SARS-CoV-2 infection, comprising administering to a subject in need thereof an amount effective to treat or limit development of the infection the polypeptide, nanoparticle, composition, nucleic acid, pharmaceutical composition, or vaccine disclosed herein. In one aspect, the present disclosure provides use of any one of the polypeptide, nanoparticle, composition, nucleic acid, pharmaceutical composition, or vaccine disclosed herein in the
30 manufacture of a medicament for treating or limiting development of a SARS-CoV-2 infection in a subject in need thereof.

Description of the Figures

Figure 1 (A-H). Design, *In Vitro* Assembly, and Characterization of SARS-CoV-2
35 **RBD Nanoparticle Immunogens** (A) Molecular surface representation of the SARS-CoV-2 S-2P trimer in the prefusion conformation (PDB 6VYB). Each protomer is colored distinctly, and N-linked glycans are rendered dark blue (the glycan at position N343 was modeled based on PDB 6WPS and the receptor-binding motif (RBM) was modeled from PDB 6M0J). The single open RBD is boxed. (B) Molecular surface representation of the SARS-CoV-2 S RBD,
40 including the N-linked glycans at positions 331 and 343. The ACE2 receptor-binding site or RBM is indicated with a black outline. (C) Structural models of the trimeric RBD-I53-50A (RBD in light blue and I53-50A in light gray) and pentameric I53-50B (orange) components.

We claim:

1. A polypeptide comprising an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequence
5 selected from the group consisting of SEQ ID NOS: 1-84, 138-146, and 167-184, wherein X1 is absent or is an amino acid linker, and wherein residues in parentheses are optional and may be present or some or all of the optional residues may be absent.
2. The polypeptide of claim 1, comprising the amino acid sequence selected from
10 the group consisting of SEQ ID NOS:1-12 and 142-151.
3. The polypeptide of claim 1, comprising the amino acid sequence selected from the group consisting of SEQ ID NOS: 1-8.
- 15 4. The polypeptide of claim 1, comprising the amino acid sequence selected from the group consisting of SEQ ID NOS: 1-4
5. The polypeptide of claim 1, comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:5-8.
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6. The polypeptide of claim 1, comprising the amino acid sequence selected from the group consisting of SEQ ID NOS:1 and 5.
7. The polypeptide of claim 1, comprising the amino acid sequence of SEQ ID
25 NO:1.
8. The polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:5.
- 30 9. A nanoparticle comprising a plurality of polypeptides according to any one of claims 1-8.
10. A nanoparticle, comprising:

(a) a plurality of first assemblies, each first assembly comprising a plurality of identical first proteins; and,

5 (b) a plurality of second assemblies, each second assembly comprising a plurality of second proteins;

wherein the amino acid sequence of the first protein differs from the sequence of the second protein;

wherein the plurality of first assemblies non-covalently interact with the plurality of second assemblies to form the nanoparticle; and

10 wherein the nanoparticle displays on its surface an immunogenic portion of a SARS-CoV-2 antigen or a variant or homolog thereof, present in the at least one second protein.

11. The nanoparticle of claim 10, wherein the second proteins comprise an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least
15 100% identical to the amino acid sequence selected from the group consisting of SEQ ID NOS:85-124 or 185-193, wherein X1 for at least one second protein comprises an immunogenic portion of a SARS-CoV-2 antigen or a variant or homolog thereof, X2 is absent or an amino acid linker, and residues in parentheses are optional.

20 12. The nanoparticle of claim 11, wherein the second proteins comprise the amino acid sequence selected from the group consisting of SEQ ID NOS:85-88.

13. The nanoparticle of claim 11, wherein the second proteins comprise the amino acid sequence selected from the group consisting of SEQ ID NO:85-86.

25 14. The nanoparticle of claim 11, wherein the second proteins comprise the amino acid sequence of SEQ ID NO:85.

15. The nanoparticle of any one of claims 11-14, wherein X1 in at least 20%,
30 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprises an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to a Spike (S) protein extracellular domain (ECD) amino acid sequence, an S1 subunit amino acid sequence, an S2 subunit amino acid

sequence, an S1 receptor binding domain (RBD) amino acid sequence, and/or an N-terminal domain (NTD) amino acid sequence, from SARS-CoV-2, or a variant or homolog thereof.

16. The nanoparticle of any one of claims 11-15, wherein X1 in at least 20%,
5 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprises an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NO:125-137.

10 17. The nanoparticle of any one of claims 11-16, wherein X1 in at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprises an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to the amino acid sequence of SEQ ID NO:125.

15 18. The nanoparticle of claim 17, wherein:

(a) X1 in at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprise mutations at 1, 2, 3, 4, 5, 6, 7, or all 8 positions relative to SEQ ID NO:125 selected from the group consisting of K90N, K90T, G119S, Y126F, T151I, E157K,
20 E157A, S167P, N174Y, and L125R, including but not limited to mutations comprising one of the following naturally occurring mutations or combinations of mutations:

N174Y (UK variant);

K90N/E157K/N174Y (South African variant);

K90N or T/E157K/N174Y (Brazil variant); or

25 L125R (LA variant).; or

(b) X1 in at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprise mutations at 1, 2, 3, 4, 5, 6, 7, or all 8 positions relative to SEQ ID NO:130 selected from the group consisting of L18F, T20N, P26S, deletion of residues 69-70, D80A, D138Y, R190S, D215G, K417N, K417T, G446S, L452R, Y453F, T478I, E484K,
30 S494P, N501Y, A570D, D614G, H655Y, P681H, A701V, T716L including but not limited to mutations comprising one of the following naturally occurring mutations or combinations of mutations:

N501Y, optionally further including 1, 2, 3, 4, or 5 of deletion of one or both of residues 69-70, A570D, D614G, P681H, and/or T716L (UK variant);

K417N/E484K/N501Y, optionally further including 1, 2, 3, 4, or 5 of L18F, D80A, D215G, D614G, and/or A701V (South African variant);

5 K417N or T/E484K/N501Y, optionally further including 1, 2, 3, 4, or 5 of L18F, T20N, P26S, D138Y, R190S, D614G, and/or H655Y (Brazil variant); or L452R (LA variant).

19. The nanoparticle of claim 17, wherein X1 in at least 20%, 30%, 40%, 50%,
10 60%, 70%, 80%, 90%, or 100% of the second proteins comprise 1, 2, 3, or all 4 mutations relative to SEQ ID NO:125 selected from the group consisting of K90N, K90T, E157K, and N174Y.

20. The nanoparticle of any one of claims 11-19, wherein X1 in at least 20%,
15 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprises the amino acid sequence of SEQ ID NO:125.

21. The nanoparticle of any one of claims 11-20, wherein X1 in 100% of the
20 second proteins comprises the amino acid sequence of SEQ ID NO:125, and all second proteins are identical.

22. The nanoparticle of any one of claims 10-21, wherein the plurality of second assemblies in total comprise 2, 3, 4, 5, 6, 7, 8, or more different SARS-CoV-2 antigens.

23. The nanoparticle of any one of claims 10-22, wherein the plurality of second
25 assemblies in total comprise 2, 3, 4, 5, 6, 7, 8, or more polypeptides comprising the amino acid sequence of the polypeptide of any one of claims 1-8.

24. The nanoparticle of any one of claims 10-23, wherein all second assemblies
30 comprise at least one second protein comprising the amino acid sequence of the polypeptide of any one of claims 1-8.

25. The nanoparticle of any one of claims 10-24, wherein all second proteins comprise the amino acid sequence of the polypeptide of any one of claims 1-8.

26. The nanoparticle of any one of claims 10-25, wherein the first protein comprises an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or some or all of the optional residues may be absent.

27. The nanoparticle of any one of claims 10-26, wherein the first protein comprises an amino acid sequence at least at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159.

28. The nanoparticle of any one of claims 10-27, wherein the first protein comprises the amino acid sequence of SEQ ID NO:155.

29. The nanoparticle of claim 28, wherein the at least one second assembly comprises at least one second protein comprising the amino acid sequence selected from the group consisting of SEQ ID NO:85-88.

30. The nanoparticle of claim 28, wherein all second assemblies comprise at least one second protein comprising the amino acid sequence selected from the group consisting of SEQ ID NO:85-88.

31. The nanoparticle of claim 28, wherein all second proteins comprise the amino acid sequence selected from the group consisting of SEQ ID NO:85-88.

32. The nanoparticle of any one of claims 10-31, wherein each first assembly is pentameric and each second assembly is trimeric.

33. The nanoparticle of any one of claims 10-32, wherein:

(a) the first protein comprises the amino acid sequence of SEQ ID NO:155;

- (b) all second proteins comprise the amino acid sequence of SEQ ID NO:85, wherein X1 in at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprise an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to the amino acid sequence of SEQ ID NO:125.
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34. The nanoparticle of any one of claims 10-33, wherein:
- (a) the first protein comprises the amino acid sequence of SEQ ID NO:155;
- (b) all second proteins comprise the amino acid sequence of SEQ ID NO:85,
- 10 wherein X1 in at least 50%, 60%, 70%, 80%, 90%, or 100% of the second proteins comprise an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to the amino acid sequence of SEQ ID NO:125.
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35. The nanoparticle of any one of claims 10-34, wherein:
- (a) the first protein comprises the amino acid sequence of SEQ ID NO:155;
- (b) all second proteins comprise the amino acid sequence selected from the group consisting of SEQ ID NO:1-8.
- 20
36. The nanoparticle of any one of claims 10-35, wherein:
- (a) the first protein comprises the amino acid sequence of SEQ ID NO:155;
- (b) all second proteins comprise the amino acid sequence of SEQ ID NO:1 or 5.
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37. A composition, comprising a plurality of nanoparticles of any one of claims 10-36, preferably comprising a plurality of the nanoparticles of any one of claims 33-36.
38. A nucleic acid molecule encoding the polypeptide of any one of claims 1-8, preferably encoding the amino acid sequence of SEQ ID NO:1-12.
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39. The nucleic acid molecule of claim 42, wherein the polynucleotide comprises an mRNA.

40. An expression vector comprising the nucleic acid molecule of claim 38 or 39 operatively linked to a suitable control sequence.
41. A cell comprising the polypeptide, the nanoparticle, the composition, the nucleic acid, and/or the expression vector of any preceding claim.
42. A pharmaceutical composition comprising
- (a) the polypeptide, the nanoparticle, the composition, the nucleic acid, the expression vector, and/or the cell of any preceding claim; and
- (b) a pharmaceutically acceptable carrier.
43. The pharmaceutical composition of claim 46, comprising a plurality of the nanoparticles of any one of claims 33-36.
44. The composition or the pharmaceutical composition of any preceding claim, further comprising an adjuvant.
45. A vaccine comprising the polypeptide, the nanoparticle, the composition, the nucleic acid, and/or the composition of any preceding claim.
46. The vaccine of claim 45, comprising a plurality of the nanoparticles of any one of claims 33-36.
47. Use of the polypeptide, nanoparticle, composition, nucleic acid, pharmaceutical composition, or vaccine of any preceding claim in the manufacture of a medicament for treating or limiting development of a SARS-CoV-2 infection in a subject in need thereof.
48. The use of claim 47, wherein a plurality of the nanoparticles of any one of claims 33-36, the pharmaceutical composition of claim 43, or the vaccine of claim 46 is to be administered to the subject.
49. The use of claim 47 or 48, wherein the subject is not infected with SARS-CoV-2, wherein an immune response against SARS-CoV-2 is to be elicited in the subject

upon administration of the medicament that limits development of a SARS-CoV-2 infection in the subject.

50. The use of claim 49, wherein a first dose and a second dose are to be administered, wherein the second dose is to be administered about 2 weeks to about 12 weeks, or about 4 weeks to about 12 weeks the first dose is administered.

51. The use of claim 50, wherein

(a) a prime dose of a DNA, mRNA, or adenoviral vector vaccine is to be administered to the subject, wherein the DNA, mRNA, or adenoviral vector vaccine encodes an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to the amino acid sequence of SEQ ID NO:125-137; and

(b) a boost dose of the polypeptide, nanoparticle, composition, nucleic acid, pharmaceutical composition, or vaccine of any preceding claim is to be administered to the subject.

52. The use of claim 50, wherein

(a) a prime dose of the polypeptide, nanoparticle, composition, nucleic acid, pharmaceutical composition, or vaccine of any preceding claim is to be administered to the subject; and

(b) a boost dose of a DNA, mRNA, or adenoviral vector vaccine, wherein the DNA, mRNA, or adenoviral vector vaccine encodes an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to the amino acid sequence of SEQ ID NO:125-137 is to be administered to the subject.

53. The use of any one of claims 47-52, wherein the immune response comprises generation of neutralizing antibodies against SARS-CoV-2.

54. The use of any one of claims 47-53, wherein the immune response comprises generation of SARS-CoV-2 spike protein antibody-specific responses with a mean geometric titer of at least 1×10^5 .

55. The use of any one of claims 47-48 or 53-54, wherein the subject is infected with a severe acute respiratory (SARS) virus, including but not limited to SARS-CoV-2, wherein an immune response against the SARS virus is to be elicited in the subject upon administration of the medicament that treats a SARS virus infection in the subject.

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56. A kit, comprising:

(a) the polypeptide of any one of claims 1-8, preferably wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1 or 5; and

(b) a first protein comprising an amino acid sequence at least at least 75%,
10 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or absent, preferably wherein the first protein comprises the amino acid sequence of SEQ ID NO:155.

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57. A kit, comprising:

(a) a nucleic acid encoding the polypeptide of any one of claims 1-8, preferably wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1 or 5; and

(b) a nucleic acid encoding first protein comprising an amino acid
sequence at least at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%,
20 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or absent, preferably wherein the first protein comprises the amino acid sequence of SEQ ID NO:155.

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58. A kit, comprising:

(a) an expression vector comprising a nucleic acid encoding the polypeptide of any one of claims 1-8 operatively linked to a suitable control sequence, preferably wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1 or 5; and

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(b) an expression vector comprising a nucleic acid encoding first protein comprising an amino acid sequence at least at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or absent, wherein the nucleic acid is operatively linked to a suitable control

sequence, preferably wherein the first protein comprises the amino acid sequence of SEQ ID NO:155.

59. A kit, comprising:

- 5 (a) a cell comprising an expression vector, wherein the expression vector comprises a nucleic acid encoding the polypeptide of any one of claims 1-8 operatively linked to a suitable control sequence, preferably wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:1 or 5; and
- 10 (b) a cell comprising an expression vector, wherein the expression vector comprises a nucleic acid encoding first protein comprising an amino acid sequence at least at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence selected the group consisting of SEQ ID NOS:152-159, wherein residues in parentheses are optional and may be present or absent, wherein the nucleic acid is operatively linked to a suitable control sequence, preferably wherein the first
- 15 protein comprises the amino acid sequence of SEQ ID NO:155.