CLAIMS:

1. A structurally-stabilized peptide comprising an amino acid sequence that is at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 94% identical to sequence set forth in SEQ ID NO: 6 (DISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGK), wherein amino acids at positions of SEQ ID NO: 6 selected from (wherein position 1 is the N-terminal Aspartic Acid and position 38 is the C-terminal Lysine of SEQ ID NO: 6):

(i) positions 14 and 21,

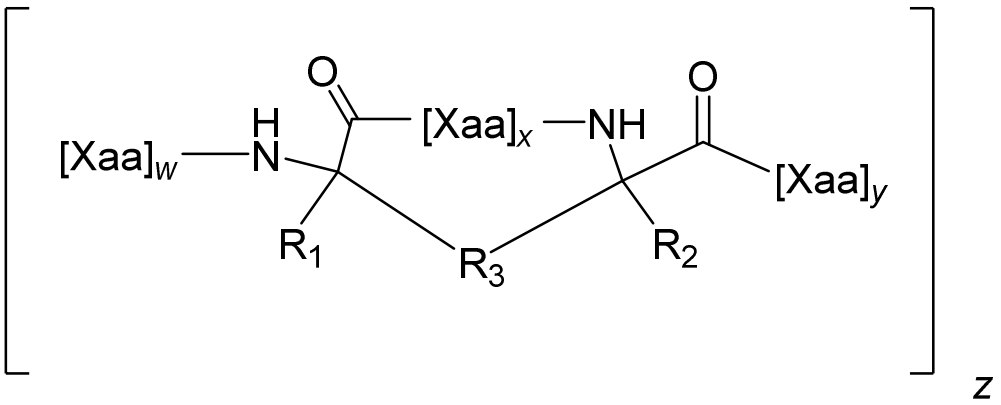
(ii) positions 17 and 24,

(iii) positions 21 and 28, or

(iv) positions 24 and 31;

are replaced by α, α-disubstituted non-natural amino acids with olefinic side chains; wherein the structurally-stabilized peptide is 38 to 60 amino acids in length, optionally 38 to 50 amino acids in length; and wherein the structurally-stabilized peptide inhibits infection of a cell by SARS-CoV-2 in SARS-CoV-2 pseudovirus and/or live SARS-CoV-2 virus assays and/or wherein the structurally-stabilized peptide prevents infection of a cell by SARS-CoV-2 in the SARS-CoV-2 pseudovirus and/or the live SARS-CoV-2 virus assays, optionally wherein the amino acid sequence comprises or consists of the amino acid sequence of any one of SEQ ID NOs: 10, 13, 17, and 20.

2. A structurally-stabilized peptide comprising the formula:



Formula (I),

or a pharmaceutically acceptable salt thereof, wherein:

each R_1 and R_2 is H or a C_1 to C_{10} alkyl, alkenyl, alkynyl, arylalkyl, cycloalkylalkyl, heteroarylalkyl, or heterocyclylalkyl, any of which is substituted or unsubstituted;

each R_3 is independently alkane alkylene, alkenylene, or alkynylene, any of which is substituted or unsubstituted;

z is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

(a) each $[Xaa]_w$ is DISGINASVVNIQ (SEQ ID NO: 35), each $[Xaa]_x$ is EIDRLN (SEQ ID NO: 36), and each $[Xaa]_y$ is VAKNLNESLIDLQELGK (SEQ ID NO: 37);

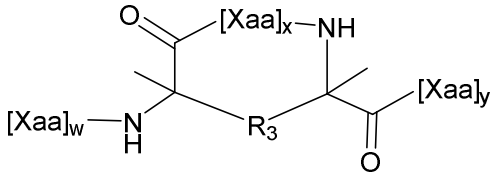
(b) each $[Xaa]_w$ is DISGINASVVNIQKEI (SEQ ID NO: 44), each $[Xaa]_x$ is RLNEVA (SEQ ID NO: 45), and each $[Xaa]_y$ is NLNESLIDLQELGK (SEQ ID NO: 46);

(c) each $[Xaa]_w$ is DISGINASVVNIQKEIDRLN (SEQ ID NO: 56), each $[Xaa]_x$ is VAKNLN (SEQ ID NO: 57), and each $[Xaa]_y$ is SLIDLQELGK (SEQ ID NO: 58); or

(d) each $[Xaa]_w$ is DISGINASVVNIQKEIDRLNEVA (SEQ ID NO: 65), each $[Xaa]_x$ is NLNESL (SEQ ID NO: 66), and each $[Xaa]_y$ is DLQELGK (SEQ ID NO: 67);

and wherein the structurally-stabilized peptide inhibits infection of a cell by SARS-CoV-2 in SARS-CoV-2 pseudovirus and/or live SARS-CoV-2 virus assays and/or wherein the structurally-stabilized peptide prevents infection of a cell by SARS-CoV-2 in the SARS-CoV-2 pseudovirus and/or the live SARS-CoV-2 virus assays.

3. The structurally stabilized peptide or the pharmaceutically acceptable salt thereof of claim 2 comprising Formula I-A, wherein Formula I-A is defined by:



or a pharmaceutically acceptable salt thereof;

R_3 is $-(CH_2)_6-CH=CH-(CH_2)_3$;

(a) $[Xaa]_w$ is DISGINASVVNIQ (SEQ ID NO: 35); $[Xaa]_x$ is EIDRLN (SEQ ID NO: 36); and $[Xaa]_y$ is VAKNLNESLIDLQELGK (SEQ ID NO: 37);

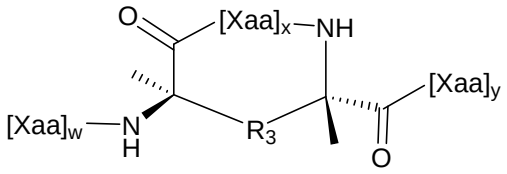
(b) $[Xaa]_w$ is DISGINASVVNIQKEI (SEQ ID NO: 44), $[Xaa]_x$ is RLNEVA (SEQ ID NO: 45), and $[Xaa]_y$ is NLNESLIDLQELGK (SEQ ID NO: 46);

(c) $[Xaa]_w$ is DISGINASVVNIQKEIDRLN (SEQ ID NO: 56), $[Xaa]_x$ is VAKNLN (SEQ ID NO: 57), and $[Xaa]_y$ is SLIDLQELGK (SEQ ID NO: 58); or

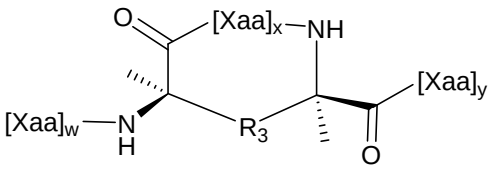
(d) $[Xaa]_w$ is DISGINASVVNIQKEIDRLNEVA (SEQ ID NO: 65), $[Xaa]_x$ is NLNESL (SEQ ID NO: 66), and $[Xaa]_y$ is DLQELGK (SEQ ID NO: 67);
wherein the amino group of the N-terminal aspartic acid in $[Xaa]_w$ is replaced with -N(H)C(O)CH_3, and the carboxylic acid group of the C-terminal lysine in $[Xaa]_y$ is replaced with -C(O)NH_2.

4. The structurally stabilized peptide or the pharmaceutically acceptable salt thereof of claim 3, wherein the structurally stabilized peptide or the pharmaceutically acceptable salt thereof consists of Formula I-A.

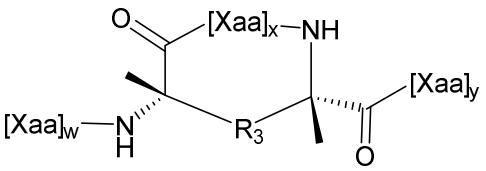
5. The structurally stabilized peptide or the pharmaceutically acceptable salt thereof of claim 3, wherein the structurally stabilized peptide comprises or consists of:



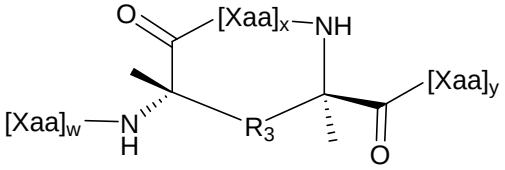
Formula Ia; or



Formula (Ib); or



Formula (Ic); or



Formula (Id);

or a pharmaceutically acceptable salt thereof.

6. The structurally-stabilized polypeptide of claim 1, wherein the structurally-stabilized polypeptide comprises the amino acid sequence set forth in SEQ ID NO: 10 (DISGINASVVNIQ**8**EIDRLN**X**VAKNLNESLIDLQELGK), or variant thereof in which there is one amino acid substitution in SEQ ID NO:10, wherein **8** is a (R)-α-(7′-octenyl)alanine group, and **X** is a (S)-α-(4′-pentenyl)alanine group.

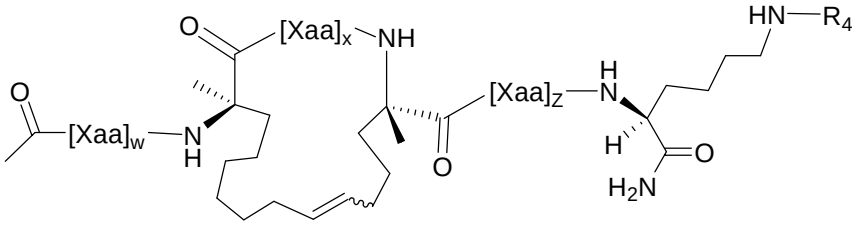
7. The structurally-stabilized polypeptide of claim 1 or claim 6 wherein

(a) the structurally-stabilized polypeptide is 38 to 45 amino acids in length; or

(b) the structurally-stabilized polypeptide is 38 to 40 amino acids in length.

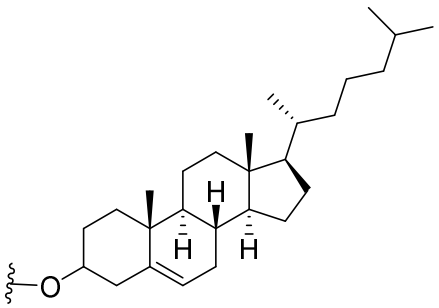
8. The structurally-stabilized polypeptide of any one of claims 1 and 6-7, wherein positions 37 and/or 38 of SEQ ID NO: 6 are not substituted.

9. A structurally stabilized peptide conjugate represented by Formula VI or a pharmaceutically acceptable salt thereof, wherein Formula VI is defined by:



wherein

R_4 is -C(O)-(CH_2CH_2)-[O-CH_2CH_2]$_8$-N(H)C(O)-(CH_2)-R_6;

R_6 is 

;

$[Xaa]_w$ is DISGINASVVNIQ (SEQ ID NO: 35);

$[Xaa]_x$ is EIDRLN (SEQ ID NO: 36); and

$[Xaa]_z$ is VAKNLNESLIDLQELG (SEQ ID NO: 77).

10. A conjugate comprising

(i) the structurally-stabilized polypeptide of any one of claims 1 and 6-8 and a polyethylene glycol (PEG) and/or a cholesterol, wherein the PEG and/or cholesterol are linked to the C-terminus of the structurally-stabilized polypeptide; or

(ii) the structurally-stabilized peptide or pharmaceutically acceptable salt thereof of any one of claims 2 to 6 and PEG and/or cholesterol;

optionally wherein the conjugate (i) or (ii) comprises PEG and cholesterol.

11. The conjugate of claim 10, wherein

(a) the cholesterol is thiocholesterol; or

(b) the conjugate comprises PEG(n)-cholesterol, wherein n is 1-36, optionally wherein n is 4, 5, 6, 7, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, or 36.

12. The conjugate of any one of claims 10 to 11, wherein the conjugate comprises:

(i) PEG(n)-thiocholesterol, wherein n is 2-36, optionally wherein n is 4, 5, 6, 7, 8, 10, 12, 14, 16,18, 20, 22, 24, 26, 28, 30, 32, 34, or 36 according to the conjugate of claim 10; or

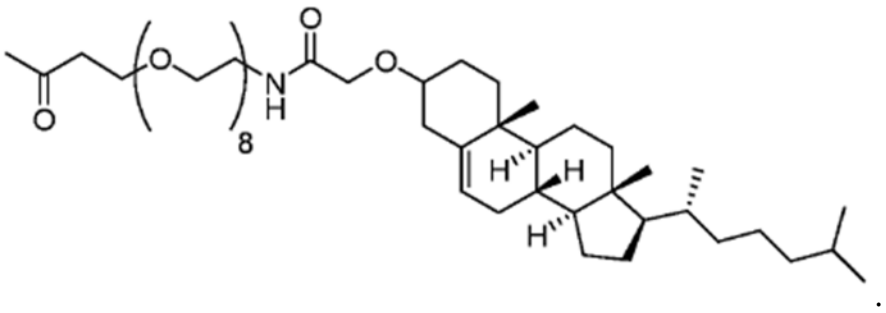
(ii) PEG(n)-thiocholesterol, wherein n is 1-36, optionally wherein n is 4, 5, 6, 7, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, or 36 according to the conjugate of claim 10.

13. A conjugate comprising:

a structurally-stabilized peptide of SEQ ID NO: 10 (DISGINASVVNIQ**8**EIDRLN**X**VAKNLNESLIDLQELGK), wherein **8** is a (R)-α-(7′-octenyl)alanine group, and **X** is a (S)-α-(4′-pentenyl)alanine group; and

a PEG(8)-cholesterol moiety linked to the C-terminal lysine of the structurally-stabilized peptide,

optionally wherein the PEG(8)-cholesterol moiety comprises the formula:



14. A pharmaceutical compound comprising (i) the structurally-stabilized peptide, pharmaceutically acceptable salt thereof, or the conjugate, of any one of claims 1-8 and 10-13, or (ii) the structurally-stabilized peptide conjugate or pharmaceutically acceptable salt thereof of claim 9, and a pharmaceutically acceptable carrier.

15. Use of a structurally-stabilized peptide or a pharmaceutically acceptable salt thereof, a conjugate, a structurally-stabilized peptide conjugate or a pharmaceutically acceptable salt thereof, or a pharmaceutical compound of any one of claims 1 to 14 in the manufacture of a medicament for treating or preventing a coronavirus infection in a human subject in need thereof, wherein a therapeutically-effective amount of the structurally-stabilized peptide or the pharmaceutically acceptable salt thereof, the conjugate, the structurally-stabilized peptide conjugate or the pharmaceutically acceptable salt thereof, or the pharmaceutical compound of any one of claims 1 to 14 is to be administered to said human subject, optionally wherein the structurally-stabilized peptide or the pharmaceutically acceptable salt thereof, the conjugate, the structurally-stabilized peptide conjugate or the pharmaceutically acceptable salt thereof, or the pharmaceutical compound is to be administered to the human subject intranasally.

16. The use of claim 15, wherein the coronavirus infection is caused by

(a) a betacoronavirus;

(b) SARS-CoV-2; and/or

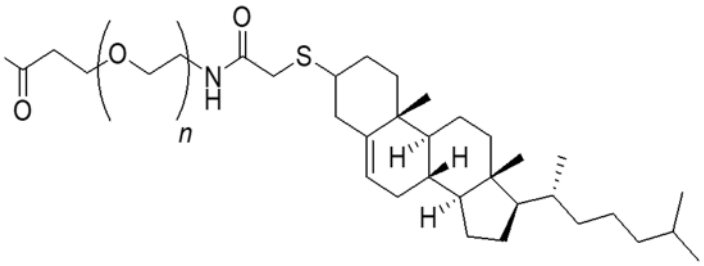
(c) a variant of SARS-CoV-2, optionally wherein the variant is selected from Wuhan-Hu-1, B.1.427/B.1.429, B.1.617.2, D614G B.1, Brazilian variant P.1, B.1.1.7, B.1.351, B.1.525, B.1.526, B.1.617.1, B.1.617.3, P.2, B.1.621, B.1.621.1, B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4 and BA.5, further optionally wherein the variant is selected from B.1.351,

Cluster 5, Lineage B.1.1.207, Lineage B.1.1.7, Variant of Concern 202102/02, Lineage B.1.1.317, Lineage B.1.1.318, Lineage B.1.351, Lineage B.1.429, Lineage B.1.525, Lineage P.1 (also known as Lineage B.1.1.28), Lineage B.1.1.529, Lineage BA.1, Lineage BA.1.1, Lineage BA.2, Lineage BA.3, Lineage BA.4 Lineage BA.5, D614G, E484K, N501Y, S477G/N, and P681H.

17. A nanoparticle composition comprising the structurally-stabilized peptide or the pharmaceutically acceptable salt thereof, the structurally-stabilized peptide conjugate or the pharmaceutically acceptable salt thereof, or the conjugate of any one of claims 1 to 13, optionally wherein the nanoparticle composition is a PLGA nanoparticle, and further optionally, wherein the nanoparticle composition comprises a lactic acid:glycolic acid ratio of the PLGA nanoparticle in the range of 2:98 to 100:0, optionally wherein the nanoparticle composition further comprises chitosan, a dextrin, or both.

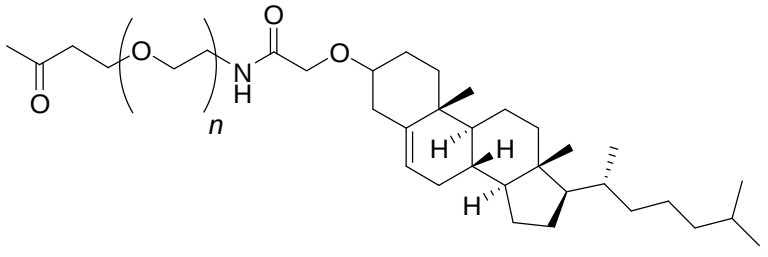
18. A linker comprising:

(i) a PEG(n)-thiocholesterol comprising the formula:



, or

(ii) a PEG(n)-cholesterol comprising the formula:



,

wherein n is 1-36, optionally wherein n is 4, 5, 6, 7, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, or 36, and/or further comprising a lysine affixed to the PEG.

19. A structurally-stabilized peptide or a pharmaceutically acceptable salt thereof, a conjugate, a structurally-stabilized peptide conjugate or a pharmaceutically acceptable salt thereof, or a pharmaceutical compound of any one of claims 1 to 14, for use in therapy.