

POLYPEPTIDES TARGETING SARS-COV-2 AND RELATED COMPOSITIONS AND METHODS

Field

The present invention relates to polypeptides. In particular, the present invention relates to SARS-CoV-2-specific polypeptides and related constructs, compositions, and methods.

Background

Nanoparticles have contributed to advancements in various disciplines. Their use has the potential to confer targeted delivery and allows the engineering of ordered micro-arrays, slow release and caged micro-environments for catalytic processes.

For the fabrication of nanoparticles that contain sensitive and metastable proteins, protein self-assembly is an attractive method. Indeed, self-assembled nanoparticles form under physiological conditions through non-covalent interactions and reliably yield uniform and often symmetric nanocapsules or nanocages.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the strain of coronavirus that causes coronavirus disease 2019 (COVID-19), the respiratory illness responsible for the COVID-19 pandemic.

A need exists for improved compositions and methods for treating and/or preventing SARS-CoV-2.

Summary of the Invention

In accordance with an aspect, there is provided a fusion protein comprising a nanocage monomer linked to a SARS-CoV-2 binding moiety, wherein a plurality of the fusion proteins self-assemble to form a nanocage.

In an [aspectexample](#), the SARS-CoV-2 binding moiety targets the SARS-CoV-2 S glycoprotein.

In an [aspectexample](#), the SARS-CoV-2 binding moiety decorates the interior and/or exterior surface, preferably the exterior surface, of the assembled nanocage.

In an [aspectexample](#), the SARS-CoV-2 binding moiety comprises an antibody or fragment thereof.

In an [aspectexample](#), the antibody or fragment thereof comprises a Fab fragment.

In an [aspectexample](#), the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domains or a combination thereof.

In an [aspectexample](#), the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an [aspectexample](#), the SARS-CoV-2 binding moiety comprises single chain variable domain VHH-72, BD23 and/or 4A8.

In an [aspectexample](#), the SARS-CoV-2 binding moiety comprises an mAb listed in Table 4.

In an [aspectexample](#), the SARS-CoV-2 binding moiety comprises mAb 298, 324, 46, 80, 52, 82, or 236 from Table 4.

In an [aspectexample](#), the SARS-CoV-2 binding moiety is linked at the N- or C-terminus of the nanocage monomer, or wherein there is a first SARS-CoV-2 binding moiety linked at the N-terminus

and a second SARS-CoV-2 binding moiety linked at the C-terminus of the nanocage monomer, wherein the first and second SARS-CoV-2 binding moieties are the same or different.

In an [aspectexample](#), the nanocage monomer comprises a first nanocage monomer subunit linked to the SARS-CoV-2 binding moiety; wherein the first nanocage monomer subunit self-assembles with a second nanocage monomer subunit to form the nanocage monomer.

In an [aspectexample](#), the SARS-CoV-2 binding moiety is linked at the N- or C-terminus of the first nanocage monomer, or wherein there is a first SARS-CoV-2 binding moiety linked at the N-terminus and a second SARS-CoV-2 binding moiety linked at the C-terminus of the first nanocage monomer subunit, wherein the first and second SARS-CoV-2 binding moieties are the same or different.

In an [aspectexample](#), the fusion protein is provided in combination with the second nanocage monomer subunit.

In an [aspectexample](#), the second nanocage monomer subunit is linked to a bioactive moiety.

In an [aspectexample](#), the bioactive moiety comprises an Fc fragment.

In an [aspectexample](#), the Fc fragment is an IgG1 Fc fragment.

In an [aspectexample](#), the Fc fragment comprises one or more mutations, such as LS, YTE, LALA, I253A, and/or LALAP, that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.

In an [aspectexample](#), the Fc fragment is an scFc fragment.

In an [aspectexample](#), from about 3 to about 100 nanocage monomers, such as 24, 32, or 60 monomers, or from about 4 to about 200 nanocage monomer subunits, such as 4, 6, 8, 10, 12, 14, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or more, optionally in combination with one or more whole nanocage monomers, self-assemble to form a nanocage.

In an [aspectexample](#), the nanocage monomer is selected from ferritin, apoferritin, encapsulin, SOR, lumazine synthase, pyruvate dehydrogenase, carboxysome, vault proteins, GroEL, heat shock protein, E2P, MS2 coat protein, fragments thereof, and variants thereof.

In an [aspectexample](#), the nanocage monomer is apoferritin, optionally human apoferritin.

In an [aspectexample](#), the first and second nanocage monomer subunits interchangeably comprise the "N" and "C" regions of apoferritin.

In an [aspectexample](#), the "N" region of apoferritin comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:

MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREGYER
LLKMQNQRGGRALFQDIKKPAEDEV.

In an [aspectexample](#), the "C" region of apoferritin comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:

GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKMGDHLTNLHRL
GGPEAGLGEYLFERLTLRHD

or

GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKMGDHLTNLHRL
GGPEAGLGEYLFERLTLKHD.

In an [aspectexample](#), the fusion protein further comprises a linker between the nanocage monomer subunit and the bioactive moiety.

In an [aspectexample](#), the linker is flexible or rigid and comprises from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

In an [aspectexample](#), the linker comprises a GGS repeat, such as 1, 2, 3, 4, or more GGS repeats.

In an [aspectexample](#), the linker comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:

GGGSGGGSGGGSGGGSGGGSGGGSGG.

In an [aspectexample](#), the fusion protein further comprises a C-terminal linker.

In an [aspectexample](#), a C-terminal linker comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:

GGSGSGSGSGSGSGSGSGSGSGSG

In accordance with an aspect, there is provided a nanocage comprising at least one fusion protein described herein and at least one second nanocage monomer subunit that self-assembles with the fusion protein to form a nanocage monomer.

In an [aspectexample](#), each nanocage monomer comprises the fusion protein described herein.

In an [aspectexample](#), from about 20% to about 80% of the nanocage monomers comprise the fusion protein described herein.

In an [aspectexample](#), the nanocage comprises at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different SARS-CoV-2 binding moieties, such as 3 different SARS-CoV-2 binding moieties.

In an [aspectexample](#), the nanocage is multivalent and/or multispecific.

In an [aspectexample](#), the nanocage comprises one of more mAbs from Table 4.

In an [aspectexample](#), the nanocage comprises 3 mAbs from Table 4.

In an [aspectexample](#), the nanocage comprises mAbs 298, 324, 46, 52, 80, 82 and/or 236 from Table 4.

In an [aspectexample](#), the nanocage comprises a 4:2:1:1: ratio of scFab1-human apoferritin: scFc-human N-Ferritin: scFab2-C-Ferritin: scFab3-C-Ferritin.

In an [aspectexample](#), the nanocage carries a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

In an [aspectexample](#), the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally.

In an [aspectexample](#), the cargo molecule is a protein and is fused to the fusion protein such that the cargo molecule is contained in the nanocage internally.

In an [aspectexample](#), the cargo molecule is a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.

In accordance with an [aspectexample](#), there is provided a tri-specific antibody construct targeting SARS-CoV-2.

In accordance with an aspect, there is provided a SARS-CoV-2 therapeutic or prophylactic composition comprising the nanocage or the antibody described herein.

In accordance with an aspect, there is provided a nucleic acid molecule encoding the fusion protein described herein.

In accordance with an aspect, there is provided a vector comprising the nucleic acid molecule described herein.

In accordance with an aspect, there is provided a host cell comprising the vector described herein and producing the fusion protein described herein.

In one aspect, the present disclosure provides the nanocage as described herein or the composition as described herein for use in therapy. In another aspect, the present disclosure provides a use of the nanocage as described herein or the composition as described herein in the preparation of a medicament for the treatment and/or prevention of SARS-CoV-2.

In accordance with an aspectexample, there is provided a method for treating and/or preventing SARS-CoV-2, the method comprising administering the nanocage or the antibody or the composition described herein.

In accordance with an aspectexample, there is provided a use of the nanocage or the antibody or the composition described herein for treating and/or preventing SARS-CoV-2.

In accordance with an aspectexample, there is provided the nanocage or the antibody or the composition described herein for use in treating and/or preventing SARS-CoV-2.

In accordance with an aspectexample, there is provided a polypeptide comprising an amino acid sequence having at least 70% identity to any sequence listed in the following Table:

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGIS WVRQAPGQGLEWMGWISAYNGNTNYAQKLQGRV TMTRDTSTSTVYMELSSLRSEDTAVYYCARDIGPID YWGQGTLLTVSS	DIQMTQSPSSLSASVGDRVTITCRASQGISSYLAWY QQKPGKAPKLLIYDASNLQSGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQANSFPSTFGQGKVEIK R
EVQLLESGLVQPGGSLRLSCAASGFTFSNYGM HWVRQAPGQGLEWVSGISSAGSITNYADSVKGRFT ISRDNSTNTLYQMNSLRSEDVAVYYCAGNHAGTT VTSEYFQHWGQGTLLTVSS	DIQMTQSPSSLSASVGDRVTITCRASQSISSWLAW YQQKPGKAPKLLIYDTSNLETGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQSYTTPWTFGQGTRLEI KR
QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYHM HWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGR VTMTRDTSTSTVYMELSSLRSEDTAVYYCARDISS WYEITKFDWPWGQGTLLTVSS	EIVMTQSPATLSVSPGERATLSCKASQSVSGTYLA WYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGT EFTLTISSLQSEDFAVYYCLQTHSYPTFGQGKVEI KR
QVQLVQSGAEVKKPGASVKVSCKASGYIFSRYAIH WVRQAPGQGLEWMGMNPISGNTDYAPNFQGRV TMTRDTSTSTVYMELSSLRSEDTAVYYCAKDGSQ AYLVEYFQHWGQGTLLTVSS	DIQMTQSPSSLSASVGDRVTITCRASQVITNNLAWY QQKPGKAPKLLIYDASTLETGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQSYTFPYTFGQGKVEIK R
QVQLVQSGAEVKKPGASVKVSCKASGYTFTHYHM HWVRQAPGQGLEWMGIINPSSSSASYSQKFQGRV TMTRDTSTSTVYMELSSLRSEDTAVYYCARDGRYG SGSYFPDYWGQGTLLTVSS	DIQMTQSPSSLSASVGDRVTITCRASQNISSRYLNWY QQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQANGFPPTFGQGKLEIK R
QVQLVQSGAEVKKPGASVKVSCKASGYTFTGHDM HWVRQAPGQGLEWMGIINPSSGTSYAQKFQGRV TMTRDTSTSTVYMELSSLRSEDTAVYYCARANSLR YYYGMDVWGQGTMTVSS	DIQMTQSPSSLSASVGDRVTITCRASQSVSSWLAW YQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQGYTTPYTFGQGKLEI KR
QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYDIN WVRQAPGQGLEWMGAIMPMFGTANYAQKFQGRV TITADESTSTAYMELSSLRSEDTAVYYCARGSSGY YWGQGTLLTVSS	DIVMTQSPSLPVPVTPGEPASISCRSSQSLLSHNGYN YLDWYLQKPGQSPQLLIYLGSNRASGVDRFSGSG SGTDFTLKISRVEAEDVGVYYCMQALQTPATFGPG TKVDIKR
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAIS WVRQAPGQGLEWMGWINPNSGGANYAQKFQGRV TITADESTSTAYMELSSLRSEDTAVYYCSTYYDSS GYSTDYWGQGTLLTVSS	DIVMTQSPSLPVPVTPGEPASISCRSSQSLLSHNGYN YLDWYLQKPGQSPQLLIYAASSLQSGVPDRFSGSG SGTDFTLKISRVEAEDVGVYYCMQALQTPYTFGQG TKLEIKR
QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYM HWVRQAPGQGLEWMGWINPLNGGTNFAKPFQGR VTMTRDTSTSTVYMELSSLRSEDTAVYYCARDPGG SYSNDAFDIWGQGTLLTVSS	DIQMTQSPSSLSASVGDRVTITCRASQSISSRYLNWY QQKPGKAPKLLIYDASNLQSGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQANSFPLTFGGGKVDIK R
QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYAM HWVRQAPGQGLEWMGRISPRSGGTKYAQRQGR VTITADESTSTAYMELSSLRSEDTAVYYCAREAVAG THPQAGDFDLWGRGTLTVSS	DIVMTQSPSLPVPVTPGEPASISCRSSQSLLSHNGYN YLDWYLQKPGQSPQLLIYAASSLQSGVPDRFSGSG SGTDFTLKISRVEAEDVGVYYCQQYYSSPYTFGQG TKLEIKR

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSSAMH WVRQAPGKGLEWWSAIGTGGDTYYADSVKGRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCAREGDGYNF YFDYWGGGTLTVSS	DIQMTQSPSSLSASVGDRVTITCRASQGISSYLAWY QQKPGKAPKLLIYDASSLQIGVPSRFSGSGSGTDFT LTISSLQPEDFATYYCLQSYSTPPWTFGQGTKVEIK R
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDIN WVRQAPGQGLEWMGMIDPSGGSTSYAQKFQGRV TMTRDTSTSTVYMELSSLRSEDVAVYYCAKDFGGG TRYDYWYFDLWGRGTLTVSS	EIVMTQSPATLSVSPGERATLSCRASQSVSSRYLA WYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGT EFTLTISSLQSEDFAVYYCQQYYTTPRTFGQGTRLE IKR

EVQLLESGGGLVQPGGSLRLSCAASGFPFSQHGM HWVRQAPGKGLEWWSAIDRSGSYIYYADSVKGRFT ISRDN SKNTLYLQMNSLRAEDTAVYYCARDTYGGK VTYFDYWGGQGLTVTVSS	DIQMTQSPSSLSASVGDRVITITCRASQGISHLAWY QQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQTYSTPWTFGQGTKVEIK R
QVQLVQSGAEVKKPGASVKVCKASGGTFSTYGIS WVRQAPGQGLEWMGWISPNSSGGTDLAQKFQGRV TMTTRDTSTSTVYMESSLRSED TAVYYCASDPRDD IAGGYWGQGLTVTVSS	DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNK NYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSG SGSGTDFTLTISSLQAEDVAVYYCQYYSTPPTFG QGKLEIKR
QVQLVQSGAEVKKPGASVKVCKASGGSFSTSAF YWVRQAPGQGLEWMGWINPYTG GTNYAQKFQGR VTMTRDTSTSTVYMESSLRSED TAVYYCARSRAL YSGSYFDYWGGQGLTVTVSS	DIQMTQSPSSLSASVGDRVITITCRASQVISNYLAWY QQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQSFSPPTFGQGTREIK R
EVQLLESGGGLVQPGRLRLSCAASGFTFSSYAMS WVRQAPGKGLEWVSTIYSGGSTYYADSVKGRFTIS RDNSKNTLYLQMNSLRAEDTAVYYCARGDSRDAF DIWGQGTMTVTVSS	DIQMTQSPSSLSASVGDRVITITCRASQSISSWLAW YQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQSYSTPPTFGPGTKVDIK R
QVQLVQSGAEVKKPGASVKVCKASGGTFNNYGIS WVRQAPGQGLEWMGWMNPNSGNTGYAQKFQGR VTMTRDTSTSTVYMESSLRSED TAVYYCARVGDY GDYIVSPFDLWGRGTLTVTVSS	DIQMTQSPSSLSASVGDRVITITCRASQSITTYLNWY QQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQSYSTPPTFGQGTKVEIK R
QVQLVQSGAEVKKPGASVKVCKASGGTFTSYGIN WVRQAPGQGLEWMGWMNPNSGNTGYAQKFQGR VTMTRDTSTSTVYMESSLRSED TAVYYCASRGQL LPRGMDVWGQGTITVTVSS	DIVMTQSPSLPVTTPGEPASISCRSSQSLLSHNGYN YLDWYLLQKPGQSPQLLIYLGSNRASGVPDRFSGSG SGTDFTLKISRVEAEDVGVYYCMQALQTPPTFGQG TRLEIKR
QVQLVQSGAEVKKPGSSVKVCKASGYTFTSYGIS WVRQAPGQGLEWMGGIIPMGFTTNYAQKFQGRVT ITADKSTSTAYMESSLRSED TAVYYCARDRGDTID YWGQGLTVTVSS	DIQMTQSPSSLSASVGDRVITITCRASQGISNNLNW YQQKPGKAPKLLIYAASSLES GVPDRFSGSGSGTD FTLTISSLQPEDFATYYCQQNGFPLTFGPGTKVDI KR
QVQLVQSGAEVKKPGSSVKVCKASGGTFNRYAF SWVRQAPGQGLEWMGGIIPFGTANYAQKFQGRVT ITADESTSTAYMESSLRSED TAVYYCARSTRELPE VVDWYFDLWGRGTLTVTVSS	DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNK NYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSG SGSGTDFTLTISSLQAEDVAVYYCQYY SAPLTFG GGTKVEIKR

or a functional fragment thereof.

In an [aspectexample](#), the polypeptide comprises at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the listed sequence.

In an [aspectexample](#), the polypeptide consists of at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the listed sequence.

In accordance with an [aspectexample](#), there is provided an antibody or fragment thereof comprising the polypeptide described herein.

In accordance with an [aspectexample](#), there is provided a fusion polypeptide comprising (1) a fragment crystallizable (Fc) region linked to (2) a nanocage monomer or subunit thereof, wherein the Fc region comprises the I253A mutation, wherein numbering is according to the EU index.

In an [aspectexample](#), the Fc region further comprises the LALAP (L234A/L235A/P329G) mutations, wherein numbering is according to the EU index.

In an [aspectexample](#), the Fc region is an IgG1 Fc region.

In an [aspectexample](#), the nanocage monomer is a ferritin monomer.

In an [aspectexample](#), the ferritin monomer is a ferritin light chain.

In an [aspectexample](#), the ferritin light chain is a human ferritin light chain.

In an [aspectexample](#), the Fc region is linked via an amino acid linker to the nanocage monomer or subunit thereof.

In an [aspectexample](#), the Fc region is linked to the N-terminus of the nanocage monomer or subunit thereof.

In an [aspectexample](#), the Fc region is a single chain Fc (scFc).

In an [aspectexample](#), the Fc region is an Fc monomer.

In accordance with an [aspectexample](#), there is provided a self-assembled polypeptide complex comprising:

(a) a plurality of first fusion polypeptides, each first fusion polypeptide comprising (1) an Fc region linked to (2) a nanocage monomer or subunit thereof, and

(b) a plurality of second fusion polypeptides, each second fusion polypeptide comprising (1) a SARS-CoV-2-binding antibody fragment linked to (2) a nanocage monomer or subunit thereof.

In an [aspectexample](#), the nanocage monomer is a ferritin monomer.

In an [aspectexample](#), the nanocage monomer is a ferritin light chain.

In an [aspectexample](#), the self-assembled polypeptide complex does not comprise any ferritin heavy chains or subunits of ferritin heavy chains.

In an [aspectexample](#), the nanocage monomer is a human ferritin light chain.

In an [aspectexample](#), the SARS-CoV-2-binding antibody fragment binds to the receptor binding domain or the Spike protein of SARS-CoV-2.

In an [aspectexample](#), the SARS-CoV-2-binding antibody fragment comprises a light chain variable domain and a heavy chain variable domain.

In an [aspectexample](#), the SARS-CoV-2-binding antibody fragment comprises an Fab of an antibody that is capable of binding to SARS-CoV-2.

In an [aspectexample](#), the SARS-CoV-2-binding antibody fragment comprises a VK domain and a VH domain.

In an [aspectexample](#), the self-assembled polypeptide complex is characterized by a 1:1 ratio of first fusion polypeptides to second fusion polypeptides.

In an [aspectexample](#), the Fc region is an IgG1 Fc region.

In an [aspectexample](#), the Fc region is linked to the nanocage monomer or subunit thereof via an amino acid linker.

In an [aspectexample](#), the Fc region is linked to the N-terminus of the nanocage monomer or subunit thereof.

In an [aspectexample](#), the self-assembled polypeptide complex comprises at total of least 24 fusion polypeptides.

In an [aspectexample](#), the self-assembled polypeptide complex comprises a total of at least 32 fusion polypeptides.

In an [aspectexample](#), the self-assembled polypeptide complex has a total of about 32 fusion polypeptides.

In accordance with an [aspectexample](#), there is provided a self-assembled polypeptide complex comprising:

(a) a plurality of first fusion polypeptides, each first fusion polypeptide comprising (1) an IgG1 Fc region linked to (2) a human ferritin monomer or subunit thereof, wherein the IgG1 Fc region comprises the LALAP (L234A/L235A/P329G) and I253A mutations, wherein numbering is according to the EU index, and

(b) a plurality of second fusion polypeptides, each second fusion polypeptide comprising (1) a Fab fragment of an antibody that is capable of binding to a SARS-CoV-2 protein, the Fab fragment being linked to (2) a human ferritin monomer or subunit thereof.

In an aspectexample:

(1) each first fusion polypeptide comprises a ferritin monomer subunit which is C-half-ferritin and each second fusion polypeptide comprises a ferritin monomer subunit which is N-half-ferritin; or

(2) each first fusion polypeptide comprises a ferritin monomer subunit which is N-half-ferritin and each second fusion polypeptide comprises a ferritin monomer subunit which is C-half-ferritin.

In an aspectexample, the self-assembled polypeptide complex is characterized by a 1:1 ratio of first fusion polypeptides to second fusion polypeptides.

In an aspectexample, each first fusion polypeptide comprises a ferritin monomer subunit which is C-half-ferritin.

In an aspectexample, the IgG1 Fc region is linked to the C-half-ferritin via an amino acid linker.

In an aspectexample, the IgG1 Fc region is linked to the C-half-ferritin via the N-terminus of the C-half-ferritin.

In an aspectexample, each second fusion polypeptide comprises a ferritin monomer subunit which is N-half-ferritin.

In an aspectexample, the Fab fragment is linked to the N-half-ferritin via an amino acid linker.

In an aspectexample, the Fab fragment is linked to the N-half-ferritin via the N-terminus of the N-half-ferritin.

In an aspectexample, the self-assembled polypeptide complex further comprises a plurality of third fusion polypeptides, each third fusion polypeptide comprising (1) a human ferritin monomer linked to (2) a Fab fragment of an antibody that is capable of binding to a SARS-CoV-2 protein.

In an aspectexample, the self-assembled polypeptide complex is characterized by a 1:1:2 ratio of first fusion polypeptides to second fusion polypeptides to third fusion polypeptides.

In an aspectexample, the self-assembled polypeptide complex comprises at total of least 24 fusion polypeptides.

In an aspectexample, the self-assembled polypeptide complex comprises a total of at least 32 fusion polypeptides.

In an aspectexample, the self-assembled polypeptide complex has a total of 32 fusion polypeptides.

In an aspectexample, wherein the Fab fragment comprises a VK domain and a VH domain, wherein

(1) the VK domain has an amino acid sequence of SEQ ID NO:11 and the VH domain has an amino acid sequence of SEQ ID NO:12;

(2) the VK domain has an amino acid sequence of SEQ ID NO:17 and the VH domain has an amino acid sequence of SEQ ID NO:18;

(3) the VK domain has an amino acid sequence of the VK within SEQ ID NO:25 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:26;

(4) the VK domain has an amino acid sequence of the VK within SEQ ID NO:27 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:28;

- (5) the VK domain has an amino acid sequence of the VK within SEQ ID NO:29 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:30;
- (6) the VK domain has an amino acid sequence of the VK within SEQ ID NO:31 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:32;
- (7) the VK domain has an amino acid sequence of the VK within SEQ ID NO:33 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:34;
- (8) the VK domain has an amino acid sequence of the VK within SEQ ID NO:35 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:36;
- (9) the VK domain has an amino acid sequence of the VK within SEQ ID NO:37 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:38;
- (10) the VK domain has an amino acid sequence of the VK within SEQ ID NO:39 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:40;
- (11) the VK domain has an amino acid sequence of the VK within SEQ ID NO:41 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:42;
- (12) the VK domain has an amino acid sequence of the VK within SEQ ID NO:43 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:44;
- (13) the VK domain has an amino acid sequence of the VK within SEQ ID NO:45 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:46;
- (14) the VK domain has an amino acid sequence of the VK within SEQ ID NO:47 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:48;
- (15) the VK domain has an amino acid sequence of the VK within SEQ ID NO:49 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:50;
- (16) the VK domain has an amino acid sequence of the VK within SEQ ID NO:51 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:52;
- (17) the VK domain has an amino acid sequence of the VK within SEQ ID NO:53 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:54;
- (18) the VK domain has an amino acid sequence of the VK within SEQ ID NO:55 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:56;
- (19) the VK domain has an amino acid sequence of the VK within SEQ ID NO:57 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:58;
- (20) the VK domain has an amino acid sequence of the VK within SEQ ID NO:59 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:60;
- (21) the VK domain has an amino acid sequence of the VK within SEQ ID NO:61 or SEQ ID NO:62 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:63; or
- (22) the VK domain has an amino acid sequence of the VK within SEQ ID NO:64 and the VH domain has an amino acid sequence of the VH within SEQ ID NO:65.

In an aspectexample, the human ferritin monomer is human ferritin light chain.

In an aspectexample, the self-assembled polypeptide complex does not comprise any ferritin heavy chains or subunits of ferritin heavy chains.

In accordance with an aspectexample, there is provided a method of treating, ameliorating, or preventing a SARS-CoV-2-related condition, the method comprising administering to a subject a composition comprising the self-assembled polypeptide complex described herein.

In an aspectexample, the subject is a mammal.

In an aspectexample, the subject is human.

The novel features of the present inventiondisclosure will become apparent to those of skill in the art upon examination of the following detailed description of the inventiondisclosure. It should be understood, however, that the detailed description of the inventiondisclosure and the specific examples presented, while indicating certain aspectexamples of the present inventiondisclosure, are provided for illustration purposes only because various changes and modifications within the spirit and scope of the inventiondisclosure will become apparent to those of skill in the art from the detailed description of the inventiondisclosure and claims that follow.

Brief Description of the Drawings

The present invention will be further understood from the following description with reference to the Figures, in which:

Figure 1. Avidity enhances binding and neutralization of VHH against SARS-CoV-2.

a Schematic representation of a monomeric VHH domain and its multimerization using a conventional Fc (dark red) scaffold or human apoferritin (gray). **b** Size exclusion chromatography and SDS-PAGE of apoferritin alone (gray) and VHH-72 apoferritin particles (gold). **c** Negative stain electron microscopy of VHH-72 apoferritin particles. (Scale bar 50 nm, representative of two independent experiments). **d** Comparison of the binding avidity (apparent K_D) of VHH-72 to SARS-CoV-2 S protein when displayed in a bivalent (dark red) or 24-mer (gold) format. Bars indicate the mean values of $n = 2$ biologically independent experiments. Apparent K_D lower than 10^{-12} M (dash line) is beyond the instrument detection limit. **e** Neutralization potency against SARS-CoV-2 PsV (color coding is as in **(d)**). One representative out of two biologically independent replicates with similar results is shown. Mean values $\pm$ SD of two technical replicates is represented in the plot. Median IC_{50} values of the two biologically independent replicates are shown.

Figure 2. Binding interfaces of Fabs 52 and 298 and the RBD. Interaction of Fab 298 (**a**) and 52 (**b**) with RBD (light and dark green for the core and RBM regions, respectively) is mediated by complementarity determining regions (CDR) heavy (H) 1 (yellow), H2 (orange), H3 (red), kappa light (K) 1 (light blue) and K3 (purple). Critical binding residues are shown as sticks (insets). H-bonds and salt bridges are depicted as black dashed lines. L and H chains of Fabs are shown in tan and white, respectively. **c**) Bottom and side views of ACE2 (left) and Fab 298 (right) bound to RBD. RBD side-chains that are part of the binding interface of the ACE2-RBD and Fab 298-RBD complexes are depicted in pink, while RBD side-chains unique to a given interface are shown in yellow. Surfaces of ACE2, variable regions of Fab 298 HC and Fab 298 KC are shown in white, grey and tan, respectively. The RBD is colored as in **(a)**. **d**) Superposition of Fabs 46 (light pink) and 52 (dark pink) when bound to the RBD (green) reveals a distinct angle of approach for the two mAbs. Stereo-image of the composite omit map electron density contoured at 1.3 sigma at the interfaces of **e**) 298-RBD and **f**) 52-RBD.

WHAT IS CLAIMED IS:

1. A fusion protein comprising a nanocage monomer linked to a SARS-CoV-2 binding moiety, wherein a plurality of the fusion proteins self-assemble to form a nanocage.
2. The fusion protein of claim 1, wherein the SARS-CoV-2 binding moiety targets the SARS-CoV-2 S glycoprotein.
- ~~3. The fusion protein of claim 1 or 2, wherein the SARS-CoV-2 binding moiety decorates the interior and/or exterior surface, preferably the exterior surface, of the assembled nanocage.~~
- ~~43.~~ The fusion protein of ~~any one of claims 1 to 3~~claim 1, wherein the SARS-CoV-2 binding moiety comprises an antibody or fragment thereof.
- ~~54.~~ The fusion protein of claim ~~42~~, wherein the antibody or fragment thereof comprises a Fab fragment.
- ~~65.~~ The fusion protein of claim 4, wherein the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domains or a combination thereof.
- ~~76.~~ The fusion protein of claim 4, wherein the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.
- ~~87.~~ The fusion protein of any one of claims 4 ~~to 76~~, wherein the SARS-CoV-2 binding moiety comprises single chain variable domain VHH-72, BD23 and/or 4A8.
- ~~98.~~ The fusion protein of any one of claims 4 ~~to 87~~, wherein the SARS-CoV-2 binding moiety comprises an mAb listed in Table 4.
- ~~109.~~ The fusion protein of claim ~~9-8~~ wherein the SARS-CoV-2 binding moiety comprises mAb 298, 324, 46, 80, 52, 82, or 236 from Table 4, or variants thereof.
- ~~10a10.~~ The fusion protein of claim ~~109~~, wherein the SARS-CoV-2 binding moiety comprises mAb 298, 80, and 52 from Table 4, or variants thereof.
11. The fusion protein of any one of claims 1 ~~to 10~~, wherein the SARS-CoV-2 binding moiety is linked at the N- or C-terminus of the nanocage monomer, or wherein there is a first SARS-CoV-2 binding moiety linked at the N-terminus and a second SARS-CoV-2 binding moiety linked at the C-terminus of the

nanocage monomer, wherein the first and second SARS-CoV-2 binding moieties are the same or different.

12. The fusion protein of any one of claims 1-11, wherein the nanocage monomer comprises a first nanocage monomer subunit linked to the SARS-CoV-2 binding moiety; wherein the first nanocage monomer subunit self-assembles with a second nanocage monomer subunit to form the nanocage monomer.

~~13. The fusion protein of claim 12, wherein the SARS-CoV-2 binding moiety is linked at the N- or C-terminus of the first nanocage monomer, or wherein there is a first SARS-CoV-2 binding moiety linked at the N-terminus and a second SARS-CoV-2 binding moiety linked at the C-terminus of the first nanocage monomer subunit, wherein the first and second SARS-CoV-2 binding moieties are the same or different.~~

~~14. The fusion protein of claim 12 or 13, in combination with the second nanocage monomer subunit.~~

~~15. The fusion protein of any one of claims 12 to 14, wherein the second nanocage monomer subunit is linked to a bioactive moiety.~~

~~16. The fusion protein of claim 15, wherein the bioactive moiety comprises an Fc fragment.~~

~~17. The fusion protein of claim 16, wherein the Fc fragment is an IgG1 Fc fragment.~~

~~18. The fusion protein of claim 15 or 16, wherein the Fc fragment comprises one or more mutations, such as LS, YTE, LALA, I253A, and/or LALAP, that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.~~

~~19. The fusion protein of any one of claims 15 to 18, wherein the Fc fragment is an scFc fragment.~~

~~20. The fusion protein of any one of claims 1 to 19, wherein from about 3 to about 100 nanocage monomers, such as 24, 32, or 60 monomers, or from about 4 to about 200 nanocage monomer subunits, such as 4, 6, 8, 10, 12, 14, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, or more, optionally in combination with one or more whole nanocage monomers, self-assemble to form a nanocage.~~

~~21~~13. The fusion protein of any one of claims 1-~~12~~ to 20, wherein the nanocage monomer is selected from ferritin, apoferritin, encapsulin, SOR, lumazine synthase, pyruvate dehydrogenase, carboxysome, vault proteins, GroEL, heat shock protein, E2P, MS2 coat protein, fragments thereof, and variants thereof.

~~22~~14. The fusion protein of claim ~~13~~ 21, wherein the nanocage monomer is apoferritin, optionally human apoferritin.

~~23~~15. The fusion protein of claim ~~13 or 14~~ 22, wherein the first and second nanocage monomer subunits interchangeably comprise the “N” and “C” regions of apoferritin.

~~24. The fusion protein of claim 23, wherein the “N” region of apoferritin comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:~~

~~MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREGYERLLKMQ
NQRGGRALFQDIKKPAEDEW.~~

~~25. The fusion protein of claim 22 or 23, wherein the “C” region of apoferritin comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:~~

~~GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKMGDHLTNLHRLGGPEA
GLGEYLFERLTLRHD~~

~~or~~

~~GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKMGDHLTNLHRLGGPEA
GLGEYLFERLTLKHD.~~

~~2616.~~ The fusion protein of any one of claims 1-~~15 to 25~~, further comprising a linker between the nanocage monomer subunit and the bioactive moiety.

~~2717.~~ The fusion protein of claim ~~1626~~, wherein the linker is flexible or rigid and comprises from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

~~2818.~~ The fusion protein of claim ~~1626~~ or ~~1727~~, wherein the linker comprises a GGS repeat, such as 1, 2, 3, 4, or more GGS repeats.

~~29. The fusion protein of claim 28, wherein the linker comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:~~

~~GGGSGGGSGGGSGGGSGGGSGGGSGG.~~

~~3019.~~ The fusion protein of any one of claims 1-~~18 to 29~~, further comprising a C-terminal linker.

~~31. The fusion protein of claim 30, wherein a C-terminal linker comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:~~

~~GGSGGSGGSGGSGGSGGSGGSGGSGG~~

~~3220.~~ A nanocage comprising at least one fusion protein of any one of claims 1-~~19 to 31~~ and at least one second nanocage monomer subunit that self-assembles with the fusion protein to form a nanocage monomer.

~~3321.~~ The nanocage of claim ~~320~~, wherein each nanocage monomer comprises the fusion protein of any one of claims 1-~~19 to 31~~.

~~34. The nanocage of claim 32 or 33, wherein from about 20% to about 80% of the nanocage monomers comprise the fusion protein of any one of claims 1 to 27.~~

~~3522.~~ The nanocage of ~~any one of claims 32 to 34~~claim 20 or 21, comprising at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different SARS-CoV-2 binding moieties, such as 3 different SARS-CoV-2 binding moieties.

~~3623.~~ The nanocage of any one of claims ~~2032 to 2235~~, wherein the nanocage is multivalent and/or multispecific.

~~3724.~~ The nanocage of any one of claims ~~2032 to 2336~~, comprising one of more mAbs from Table 4.

~~3825.~~ The nanocage of claim ~~2437~~, comprising 3 mAbs from Table 4.

~~3926.~~ The nanocage of claims ~~2437~~ or ~~2538~~ comprising mAbs 298, 324, 46, 52, 80, 82 and/or 236 from Table 4.

~~4027.~~ The nanocage of any one of claims ~~32-20 to 3926~~, comprising a 4:2:1:1: ratio of scFab1-human apoferritin: scFc-human N-Ferritin: scFab2-C-Ferritin: scFab3-C-Ferritin.

~~4128.~~ The nanocage of any one of claims ~~32 to 4020-27~~, carrying a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

~~42. The nanocage of claim 41, wherein the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally.~~

~~43. The nanocage of claim 42, wherein the cargo molecule is a protein and is fused to the fusion protein such that the cargo molecule is contained in the nanocage internally.~~

~~44. The nanocage of any one of claims 41 to 43, wherein the cargo molecule is a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.~~

~~45. A tri-specific antibody construct targeting SARS-CoV-2.~~

~~4629.~~ A SARS-CoV-2 therapeutic or prophylactic composition comprising the nanocage of any one of claims ~~32-20 to 2844~~ or the antibody of claim 45.

~~4730.~~ A nucleic acid molecule encoding the fusion protein of any one of claims 1-~~19 to 31~~.

~~3148.~~ A vector comprising the nucleic acid molecule of claim ~~3047~~.

~~3249.~~ A host cell comprising the vector of claim ~~3148~~ and producing the fusion protein of any one of claims ~~1-19 to 31~~.

~~50.~~ A method for treating and/or preventing SARS-CoV-2, the method comprising administering the nanocage of any one of claims ~~32 to 33~~ or the antibody of claim ~~45~~, or the composition of claim ~~46~~.

~~5331.~~ Use of ~~the~~ the nanocage of any one of claims ~~32-20-28 to 33~~ or the antibody of claim ~~45~~, or the composition of claim ~~2946~~ for ~~treating and/or preventing SARS-CoV-2~~ use in therapy.

~~5234.~~ The Use of the nanocage of any one of claims ~~20-2832 to 33~~ or the antibody of claim ~~45~~, or the composition of claim ~~2946~~ for use in the preparation of a medicament for the treatment and/or prevention of in treating and/or preventing SARS-CoV-2.

~~53.~~ A polypeptide comprising an amino acid sequence having at least 70% identity to any sequence listed in the following Table:

QVQLVQSGAEVKKPGASVKVSCKASGYTFTS YGISWVRQAPGQGLEWMGWISAYNGNTNYA QKLQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARDIGPIDYWGQGTLVTVSS	DIQMTQSPSSLSASVGDRVITTCRASQGISSYL AWYQQKPGKAPKLLIYDASNLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQANSFPS TFGQGTKVEIKR
EVQLLESQGGGLVQPGGSLRLSCAASGFTFSN YGMHWVRQAPGKGLEWVSGISSAGSITNYAD SVKGRFTISRDN SKNTLYLQMNSLRAEDTAVY YCAGNHAGTTVTSEYFQHWGQGTLVTVSS	DIQMTQSPSSLSASVGDRVITTCRASQSISW LAWYQQKPGKAPKLLIYDTSNLETGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQSYTTPW TFGQGTRLEIKR
QVQLVQSGAEVKKPGASVKVSCKASGYTFTD YHMHWVRQAPGQGLEWMGWINPNSGGTNY AQKFQGRVTMTRDTSTSTVYMELSSLRSED AVYYCARDISSWYEITKFDPPWGQGTLVTVSS	EIVMTQSPATLSVSPGERATLSCKASQSVSGT YLAWYQQKPGQAPRLIYGASTRATGIPARFS GSGSGTEFTLTISLQSEDFAVYYCLQTHSYP PTFGQGTKVEIKR
QVQLVQSGAEVKKPGASVKVSCKASGYIFSR YAIHWVRQAPGQGLEWMGWMNPISGNTDYA PNFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCAKDGSQLAYLVEYFQHWGQGTLVTVSS	DIQMTQSPSSLSASVGDRVITTCRASQVITNNL AWYQQKPGKAPKLLIYDASTLETGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQSYTFPYT FGQGTKVEIKR
QVQLVQSGAEVKKPGASVKVSCKASGYTFTH YYMHWVRQAPGQGLEWMGIINPSSSSASYS QKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARDGRYGSQSYFDYWGQGTLVTVSS	DIQMTQSPSSLSASVGDRVITTCRASQNISSYL NWWYQQKPGKAPKLLIYDASNLETGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQANGFPF TFGQGTKLEIKR
QVQLVQSGAEVKKPGASVKVSCKASGYTFTG HDMHWVRQAPGQGLEWMGIINPSSGGSTSYA QKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARANSLRYYYGMDVWGQGTMTVTVSS	DIQMTQSPSSLSASVGDRVITTCRASQSVSSW LAWYQQKPGKAPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQGYTTPY TFGQGTKLEIKR

QVQLVQSGAEVKKPGSSVKVSCKASGYTFTS YDINWVRQAPGQGLEWMGAIMPMEGTANYA QKFQGRVTITADESTSTAYMELSSLRSED TAVYYCARGSSGYYYGWGQGTTLTVSS	DIVMTQSPLSLPVTPGEPASISCRSSQSLH SN GYN YLDWYLQKPGQSPQLLIYLG SNRASGVPRFSGSGSGTDFTLKISR VEAEDVGVYYCMQALQTPATFGPGTK VDIKR
QVQLVQSGAEVKKPGSSVKVSCKASGGTFSS YAIWVRQAPGQGLEWMGWINPNSGGANYA QKFQGRVTITADESTSTAYMELSSLRSED TAVYYCSTYYYDSSGYSTDYWGQGTTL TVSS	DIVMTQSPLSLPVTPGEPASISCRSSQSLH SN GYN YLDWYLQKPGQSPQLLIYAAS SLQSGVPRFSGSGSGTDFTLKISRVEA EDVGVYYCMQALQTPYTFGQGCKLEIKR
QVQLVQSGAEVKKPGASVKVSCKASGYTFTG YYMHWVRQAPGQGLEWMGWINPLNGGTNF APKFQGRVTMTRDTSTSTVYMELSSLRSE DTAVYYCARGDPGGSYSNDAFDIWGQGT LTVSS	DIQMTQSPSSLSASVGDRVTITCRASQSI SRYL N WYQQKPKGKAPKLLIYDASN LESQVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQQANSFPLTFGGGKVDIKR
QVQLVQSGAEVKKPGSSVKVSCKASGYTFTS YAMHWVRQAPGQGLEWMGRISPRSGGTYA QRFQGRVTITADESTSTAYMELSSLRSED TAVYYCAREAVAGTHPQAGDFDLWGRGT LTVSS	DIVMTQSPLSLPVTPGEPASISCRSSQSLH SN GYN YLDWYLQKPGQSPQLLIYAAS SLQSGVPRFSGSGSGTDFTLKISRVEA EDVGVYYCQQYYSSPYTFGQGCKLEIKR
EVQLLESGGGLVQPGGSLRLSCAASGFTFSS SAMHWVRQAPGKGLEWVSAIGTGGDTYYAD SVKGRFTISRDN SKNTLYLQMNSLRAED TAVYYCAREGDGYNFYFDYWGQGTTLTV SS	DIQMTQSPSSLSASVGDRVTITCRASQG ISSYLAWYQQKPKGKAPKLLIYDASSL QIGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCLQSYSTPPWTFGQGCKVEIKR
QVQLVQSGAEVKKPGASVKVSCKASGYTFTS YDINWVRQAPGQGLEWMGMIDPSGGSTSYA QKFQGRVTMTRDTSTSTVYMELSSLRSE DTAVYYCAKDFGGGTRYDYWYFDLWGRGT LTVSS	EIVMTQSPATLSVSPGERATLSCRASQSV SSR YLAWYQQKPGQAPRLLIYGASTRA TGIPARFSGSGSGTEFTLTISSLQSEDF AVYYCQQYYTTPRTFGQGRLEIKR
EVQLLESGGGLVQPGGSLRLSCAASGFPPFSQ HGMHWVRQAPGKGLEWVSAIDRSGSYIYYAD SVKGRFTISRDN SKNTLYLQMNSLRAED TAVYYCARDTYGGKVTFDYWGQGTTLTV SS	DIQMTQSPSSLSASVGDRVTITCRASQG ISSHLAWYQQKPKGKAPKLLIYDASN LETGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQQTYSTPWTFGQGCKVEIKR
QVQLVQSGAEVKKPGASVKVSCKASGGTFST YGISWVRQAPGQGLEWMGWISPNSGGTDLA QKFQGRVTMTRDTSTSTVYMELSSLRSE DTAVYYCASDPRDDIAGGYWGQGTTLTV SS	DIVMTQSPDSLAVSLGERATINCKSSQSV LYS SNNKNYLAWYQQKPGQPPKLLIY WASTRESGVPRFSGSGSGTDFTLTIS SLQAEDVAVYYCQQYYSTPPTFGQGCK LEIKR
QVQLVQSGAEVKKPGASVKVSCKASGGSFST SAFYWVRQAPGQGLEWMGWINPYTGGTNYA QKFQGRVTMTRDTSTSTVYMELSSLRSE DTAVYYCARSRALYGSYSYFDYWGQGT LTVSS	DIQMTQSPSSLSASVGDRVTITCRASQV ISNYLAWYQQKPKGKAPKLLIYDASN LETGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQQSFSPPTFGQGRLEIKR

EVQLLESQGGGLVQPGRSRLSCAASGFTFSS YAMSWVRQAPGKGLEWVSTIYSGGSTYYADS VKGRFTISRDN SKNTLYLQMNSLRAEDTAVYY CARGDSRDAFDIWGQGTMVTVSS	DIQMTQSPSSLSASVGDRVITTCRASQSISSW LAWYQQKPGKAPKLLIYDASNLETGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQSYSTPF TFGPGTKVDIKR
QVQLVQSGAEVKKPGASVKVSKASGGTFNN YGISWVRQAPGQGLEWMGWMNPNSGNTGY AQKFQGRVTMTRDTSTSTVYMELSSLRSED TAVYYCARVGDYGDYIVSPFDLWGRGTLTVS S	DIQMTQSPSSLSASVGDRVITTCRASQSITTYL NWAYQQKPGKAPKLLIYDASNLETGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQSYSTPP TFGQGTKVEIKR
QVQLVQSGAEVKKPGASVKVSKASGGTFTS YGINWVRQAPGQGLEWMGWMNPNSGNTGY AQKFQGRVTMTRDTSTSTVYMELSSLRSED TAVYYCASRGIQLLRGMDVWGQGTITVTVSS	DIVMTQSPSLPVTTPGEPASISCRSSQSLLHSN GYNYL DWYLQKPGQSPQLLIYLGSNRASGVP DRFSGSGSGTDFTLKISRVEAEDVGVYYCMQ ALQTPPTFGQGRLEIKR
QVQLVQSGAEVKKPGSSVKVSKASGYTFTS YGISWVRQAPGQGLEWMGGIIPMFGTTNYAQ KFQGRVTITADKSTSTAYMELSSLRSED TAVYYCARDRGDTIDYWGQGTITVTVSS	DIQMTQSPSSLSASVGDRVITTCRASQGISNN LNWAYQQKPGKAPKLLIYAASSLESQVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQGNGFPL TFGPGTKVDIKR
QVQLVQSGAEVKKPGSSVKVSKASGGTFNR YAFSWVRQAPGQGLEWMGGIIPFGTANYAQ KFQGRVTITADESTSTAYMELSSLRSED TAVYYCARSTRELPEVVDWYFDLWGRGTLTVSS	DIVMTQSPDSLAVSLGERATINCKSSQSVLYS SNNKNYLAWYQQKPGQPPKLLIYWASTRESG VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQ QYYSAPLTFGGGTKVEIKR

or a functional fragment thereof.

54. — The polypeptide of claim 53, comprising at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the listed sequence.

55. — The polypeptide of claim 54 consisting of at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the listed sequence.

56. — An antibody or fragment thereof comprising the polypeptide of any one of claims 53 to 55.

57. — A fusion polypeptide comprising (1) a fragment crystallizable (Fc) region linked to (2) a nanocage monomer or subunit thereof, wherein the Fc region comprises the I253A mutation, wherein numbering is according to the EU index.

58. — The fusion polypeptide of claim 57, wherein the Fc region further comprises the LALAP (L234A/L235A/P329G) mutations, wherein numbering is according to the EU index.

59. — The fusion polypeptide of claim 57 or 58, wherein the Fc region is an IgG1 Fc region.

60. — The fusion polypeptide of any one of claims 57 to 59, wherein the nanocage monomer is a ferritin monomer.

61. — The fusion polypeptide of claim 60, wherein the ferritin monomer is a ferritin light chain.

~~62. The fusion polypeptide of claim 61, wherein the ferritin light chain is a human ferritin light chain.~~

~~63. The fusion polypeptide of any one of claims 57 to 62, wherein the Fc region is linked via an amino acid linker to the nanocage monomer or subunit thereof.~~

~~64. The fusion polypeptide of any one of claims 57 to 63, wherein the Fc region is linked to the N-terminus of the nanocage monomer or subunit thereof.~~

~~65. The fusion polypeptide of any one of claims 57 to 64, wherein the Fc region is a single chain Fc (scFc).~~

~~66. The fusion polypeptide of any one of claims 57 to 65, wherein the Fc region is an Fc monomer.~~

~~67. A self-assembled polypeptide complex comprising:~~
~~— (a) a plurality of first fusion polypeptides, each first fusion polypeptide comprising (1) an Fc region linked to (2) a nanocage monomer or subunit thereof, and~~
~~— (b) a plurality of second fusion polypeptides, each second fusion polypeptide comprising (1) a SARS-CoV-2-binding antibody fragment linked to (2) a nanocage monomer or subunit thereof.~~

~~68. The self-assembled polypeptide complex of claim 67, wherein the nanocage monomer is a ferritin monomer.~~

~~69. The self-assembled polypeptide complex of claim 68, wherein the nanocage monomer is a ferritin light chain.~~

~~70. The self-assembled polypeptide complex of claim 69, which does not comprise any ferritin heavy chains or subunits of ferritin heavy chains.~~

~~71. The self-assembled polypeptide complex of claim 68 or 69, wherein the nanocage monomer is a human ferritin light chain.~~

~~72. The self-assembled polypeptide complex of any one of claims 67 to 71, wherein the SARS-CoV-2-binding antibody fragment binds to the receptor binding domain or the Spike protein of SARS-CoV-2.~~

~~73. The self-assembled polypeptide complex of any one of claims 67 to 72, wherein the SARS-CoV-2-binding antibody fragment comprises a light chain variable domain and a heavy chain variable domain.~~

~~74. The self-assembled polypeptide complex of any one of claims 67 to 73, wherein the SARS-CoV-2-binding antibody fragment comprises an Fab of an antibody that is capable of binding to SARS-CoV-2.~~

~~75. The self-assembled polypeptide complex of claim 73 or 74, wherein the SARS-CoV-2-binding antibody fragment comprises a V_K domain and a V_H domain.~~

~~76. The self-assembled polypeptide complex of any one of claims 67 to 75, wherein the self-assembled polypeptide complex is characterized by a 1:1 ratio of first fusion polypeptides to second fusion polypeptides.~~

~~77. The self-assembled polypeptide complex of any one of claims 67 to 76, wherein the Fc region is an IgG1 Fc region.~~

~~78. The self-assembled polypeptide complex of any one of claims 67 to 77, wherein the Fc region is linked to the nanocage monomer or subunit thereof via an amino acid linker.~~

~~79. The self-assembled polypeptide complex of any one of claims 67 to 78, wherein the Fc region is linked to the N-terminus of the nanocage monomer or subunit thereof.~~

~~80. The self-assembled polypeptide complex of any one of claims 67 to 79, comprising at total of least 24 fusion polypeptides.~~

~~81. The self-assembled polypeptide complex of claim 80, comprising a total of at least 32 fusion polypeptides.~~

~~82. The self-assembled polypeptide complex of claim 81, having a total of about 32 fusion polypeptides.~~

~~83. A self-assembled polypeptide complex comprising:~~

~~—— (a) a plurality of first fusion polypeptides, each first fusion polypeptide comprising (1) an IgG1 Fc region linked to (2) a human ferritin monomer or subunit thereof, wherein the IgG1 Fc region comprises the L234A/L235A/P329G and I253A mutations, wherein numbering is according to the EU index, and~~

~~—— (b) a plurality of second fusion polypeptides, each second fusion polypeptide comprising (1) a Fab fragment of an antibody that is capable of binding to a SARS-CoV-2 protein, the Fab fragment being linked to (2) a human ferritin monomer or subunit thereof.~~

~~84. The self-assembled polypeptide complex of claim 83, wherein:~~

~~—— (1) each first fusion polypeptide comprises a ferritin monomer subunit which is C-half-ferritin and each second fusion polypeptide comprises a ferritin monomer subunit which is N-half-ferritin; or~~

~~—— (2) each first fusion polypeptide comprises a ferritin monomer subunit which is N-half-ferritin and each second fusion polypeptide comprises a ferritin monomer subunit which is C-half-ferritin.~~

~~85. The self-assembled polypeptide complex of claim 83 or 84, wherein the self-assembled polypeptide complex is characterized by a 1:1 ratio of first fusion polypeptides to second fusion polypeptides.~~

~~86. The self-assembled polypeptide complex of any one of claims 83 to 85, wherein each first fusion polypeptide comprises a ferritin monomer subunit which is C-half-ferritin.~~

~~87. The self-assembled polypeptide complex of claim 86, wherein the IgG1 Fc region is linked to the C-half-ferritin via an amino acid linker.~~

~~88. The self-assembled polypeptide complex of claim 86 or 87, wherein the IgG1 Fc region is linked to the C-half-ferritin via the N-terminus of the C-half-ferritin.~~

~~89. The self-assembled polypeptide complex of any one of claims 83 to 88, wherein each second fusion polypeptide comprises a ferritin monomer subunit which is N-half-ferritin.~~

~~90. The self-assembled polypeptide complex of claim 89, wherein the Fab fragment is linked to the N-half-ferritin via an amino acid linker.~~

~~91. The self-assembled polypeptide complex of claim 89 or 90, wherein the Fab fragment is linked to the N-half-ferritin via the N-terminus of the N-half-ferritin.~~

~~92. — The self-assembled polypeptide complex of any one of claims 83 to 91, further comprising a plurality of third fusion polypeptides, each third fusion polypeptide comprising (1) a human ferritin monomer linked to (2) a Fab fragment of an antibody that is capable of binding to a SARS-CoV-2 protein.~~

~~93. — The self-assembled polypeptide complex of claim 92, wherein the self-assembled polypeptide complex is characterized by a 1:1:2 ratio of first fusion polypeptides to second fusion polypeptides to third fusion polypeptides.~~

~~94. — The self-assembled polypeptide complex of any one of claims 83 to 93, comprising at total of least 24 fusion polypeptides.~~

~~95. — The self-assembled polypeptide complex of claim 94, comprising a total of at least 32 fusion polypeptides.~~

~~96. — The self-assembled polypeptide complex of claim 95, having a total of 32 fusion polypeptides.~~

~~97. — The self-assembled polypeptide complex of any one of claims 74 or 83 to 93, wherein the Fab fragment comprises a V_K domain and a V_H domain, wherein~~

~~(1) the V_K domain has an amino acid sequence of SEQ ID NO:11 and the V_H domain has an amino acid sequence of SEQ ID NO:12;~~

~~(2) the V_K domain has an amino acid sequence of SEQ ID NO:17 and the V_H domain has an amino acid sequence of SEQ ID NO:18;~~

~~(3) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:25 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:26;~~

~~(4) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:27 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:28;~~

~~(5) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:29 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:30;~~

~~(6) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:31 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:32;~~

~~(7) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:33 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:34;~~

~~(8) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:35 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:36;~~

~~(9) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:37 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:38;~~

~~(10) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:39 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:40;~~

~~(11) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:41 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:42;~~

~~(12) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:43 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:44;~~

~~(13) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:45 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:46;~~

~~(14) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:47 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:48;~~

~~(15) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:49 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:50;~~

~~(16) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:51 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:52;~~

~~(17) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:53 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:54;~~

~~(18) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:55 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:56;~~

~~(19) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:57 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:58;~~

~~(20) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:59 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:60;~~

~~(21) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:61 or SEQ ID NO:62 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:63; or~~

~~(22) the V_K domain has an amino acid sequence of the V_K within SEQ ID NO:64 and the V_H domain has an amino acid sequence of the V_H within SEQ ID NO:65.~~

~~98. — The self-assembled polypeptide complex of any one of claims 83 to 97, wherein the human ferritin monomer is human ferritin light chain.~~

~~99. — The self-assembled polypeptide complex of claim 98, which does not comprise any ferritin heavy chains or subunits of ferritin heavy chains.~~

~~100. — A method of treating, ameliorating, or preventing a SARS-CoV-2-related condition, the method comprising administering to a subject a composition comprising the self-assembled polypeptide complex of any one of claims 67 to 99.~~

~~101. — The method of claim 100, wherein the subject is a mammal.~~

~~102. — The method of claim 101, wherein the subject is human.~~