MULTABODY CONSTRUCTS, COMPOSITIONS, AND METHODS

Cross-reference to Related Applications

The present application claims the benefit of and priority to U.S. Provisional Patent Application No. 63/142,704, filed January 28, 2021, the entire content of which is hereby incorporated by reference in its entirety for all purposes.

Sequence Listing

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on January 28, 2022, is named “Sequence Listing Jan-2022 3206-5048_ST25.txt” and is 8100 bytes in size.

Field

The present invention relates to polypeptides. In particular, the present invention relates to Multabody 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. Self-assembling protein nanoparticles possess three distinct surfaces that can all be tweaked to convey added functionalities: exterior, interior and inter-subunits surfaces.

Fusion proteins comprising self-assembling proteins have been described. For example, it is known to display antigens on the exterior surface of assembled nanocages for use as vaccines.

A need exists for improved constructs, compositions, and methods for designing nanoparticles and treating and/or preventing disease.

Summary ~~of the Invention~~

In accordance with an aspect, there is provided a fusion protein comprising a first nanocage monomer or a subunit thereof linked to an Fc monomer, wherein a plurality of the fusion proteins are capable of self-assembling to form a nanocage comprising one or more Fc dimers.

In an ~~aspect~~example, the Fc monomer is linked to the first nanocage monomer or subunit thereof at the N- or C-terminus of the first nanocage monomer or subunit thereof, preferably at the C-terminus.

In an ~~aspect~~example, the subunit comprises an N-subunit or a C-subunit, corresponding substantially to the N-terminal half of a nanocage monomer and the C-terminal half of a nanocage monomer, respectively, wherein the N-subunit and the C-subunit are capable of self-assembling to form a nanocage monomer.

In an ~~aspect~~example, the Fc monomer is linked to the N-subunit or C-subunit at the C-terminus of the N-subunit or C-subunit, preferably wherein the Fc monomer is linked to the C-subunit at the C-terminus.

In an ~~aspect~~example, the first nanocage monomer or subunit thereof is further linked to a first bioactive moiety.

In an ~~aspect~~example, the first bioactive moiety is linked to the first nanocage monomer or subunit thereof at the N- or C-terminus of the first nanocage monomer or subunit thereof, preferably the N-terminus.

In an ~~aspect~~example, the first bioactive moiety is linked to the N-subunit or C-subunit at the N-terminus of the N-subunit or C-subunit, preferably wherein the first bioactive moiety is linked to the C-subunit at the N-terminus.

In an ~~aspect~~example, the first bioactive moiety decorates the interior and/or exterior surface, preferably the exterior surface, of the assembled nanocage.

In an ~~aspect~~example, the first bioactive moiety comprises a first antigen-binding moiety.

In an ~~aspect~~example, the first antigen-binding moiety comprises an antibody or fragment thereof.

In an ~~aspect~~example, the first antigen-binding moiety comprises a Fab fragment.

In an ~~aspect~~example, the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

In an ~~aspect~~example, the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an ~~aspect~~example, the first antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, the first antigen-binding moiety comprises an HIV-1 specific antigen-binding moiety.

In an ~~aspect~~example, the HIV-1-specific antigen-binding moiety binds to BG505 SOSIP_D368R, 93TH057 gp120, and/or an MPER peptide.

In an ~~aspect~~example, the HIV-1 specific antigen-binding moiety comprises an HIV-1 specific antigen-binding moiety from PGDM1400, 10E8v4, and/or N49P7.

In an ~~aspect~~example, the fusion protein comprises the first nanocage monomer or subunit thereof linked to the Fc monomer at the C-terminus of the first nanocage monomer or subunit thereof and linked to the first bioactive moiety at the N-terminus of the first nanocage monomer or subunit thereof.

In an ~~aspect~~example, the fusion protein comprises the C-subunit linked to the Fc monomer at the C-terminus of the C-subunit and linked to the first bioactive moiety at the N-terminus of the C-subunit.

In an ~~aspect~~example, the fusion protein is provided in combination with an N-subunit or with a fusion protein comprising an N-subunit.

In an ~~aspect~~example, the N-subunit is linked to a second bioactive moiety at the N- or C-terminus, preferably the N-terminus.

In an ~~aspect~~example, the second bioactive moiety comprises a second antigen-binding moiety, and wherein, if the first bioactive moiety comprises the first antigen-binding moiety, the second antigen-binding moiety may be the same or different from the first antigen-binding moiety.

In an ~~aspect~~example, the second antigen-binding moiety comprises an antibody or fragment thereof.

In an ~~aspect~~example, the second antigen-binding moiety comprises a Fab fragment.

In an ~~aspect~~example, the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

In an ~~aspect~~example, the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an ~~aspect~~example, the N-subunit is further linked to an Fc monomer at the N- or C-terminus of the N-subunit, preferably the C-terminus.

In an ~~aspect~~example, the Fc monomer is derived from an IgG, IgA, IgD, IgM, or IgE, and is preferably human.

In an ~~aspect~~example, the Fc monomer is derived from an IgG, such as IgG1, IgG2, IgG3, or IgG4.

In an ~~aspect~~example, the Fc monomer is an IgG1 Fc monomer.

In an ~~aspect~~example, the Fc monomer comprises one or more mutations or sets of mutations that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.

In an ~~aspect~~example, the Fc monomer comprises a mutation at one or more of L234, L235, G236, G237, M252, I253, S254, T256, P329, A330, M428, N434, or a combination thereof (wherein numbering is according to the EU index), such as M428L and N434S (“LS”); M252Y, S254T and T256E (“YTE”); L234A and L235A (“LALA”); I253A; L234A, L235A, and P329G (“LALAP”); G236R; G237A; and/or A330L or a combination thereof.

In an ~~aspect~~example, from about 3 to about 100 nanocage monomers, such as 24, 32, 48, or 60 nanocage 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, are capable of self-assembling to form a nanocage.

In an ~~aspect~~example, the first nanocage monomer or subunit thereof 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 ~~aspect~~example, the first nanocage monomer or subunit thereof is apoferritin, optionally human apoferritin.

In an ~~aspect~~example, the first nanocage monomer or subunit thereof is an apoferritin light chain, optionally human apoferritin light chain.

In an ~~aspect~~example, the fusion protein comprises a first apoferritin subunit, optionally a first human apoferritin subunit, and wherein the first apoferritin subunit is capable of self-assembling with a second apoferritin subunit.

In an ~~aspect~~example, the first and second apoferritin monomer subunits interchangeably comprise the “N” and “C” regions of apoferritin.

In an ~~aspect~~example, 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:

MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREG YERLLKMQNQRGGRALFQDIKKPAEDEW (SEQ ID NO:1) or

SSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREGY ERLLKMQNQRGGRALFQDIKKPAEDEW (SEQ ID NO:15).

In an ~~aspect~~example, 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:

GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNL HRLGGPEAGLGEYLFERLTLRHD (SEQ ID NO:2) or

GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNL HRLGGPEAGLGEYLFERLTLKHD (SEQ ID NO:16).

In an ~~aspect~~example, the Fc monomer is linked to the first nanocage monomer or subunit thereof through a linker.

In an ~~aspect~~example, the first bioactive moiety is linked to the first nanocage monomer or subunit thereof through a linker.

In an ~~aspect~~example, the second bioactive moiety is linked to the N-subunit through a linker.

In an ~~aspect~~example, the linker is flexible or rigid and comprises from about 1 to about 100 amino acid residues, such as from about 1 to about 70 amino acid residues, such as from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

In an ~~aspect~~example, the linker comprises a GS domain.

In an ~~aspect~~example, the GS domain comprises a GS repeat, a GGS repeat, a GGGS (SEQ ID NO:11) repeat, and/or a GGGGS (SEQ ID NO:12) repeat, such as 1, 2, 3, 4, or more GGGGS (SEQ ID NO:12) repeats.

In an ~~aspect~~example, 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:

GGGGSGGGGSGGGGSGGGGSGGGGSGG (SEQ ID NO:4).

In an ~~aspect~~example, 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:

GGSGGSGGSGGSGGGSGGSGGSGGSG (SEQ ID NO:5).

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

In an ~~aspect~~example, the fusion protein comprises a first nanocage monomer subunit, the second nanocage monomer or subunit thereof is a second nanocage monomer subunit, and the second nanocage monomer subunit self-assembles with the fusion protein to form the nanocage monomer.

In an ~~aspect~~example, from about 1% to about 100%, such as from about 1%, 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, to about 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, such as from about 20% to about 80%, of the nanocage monomers or subunits thereof are comprised within a fusion protein described herein.

In an ~~aspect~~example, each nanocage monomer or subunit thereof is comprised within a fusion protein described herein.

In an ~~aspect~~example, the nanocage comprises 1 bioactive moiety or at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different bioactive moieties, such as 2 or 3 different bioactive moieties.

In an ~~aspect~~example, the nanocage is multivalent.

In an ~~aspect~~example, the nanocage is multispecific.

In an ~~aspect~~example, at least one bioactive moiety decorates the exterior surface of the nanocage and at least one Fc dimer decorates the exterior surface of the nanocage.

In an ~~aspect~~example, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 bioactive moieties decorate the exterior surface of the nanocage and at least two Fc dimers decorate the exterior surface of the nanocage.

In an ~~aspect~~example, the nanocage comprises:

(a) at least one nanocage monomer fused to a first antigen-binding moiety, such as a Fab,

(b) at least one N-subunit fused to a second antigen-binding moiety, such as a Fab, and

(c) and at least one C-subunit fused to:

(i) a third antigen-binding moiety, such as a Fab at one terminus, and

(ii) a Fc monomer at the other terminus.

In an ~~aspect~~example, each antigen-binding moiety is linked to the N-terminus of the nanocage monomer or subunit thereof and wherein the Fc monomer is linked to the C-terminus of the C-subunit.

In an ~~aspect~~example, the antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, each antigen-binding moiety is a different HIV-1-specific Fab.

In an ~~aspect~~example, the HIV-1-specific Fab binds to BG505 SOSIP_D368R, 93TH057 gp120, and/or an MPER peptide.

In an ~~aspect~~example, the HIV-1 specific Fab comprises PGDM1400 Fab, 10E8v4 Fab, and/or N49P7 Fab.

In an ~~aspect~~example, the HIV-1 specific Fab comprises PGDM1400 Fab, 10E8v4 Fab, and N49P7 Fab.

In an ~~aspect~~example, the nanocage comprises at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 antigen-binding moieties.

In an ~~aspect~~example, the nanocage comprises at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 Fc monomers.

In an ~~aspect~~example, the nanocage is carrying a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

In an ~~aspect~~example, the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally or wherein the cargo molecule is linked to the fusion protein or bound to the nanocage either internally or externally.

In an ~~aspect~~example, 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 ~~aspect~~example, the cargo molecule comprises a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.

In an ~~aspect~~example, the nanocage exhibits pan-virus neutralization breadth.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 0.1 ug/mL, such as less than about 0.01 ug/mL, such as less than about 0.001 ug/mL.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 42 pM, such as less than about 4.2 pM, such as less than about 0.42 pM.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) that is at least about 10, at least about 100, at least about 1000, at least about 10,000, or at least about 100,000 more potent than a cocktail of the corresponding bNAbs on a mass and/or molar basis.

In accordance with another aspect, there is provided a fusion protein comprising a first nanocage monomer or a subunit thereof linked to an scFc fragment at the C-terminus of the first nanocage monomer or subunit thereof, wherein a plurality of the fusion proteins are capable of self-assembling to form a nanocage.

In an ~~aspect~~example, the subunit comprises an N-subunit or a C-subunit, corresponding substantially to the N-terminal half of a nanocage monomer and the C-terminal half of a nanocage monomer, respectively, wherein the N-subunit and the C-subunit are capable of self-assembling to form a nanocage monomer.

In an ~~aspect~~example, the scFc fragment is linked to the N-subunit or C-subunit at the C-terminus of the N-subunit or C-subunit.

In an ~~aspect~~example, the first nanocage monomer or subunit thereof is further linked to a first bioactive moiety.

In an ~~aspect~~example, the first bioactive moiety is linked to the first nanocage monomer or subunit thereof at the N- or C-terminus of the first nanocage monomer or subunit thereof, preferably the N-terminus.

In an ~~aspect~~example, the first bioactive moiety is linked to the N-subunit or C-subunit at the N-terminus of the N-subunit or C-subunit, preferably wherein the first bioactive moiety is linked to the C-subunit at the N-terminus.

In an ~~aspect~~example, the first bioactive moiety decorates the interior and/or exterior surface, preferably the exterior surface, of the assembled nanocage.

In an ~~aspect~~example, the first bioactive moiety comprises a first antigen-binding moiety.

In an ~~aspect~~example, the first antigen-binding moiety comprises an antibody or fragment thereof.

In an ~~aspect~~example, the first antigen-binding moiety comprises a Fab fragment.

In an ~~aspect~~example, the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

In an ~~aspect~~example, the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an ~~aspect~~example, the first antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, the first antigen-binding moiety comprises an HIV-1 specific antigen-binding moiety.

In an ~~aspect~~example, the HIV-1 specific antigen-binding moiety binds to BG505 SOSIP_D368R, 93TH057 gp120, and/or an MPER peptide.

In an ~~aspect~~example, the HIV-1 specific antigen-binding moiety comprises an HIV-1 specific antigen-binding moiety from PGDM1400, 10E8v4, and/or N49P7.

In an ~~aspect~~example, the fusion protein comprises the first nanocage monomer or a subunit thereof linked to the scFc fragment at the C-terminus of the first nanocage monomer or a subunit thereof and linked to a first bioactive moiety at the N-terminus of the nanocage monomer or a subunit thereof.

In an ~~aspect~~example, the fusion protein comprises the C-subunit linked to the scFc fragment at the C-terminus of the C-subunit and linked to a first bioactive moiety at the N-terminus of the C-subunit.

In an ~~aspect~~example, the fusion protein is provided in combination with an N-subunit or a fusion protein comprising an N-subunit.

In an ~~aspect~~example, the N-subunit is linked to a second bioactive moiety at the N- or C-terminus, preferably the N-terminus.

In an ~~aspect~~example, the second bioactive moiety comprises a second antigen-binding moiety, and wherein, if the first bioactive moiety comprises the first antigen-binding moiety, the second antigen-binding moiety may be the same or different from the antigen-binding moiety that is linked to the C-subunit.

In an ~~aspect~~example, the second antigen-binding moiety comprises an antibody or fragment thereof.

In an ~~aspect~~example, the second antigen-binding moiety comprises a Fab fragment.

In an ~~aspect~~example, the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

In an ~~aspect~~example, the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an ~~aspect~~example, the N-subunit is further linked to a second scFc fragment at the N- or C-terminus of the N-subunit, preferably the C-terminus.

In an ~~aspect~~example, the scFc fragment is derived from an IgG, IgA, IgD, IgM, or IgE, and is preferably human.

In an ~~aspect~~example, the scFc fragment is derived from an IgG, such as IgG1, IgG2, IgG3, or IgG4.

In an ~~aspect~~example, the scFc fragment is an IgG1 scFc fragment.

In an ~~aspect~~example, the scFc fragment comprises one or more mutations or sets of mutations that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.

In an ~~aspect~~example, the scFc fragment comprises a mutation at one or more of L234, L235, G236, G237, M252, I253, S254, T256, P329, A330, M428, N434, or a combination thereof (wherein numbering is according to the EU index), such as M428L and N434S ("LS"); M252Y, S254T and T256E ("YTE"); L234A and L235A ("LALA"); I253A; L234A, L235A, and P329G ("LALAP"); G236R; G237A; and/or A330L or a combination thereof.

In an ~~aspect~~example, from about 3 to about 100 nanocage monomers, such as 24, 32, 48, or 60 nanocage 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, are capable of self-assembling to form a nanocage.

In an ~~aspect~~example, the first nanocage monomer or subunit thereof 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 ~~aspect~~example, the first nanocage monomer or subunit thereof is apoferritin, optionally human apoferritin.

In an ~~aspect~~example, the first nanocage monomer or subunit thereof is an apoferritin light chain, optionally human apoferritin light chain.

In an ~~aspect~~example, the fusion protein comprises a first apoferritin subunit, optionally a first human apoferritin subunit, and wherein the first apoferritin subunit is capable of self-assembling with a second apoferritin subunit.

In an ~~aspect~~example, the first and second apoferritin monomer subunits interchangeably comprise the "N" and "C" regions of apoferritin.

In an ~~aspect~~example, 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:

MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREG YERLLKMQNQRGGRALFQDIKKPAEDEW (SEQ ID NO:1) or

SSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREGY ERLLKMQNQRGGRALFQDIKKPAEDEW (SEQ ID NO:15).

In an ~~aspect~~example, 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:

GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNL HRLGGPEAGLGEYLFERLTLRHD (SEQ ID NO:2) or

GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNL HRLGGPEAGLGEYLFERLTLKHD (SEQ ID NO:16).

In an ~~aspect~~example, the scFc fragment is linked to the first nanocage monomer or subunit thereof through a linker.

In an ~~aspect~~example, the first bioactive moiety is linked to the first nanocage monomer or subunit thereof through a linker.

In an ~~aspect~~example, the second bioactive moiety is linked to the N-subunit through a linker.

In an ~~aspect~~example, the linker is flexible or rigid and comprises from about 1 to about 100 amino acid residues, such as from about 1 to about 70 amino acid residues, such as from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

In an ~~aspect~~example, the linker comprises a GS domain.

In an ~~aspect~~example, the GS domain comprises a GS repeat, a GGS repeat, a GGGS (SEQ ID NO:11) repeat, and/or a GGGGS (SEQ ID NO:12) repeat, such as 1, 2, 3, 4, or more GGGGS (SEQ ID NO:12) repeats.

In an ~~aspect~~example, 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:

GGGGSGGGGSGGGGSGGGGSGGGGSGG (SEQ ID NO:4).

In an ~~aspect~~example, 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:

GGSGGSGGSGGSGGGSGGSGGSGGSG (SEQ ID NO:5)

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

In an ~~aspect~~example, the fusion protein comprises a first nanocage monomer subunit, the second nanocage monomer or subunit thereof is a second nanocage monomer subunit, and the second nanocage monomer subunit self-assembles with the fusion protein to form the nanocage monomer.

In an ~~aspect~~example, from about 1% to about 100%, such as from about 1%, 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, to about 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, such as from about 20% to about 80%, of the nanocage monomers or subunits thereof is comprised within the fusion protein described herein.

In an ~~aspect~~example, each nanocage monomer or subunit thereof is comprised within a fusion protein described herein.

In an ~~aspect~~example, the nanocage comprises 1 bioactive moiety or at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different bioactive moieties, such as 2 or 3 different bioactive moieties.

In an ~~aspect~~example, the nanocage is multivalent.

In an ~~aspect~~example, the nanocage is multispecific.

In an ~~aspect~~example, at least one bioactive moiety decorates the exterior surface of the nanocage and at least one scFc fragment decorates the exterior surface of the nanocage.

In an ~~aspect~~example, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 bioactive moieties decorate the exterior surface of the nanocage and at least two scFc fragments decorate the exterior surface of the nanocage.

In an ~~aspect~~example, the nanocage comprises:

(a) at least one nanocage monomer fused to a first antigen-binding moiety, such as a Fab,

(b) at least one N-subunit fused to a second antigen-binding moiety, such as a Fab, and

(c) and at least one C-subunit fused to:

(i) a third antigen-binding moiety, such as a Fab at one terminus and

(ii) a scFc fragment at the other terminus.

In an ~~aspect~~example, each antigen-binding moiety is linked to the N-terminus of the nanocage monomer or subunit thereof and wherein the scFc fragment is linked to the C-terminus of the C-subunit.

In an ~~aspect~~example, the first and/or second antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, each antigen-binding moiety is a different HIV-1-specific Fab.

In an ~~aspect~~example, the HIV-1-specific Fab binds to BG505 SOSIP_D368R, 93TH057 gp120, and/or an MPER peptide.

In an ~~aspect~~example, the HIV-1 specific Fab comprises PGDM1400 Fab, 10E8v4 Fab, and/or N49P7 Fab.

In an ~~aspect~~example, the HIV-1 specific Fab comprises PGDM1400 Fab, 10E8v4 Fab, and N49P7 Fab.

In an ~~aspect~~example, the nanocage comprises at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 antigen-binding moieties.

In an ~~aspect~~example, the nanocage comprises at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 scFc fragments.

In an ~~aspect~~example, the nanocage is carrying a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

In an ~~aspect~~example, the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally or wherein the cargo molecule is linked to the fusion protein or bound to the nanocage either internally or externally.

In an ~~aspect~~example, 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 ~~aspect~~example, the cargo molecule comprises a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.

In an ~~aspect~~example, the nanocage exhibits pan-virus neutralization breadth.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 0.1 ug/mL, such as less than about 0.01 ug/mL, such as less than about 0.001 ug/mL.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 42 pM, such as less than about 4.2 pM, such as less than about 0.42 pM.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) that is at least about 10, at least about 100, at least about 1000, at least about 10,000, or at least about 100,000 more potent than a cocktail of the corresponding bNAbs on a mass and/or molar basis.

In another aspect, there is provided a therapeutic or prophylactic composition comprising the nanocage described herein.

In an ~~aspect~~example, the composition is for treating and/or preventing an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, the composition is for treating and/or preventing an HIV-1-related condition.

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

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

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

In a further aspect, the present disclosure provides a use of the nanocage as described herein or the composition as described herein in the manufacture of a medicament for treating and/or preventing a condition in a subject in need thereof. In a further aspect, the present disclosure provides the nanocage as described herein or the composition as described herein for use in therapy. In accordance with an ~~aspect~~example, there is provided a method for treating and/or preventing a condition, the method comprising administering the nanocage or the composition described herein to a subject in need thereof.

In an ~~aspect~~example, the condition is an HIV-1-related condition.

In accordance with an ~~aspect~~example, there is provided a use of the nanocage or the composition described herein for treating and/or preventing a condition.

In an ~~aspect~~example, the condition is an HIV-1-related condition.

In accordance with an ~~aspect~~example, there is provided the nanocage or the composition described herein for use in treating and/or preventing a condition.

In an ~~aspect~~example, the condition is an HIV-1-related condition.

In an ~~aspect~~example, the nanocage does not include any ferritin heavy chains.

In an ~~aspect~~example, the nanocage does not include any components capable of ferroxidase activity.

In an ~~aspect~~example, the nanocage comprises at least one bioactive moiety comprising an antibody or antigen-binding fragment thereof, and the ratio of the total number of bioactive moieties to the number of Fc dimers is 6:1.

In an ~~aspect~~example, the nanocage comprises at least one bioactive moiety comprising an antibody or antigen-binding fragment thereof, and the ratio of the total number of bioactive moieties to the number of scFcs is 3:1.

In an ~~aspect~~example, the nanocage comprises at least one bioactive moiety comprising an antibody or antigen-binding fragment thereof, and the ratio of the total number of bioactive moieties to the number of Fc dimers or scFcs is at least 7:1.

In an ~~aspect~~example, the nanocage comprises at least one bioactive moiety comprising an antibody or antigen-binding fragment thereof, and the ratio of the total number of bioactive moieties to the number of Fc dimers or scFcs is at least 4:1.

In accordance with an ~~aspect~~example, there is provided a fusion protein comprising a nanocage monomer or a subunit thereof linked to an Fc monomer, wherein a plurality of the fusion proteins self-assemble to form a nanocage comprising one or more Fc dimers.

In an ~~aspect~~example, the subunit comprises an N-subunit or a C-subunit, corresponding substantially to the N-terminal half of the nanocage monomer and the C-terminal half of the nanocage monomer, respectively, wherein the N-subunit and the C-subunit are capable of self-assembling to form the nanocage monomer.

In an ~~aspect~~example, the Fc monomer is linked to the nanocage monomer or subunit thereof at the N- or C-terminus of the nanocage monomer or subunit thereof, preferably at the C-terminus.

In an ~~aspect~~example, the Fc monomer is linked to the N-subunit or C-subunit at the C-terminus of the N-subunit or C-subunit, preferably wherein the Fc monomer is linked to the C-subunit at the C-terminus.

In an ~~aspect~~example, the nanocage monomer or subunit thereof is further linked to a bioactive moiety.

In an ~~aspect~~example, the bioactive moiety is linked to the nanocage monomer or subunit thereof at the N- or C-terminus of the nanocage monomer or subunit thereof, preferably the N-terminus.

In an ~~aspect~~example, the bioactive moiety is linked to the N-subunit or C-subunit at the N-terminus of the N-subunit or C-subunit, preferably wherein the bioactive moiety is linked to the C-subunit at the N-terminus.

In an ~~aspect~~example, the antigen-binding moiety decorates the interior and/or exterior surface, preferably the exterior surface, of the assembled nanocage.

In an ~~aspect~~example, the bioactive moiety comprises an antigen-binding moiety.

In an ~~aspect~~example, the antigen-binding moiety comprises an antibody or fragment thereof.

In an ~~aspect~~example, the antigen-binding moiety comprises a Fab fragment.

In an ~~aspect~~example, the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

In an ~~aspect~~example, the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an ~~aspect~~example, the antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, the antigen-binding moiety comprises an HIV-1 antigen-binding moiety.

In an ~~aspect~~example, the HIV-1-specific antigen-binding moiety binds to BG505 SOSIP D368R, 93TH057 gp120, and/or an MPER peptide.

In an ~~aspect~~example, the HIV-1 antigen-binding moiety comprises PGDM1400, 10E8v4, and/or N49P7.

In an ~~aspect~~example, the fusion protein comprises the nanocage monomer linked to the Fc monomer at the C-terminus of the nanocage monomer and linked to the bioactive moiety at the N-terminus of the nanocage monomer.

In an ~~aspect~~example, the fusion protein comprises the C-subunit linked to the Fc monomer at the C-terminus of the C-subunit and linked to the bioactive moiety at the N-terminus of the C-subunit.

In an ~~aspect~~example, the C-subunit is provided in combination with the N-subunit.

In an ~~aspect~~example, the N-subunit is linked to a bioactive moiety at the N- or C-terminus, preferably the N-terminus.

In an ~~aspect~~example, the bioactive moiety comprises an antigen-binding moiety, which may be the same or different from the antigen-binding moiety that is linked to the C-subunit.

In an ~~aspect~~example, the antigen-binding moiety comprises an antibody or fragment thereof.

In an ~~aspect~~example, the antigen-binding moiety comprises a Fab fragment.

In an ~~aspect~~example, the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

In an ~~aspect~~example, the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an ~~aspect~~example, the N-subunit is further linked to an Fc monomer at the N- or C-terminus of the N-subunit, preferably the C-terminus.

In an ~~aspect~~example, the Fc monomer is derived from an IgG, IgA, IgD, IgM, or IgE, and is preferably human.

In an ~~aspect~~example, the Fc monomer is derived from an IgG, such as IgG1, IgG2, IgG3, or IgG4.

In an ~~aspect~~example, the Fc monomer is an IgG1 Fc monomer.

In an ~~aspect~~example, the Fc monomer comprises one or more mutations or sets of mutations that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.

In an ~~aspect~~example, the Fc monomer comprises a mutation at one or more of L234, L235, G236, G237, M252, I253, S254, T256, P329, A330, M428, N434, or a combination thereof (wherein numbering is according to the EU index), such as M428L and N434S (“LS”); M252Y, S254T and T256E (“YTE”); L234A and L235A (“LALA”); I253A, and/or L234A, L235A, and P329G (“LALAP”), G236R, G237A, A330L or a combination thereof.

In an ~~aspect~~example, from about 3 to about 100 nanocage monomers, such as 24, 32, 48, 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, are capable of self-assembling to form a nanocage.

In an ~~aspect~~example, the nanocage monomer or subunit thereof 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 ~~aspect~~example, the nanocage monomer or subunit thereof is apoferritin, optionally human apoferritin.

In an ~~aspect~~example, the nanocage monomer or subunit thereof is an apoferritin light chain, optionally human apoferritin light chain.

In an ~~aspect~~example, the fusion protein comprises a first apoferritin subunit, optionally a first human apoferritin subunit, and wherein the first apoferritin subunit is capable of self-assembling with a second apoferritin subunit.

In an ~~aspect~~example, the first and second apoferritin monomer subunits interchangeably comprise the “N” and “C” regions of apoferritin.

In an ~~aspect~~example, 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:

MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREG YERLLKMQNQRGGRALFQDIKKPAEDEW.

In an ~~aspect~~example, 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:

GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNL HRLGGPEAGLGEYLFERLTLRHD.

In an ~~aspect~~example, the Fc monomer and/or the bioactive moiety is linked to the nanocage monomer or subunit thereof through a linker.

In an ~~aspect~~example, the linker is flexible or rigid and comprises from about 1 to about 100 amino acid residues, such as from about 1 to about 70 amino acid residues, such as from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

In an ~~aspect~~example, the linker comprises a GS domain.

In an ~~aspect~~example, the GS domain comprises a GS repeat, a GGS repeat, a GGGS repeat, and/or a GGGGS repeat, such as 1, 2, 3, 4, or more GGGGS repeats.

In an ~~aspect~~example, 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:

GGGGSGGGGSGGGGSGGGGSGGGGSGG.

In an ~~aspect~~example, 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:

GGSGGSGGSGGSGGGSGGSGGSGGSG.

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

In an ~~aspect~~example, the fusion protein comprises a first nanocage monomer subunit, the second nanocage monomer or subunit thereof is a second nanocage monomer subunit, and the second nanocage monomer subunit self-assembles with the fusion protein to form the nanocage monomer.

In an ~~aspect~~example, each nanocage monomer comprises a fusion protein described herein.

In an ~~aspect~~example, from about 1% to about 100%, such as from about 1%, 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, to about 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, such as from about 20% to about 80%, of the nanocage monomers or subunits thereof comprise the fusion protein described herein.

In an ~~aspect~~example, the nanocage comprises 1 bioactive moiety or at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different bioactive moieties, such as 2 or 3 different bioactive moieties.

In an ~~aspect~~example, the nanocage is multivalent.

In an ~~aspect~~example, the nanocage is multispecific.

In an ~~aspect~~example, at least one bioactive moiety decorates the exterior surface of the nanocage and at least one Fc dimer decorates the exterior surface of the nanocage.

In an ~~aspect~~example, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 bioactive moieties decorate the exterior surface of the nanocage and at least two Fc dimers decorate the exterior surface of the nanocage.

In an ~~aspect~~example, the nanocage comprises at least one nanocage monomer fused to a first antigen-binding moiety, such as a Fab, at least one N-subunit fused to a second antigen-binding moiety, such as a Fab, and at least one C-subunit fused to a third antigen-binding moiety, such as a Fab at one terminus and a Fc monomer at the other terminus.

In an ~~aspect~~example, each antigen-binding moiety is linked to the N-terminus of the nanocage monomer or subunit thereof and wherein the Fc monomer is linked to the C-terminus of the C-subunit.

In an ~~aspect~~example, the antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, each antigen-binding moiety is a different HIV-1-specific Fab.

In an ~~aspect~~example, the HIV-1-specific Fab binds to BG505 SOSIP D368R, 93TH057 gp120, and/or an MPER peptide.

In an ~~aspect~~example, the HIV-1 specific Fab comprises PGDM1400, 10E8v4, and/or N49P7.

In an ~~aspect~~example, the nanocage comprises PGDM1400, 10E8v4, and N49P7.

In an ~~aspect~~example, the nanocage comprises at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 antigen-binding moieties.

In an ~~aspect~~example, the nanocage comprises at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 Fc monomers.

In an ~~aspect~~example, the nanocage is carrying a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

In an ~~aspect~~example, the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally or wherein the cargo molecule is linked to the fusion protein or bound to the nanocage either internally or externally.

In an ~~aspect~~example, 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 ~~aspect~~example, the cargo molecule comprises a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.

In an ~~aspect~~example, the nanocage exhibits pan-virus neutralization breadth.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 0.1 ug/mL, such as less than about 0.01 ug/mL, such as less than about 0.001 ug/mL.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 42 pM, such as less than about 4.2 pM, such as less than about 0.42 pM.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) that is at least about 10, at least about 100, at least about 1000, at least about 10,000, or at least about 100,000 more potent than a cocktail of the corresponding bNAbs on a mass and/or molar basis.

In accordance with an ~~aspect~~example, there is provided a fusion protein comprising a nanocage monomer or a subunit thereof linked to an scFc fragment at the C-terminus of the nanocage monomer or subunit thereof, wherein a plurality of the fusion proteins self-assemble to form a nanocage.

In an ~~aspect~~example, the subunit comprises an N-subunit or a C-subunit, corresponding substantially to the N-terminal half of the nanocage monomer and the C-terminal half of the nanocage monomer, respectively, wherein the N-subunit and the C-subunit are capable of self-assembling to form the nanocage monomer.

In an ~~aspect~~example, the scFc fragment is linked to the nanocage monomer at the C-terminus of the nanocage monomer.

In an ~~aspect~~example, the scFc fragment is linked to the N-subunit or C-subunit at the C-terminus of the N-subunit or C-subunit.

In an ~~aspect~~example, the nanocage monomer or subunit thereof is further linked to a bioactive moiety.

In an ~~aspect~~example, the bioactive moiety is linked to the nanocage monomer or subunit thereof at the N- or C-terminus of the nanocage monomer or subunit thereof, preferably the N-terminus.

In an ~~aspect~~example, the bioactive moiety is linked to the N-subunit or C-subunit at the N-terminus of the N-subunit or C-subunit, preferably wherein the bioactive moiety is linked to the C-subunit at the N-terminus.

In an ~~aspect~~example, the antigen-binding moiety decorates the interior and/or exterior surface, preferably the exterior surface, of the assembled nanocage.

In an ~~aspect~~example, the bioactive moiety comprises an antigen-binding moiety.

In an ~~aspect~~example, the antigen-binding moiety comprises an antibody or fragment thereof.

In an ~~aspect~~example, the antigen-binding moiety comprises a Fab fragment.

In an ~~aspect~~example, the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

In an ~~aspect~~example, the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an ~~aspect~~example, the antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, the antigen-binding moiety comprises an HIV-1 antigen-binding moiety.

In an ~~aspect~~example, the HIV-1-specific antigen-binding moiety binds to BG505 SOSIP D368R, 93TH057 gp120, and/or an MPER peptide.

In an ~~aspect~~example, the HIV-1 antigen-binding moiety comprises PGDM1400, 10E8v4, and/or N49P7.

In an ~~aspect~~example, the fusion protein comprises the nanocage monomer linked to the scFc fragment at the C-terminus of the nanocage monomer and linked to the bioactive moiety at the N-terminus of the nanocage monomer.

In an ~~aspect~~example, the fusion protein comprises the C-subunit linked to the scFc fragment at the C-terminus of the C-subunit and linked to the bioactive moiety at the N-terminus of the C-subunit.

In an ~~aspect~~example, the C-subunit is provided in combination with the N-subunit.

In an ~~aspect~~example, the N-subunit is linked to a bioactive moiety at the N- or C-terminus, preferably the N-terminus.

In an ~~aspect~~example, the bioactive moiety comprises an antigen-binding moiety, which may be the same or different from the antigen-binding moiety that is linked to the C-subunit.

In an ~~aspect~~example, the antigen-binding moiety comprises an antibody or fragment thereof.

In an ~~aspect~~example, the antigen-binding moiety comprises a Fab fragment.

In an ~~aspect~~example, the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

In an ~~aspect~~example, the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.

In an ~~aspect~~example, the N-subunit is further linked to an scFc fragment at the N- or C-terminus of the N-subunit, preferably the C-terminus.

In an ~~aspect~~example, the scFc fragment is derived from an IgG, IgA, IgD, IgM, or IgE, and is preferably human.

In an ~~aspect~~example, the scFc fragment is derived from an IgG, such as IgG1, IgG2, IgG3, or IgG4.

In an ~~aspect~~example, the scFc fragment is an IgG1 scFc fragment.

In an ~~aspect~~example, the scFc fragment comprises one or more mutations or sets of mutations that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.

In an ~~aspect~~example, the scFc fragment comprises a mutation at one or more of L234, L235, G236, G237, M252, I253, S254, T256, P329, A330, M428, N434, or a combination thereof (wherein numbering is according to the EU index), such as M428L and N434S (“LS”); M252Y, S254T and T256E (“YTE”); L234A and L235A (“LALA”); I253A, and/or L234A, L235A, and P329G (“LALAP”), G236R, G237A, A330L or a combination thereof.

In an ~~aspect~~example, from about 3 to about 100 nanocage monomers, such as 24, 32, 48, 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, are capable of self-assembling to form a nanocage.

In an ~~aspect~~example, the nanocage monomer or subunit thereof 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 ~~aspect~~example, the nanocage monomer or subunit thereof is apoferritin, optionally human apoferritin.

In an ~~aspect~~example, the nanocage monomer or subunit thereof is an apoferritin light chain, optionally human apoferritin light chain.

In an ~~aspect~~example, the fusion protein comprises a first apoferritin subunit, optionally a first human apoferritin subunit, and wherein the first apoferritin subunit is capable of self-assembling with a second apoferritin subunit.

In an ~~aspect~~example, the first and second apoferritin monomer subunits interchangeably comprise the “N” and “C” regions of apoferritin.

In an ~~aspect~~example, 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:

MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREG YERLLKMQNQRGGRALFQDIKKPAEDEW.

In an ~~aspect~~example, 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:

GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNL HRLGGPEAGLGEYLFERLTLRHD.

In an ~~aspect~~example, the scFc fragment and/or the bioactive moiety is linked to the nanocage monomer or subunit thereof through a linker.

In an ~~aspect~~example, the linker is flexible or rigid and comprises from about 1 to about 100 amino acid residues, such as from about 1 to about 70 amino acid residues, such as from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

In an ~~aspect~~example, the linker comprises a GS domain.

In an ~~aspect~~example, the GS domain comprises a GS repeat, a GGS repeat, a GGGS repeat, and/or a GGGGS repeat, such as 1, 2, 3, 4, or more GGGGS repeats.

In an ~~aspect~~example, 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:

GGGGSGGGGSGGGGSGGGGSGGGGSGG.

In an ~~aspect~~example, 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:

GGSGGSGGSGGSGGGSGGSGGSGGSG

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

In an ~~aspect~~example, the fusion protein comprises a first nanocage monomer subunit, the second nanocage monomer or subunit thereof is a second nanocage monomer subunit, and the second nanocage monomer subunit self-assembles with the fusion protein to form the nanocage monomer.

In an ~~aspect~~example, each nanocage monomer comprises the fusion protein described herein.

In an ~~aspect~~example, from about 1% to about 100%, such as from about 1%, 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, to about 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, such as from about 20% to about 80%, of the nanocage monomers or subunits thereof comprise the fusion protein described herein.

In an ~~aspect~~example, the nanocage comprises 1 bioactive moiety or at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different bioactive moieties, such as 2 or 3 different bioactive moieties.

In an ~~aspect~~example, the nanocage is multivalent.

In an ~~aspect~~example, the nanocage is multispecific.

In an ~~aspect~~example, at least one bioactive moiety decorates the exterior surface of the nanocage and at least one scFc fragment decorates the exterior surface of the nanocage.

In an ~~aspect~~example, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 bioactive moieties decorate the exterior surface of the nanocage and at least two scFc fragments decorate the exterior surface of the nanocage.

In an ~~aspect~~example, the nanocage comprises at least one nanocage monomer fused to a first antigen-binding moiety, such as a scFab, at least one N-subunit fused to a second antigen-binding moiety, such as a scFab, and at least one C-subunit fused to a third antigen-binding moiety, such as a scFab at one terminus and a scFc fragment at the other terminus.

In an ~~aspect~~example, each antigen-binding moiety is linked to the N-terminus of the nanocage monomer or subunit thereof and wherein the scFc fragment is linked to the C-terminus of the C-subunit.

In an ~~aspect~~example, the antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, each antigen-binding moiety is a different HIV-1-specific Fab.

In an ~~aspect~~example, the HIV-1-specific Fab binds to BG505 SOSIP D368R, 93TH057 gp120, and/or an MPER peptide.

In an ~~aspect~~example, the HIV-1 specific Fab comprises PGDM1400, 10E8v4, and/or N49P7.

In an ~~aspect~~example, the nanocage comprises PGDM1400, 10E8v4, and N49P7.

In an ~~aspect~~example, the nanocage comprises at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 antigen-binding moieties.

In an ~~aspect~~example, the nanocage comprises at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 Fc monomers.

In an ~~aspect~~example, the nanocage is carrying a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

In an ~~aspect~~example, the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally or wherein the cargo molecule is linked to the fusion protein or bound to the nanocage either internally or externally.

In an ~~aspect~~example, 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 ~~aspect~~example, the cargo molecule comprises a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.

In an ~~aspect~~example, the nanocage exhibits pan-virus neutralization breadth.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 0.1 ug/mL, such as less than about 0.01 ug/mL, such as less than about 0.001 ug/mL.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 42 pM, such as less than about 4.2 pM, such as less than about 0.42 pM.

In an ~~aspect~~example, the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) that is at least about 10, at least about 100, at least about 1000, at least about 10,000, or at least about 100,000 more potent than a cocktail of the corresponding bNAbs on a mass and/or molar basis.

In accordance with an ~~aspect~~example, there is provided a therapeutic or prophylactic composition comprising the nanocage described herein.

In an ~~aspect~~example, the composition is for treating and/or preventing an antibody-preventable and/or antibody-treatable condition.

In an ~~aspect~~example, the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

In an ~~aspect~~example, the composition is for treating and/or preventing HIV-1.

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

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

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

In accordance with an ~~aspect~~example, there is provided a method for treating and/or preventing a condition, the method comprising administering the nanocage or the composition described herein.

In an ~~aspect~~example, the condition is HIV-1.

In accordance with an ~~aspect~~example, there is provided a use of the nanocage or the composition described herein for treating and/or preventing a condition.

In an ~~aspect~~example, the condition is HIV-1.

In an ~~aspect~~example, the use is for treating and/or preventing a condition.

In an ~~aspect~~example, the condition is HIV-1.

The novel features of the present ~~invention~~disclosure will become apparent to those of skill in the art upon examination of the following detailed description of the ~~invention~~disclosure. It should be understood, however, that the detailed description of the ~~invention~~disclosure and the specific examples presented, while indicating certain ~~aspect~~examples of the present ~~invention~~disclosure, are provided for illustration purposes only because various changes and modifications within the spirit and scope of the ~~invention~~disclosure will become apparent to those of skill in the art from the detailed description of the ~~invention~~disclosure 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. HIV-1 bNAb multimerization drives increases in neutralization potency. Schematic of the self-assembly of (a) apoferritin (24 subunits) and (b) single-chain Fab-apoferritin fusions. Fab light chain (LC) and heavy chain (HC) are shown in light and dark pink, respectively, and are connected to the N terminus of the light chain of human apoferritin (grey) through a GGS-like

flexible linker (dark). (c) Schematic representation of different Fab densities displayed on human apoferritin. Co-transfection of scFab-human apoferritin-encoding plasmids together with unconjugated apoferritin at ratios of 1:4 (dark yellow), 1:1 (black), 4:1 (blue) and 1:0 (red) resulted in molecules with

WHAT IS CLAIMED IS:

1. A fusion protein comprising a first nanocage monomer or a subunit thereof linked to an Fc monomer, wherein a plurality of the fusion proteins are capable of self-assembling to form a nanocage comprising one or more Fc dimers.

2. The fusion protein of claim 1, wherein the Fc monomer is linked to the first nanocage monomer or subunit thereof at the N- or C-terminus of the first nanocage monomer or subunit thereof, preferably at the C-terminus.

3. The fusion protein of claim 1 or 2, wherein the subunit comprises an N-subunit or a C-subunit, corresponding substantially to the N-terminal half of a nanocage monomer and the C-terminal half of a nanocage monomer, respectively, wherein the N-subunit and the C-subunit are capable of self-assembling to form a nanocage monomer.

4. The fusion protein of claim 3, wherein the Fc monomer is linked to the N-subunit or C-subunit at the C-terminus of the N-subunit or C-subunit, preferably wherein the Fc monomer is linked to the C-subunit at the C-terminus.

5. The fusion protein of any one of claims 1 to 4, wherein the first nanocage monomer or subunit thereof is further linked to a first bioactive moiety.

6. The fusion protein of claim 5, wherein the first bioactive moiety is linked to the first nanocage monomer or subunit thereof at the N- or C-terminus of the first nanocage monomer or subunit thereof, preferably the N-terminus.

7. The fusion protein of claim 6, wherein the first bioactive moiety is linked to the N-subunit or C-subunit at the N-terminus of the N-subunit or C-subunit, preferably wherein the first bioactive moiety is linked to the C-subunit at the N-terminus.

~~8. The fusion protein of any one of claims 5 to 7, wherein the first bioactive moiety decorates the interior and/or exterior surface, preferably the exterior surface, of the assembled nanocage.~~

~~9~~8. The fusion protein of any one of claims 5 to ~~8~~7, wherein the first bioactive moiety comprises a first antigen-binding moiety.

~~10~~9. The fusion protein of claim ~~8~~9, wherein the first antigen-binding moiety comprises an antibody or fragment thereof.

~~11~~10. The fusion protein of claim ~~9~~10, wherein the first antigen-binding moiety comprises a Fab fragment, preferably a single chain Fab (scFab) fragment.

~~12. The fusion protein of claim 10 or 11, wherein the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.~~

~~13~~11. The fusion protein of claim ~~9~~10, wherein the antibody or fragment thereof comprises a heavy chain and/or light chain of a Fab fragment.

12. The fusion protein of any one of claims 5 to ~~13~~11, wherein the first antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.

13. The fusion protein of claim 12, wherein the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.

14. The fusion protein of claim 13, wherein the first antigen-binding moiety comprises an HIV-1 specific antigen-binding moiety.

15. The fusion protein of claim 14, wherein the HIV-1-specific antigen-binding moiety binds to BG505 SOSIP_D368R, 93TH057 gp120, and/or an MPER peptide.

16. The fusion protein of claim 15, wherein the HIV-1 specific antigen-binding moiety comprises an HIV-1 specific antigen-binding moiety from PGDM1400, 10E8v4, and/or N49P7.

~~19~~17. The fusion protein of any one of claims 1 to ~~18~~16, wherein the fusion protein comprises the first nanocage monomer or subunit thereof linked to the Fc monomer at the C-terminus of the first nanocage monomer or subunit thereof and linked to the first bioactive moiety at the N-terminus of the first nanocage monomer or subunit thereof.

~~20~~18. The fusion protein of any one of claims 5 to 17~~19~~, wherein the fusion protein comprises the C-subunit linked to the Fc monomer at the C-terminus of the C-subunit and linked to the first bioactive moiety at the N-terminus of the C-subunit.

~~21~~19. The fusion protein of claim ~~20~~18, in combination with an N-subunit or with a fusion protein comprising an N-subunit.

~~22~~20. The fusion protein of claim ~~21~~19, wherein the N-subunit is linked to a second bioactive moiety at the N- or C-terminus, preferably the N-terminus.

~~23~~21. The fusion protein of claim ~~22~~20, wherein the second bioactive moiety comprises a second antigen-binding moiety, and wherein, if the first bioactive moiety comprises the first

antigen-binding moiety, the second antigen-binding moiety may be the same or different from the first antigen-binding moiety.

2422. The fusion protein of claim 2321, wherein the second antigen-binding moiety comprises an antibody or fragment thereof.

2523. The fusion protein of claim 2422, wherein the second antigen-binding moiety comprises a Fab fragment, preferably an scFab fragment.

26. The fusion protein of claim 24, wherein the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.

2724. The fusion protein of claim 2422, wherein the antibody or fragment thereof comprises a heavy chain and/or light chain of a Fab fragment.

2825. The fusion protein of any one of claims 2119 to 2724, wherein the N-subunit is further linked to an Fc monomer at the N- or C-terminus of the N-subunit, preferably the C-terminus.

269. The fusion protein of any one of claims 1 to 258, wherein the Fc monomer is derived from an IgG, IgA, IgD, IgM, or IgE, and is preferably human.

2730. The fusion protein of claim 269, wherein the Fc monomer is derived from an IgG, such as IgG1, IgG2, IgG3, or IgG4.

2831. The fusion protein of claim 2730, wherein the Fc monomer is an IgG1 Fc monomer.

32. The fusion protein any one of claims 1 to 31, wherein the Fc monomer comprises one or more mutations or sets of mutations that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.

33. The fusion protein of claim 32, wherein the Fc monomer comprises a mutation at one or more of L234, L235, G236, G237, M252, I253, S254, T256, P329, A330, M428, N434, or a combination thereof (wherein numbering is according to the EU index), such as M428L and N434S ("LS"); M252Y, S254T and T256E ("YTE"); L234A and L235A ("LALA"); I253A; L234A, L235A, and P329G ("LALAP"); G236R; G237A; and/or A330L or a combination thereof.

34. The fusion protein of any one of claims 1 to 33, wherein from about 3 to about 100 nanocage monomers, such as 24, 32, 48, or 60 nanocage 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, are capable of self-assembling to form a nanocage.

~~35~~29. The fusion protein of any one of claims 1 to ~~34~~28, wherein the first nanocage monomer or subunit thereof 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.

~~36~~30. The fusion protein of claim ~~35~~29, wherein the first nanocage monomer or subunit thereof is apoferritin, optionally human apoferritin.

~~37~~31. The fusion protein of claim 30~~36~~, wherein the first nanocage monomer or subunit thereof is an apoferritin light chain, optionally human apoferritin light chain.

~~38~~32. The fusion protein of claim 30~~36~~ or 31~~37~~, wherein the fusion protein comprises a first apoferritin subunit, optionally a first human apoferritin subunit, and wherein the first apoferritin subunit is capable of self-assembling with a second apoferritin subunit.

~~39~~33. The fusion protein of claim 32~~38~~, wherein the first and second apoferritin monomer subunits interchangeably comprise the “N” and “C” regions of apoferritin.

~~40. The fusion protein of claim 39, 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: MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREG YERLLKMQNQRGGRALFQDIKKPAEDEW (SEQ ID NO:1) or SSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREGY ERLLKMQNQRGGRALFQDIKKPAEDEW (SEQ ID NO:15).~~

~~41. The fusion protein of claim 39 or 40, 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: GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNLH RLGGPEAGLGEYLFERLTLRHD (SEQ ID NO:2) or GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNLH RLGGPEAGLGEYLFERLTLKHD (SEQ ID NO:16).~~

~~42~~34. The fusion protein of any one of claims 1 to 33~~41~~, wherein the Fc monomer is linked to the first nanocage monomer or subunit thereof through a linker.

~~43~~35. The fusion protein of any one of claims 5-34~~42~~, wherein the first bioactive moiety is linked to the first nanocage monomer or subunit thereof through a linker.

~~44~~36. The fusion protein of any of claims 20~~22~~-35~~43~~, wherein the second bioactive moiety is linked to the N-subunit through a linker.

~~45~~37. The fusion protein of any one of claims 34~~42~~-36~~44~~, wherein the linker is flexible or rigid and comprises from about 1 to about 100 amino acid residues, such as from about 1 to about 70 amino acid residues, such as from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

~~46~~38. The fusion protein of any one of claims 34~~42~~ to 37~~45~~, wherein the linker comprises a GS domain.

~~47~~39. The fusion protein of claim 38~~46~~, wherein the GS domain comprises at least one GS repeat, a GGS repeat, a GGGS (SEQ ID NO:11) repeat, and/or a GGGGS (SEQ ID NO:12) repeat, such as 1, 2, 3, 4, or more GGGGS (SEQ ID NO:12) repeats.

~~48. The fusion protein of claim 47, 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:~~
~~GGGGSGGGGSGGGGSGGGGSGGGGSGG (SEQ ID NO:4).~~

~~49. The fusion protein of claim 47, 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:~~
~~GGSGGSGGSGGSGGGSGGSGGSGGSG (SEQ ID NO:5).~~

~~50~~40. A nanocage comprising at least one fusion protein of any one of claims 1 to ~~49~~ 39 and at least one second nanocage monomer or subunit thereof that self-assembles with the fusion protein.

~~51~~41. The nanocage of claim 40~~50~~, wherein the fusion protein comprises a first nanocage monomer subunit, the second nanocage monomer or subunit thereof is a second nanocage monomer subunit, and the second nanocage monomer subunit self-assembles with the fusion protein to form the nanocage monomer.

~~52. The nanocage of claim 50 or 51, wherein from about 1% to about 100%, such as from about 1%, 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, to about 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, such as from about 20% to about 80%, of the nanocage monomers or subunits thereof are comprised within a fusion protein of any one of claims 1 to 39.~~

~~53~~42. The nanocage of claim 40 or 41~~52~~, wherein each nanocage monomer or subunit thereof is comprised within a fusion protein of any one of claims 1 to ~~49~~39.

~~54. The nanocage of any one of claims 50 to 53, comprising 1 bioactive moiety or at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different bioactive moieties, such as 2 or 3 different bioactive moieties.~~

~~55~~43. The nanocage of any one of claims ~~50~~40 to 42~~54~~, wherein the nanocage is multivalent or multispecific.

~~56. The nanocage of any one of claims 50 to 55, wherein the nanocage is multispecific.~~

~~57. The nanocage of any one of claims 50 to 56, wherein at least one bioactive moiety decorates the exterior surface of the nanocage and at least one Fc dimer decorates the exterior surface of the nanocage.~~

~~58. The nanocage of claim 57, wherein at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 bioactive moieties decorate the exterior surface of the nanocage and at least two Fc dimers decorate the exterior surface of the nanocage.~~

~~59. The nanocage of any one of claims 50 to 58, comprising:~~

~~(a) at least one nanocage monomer fused to a first antigen-binding moiety, such as a Fab,~~

~~(b) at least one N-subunit fused to a second antigen-binding moiety, such as a Fab, and~~

~~(c) and at least one C-subunit fused to:~~

~~(i) a third antigen-binding moiety, such as a Fab at one terminus, and~~

~~(ii) a Fc monomer at the other terminus.~~

~~60. The nanocage of claim 59, wherein each antigen-binding moiety is linked to the N-terminus of the nanocage monomer or subunit thereof and wherein the Fc monomer is linked to the C-terminus of the C-subunit.~~

~~61. The nanocage of any one of claims 50 to 60, wherein the antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.~~

~~62. The nanocage of claim 61, wherein the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.~~

~~63. The nanocage of claim 62, wherein each antigen-binding moiety is a different HIV-1-specific Fab.~~

~~64. The nanocage of claim 63, wherein the HIV-1-specific Fab binds to BG505 SOSIP_D368R, 93TH057 gp120, and/or an MPER peptide.~~

~~65. The nanocage of claim 64, wherein the HIV-1 specific Fab comprises PGDM1400 Fab, 10E8v4 Fab, and/or N49P7 Fab.~~

~~66. The nanocage of claim 65, comprising PGDM1400 Fab, 10E8v4 Fab, and N49P7 Fab.~~

~~67. The nanocage of any one of claims 50 to 66, comprising at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 antigen-binding moieties.~~

~~68. The nanocage of any one of claims 50 to 67, comprising at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 Fc monomers.~~

~~69~~44. The nanocage of any one of claims 4~~0~~50 to 4~~3~~68, carrying a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

~~70. The nanocage of claim 69, wherein the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally or wherein the cargo molecule is linked to the fusion protein or bound to the nanocage either internally or externally.~~

~~71. The nanocage of claim 69, 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.~~

~~72. The nanocage of any one of claims 69 to 71, wherein the cargo molecule comprises a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.~~

~~73. The nanocage of any one of claims 50 to 72, wherein the nanocage exhibits pan-virus neutralization breadth.~~

~~74. The nanocage of any one of claims 50 to 73, wherein the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 0.1 ug/mL, such as less than about 0.01 ug/mL, such as less than about 0.001 ug/mL.~~

~~75. The nanocage of any one of claims 50 to 74, wherein the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 42 pM, such as less than about 4.2 pM, such as less than about 0.42 pM.~~

~~76. The nanocage of any one of claims 50 to 75, wherein the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) that is at least about 10, at least about 100, at least about 1000, at least about 10,000, or at least about 100,000 more potent than a cocktail of the corresponding bNAbs on a mass and/or molar basis.~~

~~77~~45. A fusion protein comprising a first nanocage monomer or a subunit thereof linked to an scFc fragment at the C-terminus of the first nanocage monomer or subunit thereof, wherein a plurality of the fusion proteins are capable of self-assembling to form a nanocage.

~~78~~46. The fusion protein of claim ~~77~~45, wherein the subunit comprises an N-subunit or a C-subunit, corresponding substantially to the N-terminal half of a nanocage monomer and the C-terminal half of a nanocage monomer, respectively, wherein the N-subunit and the C-subunit are capable of self-assembling to form a nanocage monomer.

~~79. The fusion protein of claim 78, wherein the scFc fragment is linked to the N-subunit or C-subunit at the C-terminus of the N-subunit or C-subunit.~~

~~80~~47. The fusion protein of ~~any one of claims 77 to 79~~claim 45 or 46, wherein the first nanocage monomer or subunit thereof is further linked to a first bioactive moiety.

~~81. The fusion protein of claim 80, wherein the first bioactive moiety is linked to the first nanocage monomer or subunit thereof at the N- or C-terminus of the first nanocage monomer or subunit thereof, preferably the N-terminus.~~

~~82. The fusion protein of claim 81, wherein the first bioactive moiety is linked to the N-subunit or C-subunit at the N-terminus of the N-subunit or C-subunit, preferably wherein the first bioactive moiety is linked to the C-subunit at the N-terminus.~~

~~83. The fusion protein of any one of claims 80 to 82, wherein the first bioactive moiety decorates the interior and/or exterior surface, preferably the exterior surface, of the assembled nanocage.~~

~~84~~48. The fusion protein of ~~any one of claims 80 to 83~~claim 47, wherein the first bioactive moiety comprises a first antigen-binding moiety.

~~85~~49. The fusion protein of claim ~~84~~48, wherein the first antigen-binding moiety comprises an antibody or fragment thereof.

~~86~~50. The fusion protein of claim ~~85~~49, wherein the first antigen-binding moiety comprises a Fab fragment, preferably an scFab fragment.

~~87. The fusion protein of claim 85 or 86, wherein the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain, or a combination thereof.~~

~~88~~51. The fusion protein of claim 49~~85~~, wherein the antibody or fragment thereof comprises a heavy chain and/or light chain of a Fab fragment.

~~89. The fusion protein of any one of claims 77 to 88, wherein the first antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.~~

~~90. The fusion protein of claim 89, wherein the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.~~

~~91. The fusion protein of claim 90, wherein the first antigen-binding moiety comprises an HIV-1 specific antigen-binding moiety.~~

~~92. The fusion protein of claim 91, wherein the HIV-1 specific antigen-binding moiety binds to BG505 SOSIP_D368R, 93TH057 gp120, and/or an MPER peptide.~~

~~93. The fusion protein of claim 92, wherein the HIV-1 specific antigen-binding moiety comprises an HIV-1 specific antigen-binding moiety from PGDM1400, 10E8v4, and/or N49P7.~~

~~94. The fusion protein of any one of claims 77 to 93, wherein the fusion protein comprises the first nanocage monomer or a subunit thereof linked to the scFc fragment at the C-terminus of the first nanocage monomer or a subunit thereof and linked to a first bioactive moiety at the N-terminus of the nanocage monomer or a subunit thereof.~~

~~95~~52. The fusion protein of any one of claims ~~79~~46 to 51~~94~~, wherein the fusion protein comprises the C-subunit linked to the scFc fragment at the C-terminus of the C-subunit and linked to a first bioactive moiety at the N-terminus of the C-subunit.

~~96~~53. The fusion protein of claim 52~~95~~, in combination with an N-subunit or a fusion protein comprising an N-subunit.

~~97~~54. The fusion protein of claim 53~~96~~, wherein the N-subunit is linked to a second bioactive moiety at the N- or C-terminus, preferably the N-terminus.

~~98~~55. The fusion protein of claim 54~~97~~, wherein the second bioactive moiety comprises a second antigen-binding moiety, and wherein, if the first bioactive moiety comprises the first antigen-binding moiety, the second antigen-binding moiety may be the same or different from the antigen-binding moiety that is linked to the C-subunit.

~~99~~56. The fusion protein of claim ~~98~~55, wherein the second antigen-binding moiety comprises an antibody or fragment thereof.

~~100~~57. The fusion protein of claim 56~~99~~, wherein the second antigen-binding moiety comprises a Fab fragment, preferably an scFab fragment.

~~101. The fusion protein of claim 99 or 100, wherein the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, a sdAb fragment, a VHH domain or a combination thereof.~~

~~102~~58. The fusion protein of claim 56~~99~~, wherein the antibody or fragment thereof comprises a heavy chain and/or light chain of a Fab fragment.

~~103~~59. The fusion protein of any one of claims ~~96~~ 53 to ~~102~~58, wherein the N-subunit is further linked to a second scFc fragment at the N- or C-terminus of the N-subunit, preferably the C-terminus.

~~104. The fusion protein of any one of claims 77 to 103, wherein the scFc fragment is derived from an IgG, IgA, IgD, IgM, or IgE, and is preferably human.~~

~~105. The fusion protein of claim 104, wherein the scFc fragment is derived from an IgG, such as IgG1, IgG2, IgG3, or IgG4.~~

~~106. The fusion protein of claim 105, wherein the scFc fragment is an IgG1 scFc fragment.~~

~~107. The fusion protein any one of claims 77 to 106, wherein the scFc fragment comprises one or more mutations or sets of mutations that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.~~

~~108. The fusion protein of claim 107, wherein the scFc fragment comprises a mutation at one or more of L234, L235, G236, G237, M252, I253, S254, T256, P329, A330, M428, N434, or a combination thereof (wherein numbering is according to the EU index), such as M428L and N434S (“LS”); M252Y, S254T and T256E (“YTE”); L234A and L235A (“LALA”); I253A;~~

~~L234A, L235A, and P329G ("LALAP"); G236R; G237A; and/or A330L or a combination thereof.~~

~~109. The fusion protein of any one of claims 77 to 108, wherein from about 3 to about 100 nanocage monomers, such as 24, 32, 48, or 60 nanocage 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, are capable of self-assembling to form a nanocage.~~

~~110~~60. The fusion protein of any one of claims 45~~77~~ to 59~~109~~, wherein the first nanocage monomer or subunit thereof 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.

~~111~~61. The fusion protein of claim 60~~110~~, wherein the first nanocage monomer or subunit thereof is apoferritin, optionally human apoferritin.

~~112~~62. The fusion protein of claim 61~~111~~, wherein the first nanocage monomer or subunit thereof is an apoferritin light chain, optionally human apoferritin light chain.

~~113~~63. The fusion protein of claim 61~~111~~ or 62~~112~~, wherein the fusion protein comprises a first apoferritin subunit, optionally a first human apoferritin subunit, and wherein the first apoferritin subunit is capable of self-assembling with a second apoferritin subunit.

~~114~~64. The fusion protein of claim 63~~113~~, wherein the first and second apoferritin monomer subunits interchangeably comprise the "N" and "C" regions of apoferritin.

~~115. The fusion protein of claim 114, 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: MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREG YERLLKMQNQRGGRALFQDIKKPAEDEW (SEQ ID NO:1) or SSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKREGY ERLLKMQNQRGGRALFQDIKKPAEDEW (SEQ ID NO:15).~~

~~116. The fusion protein of claim 114 or 115, 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: GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNLH RLGGPEAGLGEYLFERLTLRHD (SEQ ID NO:2) or~~

~~GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKKMGDHLTNLH RLGGPEAGLGEYLFERLTLKHD (SEQ ID NO:16).~~

~~117~~65. The fusion protein of any one of claims 45~~77~~ to 64~~116~~, wherein the scFc fragment is linked to the first nanocage monomer or subunit thereof through a linker.

~~118~~66. The fusion protein of any one of claims 47~~80~~ to 65~~-117~~, wherein the first bioactive moiety is linked to the first nanocage monomer or subunit thereof through a linker.

~~119~~67. The fusion protein of any one of claims ~~97-118~~54 to 66, wherein the second bioactive moiety is linked to the N-subunit through a linker.

~~120~~68. The fusion protein of any one of claims ~~117~~ 65 to 67~~119~~, wherein the linker is flexible or rigid and comprises from about 1 to about 100 amino acid residues, such as from about 1 to about 70 amino acid residues, such as from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

~~121~~69. The fusion protein of any one of claims 65~~117~~ to 68~~120~~, wherein the linker comprises a GS domain.

~~122~~70. The fusion protein of claim 69~~121~~, wherein the GS domain comprises at least one GS repeat, a GGS repeat, a GGGS (SEQ ID NO:11) repeat, and/or a GGGGS (SEQ ID NO:12) repeat, such as 1, 2, 3, 4, or more GGGGS (SEQ ID NO:12) repeats.

~~123. The fusion protein of claim 122, 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:~~
~~GGGGSGGGGSGGGGSGGGGSGGGGSGG (SEQ ID NO:4).~~

~~124. The fusion protein of claim 122, 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:~~
~~GGSGGSGGSGGSGGGSGGSGGSGGSG (SEQ ID NO:5)~~

~~125~~71. A nanocage comprising at least one fusion protein of any one of claims ~~77~~ 45 to 70~~124~~ and at least one second nanocage monomer or subunit thereof that self-assembles with the fusion protein.

~~126~~72. The nanocage of claim 71~~125~~, wherein the fusion protein comprises a first nanocage monomer subunit, the second nanocage monomer or subunit thereof is a second nanocage

monomer subunit, and the second nanocage monomer subunit self-assembles with the fusion protein to form the nanocage monomer.

~~127. The nanocage of claim 125 or 126, wherein from about 1% to about 100%, such as from about 1%, 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, to about 4%, 8%, 10%, 12%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, such as from about 20% to about 80%, of the nanocage monomers or subunits thereof is comprised within the fusion protein of any one of claims 77 to 124.~~

~~128~~73. The nanocage of claim 71~~125~~ or 72~~126~~, wherein each nanocage monomer or subunit thereof is comprised within a fusion protein of any one of claims 37~~77~~ to ~~124~~63.

~~129. The nanocage of any one of claims 125 to 128, comprising 1 bioactive moiety or at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different bioactive moieties, such as 2 or 3 different bioactive moieties.~~

~~130~~74. The nanocage of any one of claims 71~~125~~ to 73~~129~~, wherein the nanocage is multivalent or multispecific.

~~131. The nanocage of any one of claims 125 to 130, wherein the nanocage is multispecific.~~

~~132. The nanocage of any one of claims 125 to 131, wherein at least one bioactive moiety decorates the exterior surface of the nanocage and at least one scFc fragment decorates the exterior surface of the nanocage.~~

~~133. The nanocage of claim 132, wherein at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 bioactive moieties decorate the exterior surface of the nanocage and at least two scFc fragments decorate the exterior surface of the nanocage.~~

~~134. The nanocage of any one of claims 125 to 133, comprising:~~

~~(a) at least one nanocage monomer fused to a first antigen-binding moiety, such as a Fab,~~

~~(b) at least one N-subunit fused to a second antigen-binding moiety, such as a Fab, and~~

~~(c) and at least one C-subunit fused to:~~

~~(i) a third antigen-binding moiety, such as a Fab at one terminus and~~

~~(ii) a scFc fragment at the other terminus.~~

~~135. The nanocage of claim 134, wherein each antigen-binding moiety is linked to the N-terminus of the nanocage monomer or subunit thereof and wherein the scFc fragment is linked to the C-terminus of the C-subunit.~~

~~136. The nanocage of claim 134 or 135, wherein the first and/or second antigen-binding moiety binds specifically to an antigen associated with an antibody-preventable and/or antibody-treatable condition.~~

~~137. The nanocage of claim 136, wherein the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.~~

~~138. The nanocage of claim 137, wherein each antigen-binding moiety is a different HIV-1-specific Fab.~~

~~139. The nanocage of claim 138, wherein the HIV-1-specific Fab binds to BG505 SOSIP_D368R, 93TH057 gp120, and/or an MPER peptide.~~

~~140. The nanocage of claim 139, wherein the HIV-1 specific Fab comprises PGDM1400 Fab, 10E8v4 Fab, and/or N49P7 Fab.~~

~~141. The nanocage of claim 140, comprising PGDM1400 Fab, 10E8v4 Fab, and N49P7 Fab.~~

~~142. The nanocage of any one of claims 125 to 141, comprising at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 antigen-binding moieties.~~

~~143. The nanocage of any one of claims 125 to 142, comprising at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, or 48 scFc fragments.~~

~~144~~75. The nanocage of any one of claims 71~~125~~ to 74~~143~~, carrying a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

~~145. The nanocage of claim 144, wherein the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally or wherein the cargo molecule is linked to the fusion protein or bound to the nanocage either internally or externally.~~

~~146. The nanocage of claim 144, 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.~~

~~147. The nanocage of any one of claims 144 to 146, wherein the cargo molecule comprises a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.~~

~~148. The nanocage of any one of claims 125 to 147, wherein the nanocage exhibits pan-virus neutralization breadth.~~

~~149. The nanocage of any one of claims 125 to 148, wherein the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 0.1 ug/mL, such as less than about 0.01 ug/mL, such as less than about 0.001 ug/mL.~~

~~150. The nanocage of any one of claims 125 to 149, wherein the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) of less than about 42 pM, such as less than about 4.2 pM, such as less than about 0.42 pM.~~

~~151. The nanocage of any one of claims 125 to 150, wherein the nanocage exhibits an average median IC_{50} value against a multiclade panel of 118 pseudoviruses (PsV) that is at least about 10, at least about 100, at least about 1000, at least about 10,000, or at least about 100,000 more potent than a cocktail of the corresponding bNAbs on a mass and/or molar basis.~~

~~152~~76. A therapeutic or prophylactic composition comprising the nanocage of any one of claims 40~~50~~ to 44~~76~~ and 71~~125~~ to 75~~151~~.

~~153. The composition of claim 152, wherein the composition is for treating and/or preventing an antibody-preventable and/or antibody-treatable condition.~~

~~154. The composition of claim 153, wherein the antigen is associated with an infectious agent, including a virus, bacteria, a parasite, a fungus, or a yeast, a cancer, or an immune disease, including an autoimmune disease.~~

~~155. The composition of claim 154, wherein the composition is for treating and/or preventing an HIV-1-related condition.~~

~~156~~77. A nucleic acid molecule encoding the fusion protein of any one of claims 1 to 39~~49~~ and 45~~77~~ to 70~~124~~.

~~157~~78. A vector comprising the nucleic acid molecule of claim 77~~156~~.

~~158~~79. A host cell comprising the vector of claim ~~157~~ 78 and producing the fusion protein of any one of claims 1 to 39~~49~~ and 45~~77~~ to 70~~124~~.

~~159~~80. Use of the nanocage of any one of claims 40 to 44 and 71 to 75 or the composition of claim 76 in the manufacture of a medicament ~~A method~~ for treating and/or preventing a condition in~~, the method comprising administering the nanocage of any one of claims 50 to 76 and 125 to 151 or the composition of any one of claims 152 to 155 to~~ a subject in need thereof.

~~160. The method of claim 159, wherein the condition is an HIV-1-related condition.~~

~~161. Use of the nanocage of any one of claims 50 to 76 and 125 to 151 or the composition of any one of claims 152 to 155 for treating and/or preventing a condition.~~

~~162. The use of claim 161, wherein the condition is an HIV-1-related condition.~~

~~163~~81. The nanocage of any one of claims 40 to 44 and 71 to 75~~50 to 76 and 125 to 151~~ or the composition of ~~any one of claims 152 to 155~~claim 76 for use in ~~treating and/or preventing a condition~~therapy.

~~164. The nanocage of claim 163, wherein the condition is an HIV-1-related condition.~~

~~165~~82. The nanocage of any one of claims 40 to 44 and 71 to 75~~50-76, 125-151, or 163-164~~, wherein the nanocage does not include any ferritin heavy chains.

~~166~~83. The nanocage of any one of claims 40 to 44 and 71 to 75~~50-76, 125-151, or 163-164~~, wherein the nanocage does not include any components capable of ferroxidase activity.

~~167. The nanocage of any one of claims 50-76, or 163-166, wherein the nanocage comprises at least one bioactive moiety comprising an antibody or antigen-binding fragment thereof, and the ratio of the total number of bioactive moieties to the number of Fc dimers is 6:1.~~

~~168. The nanocage of any one of claims 125-151, or 163-166, wherein the nanocage comprises at least one bioactive moiety comprising an antibody or antigen-binding fragment thereof, and the ratio of the total number of bioactive moieties to the number of scFcs is 3:1.~~

~~169. The nanocage of any one of claims 50-76, or 163-166, wherein the nanocage comprises at least one bioactive moiety comprising an antibody or antigen-binding fragment thereof, and the ratio of the total number of bioactive moieties to the number of Fc dimers or scFcs is at least 7:1.~~

~~170. The nanocage of any one of claims 125-151, or 163-166, wherein the nanocage comprises at least one bioactive moiety comprising an antibody or antigen-binding fragment~~

~~thereof, and the ratio of the total number of bioactive moieties to the number of Fc dimers or scFcs is at least 4:1.~~