

WHAT IS CLAIMED IS:

1. A fusion protein comprising:
a first nanocage monomer subunit of a nanocage monomer; and
a bioactive moiety linked to the first nanocage monomer subunit;
- 5 wherein the fusion protein self-assembles with a protein comprising a second nanocage monomer subunit to form a nanocage monomer.
2. The fusion protein of claim 1, wherein the bioactive moiety decorates the interior and/or exterior surface of the assembled nanocage.
3. The fusion protein of claim 1 or 2, wherein the bioactive moiety comprises an
10 antibody or fragment thereof, an antigen, a detectable moiety, a pharmaceutical agent, a diagnostic agent, or combinations thereof.
4. The fusion protein of claim 3, wherein the antibody or fragment thereof comprises an Fc fragment.
5. The fusion protein of claim 4, wherein the Fc fragment is an IgG1 Fc
15 fragment.
6. The fusion protein of claim 4 or 5, wherein the Fc fragment comprises one or more mutations, such as LS, YTE, LALA, and/or LALAP, that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.
7. The fusion protein of claim 3, wherein the antibody or fragment thereof
20 comprises a Fab fragment.
8. The fusion protein of claim 3, wherein the antibody or fragment thereof comprises a scFab fragment, a scFv fragment, or a sdAb fragment.
9. The fusion protein of claim 3, wherein the antibody or fragment thereof comprises a heavy and/or light chain of a Fab fragment.
- 25 10. The fusion protein of claim 9, wherein the antibody or fragment thereof comprises both a light chain and a heavy chain, or in the case of a Fc fragment, a first and a second chain, optionally separated by a linker.
11. The fusion protein of claim 10, 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%,
30 or 100%) identical to:
GGSSGSGSGSTGTSSSGTGTSAGTTGTSASTSGSGSGGGGSGGGGSAGGTAT
AGASSGSGSSGSSSSGGTG.

12. The fusion protein of claim 9, in association with a separately produced Fab light chain and/or heavy chain.

13. The fusion protein of any one of claims 3 to 12, wherein the antibody or fragment thereof binds specifically to an antigen associated with an antibody-preventable
5 and/or antibody-treatable condition.

14. The fusion protein of claim 13, wherein antigen is associated with an infectious agent, including a virus (e.g., HIV, including HIV-1, influenza, RSV, rotavirus), bacteria (e.g., TB, C. difficile) parasite (e.g., malaria), fungus, or yeast, a cancer (e.g., CD19, CD22, CD79, BCMA, or CD20), including solid and liquid cancers, or an immune disease,
10 including an autoimmune disease.

15. The fusion protein of claim 14, wherein the antigen is associated with HIV-1 and the antibody or fragment thereof comprises, for example, Ibalizumab-A12P, 10E8, 10E8.v4, N49P7, PGDM1400, 10-1074, VRC01, or combinations thereof.

16. The fusion protein of claim 15, wherein the antibody or fragment thereof
15 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:

Fc chain 1:

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
20 IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSCSVLHEALHSHYTQKSLSL
SPGK;

Fc chain 2:

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN
25 WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSCSVLHEALHSHYTQKSLSL
SPGK;

Ibalizumab-A12P light chain:

30 DIVMTQSPDSLPLVSLGERVTMNCSSQSLLYSTNQKNYLAWYQQKPGQSPKLLIY
WASTRESGVPRFSGSGSGTDFTLTISVQAEDVAVYYCQQYYSYRTFGGGTKLEI
KRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQES
VTEQDSKSTYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC;

Ibalizumab-A12P heavy chain:

QVQLQQSGPEVVKPGASVKMSCKASGYTFTSYVIHWVRQKPGQGLDWIGYINPYN
DGTDYDEKFKGKATLTSDTSTSTAYMELSSLRSEDTAVYYCAREKDNYATGAWFA
YWGGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS
GALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDHKPSNTKVDKRVE
5 SKYGSR;

10E8.v4 light chain:

SELTQDPAVSVALKQTVTITCRGDSLRSYASWYQKKPGQAPVLLFYGKNNRPSGI
PDRFSGSASGNRASLTITGAQAEDADYYCSSRDKSGSRLSVFGGGTKLTVLSQPK
AAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQ
10 SNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTEC;

10E8.v4 heavy chain:

EVRLVESGGGLVKPGGSLRLSCSASGFDNDNAWMTWVRQPPGKGLEWVGRITGP
GEGWSVDYAESVKGRFTISRDNKNTLYLEMNNVRTEDTGYIFCARTGKYDFWS
GYPPGEEYFQDWGQGLTVIVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
15 EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCSR;

N49P7 light chain:

QSALTQPRSVSASPGQSVTISCTGTHNLVSWCQHQPGRAPKLLIYDFNKRPSGVPD
RFGSGSGGTASLTITGLQDDDDAEYFCWAYEAFGGGKLTVLGQPKAAPSVTLFP
20 PSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAAS
SYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTEC;

N49P7 heavy chain:

ADLVQSGAVKKPGDSVRISCEAQGYRFPDYIIHWIRRAPGQGPWMGMNPMG
GQVNIPWKFQGRVSMTRDTSIETAFDLRLGLKSDDTAVYYDRSNGSGKRFESSNW
25 FDLWGRGTAVTIQSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKK
VEPKSCDSR;

PGDM1400 light chain:

DFVLTQSPHSLSVTPGESASISCKSSHSLIHGDRNNYLAWYVQKPGRSPQLLIYLAS
SRASGVDPDRFSGSGSDKDFTLKISRVEDVGTYYCMQGRESPTWTFGGTKVDIK
30 RTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESV
TEQDSKDYSTLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRGEC;

PGDM1400 heavy chain:

QAQLVQSGPEVRKPGTSVKVSCAPGNTLKTYDLHWVRSVPGQGLQWMGWISHE
 GDKKVIVERFKAKVTIDWDRSTNTAYLQLSGLTSGDTAVYYCAKGSKHRLRDYALY
 DDDGALNWAVDVDYLSNLEFWGQGTAVTVSSASTKGPSVFPLAPSSKSTSGGTAA
 LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQT
 YICNVNHHKPSNTKVDKKVEPKSCDSR; or

combinations thereof.

17. The fusion protein of any one of claims 3 to 16, wherein the antibody or fragment thereof is conjugated to or associated with a further moiety, such as an antigen, a detectable moiety (e.g., a small molecule, fluorescent molecule, radioisotope, or magnetic particle), a pharmaceutical agent, a diagnostic agent, or combinations thereof.

18. The fusion protein of claim 17, wherein the antibody or fragment thereof comprises an antibody-drug conjugate.

19. The fusion protein of claim 3, wherein the antigen is associated with a vaccine-preventable and/or vaccine-treatable condition.

20. The fusion protein of claim 19, wherein antigen is associated with an infectious agent, including a virus, bacteria, parasite, fungus, or yeast, a cancer, including solid and liquid cancers, or an immune disease, including an autoimmune disease.

21. The fusion protein of claim 3, wherein the detectable moiety comprises a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent protein, such as a LOV-protein, such as iLOV.

22. The fusion protein of claim 3, wherein the pharmaceutical agent comprises a small molecule, peptide, lipid, carbohydrate, or toxin.

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

24. The fusion protein of any one of claims 1 to 23, wherein the nanocage monomer is selected from ferritin, apoferritin, encapsulin, SOR, lumazine synthase, pyruvate dehydrogenase, carboxysome, vault proteins, GroEL, heat shock protein, E2P, MS2 coat protein, fragments thereof, and variants thereof.

25. The fusion protein of claim 24, wherein the nanocage monomer is apoferritin.

26. The fusion protein of claim 25, wherein the first and second nanocage monomer subunits interchangeably comprise the "N" and "C" regions of apoferritin.

27. The fusion protein of claim 26, 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:

5 MSSQIRQNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELA
EEKREGYERLLKMQNQRGGRALFQDIKKPAEDEV.

28. The fusion protein of claim 26 or 27, 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:

10 GKTPDAMKAAMALEKKLNQALLDLHALGSARTDPHLCDFLETHFLDEEVKLIKMG
DHLTNLHRLGGPEAGLGEYLFERLTRHD.

29. The fusion protein of any one of claims 1 to 28, further comprising a linker between the nanocage monomer subunit and the bioactive moiety.

30. The fusion protein of claim 29, wherein the linker is flexible or rigid and comprises from about 1 to about 30 amino acid residues, such as from about 8 to about 16 amino acid residues.

31. The fusion protein of claim 29 or 30, wherein the linker comprises a GGS repeat, such as 1, 2, 3, 4, or more GGS repeats.

32. The fusion protein of claim 29, 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:

ASTASSASSGGGGGGSGGSGGSGGS.

33. The fusion protein of any one of claims 1 to 32, further comprising a C-terminal linker.

34. The fusion protein of claim 33, wherein the C-terminal linker comprises or consists of a sequence at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to:

GGSGGSGGSGGSGGGASGGS.

35. A pair of the fusion proteins of any one of claims 1 to 34, wherein the pair self-assembles to form a nanocage monomer, wherein the first and second nanocage monomer subunits are fused to different bioactive moieties.

36. A nanocage comprising at least one fusion protein of any one of claims 1 to 34 and at least one second nanocage monomer subunit that self-assembles with the fusion protein to form a nanocage monomer.

37. A nanocage comprising at least one pair of claim 35.
38. The nanocage of claim 36 or 37, wherein each nanocage monomer comprises the fusion protein of any one of claims 1 to 34 or the pair of claim 35.
39. The nanocage of claim 36 or 37, wherein from about 20% to about 80% of the
5 nanocage monomers comprise the fusion protein of any one of claims 1 to 34 or the pair of claim 35.
40. The nanocage of any one of claims 36 to 39, comprising at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 different bioactive moieties.
41. The nanocage of any one of claims 36 to 40, comprising at least one whole
10 nanocage monomer, optionally fused to a bioactive moiety that may be the same or different from the bioactive moiety of any one of claims 1 to 37.
42. The nanocage of any one of claims 36 to 41, wherein the nanocage is multivalent and/or multispecific.
43. The nanocage of any one of claims 36 to 42, comprising a first, second, and
15 third fusion protein of any one of claims 1 to 34, and at least one whole nanocage monomer, optionally fused to a bioactive moiety, wherein the bioactive moieties of the first, second, and third fusion proteins and of the whole nanocage monomer are all different from one another.
44. The nanocage of claim 43, wherein the first, second, and third fusion proteins each comprise an antibody or fragment thereof fused to N- or C-ferritin, wherein at least one
20 of the first, second, and third fusion proteins is fused to N-ferritin and at least one of the first, second, and third fusion proteins is fused to C-ferritin.
45. The nanocage of claim 44, wherein the antibody or fragment thereof of the first fusion protein is an Fc fragment; wherein the second and third fusion proteins each comprise an antibody or fragment thereof specific for a different antigen of a virus such as
25 HIV or wherein one of the second and third fusion proteins comprises an antibody or fragment thereof specific for an antigen of a virus such as HIV and the third fusion protein comprises an antibody or fragment thereof specific for a different antigen, such as the CD4 receptor; and wherein the whole nanocage monomer is fused to a bioactive moiety that is specific for another different antigen, optionally of the same virus such as HIV.
- 30 46. The nanocage of claim 45, wherein the Fc fragment comprises one or more mutations, such as LS, YTE, LALA, and/or LALAP, that modulate the half-life of the fusion protein from, for example, minutes or hours to several days, weeks, or months.

47. The nanocage of claim 45 or 46, wherein the antibody or fragment thereof of the second fusion protein is N49P7 or iMab A12P; wherein the antibody or fragment thereof of the third fusion protein is 10E8v4.

48. The nanocage of claim 47, comprising the following four fusion proteins:

- 5 a. PGDM1400 (optionally scPGDM1400) fused to full length ferritin;
- b. Fc (optionally scFc) fused to N-ferritin;
- c. N49P7 or iMab A12P (optionally scN49P7 or sciMab A12P) fused to C-ferritin; and
- d. 10E8v4 (optionally sc10E8v4) fused to C-ferritin.

49. The nanocage of claim 48, comprising a 4:2:1:1 ratio of a:b:c:d.

- 10 50. The nanocage of claim 48 or 49, comprising or consisting of sequences at least 70% (such as at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) identical to one or more of the following sequences, where ferritin subunits are in bold, linkers are underlined, light chains are italicized, and heavy chains are in lowercase:

a. PGDM1400-hFerr:

15 *DFVLTQSPHLSVTPGESASISCKSSSHLIHGDRNNYLAWYVQKPGRSPQLLIYLAS*
SRASGVPDFRFSGSGSDKDFTLKISRVEDVGYTCMQGRESPWTFGQGTKVDIK
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESV
TEQDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECGGSS
GSGSGSTGTSSSGTGTSAGTTGTSASTSGSGSGGGGGSGGGGSAGGTATAGAS
20 *SGSGSSGSSSSGGTG**qaqlvqsgpevrkpgtsvkvsckapgnltktydlhwrvspgqglqwmgwishe*
gdkkviverfkakvtidwdrstntaylqlsgltsgdtavyycaqgskhrlrdyalyddgalnwavdvdylnlefwgqgt
avtvssastkgpsvflpapskstsggtaalgclvdyfpepvtvswngaltsgvhtfpavllqssgylsssvtvpss
*slgtqtyicvnhkpsntkvdkkvepkscdsr***ASTASSASSGGGGGGSGGGSGGGSS****MSSQIR**
QNYSTDVEAAVNSLVNLYLQASYTYLSLGFYFDRDDVALEGVSHFFRELAEEKRE
25 **GYERLLKMQNQRGGRALFQDIKKPAEDEWGKTPDAMKAAMALEKKLNQALLDL**
HALGSARTDPHLCDFLETHFLDEEVKLIKMGDHLTNLHRLGGPEAGLGEYLFER
LTLRHDGGSGSGSGSGSGGGASGGS;

b. Fc-N-hFerr LS

30 *DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN*
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSVLHEALHSHYTQKSLSL
SPGKGGSSGSGSGSTGTSSSGTGTSAGTTGTSASTSGSGSGGGGGSGGGGSAG
*GTATAGASSGSGSSGSSSSGGTG**dkthtccppcpapellggpsvflfppkpkdtlmisrtpevtcvvvdv*

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vkgrftisrdntkntlylemnrvrtedtggyfcartgkyydfwsgyppgeeyfqdwgqgtlvivssastkgpsvfplapss
 kstsggtaalgclvkdyfpepvtvswngaltsgvhtfpavllqssgylssvvtvpssslgtqtyicnvnhkpsntkvdk
 kvepkscsrASTASSASSGGGGGGSGGGSGGGSGKTPDAMKAAMALEKKLNQAL
LDLHALGSARTDPHLCDFLETHFLDEEVKLIKMGDHLTNLHRLGGPEAGLGEYL
 5 **FERLTLRHDGGSGGGSGGGSGGGSGGGASGGS.**

51. The nanocage of any one of claims 36 to 50, carrying a cargo molecule, such as a pharmaceutical agent, a diagnostic agent, and/or an imaging agent.

52. The nanocage of claim 51, wherein the cargo molecule is not fused to the fusion protein and is contained in the nanocage internally.

10 53. The nanocage of claim 51, 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.

54. The nanocage of any one of claims 51 to 53, wherein the cargo molecule is a fluorescent protein, such as GFP, EGFP, Ametrine, and/or a flavin-based fluorescent
 15 protein, such as a LOV-protein, such as iLOV.

55. The nanocage of any one of claims 51 to 54, wherein the cargo molecule is contained internally to provide T-cell epitopes, but optionally not B-cell epitopes.

56. The nanocage of any one of claims 51 to 54, wherein the cargo molecule is fused to the fusion protein and contained internally to provide T-cell epitopes, but optionally
 20 not B-cell epitopes.

57. The nanocage of claim 51 or 52, wherein the cargo molecule is a small molecule, radioisotope, or magnetic particle.

58. The nanocage of any one of claims 36 to 57, further comprising an antigen on the surface.

25 59. The nanocage of claim 58, wherein the antigen is expressed as a fusion protein with a nanocage monomer.

60. A vaccine comprising the nanocage of any one of claims 36 to 59.

61. A therapeutic or prophylactic composition comprising the nanocage of any one of claims 36 to 59.

30 62. A nucleic acid molecule encoding the fusion protein of any one of claims 1 to 34 or the pair of claim 35.

63. A vector comprising the nucleic acid molecule of claim 62.

64. A host cell comprising the vector of claim 63 and producing the fusion protein of any one of claims 1 to 34 or the pair of claim 35.

65. A method of immunizing a subject, the method comprising administering the nanocage of any one of claims 36 to 59 or the vaccine of claim 60.

5 66. A method for treating and/or preventing a disease or condition, the method comprising administering the nanocage of any one of claims 36 to 59 or the vaccine of claim 60.

67. The method of claim 66, wherein the disease or condition is cancer, an infectious disease such as HIV, malaria, influenza, RSV, rotavirus, or an autoimmune
10 disease.

68. A method for diagnostic imaging, the method comprising administering the nanocage of any one of claims 36 to 59 to a subject, tissue, or sample, wherein the nanocage comprises a diagnostic label, such as a fluorescent protein or magnetic imaging moiety, and imaging the subject, tissue, or sample.

15 69. Use of the nanocage of any one of claims 36 to 59 or the vaccine of claim 60 for immunizing a subject.

70. Use of the nanocage of any one of claims 36 to 59 or the vaccine of claim 60 for treating and/or preventing a disease or condition.

71. The use of claim 70, wherein the disease or condition is cancer, an infectious
20 disease such as HIV, malaria, influenza, RSV, rotavirus, or an autoimmune disease.

72. Use of the nanocage of any one of claims 36 to 59 for diagnostic imaging of a subject, tissue, or sample, wherein the nanocage comprises a diagnostic label, such as a fluorescent protein or magnetic imaging moiety, and imaging the subject, tissue, or sample.

73. Use of the fusion protein of any one of claims 1 to 34, the pair of claim 35, or
25 the nanocage of any one of claims 36 to 59 as a research tool, such as in FACS or in an ELISA.

74. The nanocage of any one of claims 36 to 59 or the vaccine of claim 60 for use in immunizing a subject.

75. The nanocage of any one of claims 36 to 59 or the vaccine of claim 60 for use
30 in treating and/or preventing a disease or condition.

76. The nanocage of claim 70, wherein the disease or condition is cancer, an infectious disease such as HIV, malaria, influenza, RSV, rotavirus, or an autoimmune disease.

77. The nanocage of any one of claims 36 to 59 for use in diagnostic imaging of a subject, tissue, or sample, wherein the nanocage comprises a diagnostic label, such as a fluorescent protein or magnetic imaging moiety, and imaging the subject, tissue, or sample.

78. The fusion protein of any one of claims 1 to 34, the pair of claim 35, or the
5 nanocage of any one of claims 36 to 59 for use as a research tool, such as in FACS or in an ELISA.

79. A nanocage comprising a plurality of fusion proteins,
wherein each fusion protein comprises a ferritin light chain and an Fab fragment,
wherein each Fab fragment is capable of specifically binding to an antigen,
10 wherein each Fab fragment decorates the exterior surface of the nanocage, and
wherein the plurality comprises at least 12 fusion proteins.

80. The nanocage of claim 79, wherein the plurality comprises at least 19 fusion proteins.

81. The nanocage of claim 80, wherein the plurality comprises at least 24 fusion
15 proteins.

82. The nanocage of claim 82, wherein the plurality is 24 fusion proteins.

83. The nanocage of any one of claims 79-82 wherein the Fab fragments of the plurality of fusion proteins are capable of specifically binding to the same antigen.

84. The nanocage of any one of claims 79-83, wherein the nanocage does not
20 include any ferritin heavy chains.

85. The nanocage of any one of claims 79-84, wherein the Fab fragments are Fab fragments of a neutralizing antibody.

86. The nanocage of any one of claims 79-85, wherein the antigen is associated with an infectious agent.

25 87. The nanocage of claim 86, wherein the infectious agent is a virus.

88. The nanocage of claim 87, wherein the virus is a human immunodeficiency virus (HIV).

89. The nanocage of any one of claims 85-88, wherein the nanocage is capable of neutralizing the infectious agent with a neutralizing activity of at least 100-fold, 150-fold, 200-
30 fold, 250-fold, 300-fold, 350-fold, 400-fold, 450-fold, or 500-fold greater relative to a control.

90. The nanocage of claim 89, wherein the control comprises a full length version of the neutralizing antibody.

91. The nanocage of claim 90, wherein the neutralizing antibody is an IgG antibody.

5 92. A nanocage comprising a plurality of first fusion proteins and a plurality of second fusion proteins,

wherein each first fusion protein comprises a nanocage monomer or a subunit thereof and an Fab fragment capable of specifically binding to an antigen, and

10 wherein each second fusion protein comprises a nanocage monomer or a subunit thereof and an Fc fragment.

93. The nanocage of claim 92, wherein the nanocage monomer is selected from ferritin, apoferritin, encapsulin, sulfur oxygen reductase (SOR), lumazine synthase, pyruvate dehydrogenase, carboxysome, vault proteins, GroEL, heat shock protein, E2P, MS2 coat protein, fragments thereof, and variants thereof.

15 94. The nanocage of claim 93, wherein the nanocage monomer is apoferritin or ferritin.

95. The nanocage of claim 93, wherein the nanocage monomer is a ferritin light chain.

20 96. The nanocage of claim 94 or 95, wherein the nanocage monomer does not include any ferritin heavy chains.

97. A nanocage comprising a plurality of first fusion proteins and a plurality of second fusion proteins, wherein

(a) (i) the first fusion protein comprises a ferritin light chain and an Fab fragment capable of specifically binding to a first antigen, and

25 (ii) the second fusion protein comprises a ferritin light chain and an Fab fragment capable of specifically binding to a second antigen, or

(b) (i) the first fusion protein comprises N-ferritin and an Fab fragment capable of specifically binding to a first antigen, and

30 (ii) the second fusion protein comprises C-ferritin and an Fab fragment capable of specifically binding to a second antigen,

wherein, within each fusion protein, the Fab fragment is fused to the N-terminus of the ferritin light chain, the N-ferritin, or the C-ferritin, and

wherein the first antigen is distinct from the second antigen.

98. A nanocage comprising a plurality of first fusion proteins, a plurality of second
5 fusion proteins, and a plurality of third fusion proteins, wherein

(a) the first fusion protein comprises a ferritin light chain and an Fab fragment capable of specifically binding a first antigen,

(b) the second fusion protein comprises a C-ferritin and an Fab fragment capable of specifically binding a second antigen, and

10 (c) the third fusion protein comprises an N-ferritin and an Fc fragment,

wherein, within each fusion protein the Fab or Fc fragment is fused to the N-terminus of the ferritin light chain, the C-ferritin, or the N-ferritin, and

wherein the first antigen is distinct from the second antigen.

99. The nanocage of claim 97 or 98, further comprising a plurality of fourth fusion
15 proteins, wherein, the fourth fusion protein comprises a C-ferritin and an Fab fragment capable of specifically binding a third antigen, wherein the third antigen is distinct from the first and second antigens.

100. The nanocage of claim 97, 98, or 99, wherein the Fab fragments are Fab fragments of a neutralizing antibody.

20 101. The nanocage of any one of claims 97-100, wherein the first and second antigens are each associated with an infectious agent.

102. The nanocage of claim 101, wherein the first and second antigens are associated with the same infectious agent.

103. The nanocage of claims 101 or 102, wherein the infectious agent is a virus.

25 104. The nanocage of claim 103, wherein the virus is a human immunodeficiency virus (HIV).

105. The nanocage of claim 100, wherein the first and second antigens are each associated with a virus,

30 wherein the nanocage is capable of neutralizing 100% of pseudoviruses in a panel of pseudoviruses, and

wherein the panel of pseudoviruses comprises, for each Fab fragment within the nanocage capable of specifically binding to an antigen associated with the virus, at least one pseudovirus resistant to a neutralizing antibody corresponding to that Fab fragment.

106. The nanocage of claim 105, wherein the panel of pseudoviruses comprises at
5 least 10, at least 11, at least 12, at least 13, or at least 14 pseudoviruses.

107. The nanocage of any one of claims 100, 105, or 106, wherein the first and second antigens are each associated with a virus,

wherein the nanocage is capable of neutralizing a panel of pseudoviruses with an IC_{50} of less than 1 nM, less than 500 pM, less than 250 pM, less than 100 pM, less than 50 pM,
10 less than 10 pM, or less than 5 pM, and

wherein the panel of pseudoviruses comprises, for each Fab fragment within the nanocage capable of specifically binding to an antigen associated with the virus, at least one pseudovirus resistant to a neutralizing antibody corresponding to that Fab fragment.

108. The nanocage of any one of claims 100 and 105-107, wherein the first and
15 second antigens are each associated with a virus,

wherein the nanocage is capable of neutralizing a panel of pseudoviruses with an IC_{50} (molar concentration) of at least 10-fold, at least 20-fold, at least 30-fold, at least 40-fold, at least 50-fold, at least 60-fold, at least 70-fold, at least 80-fold, at least 90-fold, or at least 100-fold lower than that of one or more controls, and

20 wherein the panel of pseudoviruses comprises, for each Fab fragment within the nanocage capable of specifically binding to an antigen associated with the virus, at least one pseudovirus resistant to a neutralizing antibody corresponding to that Fab fragment.

109. The nanocage of claim 108, wherein the one or more controls comprise a neutralizing antibody corresponding to a Fab fragment within the nanocage, which Fab
25 fragment is capable of specifically binding to an antigen associated with the virus.

110. The nanocage of claim 109, wherein the neutralizing antibody is an IgG antibody.

111. The nanocage of claim 108, 109, or 110, wherein the one or more controls comprise a cocktail of neutralizing antibodies, wherein the cocktail comprises, for each Fab
30 fragment within the nanocage capable of specifically binding to an antigen associated with the virus, a neutralizing antibody corresponding to that Fab fragment.

112. The nanocage of claim 111, wherein the neutralizing antibodies are IgG antibodies.

113. The nanocage of any one of claims 108-112, wherein the one or more controls comprise one or more multispecific antibodies, wherein the one or more
5 multispecific antibodies are collectively capable of binding the first and second antigens, and, optionally, the third antigen.

114. The nanocage of claim 113, wherein the one or more controls comprise a trispecific antibody capable of specifically binding to the first, second, and third antigens.

115. The nanocage of any one of claims 99-114, wherein the first, second, and
10 third antigens are associated with HIV-1; and wherein:

the Fab fragment of the first fusion protein is a PDGM1400 Fab,

the Fab fragment of the second fusion protein is a 10E8v4 Fab,

the Fc fragment of the third fusion protein is a human IgG1 Fc fragment, and

the Fab fragment of fourth fusion protein is a N49P7 Fab.

116. The nanocage of any one of claims 99-114, wherein the first and second
15 antigens are associated with HIV-1; wherein the third antigen is associated with CD4; and wherein:

the Fab fragment of the first fusion protein is a PDGM1400 Fab,

the Fab fragment of the second fusion protein is a 10E8v4 Fab,

20 the Fc fragment of the third fusion protein is a human IgG1 Fc fragment, and

the Fab fragment of fourth fusion protein is an iMab Fab.

117. A therapeutic or prophylactic composition comprising the nanocage of any one of claims 79-116.

118. A method for treating or preventing a disease or condition, the method
25 comprising administering the nanocage of any one of claims 79-116 or the composition of claim 117 to a subject in need thereof.

119. A method of making a multispecific self-assembling nanocage, the nanocage characterized by a pre-selected ratio of different specificities, the method comprising the step of:

30 co-transfecting a host cell with one or more expression plasmids comprising a plurality of polynucleotides, each polynucleotide encoding a fusion protein,

wherein each fusion protein comprises (i) a nanocage monomer or a subunit thereof and (ii) an antibody or antibody fragment of a given specificity,

wherein the step of co-transfecting comprises co-transfecting the polynucleotides in a ratio based on the pre-selected ratio;

5 obtaining polypeptides produced by the host cell; and

purifying the polypeptides by affinity selection for all the different specificities to be present in an assembled nanocage.

120. The method of claim 119, wherein the plurality of polynucleotides comprises at least one polynucleotide encoding a first fusion protein and at least one polynucleotide
10 encoding a second fusion protein,

wherein the first fusion protein comprises a first nanocage monomer subunit, and

wherein the second fusion protein comprises a second nanocage monomer subunit capable of self-assembling with the first nanocage monomer subunit.

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