(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 December 2024 (12.12.2024)

WIPO | PCT

(10) International Publication Number
WO 2024/254544 A2

(51) International Patent Classification:
A61K 47/69 (2017.01) *A61K 39/21* (2006.01)

(21) International Application Number:
PCT/US2024/033130

(22) International Filing Date:
07 June 2024 (07.06.2024)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/506,783 07 June 2023 (07.06.2023) US

(71) Applicant: **NVELOP THERAPEUTICS, INC.** [US/US]; 100 Technology Square, Floor 5, Cambridge, Massachusetts 02139 (US).

(72) Inventors: **CABECEIRAS, Peter**; 100 Technology Square, Floor 5, Cambridge, Massachusetts 02139 (US). **PAJEROWSKI, Dave**; 100 Technology Square, Floor 5, Cambridge, Massachusetts 02139 (US). **BUDZIK, Karol**; 100 Technology Square, Floor 5, Cambridge, Massachusetts 02139 (US). **YU, Yi**; 100 Technology Square, Floor 5, Cambridge, Massachusetts 02139 (US).

(74) Agent: **TANG, Xiaoyang** et al.; Wilson Sonsini Goodrich & Rosati, 650 Page Mill Road, Palo Alto, California 94304 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(54) Title: COMPOSITIONS AND METHODS FOR PROMOTING PAYLOAD DELIVERY IN CELLS

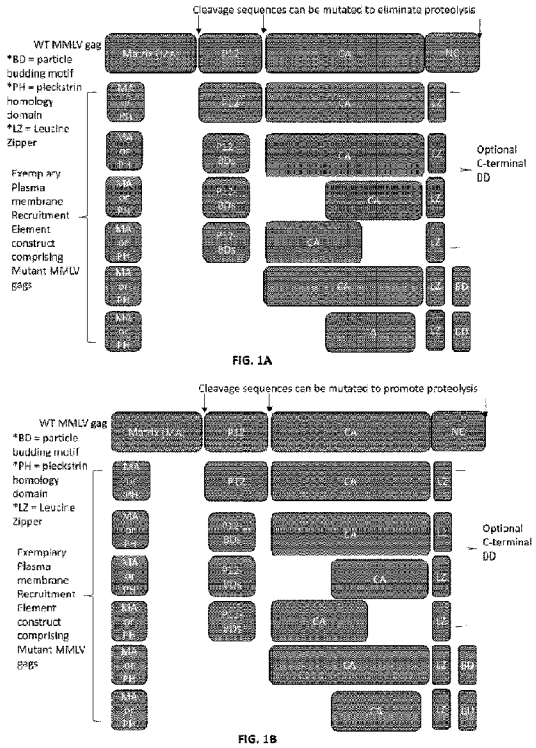


FIG. 1A

FIG. 1B

(57) Abstract: Disclosed herein, in some aspects, are compositions of lipid delivery particles used to deliver a payload to a target cell and methods of producing the like. Lipid delivery particles can comprise ectosomes, exosomes, nanoparticles, or other classes of extracellular vesicles suitable for transporting a payload. Lipid delivery particles can comprise a plasma membrane recruitment element comprising a mutant gag polyprotein.

WO 2024/254544 A2

[Continued on next page]

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *of inventorship (Rule 4.17(iv))*

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

COMPOSITIONS AND METHODS FOR PROMOTING PAYLOAD DELIVERY IN CELLS

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 63/506,783, filed June 7, 2023; which is incorporated herein by reference in their entirety.

BACKGROUND

[0002] Delivery of therapeutic payloads into the cells has been a significant challenge in drug development because payloads, such as proteins, cannot freely diffuse across the cell membrane. Although viral based constructs have been developed to deliver therapeutic payloads, these constructs often have low efficacy and/or create considerable side effects. There is a need for improved delivery of payloads into cells.

SUMMARY

[0003] In some aspects, disclosed herein is a lipid delivery particle comprising (a) a lipid membrane; (b) a plasma membrane recruitment element comprising a mutant gag polyprotein, and (c) a payload encapsulated by the lipid containing membrane, and wherein the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein; and wherein (1) the plasma membrane recruitment element comprises (i) a full-length capsid protein; (ii) a full-length matrix protein; (iii) a heterologous sequence; (iv) at least a portion of a nucleocapsid protein; (v) two or more particle budding motifs; (vi) at least a portion of a P6 domain; or (vii) two spacer peptides; (2) the lipid delivery particle further comprises an envelope protein, wherein the envelope protein comprises an envelope protein from human endogenous retrovirus (HERV) or a mutant thereof; or (3) the plasma membrane recruitment element is fused to (i) a cleavable linker; (ii) a membrane penetrating peptide; or (iii) a post-translational modification motif. In some cases, the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a retrovirus. In some cases, the retrovirus is oncoretroviruses, lentiviruses, or spumaviruses. In some cases, the retrovirus is Human Immunodeficiency Virus (HIV), Moloney Murine Leukemia Virus (MMLV), or Rous sarcoma virus (RSV). In some cases, the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a human endogenous retrovirus (HERV) or a gag homology protein (optionally human Arc). In some cases, the HERV is HERV-K or HERV-W. In some cases, the HERV-K is HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV-K11p22, or HERV-K12q13. In some cases, the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a HERV-K113. In some cases, the mutant gag polyprotein is a mutant of a wild type gag polyprotein of an alpharetrovirus, a betaretrovirus, or a deltaretrovirus, optionally the wild type gag polyprotein comprises the sequence set forth in any one of SEQ ID NOs: 285-298. In some cases, the lipid delivery particle comprises a chimeric protein comprising the plasma membrane recruitment element and the payload. In some cases, the at least a fragment of the matrix protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%,

99% or 100% of the entire amino acid sequence of the matrix protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the matrix protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the matrix protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the RNA-binding phosphoprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the RNA-binding phosphoprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the capsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the capsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the capsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the capsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the nucleocapsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the nucleocapsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the nucleocapsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the nucleocapsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a portion of the P6 domain comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the P6 domain of the corresponding wild type gag polyprotein. In some cases, the at least a portion of the P6 domain comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the P6 domain of a corresponding wild type gag polyprotein. In some cases, the plasma membrane recruitment element comprises the full-length capsid protein. In some cases, the plasma membrane recruitment element comprises the full-length matrix protein. In some cases, the plasma membrane recruitment element comprises the heterologous sequence. In some cases, the heterologous sequence is fused to a fragment of the capsid protein, a matrix protein or a fragment thereof, a nucleocapsid protein or a fragment thereof, a particle budding motif or a fragment thereof. In some cases, the plasma membrane recruitment element lacks the matrix protein. In some cases, the fragment of the capsid protein is a C-terminal fragment comprising a major homology region (MHR). In some cases, the heterologous sequence is fused to the N-terminal of the fragment of the

capsid protein or a particle budding motif (optionally a late domain of RSV). In some cases, the heterologous sequence is a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof. In some cases, the plasma membrane recruitment element comprises at least a portion of the nucleocapsid protein; optionally a N-terminal fragment of the nucleocapsid protein; optionally a C-terminal fragment of the nucleocapsid protein). In some cases, the plasma membrane recruitment element comprises two or more particle budding motifs. In some cases, (a) at least one of the two or more particle budding motifs is endogenous, (b) at least one of the two or more particle budding motifs is heterologous (optionally RSV P2B or a mutant thereof), (c) at least one of the two or more particle budding motifs comprises a PTAP motif, a PPPY motif, a PPXY motif, a YXXL motif, a YPXnL motif, or any combinations thereof, wherein n is an integer from 1 to 5; or (d) at least one of the two or more particle budding motifs comprises a sequence listed in Table 5. In some cases, the plasma membrane recruitment element comprises at least a portion of the P6 domain. In some cases, the plasma membrane recruitment element comprises at least a N-terminal fragment of the P6 domain or at least a C-terminal fragment of the P6 domain. In some cases, the plasma membrane recruitment element comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV. In some cases, the plasma membrane recruitment element is fused to the post-translational modification motif is selected from the group consisting of: a myristoylation motif, an acetylation motif, an isoprenylation motif, a palmitoylation motif, a farnesylation motif, and any combinations thereof. In some cases, the plasma membrane recruitment element comprises the two spacer peptides. In some cases, at least one of the two spacer peptides is P2 domain or P1 domain. In some cases, the two spacer peptides are P2 domain and P1 domain. In some cases, the plasma membrane recruitment element comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV. In some cases, the lipid delivery particle further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof. In some cases, the envelope protein comprises hENVH1, hENVH2, hENVH3, hENVK1, hENVK2, hENVK3, hENVK4, hENVK5, hENVK6, hENVT, hENVW, hENVFRD, hENVR, hENVR(b), hENVR(c)2, hENVR(c)1, or hENVKcon, or a mutant thereof. In some cases, the plasma membrane recruitment element is fused to the cleavable linker, and wherein the cleavable linker connects the plasma membrane recruitment element and the payload. In some cases, the plasma membrane recruitment element is fused to the membrane penetrating peptide. In some cases, (a) the membrane penetrating peptide is linked to the payload or the plasma membrane recruitment element; or (b) the membrane penetrating peptide is linked between the payload and the plasma membrane recruitment element. In some cases, the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in Table 6.

[0004] In some cases, the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of HIV, and wherein (1) the plasma membrane recruitment element is fused to the cleavable linker, the membrane penetrating peptide, or the post-translational modification motif; or (2) wherein the lipid delivery particle further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof. In some cases, the plasma membrane

recruitment element comprises (a) at least a fragment of matrix protein of an HIV gag, optionally a N-terminal fragment of the matrix protein of the HIV gag; or (b) a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof. In some cases, wherein the plasma membrane recruitment element comprises at least a fragment of capsid protein of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a full-length capsid protein of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a C-terminal fragment of capsid protein of the HIV gag. In some cases, wherein the plasma membrane recruitment element comprises a spacer peptide of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a P2 domain of the HIV gag, a P1 domain of the HIV gag, or both. In some cases, the plasma membrane recruitment element comprises (a) a heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif, optionally wherein the multimerization motif forms parallel homodimers or parallel heterodimers (optional DZF), optionally wherein the parallel homodimers comprise a coiled-coil, optionally wherein the coiled-coil is a leucine zipper, optionally wherein the plasma membrane recruitment element lacks nucleocapsid protein of the HIV gag; or (b) a full-length nucleocapsid protein of the HIV gag or a fragment thereof. In some cases, the plasma membrane recruitment element comprises a particle budding motif; optionally wherein the plasma membrane recruitment element comprises two or more particle budding motifs; optionally wherein at least one of the particle budding motifs is (a) a particle budding motif of the HIV gag (optionally a N-terminal fragment of the P6 domain of the HIV gag, a PTAP motif, or a full-length P6 domain of the HIV gag); or (b) a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5). In some cases, the plasma membrane recruitment element lacks a matrix protein of the HIV gag, and wherein the plasma membrane recruitment element comprises a N-terminal myristoylation motif, the full-length capsid protein of the HIV gag or a fragment thereof, the multimerization motif (optionally a DZF), and a heterologous particle budding motif (optionally a late domain of RSV) arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element lacks a matrix protein of the HIV gag, and wherein the plasma membrane recruitment element comprises a heterologous particle budding motif (optionally a late domain of RSV), a N-terminal myristoylation motif, the full-length capsid protein of the HIV gag or a fragment thereof, the multimerization motif (optionally a DZF), arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises (a) the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof; (b) the full-length capsid protein of the HIV gag or a fragment thereof; (c) the multimerization motif (optionally a leucine zipper) or the full-length nucleocapsid protein of the HIV gag or a fragment thereof; and (d) the particle budding motif; optionally wherein the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the plasma membrane recruitment element further comprises the P2 domain of the HIV gag located at a position between (b) and (c). In some cases,

the plasma membrane recruitment element comprises: (a) the particle budding motif; (b) the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof; (c) the full-length capsid protein of the HIV gag or a fragment thereof; and (d) the multimerization motif (optionally a leucine zipper) or the full-length nucleocapsid protein of the HIV gag or a fragment thereof; and; optionally wherein the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the plasma membrane recruitment element further comprises the P2 domain of the HIV gag located at a position between (c) and (d). In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the full-length capsid protein of the HIV gag, the P1 domain of the HIV gag, and the P6 domain of the HIV gag or a fragment thereof, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the leucine zipper, and the P6 domain of the HIV gag or a fragment thereof, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the leucine zipper, and a particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a particle budding motif, the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif, a C-terminal fragment of the HIV gag, the P2 domain of the HIV gag, the leucine zipper, and a second particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, optionally a first particle budding motif, the full-length capsid protein of the HIV gag or a fragment thereof, optionally the P2 domain of the HIV gag, the leucine zipper, and optionally a second particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the first and the second particle budding motif; optionally wherein each of the first and the second particle budding motifs independently (a) is the particle budding motif of the HIV gag; (b) is a heterologous particle budding motif (optionally RSV P2B or a mutant thereof); or (c) comprises a sequence listed in Table 5. In some cases, the plasma membrane

recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the heterologous particle budding motif, the full-length capsid protein of the HIV gag, the P2 domain, the leucine zipper, and the particle budding motif of the HIV gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the HIV gag, the P2 domain, the full-length nucleocapsid protein of the HIV gag, and the particle budding motif of the HIV gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof.

[0005] In some aspects, disclosed herein is a lipid delivery particle comprising (a) a lipid membrane; (b) a plasma membrane recruitment element comprising a mutant gag polyprotein that is not from HIV, and (c) a payload encapsulated by the lipid containing membrane, wherein the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein. In some cases, the mutant gag polyprotein is mutant of a wild-type gag polypeptide of a retrovirus; optionally wherein the retrovirus is oncoretroviruses, lentiviruses, or spumaviruses; optionally wherein the retrovirus is MMLV. In some cases, the mutant gag polyprotein is mutant of a wild-type gag polypeptide of a human endogenous retrovirus (HERV) or a gag homology protein (optionally human Arc or PEG10); optionally wherein the HERV is HERV-K or HERV-W; optionally wherein the HERV-K is HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV-K11p22, or HERV-K12q13; optionally wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of HERV-K113 or a hGAGKcon. In some cases, the mutant gag polyprotein is a mutant of a wild type gag polyprotein of an alpharetrovirus, a betaretrovirus, or a deltaretrovirus, optionally the wild type gag polyprotein comprises the sequence set forth in any one of SEQ ID NOs: 285-298. In some cases, the lipid delivery particle comprises a chimeric protein comprising the plasma membrane recruitment element and the payload. In some cases, the at least a fragment of the matrix protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the matrix protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the matrix protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the matrix protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the RNA-binding phosphoprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein. In some cases, the at

least a fragment of the RNA-binding phosphoprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the capsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the capsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the capsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the capsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the nucleocapsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the nucleocapsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the nucleocapsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the nucleocapsid protein of a corresponding wild type gag polyprotein. In some cases, the plasma membrane recruitment element lacks the at least a fragment of a matrix protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the matrix protein. In some cases, the plasma membrane recruitment element lacks the at least a fragment of a RNA-binding phosphoprotein; optionally wherein the plasma membrane recruitment element comprises a mutant of a wild-type gag polyprotein of MMLV. In some cases, the plasma membrane recruitment element lacks the at least a fragment of a capsid protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the capsid protein, a C-terminal fragment of the capsid protein, or both. In some cases, the plasma membrane recruitment element lacks the gag-endogenous protease cleavage sequence. In some cases, the plasma membrane recruitment element lacks the at least a fragment of a nucleocapsid protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the nucleocapsid protein, a C-terminal fragment of the nucleocapsid protein, or both; optionally wherein the plasma membrane recruitment element lacks the nucleocapsid protein. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of MMLV. In some cases, the plasma membrane recruitment element comprises (a) a matrix protein of the MMLV gag (optionally full-length matrix protein of the MMLV gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the MMLV gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof; (b) a capsid protein of the MMLV gag or a mutant thereof, optionally wherein the capsid protein of the MMLV gag or a mutant thereof is a full-length capsid protein of the MMLV gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the MMLV gag; (c) heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif (optionally a leucine zipper); and (d) an optional particle budding motif, optionally wherein the particle

budding motif is particle budding motif of the MMLV gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5; optionally wherein the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the plasma membrane recruitment element further comprises a P12 domain of the MMLV gag or a mutant thereof located between (a) and (b), optionally wherein the P12 domain of the MMLV gag or a mutant thereof is a full-length P12 domain of the MMLV gag, a N-terminal fragment of the full-length P12 domain of the MMLV gag, a C-terminal fragment of the full-length P12 domain of the MMLV gag, or a fragment of the full-length P12 domain of the MMLV gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5). In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and optionally the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the particle budding motif, the pleckstrin homology (PH) domain or a mutant thereof, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the particle budding motif, the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the particle budding motif,

the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of hGAGKcon; optionally wherein the plasma membrane recruitment element comprises a N-terminal myristoylation motif of the hGAGKcon gag, a full-length capsid protein of the hGAGKcon gag or a fragment thereof, a multimerization motif (optionally a DZF), and a particle budding motif (optionally a late domain of RSV); optionally wherein the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag, a full-length capsid protein of the hGAGKcon gag or a fragment thereof, a multimerization motif (optionally a DZF), and a particle budding motif (optionally a late domain of RSV). In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HERV-K113. In some cases, the plasma membrane recruitment element comprises: (a) a matrix protein of the HERV-K113 gag (optionally full-length matrix protein of the HERV-K113 gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the HERV-K113 gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof; (b) a capsid protein of the HERV-K113 gag or a mutant thereof, optionally wherein the capsid protein of the HERV-K113 gag or a mutant thereof is a full-length capsid protein of the HERV-K113 gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the HERV-K113 gag; (c) heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif (optionally a leucine zipper); and (d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the HERV-K113 gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5); (e) an optional QP1 domain of the HERV-K113 gag; and (f) an optional QP2 domain of the HERV-K113 gag; optionally wherein (a)-(f) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the plasma membrane recruitment element further comprises a P15 domain of the HERV-K113 gag or a mutant thereof, optionally wherein the P15 domain of the HERV-K113 gag or a mutant thereof is a full-length P15 domain of the HERV-K113 gag, a N-terminal fragment of the full-length P15 domain of the HERV-K113 gag, a C-terminal fragment of the full-length P15 domain of the HERV-K113 gag, or a fragment of the full-length P15 domain of the HERV-K113 gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5). In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the HERV-K113 gag, the full-length P15 domain of the HERV-K113 gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the

plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length P15 domain of the HERV-K113 gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, optionally the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the HERV-K113 gag, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the QP1 domain and the QP2 domain of the HERV-K113 gag. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of RSV; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag and a late domain of the RSV gag; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid protein of the RSV; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of the nucleocapsid protein of the RSV; optionally wherein the plasma membrane recruitment element further comprises a N-terminal myristoylation motif. In some cases, the plasma membrane recruitment element comprises one, two, or three particle budding motif, wherein each of the particle budding motif is selected from a sequence listed in Table 5. In some cases, the plasma membrane recruitment element comprises a major homology region (MHR). In some cases, the plasma membrane recruitment element comprises the heterologous sequence; optionally wherein the heterologous sequence is fused to a fragment of the matrix protein, optionally the N-terminal of the fragment of the matrix protein; optionally wherein the heterologous sequence is a pleckstrin homology (PH) domain or a mutant thereof; optionally wherein the PH domain is a human PH domain; optionally wherein the fragment of the matrix protein lacks a N-terminal myristoylation motif, a N-terminal glycine, a highly basic region (HBR), a N-terminal fragment, or any combination thereof. In some cases, the chimeric protein comprises a cleavable linker; optionally wherein the cleavable linker connects the plasma membrane recruitment element and the payload. In some cases, the chimeric protein comprises a nuclear localization signal (NLS) sequence. In some cases, the chimeric protein comprises a nuclear export signal (NES) sequence. In some cases, the chimeric protein comprises the membrane penetrating

peptide, optionally wherein (a) the membrane penetrating peptide is linked to the payload or the plasma membrane recruitment element; or (b) the membrane penetrating peptide connects the payload and the plasma membrane recruitment element; optionally wherein the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in Table 6. In some cases, the chimeric protein comprises the post-translational modification motif that is fused directly to (a) the payload; or (b) the plasma membrane recruitment element; optionally wherein the post-translational modification motif comprises a myristoylation motif, an acetylation motif, an isoprenylation motif, a palmitoylation motif, a farnesylation motif, or combinations thereof. In some cases, the chimeric protein comprises the plasma membrane recruitment element, an optional NLS, the cleavable linker, and the payload arranged in order from N-terminus of the chimeric protein to C-terminus of the chimeric protein. In some cases, the lipid delivery particle comprises the envelope protein; optionally wherein the envelope protein is a retroviral envelope protein or a mutant thereof; optionally wherein the envelope protein is an envelope protein from human endogenous retrovirus (HERV) or a mutant thereof. In some cases, the plasma membrane recruitment element forms part of a basic structure of the lipid delivery particle (optionally a protein core). In some cases, the payload comprises an antibody, a cytokine, a therapeutic protein, a small molecule therapeutics, a therapeutic DNA, and a therapeutic RNA, a ribonucleoprotein, a zinc-finger, a transcription activator-like effector (TALE), or a CRISPR-based genome editor, or any combinations thereof; optionally wherein the payload comprises a NLS, optionally wherein the NLS is an endogenous NLS or a heterologous NLS. In some cases, the lipid delivery particle further comprises a second plasma membrane recruitment element; optionally wherein the second plasma membrane recruitment element is the same as the plasma membrane recruitment element; optionally wherein the second plasma membrane recruitment element is a retroviral gag or a mutant thereof, a HERV gag or a mutant thereof, a pleckstrin homology (PH) domain or a mutant thereof, or a membrane protein or a transmembrane domain thereof or a mutant thereof. In some cases, the second plasma membrane recruitment element forms part of a basic structure of the lipid delivery particle (optionally a protein core). In some cases, the lipid delivery particle further comprises a protease; optionally wherein the protease is a retroviral protease. In some cases, the plasma membrane recruitment element is linked to the protease, optionally via a cleavable linker. In some cases, the second plasma membrane recruitment element is linked to the protease, optionally via a cleavable linker. In some cases, the plasma membrane recruitment element further comprises one or more mutant gag-endogenous protease cleavage sequences relative to a corresponding wildtype gag-endogenous protease cleavage sequence, and wherein the one or more mutant gag-endogenous protease cleavage sequences have higher cleavage efficiency than that of the corresponding wildtype gag-endogenous protease cleavage sequence.

[0006] In some aspects, disclosed herein is a recombinant protein comprising a plasma membrane recruitment element comprising a mutant gag polyprotein, wherein the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein; and wherein (1) the plasma membrane recruitment element

comprises (i) a full-length capsid protein; (ii) a full-length matrix protein; (iii) a heterologous sequence; (iv) at least a portion of a nucleocapsid protein; (v) two or more particle budding motifs; (vi) at least a portion of a P6 domain; or (vii) two spacer peptides; or (2) the plasma membrane recruitment element is fused to (i) a cleavable linker; (ii) a membrane penetrating peptide; or (iii) a post-translational modification motif. In some cases, the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a retrovirus; optionally wherein the retrovirus is oncoretroviruses, lentiviruses, or spumaviruses; optionally wherein the retrovirus is Human Immunodeficiency Virus (HIV), Moloney Murine Leukemia Virus (MMMLV), or Rous sarcoma virus (RSV). In some cases, the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a human endogenous retrovirus (HERV); optionally wherein the HERV is HERV-K or HERV-W; optionally wherein the HERV-K is HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV-K11p22, or HERV-K12q13; optionally wherein the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a HERV-K113. In some cases, the mutant gag polyprotein is a mutant of a wild type gag polyprotein of an alpharetrovirus, a betaretrovirus, or a deltaretrovirus, optionally the wild type gag polyprotein comprises the sequence set forth in any one of SEQ ID NOs: 285-298. In some cases, the at least a fragment of the matrix protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the matrix protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the matrix protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the matrix protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the RNA-binding phosphoprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the RNA-binding phosphoprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the capsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the capsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the capsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the capsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the nucleocapsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the nucleocapsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the nucleocapsid

protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the nucleocapsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a portion of the P6 domain comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the P6 domain of the corresponding wild type gag polyprotein. In some cases, the at least a portion of the P6 domain comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the P6 domain of a corresponding wild type gag polyprotein. In some cases, the plasma membrane recruitment element comprises the full-length capsid protein. In some cases, the plasma membrane recruitment element comprises the full-length matrix protein. In some cases, the plasma membrane recruitment element comprises the heterologous sequence; optionally wherein the heterologous sequence is fused to a fragment of the capsid protein, a matrix protein or a fragment thereof, a nucleocapsid protein or a fragment thereof, a particle budding motif or a fragment thereof; optionally wherein the plasma membrane recruitment element lacks the matrix protein; optionally wherein the fragment of the capsid protein is a C-terminal fragment. In some cases, the heterologous sequence is fused to the N-terminal of the fragment of the capsid protein or a particle budding motif (optionally a late domain of RSV); optionally wherein the heterologous sequence is a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof. In some cases, the plasma membrane recruitment element comprises at least a portion of a nucleocapsid protein; optionally a N-terminal fragment of the nucleocapsid protein; optionally a C-terminal fragment of the nucleocapsid protein). In some cases, the plasma membrane recruitment element comprises two or more particle budding motifs; optionally wherein (a) at least one of the two or more particle budding motifs is endogenous, (b) at least one of the two or more particle budding motifs is heterologous (optionally RSV P2B or a mutant thereof), (c) at least one of the two or more particle budding motifs comprises a PTAP motif, a PPPY motif, a PPXY motif, a YXXL motif, a YPXnL motif, or any combinations thereof, wherein n is an integer from 1 to 5, or (d) at least one of the two or more particle budding motifs comprises a sequence listed in Table 5. In some cases, the plasma membrane recruitment element comprises at least a portion of the P6 domain; optionally wherein the plasma membrane recruitment element comprises at least a N-terminal fragment of the P6 domain or at least a C-terminal fragment of the P6 domain; optionally wherein the plasma membrane recruitment element comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV. In some cases, the plasma membrane recruitment element is fused to the post-translational modification motif is selected from the group consisting of: a myristoylation motif, an acetylation motif, an isoprenylation motif, a palmitoylation motif, and a farnesylation motif. In some cases, the plasma membrane recruitment element comprises the two spacer peptides; optionally wherein at least one of the two spacer peptides is P2 domain or P1 domain; optionally wherein the two spacer peptides are P2 domain and P1 domain; optionally wherein the plasma membrane recruitment element comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV. In some

cases, the recombinant protein further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof; optionally wherein the envelope protein comprises hENVH1, hENVH2, hENVH3, hENVK1, hENVK2, hENVK3, hENVK4, hENVK5, hENVK6, hENVT, hENVW, hENVFRD, hENVR, hENVR(b), hENVR(c)2, hENVR(c)1, or hENVKcon, or a mutant thereof. In some cases, the plasma membrane recruitment element is fused to the membrane penetrating peptide; optionally wherein the membrane penetrating peptide is linked to the plasma membrane recruitment element; optionally wherein the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in Table 6. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV and wherein (1) the plasma membrane recruitment element is fused to the cleavable linker or the membrane penetrating peptide; or (2) wherein the recombinant protein further comprises the envelope protein, wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof. In some cases, the plasma membrane recruitment element comprises (a) at least a fragment of matrix protein of an HIV gag, optionally a N-terminal fragment of the matrix protein of the HIV gag; or (b) a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof. In some cases, the plasma membrane recruitment element comprises at least a fragment of capsid protein of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a full-length capsid protein of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a C-terminal fragment of capsid protein of the HIV gag. In some cases, the plasma membrane recruitment element comprises a spacer peptide of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a P2 domain of the HIV gag, a P1 domain of the HIV gag, or both. In some cases, the plasma membrane recruitment element comprises (a) a heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif, optionally wherein the multimerization motif forms parallel homodimers or parallel heterodimers (optional DZF), optionally wherein the parallel homodimers comprise a coiled-coil, optionally wherein the coiled-coil is a leucine zipper, optionally wherein the plasma membrane recruitment element lacks nucleocapsid protein of the HIV gag; or (b) a full-length nucleocapsid protein of the HIV gag or a fragment thereof. In some cases, the plasma membrane recruitment element comprises a particle budding motif; optionally wherein the plasma membrane recruitment element comprises two or more particle budding motifs; optionally wherein at least one of the particle budding motifs is (a) a particle budding motif of the HIV gag (optionally a N-terminal fragment of the P6 domain of the HIV gag, a PTAP motif, or a full-length P6 domain of the HIV gag); or (b) a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5). In some cases, the plasma membrane recruitment element lacks a matrix protein of the HIV gag and wherein the plasma membrane recruitment element comprises a N-terminal myristoylation motif, the full-length capsid protein of the HIV gag or a fragment thereof, the multimerization motif (optionally a DZF), and a heterologous particle budding motif (optionally a late domain of RSV) arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane

recruitment element. In some cases, the plasma membrane recruitment element comprises (a) the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof; (b) the full-length capsid protein of the HIV gag or a fragment thereof; (c) optionally the P2 domain of the HIV gag; (d) the multimerization motif (optionally a leucine zipper) or the full-length nucleocapsid protein of the HIV gag or a fragment thereof; and (e) the particle budding motif; optionally wherein the (a)-(e) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the full-length capsid protein of the HIV gag, the P1 domain of the HIV gag, and the P6 domain of the HIV gag or a fragment thereof, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the leucine zipper, and the P6 domain of the HIV gag or a fragment thereof, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the leucine zipper, and a particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif, a C-terminal fragment of the HIV gag, the P2 domain of the HIV gag, the leucine zipper, and a second particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, optionally a first particle budding motif, the full-length capsid protein of the HIV gag or a fragment thereof, optionally the P2 domain of the HIV gag, the leucine zipper, and optionally a second particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the first and the second particle budding motif; optionally wherein each of the first and the second particle budding motifs independently (a) is the particle budding motif of the HIV gag; (b) is a heterologous particle budding motif (optionally RSV P2B or a mutant thereof); or (c) comprises a sequence listed in Table 5. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the heterologous particle budding motif, the full-length capsid protein of the HIV gag, the P2 domain, the leucine zipper, and the particle budding motif of the HIV gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof. In some

cases, the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the HIV gag, the P2 domain, the full-length nucleocapsid protein of the HIV gag, and the particle budding motif of the HIV gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof.

[0007] In some aspects, disclosed herein is a recombinant protein comprising a plasma membrane recruitment element comprising a mutant gag polyprotein that is not from HIV, and wherein the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein. In some cases, the mutant gag polyprotein is mutant of a wild-type gag polypeptide of a retrovirus; optionally wherein the retrovirus is oncoretroviruses, lentiviruses, or spumaviruses; optionally wherein the retrovirus is MMLV or RSV. In some cases, the mutant gag polyprotein is mutant of a wild-type gag polypeptide of a human endogenous retrovirus (HERV) or a gag homology protein (optionally human Arc); optionally wherein the HERV is HERV-K or HERV-W; optionally wherein the HERV-K is HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV-K11p22, or HERV-K12q13; optionally wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of HERV-K113 or a hGAGKcon. In some cases, the mutant gag polyprotein is mutant of a wild-type gag polypeptide of an alpharetrovirus, a betaretrovirus, or a deltaretrovirus, optionally the wild type gag polyprotein comprises the sequence set forth in any one of SEQ ID NOs: 285-298. In some cases, the at least a fragment of the matrix protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the matrix protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the matrix protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the matrix protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the RNA-binding phosphoprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the RNA-binding phosphoprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the capsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the capsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the capsid protein comprises at least 1, 2, 3, 4, 5, 6,

7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the capsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the nucleocapsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the nucleocapsid protein of a corresponding wild type gag polyprotein. In some cases, the at least a fragment of the nucleocapsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the nucleocapsid protein of a corresponding wild type gag polyprotein. In some cases, the plasma membrane recruitment element lacks the at least a fragment of a matrix protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the matrix protein. In some cases, the plasma membrane recruitment element lacks the at least a fragment of a RNA-binding phosphoprotein; optionally wherein the plasma membrane recruitment element comprises a mutant of a wild-type gag polyprotein of MMLV. In some cases, the plasma membrane recruitment element lacks the at least a fragment of a capsid protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the capsid protein, a C-terminal fragment of the capsid protein, or both. In some cases, the plasma membrane recruitment element lacks the gag-endogenous protease cleavage sequence. In some cases, the plasma membrane recruitment element lacks the at least a fragment of a nucleocapsid protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the nucleocapsid protein, a C-terminal fragment of the nucleocapsid protein, or both; optionally wherein the plasma membrane recruitment element lacks the nucleocapsid protein. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of MMLV. In some cases, the plasma membrane recruitment element comprises (a) a matrix protein of the MMLV gag (optionally full-length matrix protein of the MMLV gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the MMLV gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof; (b) a capsid protein of the MMLV gag or a mutant thereof, optionally wherein the capsid protein of the MMLV gag or a mutant thereof is a full-length capsid protein of the MMLV gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the MMLV gag; (c) heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif (optionally a leucine zipper); and (d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the MMLV gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5; optionally wherein the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the plasma membrane recruitment element further comprises a P12 domain of the MMLV gag or a mutant thereof located between (a) and (b), optionally wherein the P12 domain of the MMLV gag or a mutant thereof is a full-length P12 domain of the MMLV gag, a N-

terminal fragment of the full-length P12 domain of the MMLV gag, a C-terminal fragment of the full-length P12 domain of the MMLV gag, or a fragment of the full-length P12 domain of the MMLV gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5). In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and optionally the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of hGAGKcon; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag and a late domain of the RSV gag; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid protein of the RSV gag; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of the nucleocapsid protein of the RSV; optionally wherein the plasma membrane recruitment element further comprises a N-terminal myristoylation motif of the RSV gag. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HERV-K113. In some cases, the plasma membrane recruitment element comprises (a) a matrix protein of the HERV-K113 gag (optionally full-length matrix protein of the HERV-K113 gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the HERV-K113 gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof; (b) a capsid protein of the HERV-K113 gag or a mutant thereof, optionally wherein the capsid protein of the HERV-K113 gag or a mutant thereof is a full-length capsid protein of the HERV-K113 gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the HERV-K113 gag; (c) heterologous domain, optionally wherein the heterologous domain comprises a multimerization

motif (optionally a leucine zipper); and (d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the HERV-K113 gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5); (e) an optional QP1 domain of the HERV-K113 gag; and (f) an optional QP2 domain of the HERV-K113 gag; optionally wherein (a)-(f) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the plasma membrane recruitment element further comprises a P15 domain of the HERV-K113 gag or a mutant thereof, optionally wherein the P15 domain of the HERV-K113 gag or a mutant thereof is a full-length P15 domain of the HERV-K113 gag, a N-terminal fragment of the full-length P15 domain of the HERV-K113 gag, a C-terminal fragment of the full-length P15 domain of the HERV-K113 gag, or a fragment of the full-length P15 domain of the HERV-K113 gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5). In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the HERV-K113 gag, the full-length P15 domain of the HERV-K113 gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length P15 domain of the HERV-K113 gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, optionally the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the HERV-K113 gag, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises the QP1 domain and the QP2 domain of the HERV-K113 gag. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of RSV; optionally wherein the mutant gag

polyprotein comprises a matrix protein of the RSV gag and a late domain of the RSV gag; optionally wherein the mutant gag polyprotein comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid protein of the RSV; optionally wherein the mutant gag polyprotein comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of the nucleocapsid protein of the RSV; optionally wherein the mutant gag polyprotein comprises a N-terminal myristoylation motif of the RSV gag. In some cases, the plasma membrane recruitment element comprises one, two, or three particle budding motif, wherein each of the particle budding motif is selected from a sequence listed in Table 5. In some cases, the plasma membrane recruitment element comprises a MHR. In some cases, the plasma membrane recruitment element comprises the heterologous sequence; optionally wherein the heterologous sequence is fused to at least a fragment of the matrix protein, optionally the N-terminal of the fragment of the matrix protein; optionally wherein the heterologous sequence is a pleckstrin homology (PH) domain or a mutant thereof; optionally wherein the PH domain is a human PH domain; optionally wherein the fragment of the matrix protein lacks a N-terminal myristoylation motif, a N-terminal glycine, a highly basic region (HBR), a N-terminal fragment, or any combinations thereof. In some cases, the plasma membrane recruitment element further comprises one or more mutant gag-endogenous protease cleavage sequences relative to a corresponding wildtype gag-endogenous protease cleavage sequence, and wherein the one or more mutant gag-endogenous protease cleavage sequences have higher cleavage efficiency than that of the corresponding wildtype gag-endogenous protease cleavage sequence.

[0008] In some aspects, disclosed herein is a chimeric protein comprising the recombinant protein described herein, wherein the chimeric protein comprises a cleavable linker; optionally wherein the cleavable linker connects the plasma membrane recruitment element and a payload.

In some cases, the chimeric protein comprises a nuclear localization signal (NLS) sequence. In some cases, the chimeric protein comprises a nuclear export signal (NES) sequence. In some cases, the chimeric protein comprises the membrane penetrating peptide, optionally wherein (a) the membrane penetrating peptide is linked to the payload or the plasma membrane recruitment element; or (b) the membrane penetrating peptide connects the payload and the plasma membrane recruitment element; optionally wherein the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in Table 6. In some cases, the chimeric protein comprises a post-translational modification motif that is fused directly to (a) the payload; or (b) the plasma membrane recruitment element; optionally wherein the post-translational modification motif comprises a myristoylation motif, an acetylation motif, an isoprenylation motif, a palmitoylation motif, a farnesylation motif, or combinations thereof. In some cases, the chimeric protein comprises the plasma membrane recruitment element, an optional NLS, the cleavable linker, and the payload arranged in order from N-terminus of the chimeric protein to C-terminus of the chimeric protein. In some cases, the payload comprises an antibody, a cytokine, a therapeutic protein, a small molecule therapeutics, a therapeutic DNA, and a therapeutic RNA, a ribonucleoprotein, a zinc-finger, a transcription activator-like effector

(TALE), or a CRISPR-based genome editor, or any combinations thereof; optionally wherein the payload comprises a NLS, optionally wherein the NLS is an endogenous NLS or a heterologous NLS.

[0009] In some aspects, disclosed herein is a composition comprising a first nucleic acid sequence encoding the recombinant protein described herein or the chimeric protein described herein.

In some cases, the composition comprises a second nucleic acid sequence encoding an envelope protein; optionally wherein the envelope protein is a retroviral envelope protein or a mutant thereof; optionally wherein the envelope protein is an envelope protein from human endogenous retrovirus (HERV) or a mutant thereof. In some cases, the composition further comprises a third nucleic acid sequence encoding a second plasma membrane recruitment element; optionally wherein the second plasma membrane recruitment element is the same as the plasma membrane recruitment element; optionally wherein the second plasma membrane recruitment element is a retroviral gag or a mutant thereof, a HERV gag or a mutant thereof, a pleckstrin homology (PH) domain or a mutant thereof, or a membrane protein or a transmembrane domain thereof or a mutant thereof. In some cases, the composition further comprises fourth nucleic acid encoding a protease; optionally wherein the protease is a retroviral protease. In some cases, the plasma membrane recruitment element is linked to the protease, optionally via a cleavable linker. In some cases, the second plasma membrane recruitment element is linked to the protease, optionally via a cleavable linker.

[0010] In some aspects, disclosed herein is a system comprising the lipid delivery particle described herein or the composition described herein. In some cases, the system comprises a producer cell, a cell-free extract, or a cell lysate.

[0011] In some aspects, disclosed herein is a pharmaceutical composition comprising (a) the lipid delivery particle described herein or the system described herein; and (b) a pharmaceutically acceptable excipient.

[0012] In some aspects, disclosed herein is a kit comprising (a) the lipid delivery particle described herein, the system described herein, or the pharmaceutical composition described herein; and (b) an information material containing instructions for administering a dosage of the lipid delivery particle or the system, or a dosage form of the pharmaceutical composition to a subject.

[0013] In some aspects, disclosed herein is a method of treating a disease or a condition in a subject in need thereof, comprising administering to the subject the lipid delivery particle described herein, the system described herein, or the pharmaceutical composition described herein.

[0014] In some aspects, disclosed herein is a method comprising contacting a cell with the lipid delivery particle described herein.

[0015] In some aspects, disclosed herein is a method comprising contacting a cell with the system described herein.

[0016] In some aspects, disclosed herein is a method comprising administering the lipid delivery particle described herein, the system described herein, or the pharmaceutical composition described herein to a subject in need thereof.

[0017] In some aspects, disclosed herein is a method of producing the lipid delivery particle described herein. In some cases, the method comprises contacting a producer cell with the composition described herein.

INCORPORATION BY REFERENCE

[0018] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The novel features of the disclosure are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosure will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the disclosure are utilized, and the accompanying drawings of which:

[0020] **FIG. 1A** depicts schematic representations of exemplary plasma membrane recruitment element constructs that comprise a mutant Moloney Murine leukemia virus (MMLV) gag as compared to wild-type MMLV gag according to some embodiments of the present disclosure. The schematics showing various domains of MMLV gag, truncations thereof, or replacement or fusion of a domain with another protein are for illustrative purporses only and does not represent the actual length or the relative size of one domain as compared to another domain. In some cases, the cleavage sequences can be mutated to eliminate proteolysis.

[0021] **FIG. 1B** depicts schematic representations of exemplary plasma membrane recruitment element constructs that comprise a mutant Moloney Murine leukemia virus (MMLV) gag as compared to wild-type MMLV gag according to some embodiments of the present disclosure. The schematics showing various domains of MMLV gag, truncations thereof, or replacement or fusion of a domain with another protein are for illustrative purporses only and does not represent the actual length or the relative size of one domain as compared to another domain. In some cases, the cleavage sequences can be mutated to promote proteolysis.

[0022] **FIG. 2A** depicts schematic representations of exemplary plasma membrane recruitment element constructs that comprise a mutant Human Endogenous Retrovirus (HERV) K-113 gag as compared to wild-type HERV-K113 gag according to some embodiments of the present disclosure. The schematics showing various domains of HERV-K113 gag, truncations thereof, or replacement or fusion of a domain with another protein are for illustrative purporses only and does not represent the actual length or the relative size of one domain as compared to another domain. In some cases, the cleavages sequence can be mutated to eliminate proteolysis.

[0023] **FIG. 2B** depicts schematic representations of exemplary plasma membrane recruitment element constructs that comprise a mutant Human Endogenous Retrovirus (HERV) K-113 gag as compared to wild-type HERV-K113 gag according to some embodiments of the present disclosure. The schematics

showing various domains of HERV-K113 gag, truncations thereof, or replacement or fusion of a domain with another protein are for illustrative purporses only and does not represent the actual length or the relative size of one domain as compared to another domain. In some cases, the cleavage sequences can be mutated to promote proteolysis.

[0024] **FIG. 3A** depicts schematic representations of exemplary plasma membrane recruitment element constructs that comprise a mutant Human Immunodeficiency Virus (HIV) gag as compared to wild-type HIV gag according to some embodiments of the present disclosure. The schematics showing various domains of HIV gag, truncations thereof, or replacement or fusion of a domain with another protein are for illustrative purporses only and does not represent the actual length or the relative size of one domain as compared to another domain. In some cases, the cleavage sequences can be mutated to eliminate proteolysis.

[0025] **FIG. 3B** depicts schematic representations of exemplary plasma membrane recruitment element constructs that comprise a mutant Human Immunodeficiency Virus (HIV) gag as compared to wild-type HIV gag according to some embodiments of the present disclosure. The schematics showing various domains of HIV gag, truncations thereof, or replacement or fusion of a domain with another protein are for illustrative purporses only and does not represent the actual length or the relative size of one domain as compared to another domain. In some cases, the cleavage sequences can be mutated to promote proteolysis.

[0026] **FIG. 4** depicts schematic representations of exemplary plasma membrane recruitment element constructs named RSV ML, RSV MLNC Large, and RSV MLNC Small listed in the **Table 10B**.

[0027] **FIG. 5** depicts schematic representations of exemplary plasma membrane recruitment element constructs named RSV Myr LNC Large and RSV Myr LNC Small listed in the **Table 10B**.

[0028] **FIG. 6** depicts schematic representations of exemplary plasma membrane recruitment element constructs named PH-RSV LNC Large, PH-RSV LNC Small, and HIV CAP dDZF1 listed in the **Table 10B**.

[0029] **FIG. 7** depicts schematic representations of exemplary plasma membrane recruitment element constructs named HIV CAP dDZF2, hGAGKcon Large CAP dDZF1, and hGAGKcon Large CAP dDZF2 listed in the **Table 10B**.

[0030] **FIG. 8** depicts schematic representations of exemplary plasma membrane recruitment element constructs named hGAGKcon Small CAP dDZF1 and hGAGKcon Small CAP dDZF2 listed in the **Table 10B**.

[0031] **FIG. 9** depicts schematic representations of exemplary plasma membrane recruitment element constructs named hGAGKcon Smallv2 CAP dDZF1 and hGAGKcon Smallv2 CAP dDZF2 listed in the **Table 10B**.

DETAILED DESCRIPTION

[0032] The practice of some methods disclosed herein employ, unless otherwise indicated, conventional techniques of immunology, biochemistry, chemistry, molecular biology, microbiology, cell biology,

genomics and recombinant DNA, which are within the skill of the art. See for example Sambrook and Green, Molecular Cloning: A Laboratory Manual, 4th Edition (2012); the series Current Protocols in Molecular Biology (F. M. Ausubel, *et al.* eds.); the series Methods In Enzymology (Academic Press, Inc.), PCR 2: A Practical Approach (M.J. MacPherson, B.D. Hames and G.R. Taylor eds. (1995)), Harlow and Lane, eds. (1988) Antibodies, A Laboratory Manual, and Culture of Animal Cells: A Manual of Basic Technique and Specialized Applications, 6th Edition (R.I. Freshney, ed. (2010)).

[0033] Viral-like particles (VLPs) are nanoscale structures comprising assembled proteins (*e.g.,* viral components, such as structural proteins) that lack viral genetic material. VLPs can be generated from gag-pro-pol polyproteins that are retroviral, lentiviral, or endogenous (*e.g.,* from human, such as human endogenous retrovirus). Expression of the viral components can occur in various living or cell-free expression systems, then the viral components can self-assemble and reconstruct into lipid particles. The expression of viral components through *gag-pro-pol* genes utilizes weak terminators or ribosomal framshifting or both for expressing gag, pro, and pol proteins. Payloads can be efficiently captured in VLPs by fusing to a gag polyprotein (i.e., forms a chimeric protein) for protein payloads or a other non-covalent binding mechanisms (*e.g.,* gag fused to an RNA-binding protein that can bind an RNA sequence located on the payload). After the VLPs are delivered to a target cell, the payloads can be liberated from the VLPs after membrane fusion, and in some cases, after a protease cleaves a cleavable linker between the payload and the rest of the fusion protein.

[0034] Without wishing to be bound by a certain theory, the present disclosure provides improved VLPs with higher capacity of payload delivery and reduced immunogenity by modification of the components within the VLPs (e.g, a plasma membrane reruitment element comprising a mutant gag polyprotein). By utilitzing a mutant gag polyprotein as part of the plasma membrane recruitment element, such as a mutant gag with smaller size and domain swaps (*e.g.,* swapping a nucleocapsid with a multimerization motif, such as a leucine zipper), there can be potentials for improvement in various aspects. For instance, by removing certain domains within a gag, there can be reduced packing of undesirable molecules (*e.g.,* non-therapeutic molecules, non-specific mRNA or pDNA). Smaller total DNA sequence can allow high RNA or protein expression, for example, via higher total DNA delivery, which can offer potential for titer increase. There can be more room for payload as the size of plasma membrane recruitment element is reduced. Truncation in capsid protein can eliminate the formation of capsid cage that can sequester payloads and prevent release of the payloads upon delivery to a target cell, both of which can lead to higher encapsulation rate per particle, better release of payload in a target cell, or higher instrinsic activity. There is also potential for biodiversity advantage as the particles generated can have a smaller size. Introducing a fusion of a plasma membrane recruitment element and a protease can permit increased release and downstream activity of the payload after being delivered to a target cell. Additional modifications of the plasma membrane recruitment element or a chimeric protein comprising the plasma membrane recruitment element can include introducing additional particle budding motifs (*e.g.,* either homologous or heterologous) to drive better budding of the particle in a producer cell, fusing a Pleckstrin

homology (PH) domain to the N-terminus of the mutant gag, or synthetic sequences with other advantages (*e.g.,* less immunogenecity to human subjects).

[0035] Disclosed herein, in some aspects, are lipid delivery particles comprising a lipid membrane. In some cases, the membrane encapsulates a payload. In some cases, the lipid delivery particle comprises a plasma membrane recruitment element comprising a mutant gag polyprotein, and a payload within the cavity. In some cases, the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein. In some cases, the mutant gag polyprotein is not from HIV. In some cases, the plasma membrane recruitment element comprises (i) a full-length capsid protein; (ii) a full-length matrix protein; (iii) a heterologous sequence; (iv) at least a portion of a nucleocapsid protein; (v) two or more particle budding motifs; (vi) at least a portion of a P6 domain; or (vii) two spacer peptides. In some cases, the lipid delivery particle further comprises an envelope protein, wherein the envelope protein comprises an envelope protein from human endogenous retrovirus (HERV) or a mutant thereof. In some cases, the plasma membrane recruitment element is fused to (i) a cleavable linker; (ii) a membrane penetrating peptide; or (iii) a post-translational modification motif.

[0036] Disclosed herein, in some aspects, is a recombinant protein comprising a plasma membrane recruitment element comprising a mutant gag polyprotein. In some cases, the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein. In some cases, the mutant gag polyprotein is not from HIV. In some cases, the plasma membrane recruitment element comprises (i) a full-length capsid protein; (ii) a full-length matrix protein; (iii) a heterologous sequence; (iv) at least a portion of a nucleocapsid protein; (v) two or more particle budding motifs; (vi) at least a portion of a P6 domain; or (vii) two spacer peptides. In some cases, the plasma membrane recruitment element is fused to (i) a cleavable linker; (ii) a membrane penetrating peptide; or (iii) a post-translational modification motif.

[0037] Also disclosed herein are chimeric proteins comprising the recombinant protein described herein and a cleavable linker. In some cases, the cleavable linker connects the plasma membrane recruitment element and a payload.

[0038] Also disclosed herein is a composition comprising nucleic acid sequences encoding the components within the lipid delivery particles. In some cases, the compostion comprises a first nucleic acid sequence encoding the recombinant protein described herein or the chimeric protein described herein. In some cases, the composition comprises a second nucleic acid sequence encoding an envelope protein. In some cases, the envelope protein is a retroviral envelope protein or a biologically mutant thereof. In some cases, the envelope protein is an envelope protein from human endogenous retrovirus (HERV) or a biologically active mutant thereof.

[0039] Also disclosed herein is a system, a pharmaceutical composition, a kit, method of using and making relating to the lipid delivery particle, the recombinant protein, or the chimeric protein described herein.

[0040] Without wishing to be bound by a certain theory, presence of one or more of (i) a particle budding motif; (ii) a membrane penetrating peptide motif; or (iii) a post-translational modification motif in the chimeric protein of the present disclosure can improve production of the lipid delivery particles, as well as the incorporation of lipid delivery particles into their appropriate target. In some cases, additional motifs are present in the chimeric protein of the lipid delivery particle. The motifs of the present disclosure can also include polypeptide sequences that are additionally fused to the fusion of the plasma membrane recruitment element and the payload, or in some cases replacing or modifying elements of the fusion of the plasma membrane recruitment element and payload. The plasma membrane recruitment elements and motifs can be placed at the N-terminus, C-terminus, or between the N- and C-terminus of the construct. In some cases, the plasma membrane recruitment elements and motifs can be present in repeating fashion (in tandem) or at various segments of the DNA.

DEFINITIONS

[0041] Certain specific details of this description are set forth in order to provide a thorough understanding of various embodiments. However, one skilled in the art will understand that the present disclosure may be practiced without these details. In other instances, well-known structures have not been shown or described in detail to avoid unnecessarily obscuring descriptions of the disclosure.

[0042] Unless the context requires otherwise, throughout the specification and claims which follow, the word "comprise" and variations thereof, such as, "comprises" and "comprising" are to be construed in an open, inclusive sense, that is, as "including, but not limited to." Further, headings provided herein are for convenience only and do not interpret the scope or meaning of the claimed disclosure.

[0043] As used in this specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the content clearly dictates otherwise. The use of the words "a" or "an" when used in conjunction with the term "comprising" herein may mean "one," but it is also consistent with the meaning of "one or more," "at least one," and "one or more than one."

[0044] It should also be noted that the term "or" is generally employed in its sense including "and/or" unless the content clearly dictates otherwise.

[0045] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described below.

[0046] The term "about" when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of ±20% or in some instances ±10%, or in some instances ±5%, or in some instances ±1%, or in some instances ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods. As used herein, "about" and "approximately" generally mean an acceptable degree of error for the quantity measured given the nature or precision of the

measurements. Exemplary degrees of error are within 20 percent (%), typically, within 10%, and more typically, within 5% of a given range of values.

[0047] Calculations of homology or sequence identity between sequences (the terms are used interchangeably herein) are performed as follows. To determine the percent identity of two amino acid sequences, or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (*e.g.,* gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In some cases, the length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, 60%, and even more preferably at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology").

[0048] The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In some cases, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) J. Mol. Biol. 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at http://www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In some cases, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at http://www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

[0049] The percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of E. Meyers and W. Miller ((1989) CABIOS, 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (1990) J. Mol. Biol. 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid molecule of the disclosure. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to protein molecules of

the disclosure. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) Nucleic Acids Res. 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (*e.g.,* XBLAST and NBLAST) can be used.

[0050] It is understood that the molecules of the present disclosure may have additional conservative or non-essential amino acid substitutions, which do not have a substantial effect on their functions.

[0051] The terms "peptide," "polypeptide," and "protein" are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed on the maximum number of amino acids that can comprise a protein's or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. A polypeptide includes a natural peptide, a recombinant peptide, or a combination thereof.

[0052] The term "expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, including cosmids, plasmids (*e.g.,* naked or contained in liposomes) and viruses (*e.g.,* lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

[0053] The term "promoter" refers to a DNA sequence recognized by the transcription machinery of the cell, or introduced synthetic machinery, required to initiate the specific transcription of a polynucleotide sequence.

[0054] An example of a promoter is the immediate early cytomegalovirus (CMV) promoter sequence. This promoter sequence is a strong constitutive promoter sequence capable of driving high levels of expression of any polynucleotide sequence operatively linked thereto. In some cases, a polynucleotide comprises a CMV promoter. In some cases, a polynucleotide may comprise a promoter selected from the group consisting of, but not limited to, a simian virus 40 (SV40) early promoter, a mouse mammary tumor virus (MMTV), a human immunodeficiency virus (HIV) long terminal repeat (LTR) promoter, a MoMuLV promoter, an avian leukemia virus promoter, an Epstein-Barr virus immediate early promoter, a Rous sarcoma virus (RSV) promoter, an actin promoter, a myosin promoter, an elongation factor-1a promoter, a hemoglobin promoter, and a creatine kinase promoter. In some cases, a polynucleotide comprises a sequence encoding a poly(A) tail. In some cases, a polynucleotide comprises a 3' UTR sequence. In some cases, a polynucleotide comprises a 5' UTR sequence. In some cases, a polynucleotide

comprises multiple smaller and discrete nucleotide sequences that are typically heterologous and exhibit different and measurable function(s), a promoter sequence, a translation initiating sequence, a start codon, a polyadenylation sequence, a stop codon, and/or a linker sequence.

[0055] The term "subject" is intended to include living organisms in which an immune response can be elicited (*e.g.,* mammals, human). Exemplary subjects include humans, monkeys, dogs, cats, mice, rats, cows, horses, camels, goats, rabbits, and sheep. In certain embodiments, the subject is a human. A "patient" is a subject suffering from or at risk of developing a disease, disorder or condition or otherwise in need of the compositions and methods provided herein.

[0056] The term "therapeutic" as used herein means a treatment. A therapeutic effect is obtained by reduction, suppression, remission, or eradication of a disease state.

[0057] The term "prophylaxis" as used herein means the prevention of or protective treatment for a disease or disease state.

[0058] The term "transfected" or "transformed" or "transduced" refers to a process by which exogenous nucleic acid is transferred or introduced into the host cell. A "transfected" or "transformed" or "transduced" cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny. The term "transformed cell" or "transfected cell" can be a transformed or transfected cell in which inserted DNA can replicate either as an autonomously replicating plasmid or as part of the host chromosome. In some cases, a transfected cell or transformed cell can express the inserted DNA or RNA transiently (*e.g.,* for brief periods of time).

[0059] The terms "nucleic acid," "nucleic acid sequence," "nucleotide sequence," or "polynucleotide sequence," and "polynucleotide" are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a non-natural arrangement.

[0060] The term "cell line" or "producer cell line", as used herein, refers to cultured cells that can be passed (*e.g.,* divided) more than once. In some cases, a cell like can be passed more than 2 times, more than 5 times, more than 10 times, more than 50 times, more than 100 times, or more than 150 times. In some cases, a cell line can be passed between 2-250 times. In some cases, a cell line can be passed up to 200 times.

[0061] The term "lipid delivery particle" refers to lipid vesicles secreted by the plasma membrane of a cell having a membrane or envelope that surrounds a central internal space. Lipid delivery particles can be produced via budding out of the cell's plasma membrane, secretion from lysosomes, or export by the Golgi complex. Lipid delivery particles can promote intercellular communication in vitro and in vivo.

Exemplary lipid delivery particles can include, but are not limited to, exosomes, ectosomes (*e.g.,* microvesicles and shedding vesicles), apoptotic bodies, microsomes, micelles, oncosomes, and liposomes.

[0062] Lipid delivery particles can have a range of size, such as a cross-sectional diameter, wherein the cross-sectional diameter has a range from about 1 nm to about 1200 nm, about 10 nm to about 1200 nm, about 25 nm to about 1200 nm, about 50 nm to about 1200 nm, about 100 nm to about 1200 nm, about 10 nm to about 1000 nm, about 25 nm to about 1000 nm, about 50 nm to about 1000 nm, about 100 nm to about 1000 nm, about 10 nm to about 500 nm, about 25 nm to about 500 nm, about 50 nm to about 500 nm or about 100 nm to about 500 nm (all inclusive). Lipid delivery particles can comprise a vesicle size of greater than 10 nm. Lipid delivery particles can comprise a vesicle size of less than 1000 nm.

[0063] The term "module" or "modification", used interchangeably, can refer to an addition or a motif that is added to a payload or a chimeric protein within lipid delivery particles (*e.g.,* extracellular vesicles and/or virus-like particles). The additions can enhance characteristics of particle assembly and/or payload recruitment. A module can occur in combination or alone. A module can be linked to a payload or another element (*e.g.,* domain) in a construct.

[0064] The term "purifying," "purified," and "purify," can be used interchangeably and refer to a preparation phase of a lipid delivery particle. A preparation of lipid delivery particles can comprise a known or unknown concentration of a substance. In some cases, purifying produced lipid delivery particles comprises removing, either partially removing or wholly removing, a portion of the produced lipid delivery particles from a sample containing one or more biological components (*e.g.,* producer cells). In some cases, a composition comprising lipid delivery particles, as described herein, that have been purified are enriched as compared to a starting sample. Enrichment of the lipid delivery particles can comprise 5%, 10%, 25%, 50%, 75%, 80%,, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% enrichment compared to a starting sample. In some cases, purified lipid delivery particles can be free or substantially free of residual biological products. Residual biological products can include, but are not limited to, unwanted nucleic acids, proteins, lipids, and/or or metabolites or abiotic materials such as including chemicals. In some cases, lipid delivery particles free of residual biological products comprise lipid delivery particles containing no detectable producer cells in the composition.

[0065] The terms "portion" and "fragment" are used interchangeably herein and refer to a continuous element. For example, a part of a structure such as an amino acid sequence or protein refers to a continuous element of said structure. A portion, or a fragment of a structure preferably comprises one or more functional properties of said structure. In some cases, a portion, or a fragment of a structure such as an amino acid sequence comprises of at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% of the entire structure or amino acid sequence. In some cases, a portion, or a fragment of a structure such as an amino acid sequence comprises of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the entire structure or amino acid sequence. In some cases, a portion or a fragment can be proteins having at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99,

100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more amino acids absent from the amino and/or carboxyl terminus of the amino acid sequence when compared to the reference amino acid sequence, optionally wherein the fragment has the same activity as the reference protein.

[0066] Ranges: throughout this disclosure, various aspects of the present disclosure can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the present disclosure. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. As another example, a range such as 95-99% identity, includes something with 95%, 96%, 97%, 98% or 99% identity, and includes subranges such as 96-99%, 96-98%, 96-97%, 97-99%, 97-98% and 98-99% identity. This applies regardless of the breadth of the range.

LIPID DELIVERY PARTICLE

[0067] In an aspect, described herein is a lipid delivery particle comprising a plasma membrane recrtuiment element that comprises a mutant gag polyprotein for delivery of a payload to a target cell. The chimeric protein can promote targeting of a payload to a recipient cell (*e.g.,* target cell). The lipid delivery particle can comprise a virus like particle (VLP) or an extracellular vesicle secreted by a cell. A lipid delivery particle can be secreted by cells in vivo or if cultured in vitro. Following secretion, the lipid delivery particle can deliver a payload and release its components into a recipient cell. In some cases, the lipid delivery particle can comprise a VLP, an exosome, an ectosome (*e.g.,* a microvesicle or a shedding vesicle), an apoptotic body, a microsome, a micelle, an oncosome, or a liposome. In some cases, the lipid delivery particle can comprise a nanoparticle.

[0068] Virus-like particles (VLPs) can be assemblies of viral proteins that can infect cells but lack viral general material. VLPs can be synthesized through expression of viral structural proteins. VLPs can be formed in vivo through assembly inside a producer cell via recombinant protein expression or in vitro through self-assembly in a vessel using quantities of purified protein. VLPs can be designed to deliver payloads to targeted cells and tissues. VLPs can be used to deliver to a recipient cell an agent (*e.g.,* prophylactic agent, therapeutic agent or diagnostic agent) or an enclosed circular or linear DNA or RNA molecule.

[0069] Ectosomes can be small heterogenous membrane-bound particles that are shed from the surface of the cell membrane in the extracellular space. Ectosomes can be shed by budding or outward blebbing from the plasma membrane of the cell. Ectosomes can be shed from plasma membrane micro-domains (*e.g.,* lipid rafts or caveolae domains). Ectosomes have a series of biological functions, including, but not limited to, regulation of nucleic acid metabolism, signal transduction, transport, protein metabolism, intercellular communication, apoptpsis, and cell growth. As described herein, ectosomes can comprise a payload that can be delivered to a target cell. Ectosomes can be variable in size. In some cases, an

ectosome can be between 25 and 1000 nm. In some cases, the ecostome can be about 30 nm, about 50 nm, about 75 nm, about 100 nm, about 200 nm, about 300 nm, about 400 nm, about 500 nm, about 600 nm, about 700 nm, about 800 nm, about 900 nm, or about 1000 nm in size.

[0070] Exosomes can be small vesicular particles formed by intraluminal vesicles within multivesicular bodies. Exosome can range from about 30- about 125 nm. In some cases, an exosome is about 30 nm, about 40 nm, about 50 nm, about 55 nm, about 60 nm, about 65 nm, about 70 nm, about 75 nm, about 80 nm, about 85 nm, about 90 nm, about 95 nm, or about 100 nm in size. Formation of exosomes can be regulated via the endosomal sorting complex required for transport (ESCRT), and/or by non-ESCRT-related mechanisms, including tetraspanins and membrane lipids.

[0071] Nanoparticles can be synthesized particles between about 1 and about 200 nm in size that can encapsulate payload for delivery to a recipient cell. In some cases, nanoparticles are engineered for a specific cell type and trigger endocytosis and later endosome lysis. In some cases, a nanoparticle is about 5 nm, about 10 nm, about 15 nm, about 20 nm, about 25 nm, about 30 nm, about 35 nm, about 40 nm, about 45 nm, about 50 nm, about 60 nm, about 70 nm, about 80 nm, about 90 nm, or about 100 nm in size. In some cases, a nanoparticle can be about 105 nm, about 110 nm, about 115 nm, about 120 nm, about 125 nm, about 130 nm, about 135 nm, about 140 nm, about 145 nm, about 150 nm, about 160 nm, about 170 nm, about 180 nm, about 190 nm, or about 200 nm in size (*e.g.*, a diameter). Without wishing to be bound by a theory, the small size can allow a higher intracellular uptake compared to larger molecules.

ENVELOPE PROTEIN

[0072] In some aspects, the lipid delivery particle provided herein comprises an envelope protein. The envelope protein can be associated with the outside boundary or the surface of the lipid delivery particle, for example, the membrane or envelope of the lipid delivery particle.

[0073] The membrane of the lipid delivery particle can comprise a lipid layer, such as a single layer or a lipid bilayer. In some cases, the membrane of the lipid delivery particle is from plasma membrane, endoplasmic reticulum, or a combination thereof. In some cases, the membrane of the lipid delivery particle is from Golgi complex, ER Golgi intermediate compartment, or nuclear envelope. In some cases, the membrane of the lipid delivery particle is from plasma membrane. In some cases, the membrane of the lipid delivery particle is a phospholipid bilayer.

[0074] The envelope protein can be associated with the membrane of the lipid delivery particle in various manners. For example, the envelope protein can be anchored or attached to the external membrane of the particle, or anchored or attached to the internal membrane of the particle. The envelope protein can be embedded or inserted in the membrane, spanning through the membrane, with certain portions located at the outside of the membrane, or certain portions extending to the inside of the particle, or both. The envelope protein within the lipid delivery particle described herein can be overexpressed from an exogenous source, such as plasmids or stably integrated transgenes, in the production cells.

[0075] The envelope protein can play a role in the delivery of the lipid delivery particle to a target cell and release of the components of the lipid delivery particle within the target cell. The envelope protein can contact with the surface of a target cell and participate in the fusion of the lipid delivery particle and the membrane of the target cell. The envelope protein can participate in the fusion of the lipid delivery particle with the membrane of the target cell via any appropriate mechanism, such as those described in White et al. Crit Rev Biochem Mol Biol. 2008; 43(3): 189–219. One example of the fusion mechanisms is unifying Trimer-of-Hairpins Fusion Mechanism. Membrane fusion can occur after allosteric priming by binding to a target receptor. In some cases, membrane fusion occurs after proteolysis. In some cases, membrane fusion occurs after isomerization of disulfide bridges. In some cases, membrane fusion occurs by internalization and then priming of fusion via (i) cathepsin-mediated proteolysis, or (ii) low pH/acidification. The cathepsin-mediated proteolysis can be pH dependent or pH independent. Other fusion triggering mechanisms can include low PH, binding to target cell receptors, and a receptor followed by low pH. The envelope protein can also play a role in the formation of the lipid delivery particle. The envelope protein can interact with another component within the lipid delivery particle and participate in the assembly of the lipid delivery particle, for example, in a producer cell. The envelope protein can make contact with another envelope protein and form an oligomer embedded within the membrane. The envelope protein can be a glycoprotein, for example, a transmembrane glycoprotein. In some cases, envelope protein comprises multiple membrane-spanning regions. These multiple membrane-spanning regions can oligomerize and form channels in the membrane.

[0076] In some cases, the envelope protein is fused with a targeting moiety. In some cases, the targeting moiety recognizes a specific molecule (*e.g.,* antigen, receptor, or other membrane protein) on the surface of a target cell to allow targeted cell entry with more specificity. In some cases, the targeting moiety is specific for a certain cell type or is specific for a certain target cell. The targeting moiety can be fused to the envelope protein at a position that is located at an outside of the lipid delivery particle. For example, the targeting moiety includes scFvs, antibody variable regions, nanobodies, T-cell receptor variable regions, other antigen-binding fragments or their mimetics, such as DARPins. In some cases, the targeting moiety is a protein ligand from the human ligandome. The targeting moiety can be a natural peptide or a synthetic peptide. In some cases, the targeting moiety is not fused with the envelope protein and is attached to the membrane of the lipid delivery particle from the outside, for example, via a transmembrane domain.

[0077] A targeting moiety can include, *e.g.*, an antibody or an antigen-binding fragment thereof (*e.g.*, Fab, Fab′, F(ab′)2, Fv fragments, scFv antibody fragments, disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as sdAb (either VL or VH), nanobodies, or camelid VHH domains), an antigen-binding fibronectin type III (Fn3) scaffold such as a fibronectin polypeptide minibody, a ligand, a cytokine, a chemokine, or a T cell receptor (TCRs). Membrane-fusion proteins can be re-targeted by non-covalently conjugating a targeting moiety to the membrane-fusion protein or targeting protein (*e.g.* the hemagglutinin protein). For example, the

membrane-fusion protein can be engineered to bind the Fc region of an antibody that targets an antigen on a target cell, redirecting the membrane fusion activity towards cells that display the antibody's target.

[0078] In some cases, the targeting moiety linked to the membrane-fusion protein binds a cell surface marker on the target cell, *e.g.*, a protein, glycoprotein, receptor, cell surface ligand, agonist, lipid, sugar, class I transmembrane protein, class II transmembrane protein, or class III transmembrane protein.

[0079] In some cases, the lipid delivery particles disclosed herein display targeting moieties that are not conjugated to the membrane-fusion protein or other proteins in order to redirect the fusion activity of the lipid delivery particle towards a cell that is bound by the targeting moiety, or to affect tropism of the lipid delivery particle toward the target cell.

Envelope protein of viral origin

[0080] In some cases, an envelope protein has a viral origin. For example, a suitable envelope protein is from a DNA virus, an RNA virus, or a retrovirus. The envelope protein can be envelope protein from Herpesviruses, Avian sarcoma leukosis virus, Poxviruses, Hepadnaviruses, Asfarviridae, Flaviviruses, Alphaviruses, Togaviruses, Coronaviruses, Hepatitis D, Orthomyxoviruses, Rhabdovirus, Bunyaviruses, Filoviruses, Oncoretroviruses, lentiviruses, Spumaviruses. In some cases, envelope protein can be envelope protein from lentiviruses, for example, human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), feline immunodeficiency virus (FIV) and equine infectious anemia virus (EIAV). In some cases, an envelope protein is a fusion of two different envelope proteins, wherein each comes from a different virus. Additional suitable envelope proteins that are from viral origins and their functions are described in White JM *et al.*, Crit Rev Biochem Mol Biol. 2008 May-Jun;43(3):189-219.

[0081] In some cases, the envelope protein is a vesicular stomatitis virus glycoprotein (VSVG) or a biologically active mutant thereof. A "biologically active mutant" disclosed herein in connection with a reference protein can refer to a mutant of the reference protein that remains displaying one or more biological activities that are of same nature as the reference protein, which are relevant to the context in which the reference protein is used in the lipid delivery particle disclosed herein, while the level of the one or more biological activities of the biologically active mutant can be either similar as or different than the reference protein. For instance, the biologically active mutant of a VSVG in the context of an envelope protein remains displaying the biological activities of an envelope protein, *e.g.*, mediating membrane fusion, tropism of the lipid delivery particle toward a target cell, or both. Unless otherwise noted, a mutant as described in the present disclosure is equivalent to a biologically active mutant. In some cases, the envelope protein is a Human immunodeficiency virus GP160 or a biologically active mutant thereof. In some cases, the envelope protein is a Baboon Endogenous Retrovirus (BaEVTR) glycoprotein or a biologically active mutant thereof. In some cases, the envelope protein is a modified Baboon Endogenous Retrovirus (BaEVTRless) glycoprotein or a biologically active mutant thereof. In some cases, the envelope protein is the fusion protein of Vesicular stomatitis Indiana virus and Rabies virus Glycoproteins (FuG-E) or a biologically active mutant thereof. In some cases, the envelope protein pantropic murine leukemia virus envelope protein (MLV) or a biologically active mutant thereof. In some cases, the envelope protein is a modified Fusion protein of Vesicular stomatitis Indiana virus and Rabies

virus Glycoproteins (FuG-E P440E) or a biologically active mutant thereof. In some cases, the envelope protein is an ecotrophic Murine Leukemia Virus envelope protein (MLV ENV ecotropic) or a biologically active mutant thereof. In some cases, the envelope protein is an amphotrophic Murine Leukemia Virus envelope protein (MLV ENV amphotropic) or a biologically active mutant thereof. In some cases, the envelope protein is a Moloney murine leukemia virus envelope protein (MMLV) or a biologically active mutant thereof. In some cases, the envelope protein is a Moloney murine sarcoma virus envelope protein (MoMSVg) or a biologically active mutant thereof. In some cases, the envelope protein is a moloney murine leukemia virus 10A1 strain Glycoprotein (MLV 10A1) or a biologically active mutant thereof. In some cases, the envelope protein is a xenotropic murine leukemia virus envelope protein (MLV ENV xenotropic) or a biologically active mutant thereof. In some cases, the envelope protein is a xenotropic murine leukemia virus-related envelope protein (XMRV) or a biologically active mutant thereof. In some cases, the envelope protein is a Baculovirus envelope glycoprotein (GP64) or a biologically active mutant thereof. In some cases, the envelope protein is an endogenous feline virus envelope protein (RD114 ENV) or a biologically active mutant thereof. In some cases, the envelope protein is a mammalian endogenous retrovirus protein. The mammalian endogenous retrovirus protein can be a koala retrovirus protein (KoRV) or a Jaagsiekte sheep retrovirus protein (enJSRV), or a biologically active mutant thereof.

[0082] In some cases, the envelope protein is a simian endogenous type D retrovirus protein (RD-114) or a biologically active mutant thereof. In some cases, the envelope protein is a gibbon ape leukemia virus envelope protein (GALV) or a biologically active mutant thereof. In some cases, the envelope protein is a feline leukemia virus envelope protein (FLV) or a biologically active mutant thereof. In some cases, the envelope protein is a mouse mammary tumor virus envelope protein (MMTV) or a biologically active mutant thereof. In some cases, the envelope protein is an avian leukosis virus envelope protein or a biologically active mutant thereof. In some cases, the envelope protein is a rous sarcoma virus envelope protein or a biologically active mutant thereof.

[0083] In some cases, the envelope protein can direct the lipid delivery particles to fuse with a certain type of target cells rather than other cells. For example, based on the specific type of envelope protein associated with the membrane of the lipid delivery particle, the lipid delivery particle can preferentially target different cell types (*i.e.*, tropisms of the lipid delivery particles), such as liver cells, ocular cells, nerve cells, lung cells, immune cells, muscle cells, and any other cell types of interest. For example, to fuse with a target liver cells, the envelope protein can be a glycoprotein from human hepatitis viruses or a biologically active mutant thereof, *e.g.*, Hepatitis B virus (HBV) or hepatitis C virus (HCV), VSV-G glycoprotein or a mutant thereof, a Marburg virus glycoprotein or a biologically active mutant thereof, an Ebola virus glycoprotein or a mutant thereof. To fuse with a target muscle cell, for example, a skeletal muscle cell, the envelope protein can be a Ross River virus glycoprotein or a biologically active mutant thereof, or a VSV-G or a biologically active mutant thereof. To fuse with a target ocular cell, for example, a photoreceptor cell or a retinal cell, the envelope protein can be an Ebola virus glycoprotein or a biologically active mutant thereof, a Marburg virus glycoprotein or a mutant thereof, or a VSV-G or a biologically active mutant thereof. To fuse with a target immune cell, for example, CD8+ T cell, an

HTLV-1 glycoprotein or a biologically active mutant thereof, or a VSV- G glycoprotein or a biologically active mutant thereof. To fuse with a target immune cell, for example, CD4+ T cell, the envelope protein can be a HIV-1 envelope or a biologically active mutant thereof, a HTLV-1 glycoprotein or a biologically active mutant thereof, or a VSV-G glycoprotein or a biologically active mutant thereof. To fuse with a target lung cells, the envelope protein can be a respiratory syncytial virus glycoprotein or a biologically active mutant thereof, or a SARS-CoV glycoprotein or a biologically active mutant thereof. To fuse with a target nerve cell, such as a cell from the central nervous system cell (*e.g.,* neurons, glial cells including oligodendrocytes, astrocytes and microglia), the envelope protein can be a rabies glycoprotein or a biologically active mutant thereof, a Mokola virus glycoprotein or a mutant thereof, a Semliki Forest virus glycoprotein or a mutant thereof, a Venezuelan equine encephalitis virus glycoprotein or a mutant thereof, or a VSV-G or a biologically active mutant thereof. To fuse with a target sensory cell, such as an auditory cells, including hair cells, cochlear cells, etc., the envelope protein can be an Ebola virus glycoprotein or a biologically active mutant thereof, a Marburg virus glycoprotein or a biologically active mutant thereof, or a VSV-G or a biologically active mutant thereof.

[0084] In some cases, the envelope protein includes those described in **Table 1** with at least one amino acid substitution, deletion, or insertion. For instance, N-terminal methionine can be absent from the envelope protein of the lipid delivery particle provided herein relative to the wild-type viral envelope protein. In some cases, the envelope protein includes those described in **Table 1** and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0085] In some cases, the envelope protein comprises one or more of the sequences set forth in **Table 1** with at least one amino acid substitution, deletion, or insertion. For instance, N-terminal methionine can be absent from the envelope protein of the lipid delivery particle provided herein relative to the wild-type viral envelope protein. In some cases, the envelope protein comprises one or more of the sequences set forth in **Table 1** and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0086] In some cases, the envelope protein comprises any one of the sequences set forth in **Table 1** with at least one amino acid substitution, deletion, or insertion. For instance, N-terminal methionine can be absent from the envelope protein of the lipid delivery particle provided herein relative to the wild-type viral envelope protein. In some cases, the envelope protein comprises any one of the sequences set forth in **Table 1** and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0087] In some cases, the envelope protein comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in **Table 1**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in any one of **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 50% sequence identity to a sequence set forth in any one of **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 60% sequence identity to a sequence set forth in any one of **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence

that has at least about 70% sequence identity to a sequence set forth in any one of **SEQ ID NOs: 83-104.** In some cases, the envelope protein comprises an amino acid sequence that has at least about 75% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 80% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 85% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 90% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 95% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 96% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 97% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**.In some cases, the envelope protein comprises an amino acid sequence that has at least about 98% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 99% sequence identity to a sequence set forth in **SEQ ID NOs: 83-104**.

Table 1. Exemplary envelope proteins from virus origin

Exemplary envelope proteins from virus origin	Amino Acid Sequence	SEQ ID NO:
vesicular stomatitis virus glycoprotein (VSVG)	MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDL IGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPS VEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYT GEWVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDL FAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLP ISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMIS GTTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLSS KAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASF FFIIGLIIGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK	83			KCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLI GTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSV EQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSEDG ELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLF AAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPI SPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISG TTTERELWDDWAPYEDVEIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLSSK AQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEGWFSSWKSSIASFF FIIGLIIGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK	84
Human immunodefici	MRVKEKYQHLWRWGWRWGTMLLGMLMICSATEKLWVTVYYGVPVWKEATTTL FCASDAKAYDTEVHNVWATHACVPTDPNPQEVVLVNVTENFNMWKNDMVEQM HEDIISLWDQSLKPCVKLTPLCVSLKCTDLKNDTNTNSSSGRMIMEKGEIKN	85

ency virus - GP160	CSFNISTSIRGKVQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSVITQACPKV SFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVSTVQCTHGIRPVVSTQLL LNGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEINCTRPNNNTRKRIRIQRG PGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLREQFGNNKTIIFKQS SGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTWSTEGSNNTEGSDTITL PCRIKQIINMWQKVGKAMYAPPISGQIRCSSNITGLLLTRDGGNSNNESEIF RPGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVQREKRAVGIGALFL GFLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWG IKQLQARILAVERYLKDQQLLGIWGCSGKLICTTAVPWNASWSNKSLEQIWN HTTWMEWDREINNYTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWFNIT NWLWYIKLFIMIVGGLVGLRIVFAVLSIVNRVRQGYSPLSFQTHLPTPRGPD RPEGIEEEGGERDRDRSIRLVNGSLALIWDDLRSLCLFSYHRLRDLLLIVTR IVELLGRRGWEALKYWWNLLQYWSQELKNSAVSLLNATAIAVAEGTDRVIEV VQGACRAIRHIPRRIRQGLERILL	
	RVKEKYQHLWRWGWRWGTMLLGMLMICSATEKLWVTVYYGVPVWKEATTTLF CASDAKAYDTEVHNVWATHACVPTDPNPQEVVLVNVTENFNMWKNDMVEQMH EDIISLWDQSLKPCVKLTPLCVSLKCTDLKNDTNTNSSSGRMIMEKGEIKNC SFNISTSIRGKVQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSVITQACPKVS FEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVSTVQCTHGIRPVVSTQLLL NGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEINCTRPNNNTRKRIRIQRGP GRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLREQFGNNKTIIFKQSS GGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTWSTEGSNNTEGSDTITLP CRIKQIINMWQKVGKAMYAPPISGQIRCSSNITGLLLTRDGGNSNNESEIFR PGGGDMRDNWRSELYKYKVVKIEPLGVAPTKAKRRVVQREKRAVGIGALFLG FLGAAGSTMGAASMTLTVQARQLLSGIVQQQNNLLRAIEAQQHLLQLTVWGI KQLQARILAVERYLKDQQLLGIWGCSGKLICTTAVPWNASWSNKSLEQIWNH TTWMEWDREINNYTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWFNITN WLWYIKLFIMIVGGLVGLRIVFAVLSIVNRVRQGYSPLSFQTHLPTPRGPDR PEGIEEEGGERDRDRSIRLVNGSLALIWDDLRSLCLFSYHRLRDLLLIVTRI VELLGRRGWEALKYWWNLLQYWSQELKNSAVSLLNATAIAVAEGTDRVIEVV QGACRAIRHIPRRIRQGLERILL	86
Baboon Endogenous Retrovirus glycoprotein - BaEVTR	MGFTTKIIFLYNLVLVYAGFDDPRKAIELVQKRYGRPCDCSGGQVSEPPSDR VSQVTCSGKTAYLMPDQRWKCKSIPKDTSPSGPLQECPCNSYQSSVHSSCYT SYQQCRSGNKTYYTATLLKTQTGGTSDVQVLGSTNKLIQSPCNGIKGQSICW STTAPIHVSDGGGPLDTTRIKSVQRKLEEIHKALYPELQYHPLAIPKVRDNL MVDAQTLNILNATYNLLLMSNTSLVDDCWLCLKLGPPTPLAIPNFLLSYVTR SSDNISCLIIPPLLVQPMQFSNSSCLFSPSYNSTEEIDLGHVAFSNCTSITN VTGPICAVNGSVFLCGNNMAYTYLPTNWTGLCVLATLLPDIDIIPGDEPVPI PAIDHFIYRPKRAIQFIPLLAGLGITAAFTTGATGLGVSVTQYTKLSNQLIS DVQILSSTIQDLQDQVDSLAEVVLQNRRGLDLLTAEQGGICLALQEKCCFYV NKSGIVRDKIKTLQEELERRRKDLASNPLWTGLQGLLPYLLPFLGPLLTLLL LLTIGPCIFNRLVQFVKDRISVVQALVLTQQYHQLKPLEYEP	87
	GFTTKIIFLYNLVLVYAGFDDPRKAIELVQKRYGRPCDCSGGQVSEPPSDRV SQVTCSGKTAYLMPDQRWKCKSIPKDTSPSGPLQECPCNSYQSSVHSSCYTS YQQCRSGNKTYYTATLLKTQTGGTSDVQVLGSTNKLIQSPCNGIKGQSICWS TTAPIHVSDGGGPLDTTRIKSVQRKLEEIHKALYPELQYHPLAIPKVRDNLM VDAQTLNILNATYNLLLMSNTSLVDDCWLCLKLGPPTPLAIPNFLLSYVTRS SDNISCLIIPPLLVQPMQFSNSSCLFSPSYNSTEEIDLGHVAFSNCTSITNV TGPICAVNGSVFLCGNNMAYTYLPTNWTGLCVLATLLPDIDIIPGDEPVPIP AIDHFIYRPKRAIQFIPLLAGLGITAAFTTGATGLGVSVTQYTKLSNQLISD VQILSSTIQDLQDQVDSLAEVVLQNRRGLDLLTAEQGGICLALQEKCCFYVN KSGIVRDKIKTLQEELERRRKDLASNPLWTGLQGLLPYLLPFLGPLLTLLLL LTIGPCIFNRLVQFVKDRISVVQALVLTQQYHQLKPLEYEP	88
Modified Baboon Endogenous Retrovirus	MGFTTKIIFLYNLVLVYAGFDDPRKAIELVQKRYGRPCDCSGGQVSEPPSDR VSQVTCSGKTAYLMPDQRWKCKSIPKDTSPSGPLQECPCNSYQSSVHSSCYT SYQQCRSGNKTYYTATLLKTQTGGTSDVQVLGSTNKLIQSPCNGIKGQSICW STTAPIHVSDGGGPLDTTRIKSVQRKLEEIHKALYPELQYHPLAIPKVRDNL MVDAQTLNILNATYNLLLMSNTSLVDDCWLCLKLGPPTPLAIPNFLLSYVTR	89

glycoprotein - BaEVTRless	SSDNISCLIIPPLLVQPMQFSNSSCLFSPSYNSTEEIDLGHVAFSNCTSITN VTGPICAVNGSVFLCGNNMAYTYLPTNWTGLCVLATLLPDIDIIPGDEPVPI PAIDHFIYRPKRAIQFIPLLAGLGITAAFTTGATGLGVSVTQYTKLSNQLIS DVQILSSTIQDLQDQVDSLAEVVLQNRRGLDLLTAEQGGICLALQEKCCFYV NKSGIVRDKIKTLQEELERRRKDLASNPLWTGLQGLLPYLLPFLGPLLTLLL LLTIGPCIFNRLTAFINDKLNIIHAM	
	GFTTKIIFLYNLVLVYAGFDDPRKAIELVQKRYGRPCDCSGGQVSEPPSDRV SQVTCSGKTAYLMPDQRWKCKSIPKDTSPSGPLQECPCNSYQSSVHSSCYTS YQQCRSGNKTYYTATLLKTQTGGTSDVQVLGSTNKLIQSPCNGIKGQSICWS TTAPIHVSDGGGPLDTTRIKSVQRKLEEIHKALYPELQYHPLAIPKVRDNLM VDAQTLNILNATYNLLLMSNTSLVDDCWLCLKLGPPTPLAIPNFLLSYVTRS SDNISCLIIPPLLVQPMQFSNSSCLFSPSYNSTEEIDLGHVAFSNCTSITNV TGPICAVNGSVFLCGNNMAYTYLPTNWTGLCVLATLLPDIDIIPGDEPVPIP AIDHFIYRPKRAIQFIPLLAGLGITAAFTTGATGLGVSVTQYTKLSNQLISD VQILSSTIQDLQDQVDSLAEVVLQNRRGLDLLTAEQGGICLALQEKCCFYVN KSGIVRDKIKTLQEELERRRKDLASNPLWTGLQGLLPYLLPFLGPLLTLLLL LTIGPCIFNRLTAFINDKLNIIHAM	90
Fusion protein of Vesicular stomatitis Indiana virus and Rabies virus Glycoproteins - FuG-E	MVPQVLLFVLLLGFSLCFGKFPIYTIPDELGPWSPIDIHHLSCPNNLVVEDE GCTNLSEFSYMELKVGYISAIKVNGFTCTGVVTEAETYTNFVGYVTTTFKRK HFRPTPDACRAAYNWKMAGDPRYEESLHNPYPDYHWLRTVRTTKESLIIISP SVTDLDPYDKSLHSRVFPGGKCSGITVSSTYCSTNHDYTIWMPENPRPRTPC DIFTNSRGKRASNGNKTCGFVDERGLYKSLKGACRLKLCGVLGLRLMDGTWV AMQTSDETKWCPPDQLVNLHDFRSDEIEHLVVEELVKKREECLDALESIMTT KSVSFRRLSHLRKLVPGFGKAYTIFNKTLMEADAHYKSVRTWNEIIPSKGCL KVGGRCHPHVNGVFFNGIILGPDDHVLIPEMQSSLLQQHMELLESSVIPLMH PLADPSTVFKEGDEAEDFVEVHLPKNPIELVEGWFSSWKSSIASFFFIIGLI IGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK	91
	VPQVLLFVLLLGFSLCFGKFPIYTIPDELGPWSPIDIHHLSCPNNLVVEDEG CTNLSEFSYMELKVGYISAIKVNGFTCTGVVTEAETYTNFVGYVTTTFKRKH FRPTPDACRAAYNWKMAGDPRYEESLHNPYPDYHWLRTVRTTKESLIIISPS VTDLDPYDKSLHSRVFPGGKCSGITVSSTYCSTNHDYTIWMPENPRPRTPCD IFTNSRGKRASNGNKTCGFVDERGLYKSLKGACRLKLCGVLGLRLMDGTWVA MQTSDETKWCPPDQLVNLHDFRSDEIEHLVVEELVKKREECLDALESIMTTK SVSFRRLSHLRKLVPGFGKAYTIFNKTLMEADAHYKSVRTWNEIIPSKGCLK VGGRCHPHVNGVFFNGIILGPDDHVLIPEMQSSLLQQHMELLESSVIPLMHP LADPSTVFKEGDEAEDFVEVHLPKNPIELVEGWFSSWKSSIASFFFIIGLII GLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK	92
Modified Fusion protein of Vesicular stomatitis Indiana virus and Rabies virus Glycoproteins - FuG-E (P440E)	MVPQVLLFVLLLGFSLCFGKFPIYTIPDELGPWSPIDIHHLSCPNNLVVEDE GCTNLSEFSYMELKVGYISAIKVNGFTCTGVVTEAETYTNFVGYVTTTFKRK HFRPTPDACRAAYNWKMAGDPRYEESLHNPYPDYHWLRTVRTTKESLIIISP SVTDLDPYDKSLHSRVFPGGKCSGITVSSTYCSTNHDYTIWMPENPRPRTPC DIFTNSRGKRASNGNKTCGFVDERGLYKSLKGACRLKLCGVLGLRLMDGTWV AMQTSDETKWCPPDQLVNLHDFRSDEIEHLVVEELVKKREECLDALESIMTT KSVSFRRLSHLRKLVPGFGKAYTIFNKTLMEADAHYKSVRTWNEIIPSKGCL KVGGRCHPHVNGVFFNGIILGPDDHVLIPEMQSSLLQQHMELLESSVIPLMH PLADPSTVFKEGDEAEDFVEVHLEKNPIELVEGWFSSWKSSIASFFFIIGLI IGLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK	93
	VPQVLLFVLLLGFSLCFGKFPIYTIPDELGPWSPIDIHHLSCPNNLVVEDEG CTNLSEFSYMELKVGYISAIKVNGFTCTGVVTEAETYTNFVGYVTTTFKRKH FRPTPDACRAAYNWKMAGDPRYEESLHNPYPDYHWLRTVRTTKESLIIISPS VTDLDPYDKSLHSRVFPGGKCSGITVSSTYCSTNHDYTIWMPENPRPRTPCD IFTNSRGKRASNGNKTCGFVDERGLYKSLKGACRLKLCGVLGLRLMDGTWVA MQTSDETKWCPPDQLVNLHDFRSDEIEHLVVEELVKKREECLDALESIMTTK SVSFRRLSHLRKLVPGFGKAYTIFNKTLMEADAHYKSVRTWNEIIPSKGCLK VGGRCHPHVNGVFFNGIILGPDDHVLIPEMQSSLLQQHMELLESSVIPLMHP LADPSTVFKEGDEAEDFVEVHLEKNPIELVEGWFSSWKSSIASFFFIIGLII GLFLVLRVGIHLCIKLKHTKKRQIYTDIEMNRLGK	94

Ecotropic Murine Leukemia Virus - MLV ENV (ecotropic)	MARSTLSKPLKNKVNPRGPLIPLILLMLRGVSTASPGSSPHQVYNITWEVTN GDRETVWATSGNHPLWTWWPDLTPDLCMLAHHGPSYWGLEYQSPFSSPPGPP CCSGGSSPGCSRDCEEPLTSLTPRCNTAWNRLKLDQTTHKSNEGFYVCPGPH RPRESKSCGGPDSFYCAYWGCETTGRAYWKPSSSWDFITVNNNLTSDQAVQV CKDNKWCNPLVIRFTDAGRRVTSWTTGHYWGLRLYVSGQDPGLTFGIRLRYQ NLGPRVPIGPNPVLADQQPLSKPKPVKSPSVTKPPSGTPLSPTQLPPAGTEN RLLNLVDGAYQALNLTSPDKTQECWLCLVAGPPYYEGVAVLGTYSNHTSAPA NCSVASQHKLTLSEVTGQGLCIGAVPKTHQALCNTTQTSSRGSYYLVAPTGT MWACSTGLTPCISTTILNLTTDYCVLVELWPRVTYHSPSYVYGLFERSNRHK REPVSLTLALLLGGLTMGGIAAGIGTGTTALMATQQFQQLQAAVQDDLREVE KSISNLEKSLTSLSEVVLQNRRGLDLLFLKEGGLCAALKEECCFYADHTGLV RDSMAKLRERLNQRQKLFESTQGWFEGLFNRSPWFTTLISTIMGPLIVLLMI LLFGPCILNRLVQFVKDRISVVQALVLTQQYHQLKPIEYEP	95
	ARSTLSKPLKNKVNPRGPLIPLILLMLRGVSTASPGSSPHQVYNITWEVTNG DRETVWATSGNHPLWTWWPDLTPDLCMLAHHGPSYWGLEYQSPFSSPPGPPC CSGGSSPGCSRDCEEPLTSLTPRCNTAWNRLKLDQTTHKSNEGFYVCPGPHR PRESKSCGGPDSFYCAYWGCETTGRAYWKPSSSWDFITVNNNLTSDQAVQVC KDNKWCNPLVIRFTDAGRRVTSWTTGHYWGLRLYVSGQDPGLTFGIRLRYQN LGPRVPIGPNPVLADQQPLSKPKPVKSPSVTKPPSGTPLSPTQLPPAGTENR LLNLVDGAYQALNLTSPDKTQECWLCLVAGPPYYEGVAVLGTYSNHTSAPAN CSVASQHKLTLSEVTGQGLCIGAVPKTHQALCNTTQTSSRGSYYLVAPTGTM WACSTGLTPCISTTILNLTTDYCVLVELWPRVTYHSPSYVYGLFERSNRHKR EPVSLTLALLLGGLTMGGIAAGIGTGTTALMATQQFQQLQAAVQDDLREVEK SISNLEKSLTSLSEVVLQNRRGLDLLFLKEGGLCAALKEECCFYADHTGLVR DSMAKLRERLNQRQKLFESTQGWFEGLFNRSPWFTTLISTIMGPLIVLLMIL LFGPCILNRLVQFVKDRISVVQALVLTQQYHQLKPIEYEP	96
Amphotrophic Murine Leukemia Virus - MLV ENV (amphotropic)	MARSTLSKPPQDKINPWKPLIVMGVLLGVGMAESPHQVFNVTWRVTNLMTGR TANATSLLGTVQDAFPKLYFDLCDLVGEEWDPSDQEPYVGYGCKYPAGRQRT RTFDFYVCPGHTVKSGCGGPGEGYCGKWGCETTGQAYWKPTSSWDLISLKRG NTPWDTGCSKVACGPCYDLSKVSNSFQGATRGGRCNPLVLEFTDAGKKANWD GPKSWGLRLYRTGTDPITMFSLTRQVLNVGPRVPIGPNPVLPDQRLPSSPIE IVPAPQPPSPLNTSYPPSTTSTPSTSPTSPSVPQPPPGTGDRLLALVKGAYQ ALNLTNPDKTQECWLCLVSGPPYYEGVAVVGTYTNHSTAPANCTATSQHKLT LSEVTGQGLCMGAVPKTHQALCNTTQSAGSGSYYLAAPAGTMWACSTGLTPC LSTTVLNLTTDYCVLVELWPRVIYHSPDYMYGQLEQRTKYKREPVSLTLALL LGGLTMGGIAAGIGTGTTALIKTQQFEQLHAAIQTDLNEVEKSITNLEKSLT SLSEVVLQNRRGLDLLFLKEGGLCAALKEECCFYADHTGLVRDSMAKLRERL NQRQKLFETGQGWFEGLFNRSPWFTTLISTIMGPLIVLLLILLFGPCILNRL VQFVKDRISVVQALVLTQQYHQLKPIEYEP	97
	ARSTLSKPPQDKINPWKPLIVMGVLLGVGMAESPHQVFNVTWRVTNLMTGRT ANATSLLGTVQDAFPKLYFDLCDLVGEEWDPSDQEPYVGYGCKYPAGRQRTR TFDFYVCPGHTVKSGCGGPGEGYCGKWGCETTGQAYWKPTSSWDLISLKRGN TPWDTGCSKVACGPCYDLSKVSNSFQGATRGGRCNPLVLEFTDAGKKANWDG PKSWGLRLYRTGTDPITMFSLTRQVLNVGPRVPIGPNPVLPDQRLPSSPIEI VPAPQPPSPLNTSYPPSTTSTPSTSPTSPSVPQPPPGTGDRLLALVKGAYQA LNLTNPDKTQECWLCLVSGPPYYEGVAVVGTYTNHSTAPANCTATSQHKLTL SEVTGQGLCMGAVPKTHQALCNTTQSAGSGSYYLAAPAGTMWACSTGLTPCL STTVLNLTTDYCVLVELWPRVIYHSPDYMYGQLEQRTKYKREPVSLTLALLL GGLTMGGIAAGIGTGTTALIKTQQFEQLHAAIQTDLNEVEKSITNLEKSLTS LSEVVLQNRRGLDLLFLKEGGLCAALKEECCFYADHTGLVRDSMAKLRERLN QRQKLFETGQGWFEGLFNRSPWFTTLISTIMGPLIVLLLILLFGPCILNRLV QFVKDRISVVQALVLTQQYHQLKPIEYEP	98
Moloney murine leukemia virus 10A1 strain	MARSTLSKPLKDKINPWKSLMVMGVLLRVGMAESPHQVFNVTWRVTNLMTGR TANATSLLGTVQDAFPRLYFDLCDLVGEEWDPSDQEPYVGYGCKYPGGRKRT RTFDFYVCPGHTVKSGCGGPREGYCGEWGCETTGQAYWKPTSSWDLISLKRG NTPWDTGCSKMACGPCYDLSKVSNSFQGATRGGRCNPLVLEFTDAGKKANWD GPKSWGLRLYRTGTDPITMFSLTRQVLNIGPRIPIGPNPVITGQLPPSRPVQ IRLPRPPQPPPTGAASIVPETAPPSQQPGTGDRLLNLVEGAYRALNLTNPDK	99

Glycoprotein - MLV 10A1	TQECWLCLVSGPPYYEGVAVVGTYTNHSTAPASCTATSQHKLTLSEVTGQGL CMGAVPKTHQALCNTTQSAGSGSYYLAAPAGTMWACSTGLTPCLSTTMLNLT TDYCVLVELWPRIIYHSPDYMYGQLEQRTKYKREPVSLTLALLLGGLTMGGI AAGIGTGTTALIKTQQFEQLHAAIQTDLNEVEKSITNLEKSLTSLSEVVLQN RRGLDLLFLKEGGLCAALKEECCFYADHTGLVRDSMAKLRERLNQRQKLFES GQGWFEGLFNRSPWFTTLISTIMGPLIVLLLILLFGPCILNRLVQFVKDRIS VVQALVLTQQYHQLKPIEYEP	
	ARSTLSKPLKDKINPWKSLMVMGVLLRVGMAESPHQVFNVTWRVTNLMTGRT ANATSLLGTVQDAFPRLYFDLCDLVGEEWDPSDQEPYVGYGCKYPGGRKRTR TFDFYVCPGHTVKSGCGGPREGYCGEWGCETTGQAYWKPTSSWDLISLKRGN TPWDTGCSKMACGPCYDLSKVSNSFQGATRGGRCNPLVLEFTDAGKKANWDG PKSWGLRLYRTGTDPITMFSLTRQVLNIGPRIPIGPNPVITGQLPPSRPVQI RLPRPPQPPPTGAASIVPETAPPSQQPGTGDRLLNLVEGAYRALNLTNPDKT QECWLCLVSGPPYYEGVAVVGTYTNHSTAPASCTATSQHKLTLSEVTGQGLC MGAVPKTHQALCNTTQSAGSGSYYLAAPAGTMWACSTGLTPCLSTTMLNLTT DYCVLVELWPRIIYHSPDYMYGQLEQRTKYKREPVSLTLALLLGGLTMGGIA AGIGTGTTALIKTQQFEQLHAAIQTDLNEVEKSITNLEKSLTSLSEVVLQNR RGLDLLFLKEGGLCAALKEECCFYADHTGLVRDSMAKLRERLNQRQKLFESG QGWFEGLFNRSPWFTTLISTIMGPLIVLLLILLFGPCILNRLVQFVKDRISV VQALVLTQQYHQLKPIEYEP	100
Baculovirus envelope glycoprotein - GP64	MVSAIVLYVLLAAAAHSAFAAEHCNAQMKTGPYKIKNLDITPPKETLQKDVE ITIVETDYNENVIIGYKGYYQAYAYNGGSLDPNTRVEETMKTLNVGKEDLLM WSIRQQCEVGEELIDRWGSDSDDCFRDNEGRGQWVKGKELVKRQNNNHFAHH TCNKSWRCGISTSKMYSRLECQDDTDECQVYILDAEGNPINVTVDTVLHRDG VSMILKQKSTFTTRQIKAACLLIKDDKNNPESVTREHCLIDNDIYDLSKNTW NCKFNRCIKRKVEHRVKKRPPTWRHNVRAKYTEGDTATKGDLMHIQEELMYE NDLLKMNIELMHAHINKLNNMLHDLIVSVAKVDERLIGNLMNNSVSSTFLSD DTFLLMPCTNPPAHTSNCYNNSIYKEGRVVVANTDSSQCIDFSNYKELAIDD DVEFWIPTIGNTTYHDSWKDASGWSFIAQQKSNLITTMENTKFGGVGTSLSD ITSMAEGELAAKLTSFMFGHVVNFVIILIVILFLYCMIRNRNRQY	101
	VSAIVLYVLLAAAAHSAFAAEHCNAQMKTGPYKIKNLDITPPKETLQKDVEI TIVETDYNENVIIGYKGYYQAYAYNGGSLDPNTRVEETMKTLNVGKEDLLMW SIRQQCEVGEELIDRWGSDSDDCFRDNEGRGQWVKGKELVKRQNNNHFAHHT CNKSWRCGISTSKMYSRLECQDDTDECQVYILDAEGNPINVTVDTVLHRDGV SMILKQKSTFTTRQIKAACLLIKDDKNNPESVTREHCLIDNDIYDLSKNTWN CKFNRCIKRKVEHRVKKRPPTWRHNVRAKYTEGDTATKGDLMHIQEELMYEN DLLKMNIELMHAHINKLNNMLHDLIVSVAKVDERLIGNLMNNSVSSTFLSDD TFLLMPCTNPPAHTSNCYNNSIYKEGRVVVANTDSSQCIDFSNYKELAIDDD VEFWIPTIGNTTYHDSWKDASGWSFIAQQKSNLITTMENTKFGGVGTSLSDI TSMAEGELAAKLTSFMFGHVVNFVIILIVILFLYCMIRNRNRQY	102
Endogenous feline virus - RD114 ENV	MKLPTGMVILCSLIIVRAGFDDPRKAIALVQKQHGKPCECSGGQVSEAPPNS IQQVTCPGKTAYLMTNQKWKCRVTPKISPSGGELQNCPCNTFQDSMHSSCYT EYRQCRRINKTYYTATLLKIRSGSLNEVQILQNPNQLLQSPCRGSINQPVCW SATAPIHISDGGGPLDTKRVVVTVQKRLEQIHKAMTPELQYHPLALPKVRDD LSLDARTFDILNTTFRLLQMSNFSLAQDCWLCLKLGTPTPLAIPTPSLTYSL ADSLANASCQIIPPLLVQPMQFSNSSCLSSPFINDTEQIDLGAVTFTNCTSV ANVSSPLCALNGSVFLCGNNMAYTYLPQNVVTRLCVQASLLPDIDINPGDEP VPIPAIDHYIHRPKRAVQFIPLLAGLGITAAFTTGATGLGVSVTQYTKLSHQ LISDVQVLSGTIQDLQDQVDSLAEVVLQNRRGLDLLTAEQGGICLALQEKCC FYANKSGIVRNKIRTLQEELQKRRESLATNPLVVTGLQGFLPYLLPLLGPLL TLLLILTIGPCVFSRLMAFINDRLNVVHAMVLAQQYQALKAEEEAQD	103
	KLPTGMVILCSLIIVRAGFDDPRKAIALVQKQHGKPCECSGGQVSEAPPNSI QQVTCPGKTAYLMTNQKWKCRVTPKISPSGGELQNCPCNTFQDSMHSSCYTE YRQCRRINKTYYTATLLKIRSGSLNEVQILQNPNQLLQSPCRGSINQPVCWS ATAPIHISDGGGPLDTKRVVVTVQKRLEQIHKAMTPELQYHPLALPKVRDDL SLDARTFDILNTTFRLLQMSNFSLAQDCWLCLKLGTPTPLAIPTPSLTYSLA DSLANASCQIIPPLLVQPMQFSNSSCLSSPFINDTEQIDLGAVTFTNCTSVA NVSSPLCALNGSVFLCGNNMAYTYLPQNVVTRLCVQASLLPDIDINPGDEPV	104

	PIPAIDHYIHRPKRAVQFIPLLAGLGITAAFTTGATGLGVSVTQYTKLSHQL ISDVQVLSGTIQDLQDQVDSLAEVVLQNRRGLDLLTAEQGGICLALQEKCCF YANKSGIVRNKIRTLQEELQKRRESLATNPLVVTGLQGFLPYLLPLLGPLLT LLLILTIGPCVFSRLMAFINDRLNVVHAMVLAQQYQALKAEEEAQD	

Envelope protein of human origin

[0088] In some aspects, the envelope protein in the lipid delivery particle described herein has a human origin, *e.g.,* has significant sequence similarity to a human wild-type protein, such as at least 90%, at least 95%, at least 98%, or at least 99%. Using an envelope protein of a human origin can have benefits such as providing a minimized immunogenicity and better tolerance in a human subject receiving the lipid delivery particles. The lipid delivery particle comprising an envelope protein of a human origin can comprise another component that is from human origin or from non-human origin (*e.g.,* a payload or a plasma membrane recruitment element). An envelope protein that is from human origin can include, example, envelope proteins or glycoproteins of human endogenous retroviruses (HERVs), other human endogenous envelope proteins, or other human endogenous proteins that serve a similar function of recognizing and/or fusing with membrane of a target cell (*e.g.,* clathrin adaptor protein complex-1, CHMP4C, Proteolipid protein 1, TSAP6, immunoglobulin variable domains, or a biologically active mutant thereof).

[0089] In some cases, the envelope protein is a HERV envelope protein such as any one of those listed in **Table 2.** In some cases, the envelope protein is a hENVH1 or a biologically active thereof. In some cases, the envelope protein is a hENVH2 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVH3 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVK1 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVK2 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVK3 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVK4 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVK5 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVK6 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVT or a biologically active mutant thereof. In some cases, the envelope protein is a hENVW or a biologically active mutant thereof. In some cases, the envelope protein is a hENVFRD or a biologically active mutant thereof. In some cases, the envelope protein is a hENVR or a biologically active mutant thereof. In some cases, the envelope protein is a hENVR(b) or a biologically active mutant thereof. In some cases, the envelope protein is a hENVR(c)2 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVR(c)1 or a biologically active mutant thereof. In some cases, the envelope protein is a hENVKcon or a biologically active mutant thereof. In some cases, the envelope protein is a biologically active truncated HERV protein.

Table 2. Exemplary human HERV envelope proteins

#	HERV envelope	Gene name	Accession no.	Position in sequence entry (a)
1.	hENVH1	envH/p62	AJ289709.1	6313-8067(+)
2.	hENVH2	envH/p60	AJ289710.2	5393-7084(+)
3.	hENVH3	envH/p59	AJ289711.1	5204-6871(+)
4.	hENVK1	envK1	AC074261.3	93508-95604(+)
5.	hENVK2	envK2/HML-2.HOM	AC072054.10	30365-32464(−)
6.	hENVK3	envK3/C19	Y17833.1	5581-7680(+)
7.	hENVK4	envK4/K109	AF164615.1	6412-8508(+)
8.	hENVK5	envK5/K113	AY037928.1	6451-8550(+)
9.	hENVK6	envK6/K115	AY037929.1	6442-8541(+)
10.	hENVT	envT	AC078899.1	154738-156618(+)
11.	hENVW	Syncytin-1	AC000064.1	35879-37495(+)
12.	hENVFRD	Syncytin-2	AL136139.6	21355-22972(−)
13.	hENVR	erv-3	AC073210.8	54963-56978(−)
14.	hENVR(b)	envRb	AC093488.1	78681-80225(+)
15.	hENVF(c)2	envFc2	AC016222.4	85216-86963(+)
16.	hENVF(c)1	envFc1	AL354685.2	46744-48717(−)
*17.	$hENVK_{con}$	N/A	N/A	N/A

(a) '+' and '−' refer to the orientation within the sequence entry
*$hENVK_{con}$ is a consensus sequence from ten proviral ENV sequences. The ENV sequences used to derive this consensus ENV sequence are from the following HERVs: HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV- K11p22, and HERV-K12q13.

[0090] For example, for those amino acid sequences start with a N-terminal methionine, the N-terminal methionine can be absent. In some cases, the envelope protein comprises the sequences set forth in **Table 3** and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0091] In some cases, the envelope protein comprises one or more of the sequences set forth in **Table 3** with at least one amino acid substitution, deletion, or insertion. For instance, N-terminal methionine can be absent from the envelope protein of the lipid delivery particle provided herein relative to the wild-type viral envelope protein. In some cases, the envelope protein comprises one or more of the sequences set forth in **Table 3** and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0092] In some cases, the envelope protein comprises any one of the sequences set forth in **Table 3** with at least one amino acid substitution, deletion, or insertion. For instance, N-terminal methionine can be absent from the envelope protein of the lipid delivery particle provided herein relative to the wild-type viral envelope protein. In some cases, the envelope protein comprises any one of the sequences set forth in **Table 3** and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0093] In some cases, the envelope protein comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 50% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about

60% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 70% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 75% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 80% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 85% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 90% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 95% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 96% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 97% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**.In some cases, the envelope protein comprises an amino acid sequence that has at least about 98% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**. In some cases, the envelope protein comprises an amino acid sequence that has at least about 99% sequence identity to a sequence set forth in **SEQ ID NOs: 49-82**.

Table 3. Exemplary sequences for human HERV envelope proteins

HERV envelope	Amino Acid Sequence	SEQ ID NO:
hENVT	MGPEAWVRPLKTAPKPGEAIRLILFIYLSCFFLPVMSSEPSYSFLLTSFTTGRV FANTTWRAGTSKEVSFAVDLCVLFPEPARTHEEQHNLPVIGAGSVDLAAGFGHS GSQTGCGSSKGAEKGLQNVDFYLCPGNHPDASCRDTYQFFCPDWTCVTLATYSG GSTRSSTLSISRVPHPKLCTRKNCNPLTITVHDPNAAQWYYGMSWGLRLYIPGF DVGTMFTIQKKILVSWSSPKPIGPLTDLGDPIFQKHPDKVDLTVPLPFLVPRPQ LQQQHLQPSLMSILGGVHHLLNLTQPKLAQDCWLCLKAKPPYYVGLGVEATLKR GPLSCHTRPRALTIGDVSGNASCLISTGYNLSASPFQATCNQSLLTSISTSVSY QAPNNTWLACTSGLTRCINGTEPGPLLCVLVHVLPQVYVYSGPEGRQLIAPPEL HPRLHQAVPLLVPLLAGLSIAGSAAIGTAALVQGETGLISLSQQVDADFSNLQS AIDILHSQVESLAEVVLQNCRCLDLLFLSQGGLCAALGESCCFYANQSGVIKGT VKKVRENLDRHQQERENNIPWYQSMFNWNPWLTTLITGLAGPLLILLLSLIFGP CILNSFLNFIKQRIASVKLTYLKTQYDTLVNN	49
	GPEAWVRPLKTAPKPGEAIRLILFIYLSCFFLPVMSSEPSYSFLLTSFTTGRVF ANTTWRAGTSKEVSFAVDLCVLFPEPARTHEEQHNLPVIGAGSVDLAAGFGHSG SQTGCGSSKGAEKGLQNVDFYLCPGNHPDASCRDTYQFFCPDWTCVTLATYSGG STRSSTLSISRVPHPKLCTRKNCNPLTITVHDPNAAQWYYGMSWGLRLYIPGFD VGTMFTIQKKILVSWSSPKPIGPLTDLGDPIFQKHPDKVDLTVPLPFLVPRPQL QQQHLQPSLMSILGGVHHLLNLTQPKLAQDCWLCLKAKPPYYVGLGVEATLKRG PLSCHTRPRALTIGDVSGNASCLISTGYNLSASPFQATCNQSLLTSISTSVSYQ APNNTWLACTSGLTRCINGTEPGPLLCVLVHVLPQVYVYSGPEGRQLIAPPELH PRLHQAVPLLVPLLAGLSIAGSAAIGTAALVQGETGLISLSQQVDADFSNLQSA IDILHSQVESLAEVVLQNCRCLDLLFLSQGGLCAALGESCCFYANQSGVIKGTV	50

	KKVRENLDRHQQERENNIPWYQSMFNWNPWLTTLITGLAGPLLILLLSLIFGPC ILNSFLNFIKQRIASVKLTYLKTQYDTLVNN	
hENVW	MALPYHIFLFTVLLPSFTLTAPPPCRCMTSSSPYQEFLWRMQRPGNIDAPSYRS LSKGTPTFTAHTHMPRNCYHSATLCMHANTHYWTGKMINPSCPGGLGVTVCWTY FTQTGMSDGGGVQDQAREKHVKEVISQLTRVHGTSSPYKGLDLSKLHETLRTHT RLVSLFNTTLTGLHEVSAQNPTNCWICLPLNFRPYVSIPVPEQWNNFSTEINTT SVLVGPLVSNLEITHTSNLTCVKFSNTTYTTNSQCIRWVTPPTQIVCLPSGIFF VCGTSAYRCLNGSSESMCFLSFLVPPMTIYTEQDLYSYVISKPRNKRVPILPFV IGAGVLGALGTGIGGITTSTQFYYKLSQELNGDMERVADSLVTLQDQLNSLAAV VLQNRRALDLLTAERGGTCLFLGEECCYYVNQSGIVTEKVKEIRDRIQRRAEEL RNTGPWGLLSQWMPWILPFLGPLAAIILLLLFGPCIFNLLVNFVSSRIEAVKLQ MEPKMQSKTKIYRRPLDRPASPRSDVNDIKGTPPEEISAAQPLLRPNSAGSS	51
	ALPYHIFLFTVLLPSFTLTAPPPCRCMTSSSPYQEFLWRMQRPGNIDAPSYRSL SKGTPTFTAHTHMPRNCYHSATLCMHANTHYWTGKMINPSCPGGLGVTVCWTYF TQTGMSDGGGVQDQAREKHVKEVISQLTRVHGTSSPYKGLDLSKLHETLRTHTR LVSLFNTTLTGLHEVSAQNPTNCWICLPLNFRPYVSIPVPEQWNNFSTEINTTS VLVGPLVSNLEITHTSNLTCVKFSNTTYTTNSQCIRWVTPPTQIVCLPSGIFFV CGTSAYRCLNGSSESMCFLSFLVPPMTIYTEQDLYSYVISKPRNKRVPILPFVI GAGVLGALGTGIGGITTSTQFYYKLSQELNGDMERVADSLVTLQDQLNSLAAVV LQNRRALDLLTAERGGTCLFLGEECCYYVNQSGIVTEKVKEIRDRIQRRAEELR NTGPWGLLSQWMPWILPFLGPLAAIILLLLFGPCIFNLLVNFVSSRIEAVKLQM EPKMQSKTKIYRRPLDRPASPRSDVNDIKGTPPEEISAAQPLLRPNSAGSS	52
hENVH 1	MIFAGKAPSNTSTLMKFYSLLLYSLLFSFPFLCHPLPLPSYLHHTINLTHSLLA ASNPSLVNNCWLCISLSSSAYTAVPAVQTDWATSPISLHLRTSFNSPHLYPPEE LIYFLDRSSKTSPDISHQQAAALLRTYLKNLSPYINSTPPIFGPLTTQTTIPVA APLCISWQRPTGIPLGNLSPSRCSFTLHLRSPTTNINETIGAFQLHITDKPSIN TDKLKNISSNYCLGRHLPCISLHPWLSSPCSSDSPPRPSSCLLIPSPENNSERL LVDTRRFLIHHENRTFPSTQLPHQSPLQPLTAAALAGSLGVWVQDTPFSTPSHL FTLHLQFCLAQGLFFLCGSSTYMCLPANWTGTCTLVFLTPKIQFANGTEELPVP LMTPTQQKRVIPLIPLMVGLGLSASTVALGTGIAGISTSVMTFRSLSNDFSASI TDISQTLSVLQAQVDSLAAVVLQNRRGLDLLTAEKGGLCIFLNEECCFYLNQSG LVYDNIKKLKDRAQKLANQASNYAEPPWALSNWMSWVLPIVSPLIPIFLLLLFG PCIFRLVSQFIQNRIQAITNHSIRQMFLLTSPQYHPLPQDLPSA	53
	IFAGKAPSNTSTLMKFYSLLLYSLLFSFPFLCHPLPLPSYLHHTINLTHSLLAA SNPSLVNNCWLCISLSSSAYTAVPAVQTDWATSPISLHLRTSFNSPHLYPPEEL IYFLDRSSKTSPDISHQQAAALLRTYLKNLSPYINSTPPIFGPLTTQTTIPVAA PLCISWQRPTGIPLGNLSPSRCSFTLHLRSPTTNINETIGAFQLHITDKPSINT DKLKNISSNYCLGRHLPCISLHPWLSSPCSSDSPPRPSSCLLIPSPENNSERLL VDTRRFLIHHENRTFPSTQLPHQSPLQPLTAAALAGSLGVWVQDTPFSTPSHLF TLHLQFCLAQGLFFLCGSSTYMCLPANWTGTCTLVFLTPKIQFANGTEELPVPL MTPTQQKRVIPLIPLMVGLGLSASTVALGTGIAGISTSVMTFRSLSNDFSASIT DISQTLSVLQAQVDSLAAVVLQNRRGLDLLTAEKGGLCIFLNEECCFYLNQSGL VYDNIKKLKDRAQKLANQASNYAEPPWALSNWMSWVLPIVSPLIPIFLLLLFGP CIFRLVSQFIQNRIQAITNHSIRQMFLLTSPQYHPLPQDLPSA	54
hENVH 2	MIFAGRASSNTSTLMKFYSLLLYSLLFSFPILCHPLPLPSYLHHTINLTHSLLA VSNPSLAKNCWLCISLPSSAYPAVPALQTDWGTSPVSPHLRTSFNSPHLYPPEK LIYFLDRSSKTSPDISHQQAAALLCTYLKNLSPYINSTPPTFGPLTTQTTIPVA APLCISRQRPTGIPLGNLSPSRCSFTLHLRSPTTHITETNGAFQLHITDKPSIN TDKLKNVSSNYCLGRHLSCISLHPWLFSPCSSDSPPRPSSCLLIPSPKNNSESL LVDAQRFLIYHENRTSPSTQLPHQSPLQPLTAAPLGGSLRVWVQDTPFSTPSHL FTLHLQFCLVQSLFFLCGSSTYMCLPANWTGTCTLVFLTSKIQFANGTEELPVP LMTPTRQKRVIPLIPLMVGLGLSASTVALGTGIAGISTSVTTFRILSNDFSASI TDISQTLSGLQAQVDSSAAVVLQNRQGLDLLTAEKGGLCIFLNEESYFYLNQSG LVYDNIKKLKDKAQNLANQASNYAEPPWPLSNWMSWVLPILSPLIPIFLLLFFR PCIFHLVSQFIQNHIQAITDHSI	55
	IFAGRASSNTSTLMKFYSLLLYSLLFSFPILCHPLPLPSYLHHTINLTHSLLAV SNPSLAKNCWLCISLPSSAYPAVPALQTDWGTSPVSPHLRTSFNSPHLYPPEKL IYFLDRSSKTSPDISHQQAAALLCTYLKNLSPYINSTPPTFGPLTTQTTIPVAA	56

	PLCISRQRPTGIPLGNLSPSRCSFTLHLRSPTTHITETNGAFQLHITDKPSINT DKLKNVSSNYCLGRHLSCISLHPWLFSPCSSDSPPRPSSCLLIPSPKNNSESLL VDAQRFLIYHENRTSPSTQLPHQSPLQPLTAAPLGGSLRVWVQDTPFSTPSHLF TLHLQFCLVQSLFFLCGSSTYMCLPANWTGTCTLVFLTSKIQFANGTEELPVPL MTPTRQKRVIPLIPLMVGLGLSASTVALGTGIAGISTSVTTFRILSNDFSASIT DISQTLSGLQAQVDSSAAVVLQNRQGLDLLTAEKGGLCIFLNEESYFYLNQSGL VYDNIKKLKDKAQNLANQASNYAEPPWPLSNWMSWVLPILSPLIPIFLLLFFRP CIFHLVSQFIQNHIQAITDHSI	
hENVH3	MILAGRAPSNTSTLMKFYSLLLYSLLFSFPFLYHPLPLPSYLHHTINLTHSLPA ASNPSLANNCWLCISLSSSAYIAVPTLQTDRATSPVSLHLRTSFNSPHLYPPEE LIYFLDRSSKTSPDISHQPAAALLHIYLKNLSPYINSTPPIFGPLTTQTTIPVA APLCISRQRPTGIPLGNISPSRCSFTLHLQSPTTHVTETIGVFQLHIIDKPSIN TDKLKNVSSNYCLGRHLPYISLHPWLPSPCSSDSPPRPSSCLLTPSPQNNSERL LVDTQRFLIHHENRTSSSMQLAHQSPLQPLTAAALAGSLGVWVQDTPFSTPSHP FSLHLQFCLTQGLFFLCGSSTYMCLPANWTGTCTLVFLTPKIQFANGTKELPVP LMTLTPQKRVIPLIPLMVGLGLSASTIALSTGIAGISTSVTTFRSPSNDFSASI TDISQTLSVLQAQVDSLAAVVLQNRRGLGLSILLNEECCFYLNQSGLVYENIKK LKDRAQKLANQASNYAESPWALSNWMSWVLPILSPLIPIFLLLLFGPCIFHLVS QFIQNRIQAITNHSI	57
	ILAGRAPSNTSTLMKFYSLLLYSLLFSFPFLYHPLPLPSYLHHTINLTHSLPAA SNPSLANNCWLCISLSSSAYIAVPTLQTDRATSPVSLHLRTSFNSPHLYPPEEL IYFLDRSSKTSPDISHQPAAALLHIYLKNLSPYINSTPPIFGPLTTQTTIPVAA PLCISRQRPTGIPLGNISPSRCSFTLHLQSPTTHVTETIGVFQLHIIDKPSINT DKLKNVSSNYCLGRHLPYISLHPWLPSPCSSDSPPRPSSCLLTPSPQNNSERLL VDTQRFLIHHENRTSSSMQLAHQSPLQPLTAAALAGSLGVWVQDTPFSTPSHPF SLHLQFCLTQGLFFLCGSSTYMCLPANWTGTCTLVFLTPKIQFANGTKELPVPL MTLTPQKRVIPLIPLMVGLGLSASTIALSTGIAGISTSVTTFRSPSNDFSASIT DISQTLSVLQAQVDSLAAVVLQNRRGLGLSILLNEECCFYLNQSGLVYENIKKL KDRAQKLANQASNYAESPWALSNWMSWVLPILSPLIPIFLLLLFGPCIFHLVSQ FIQNRIQAITNHSI	58
hENVK1	MHPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEQMKLPSTKKAEPPTWAQLKK LTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTNWAYVPF PPLIRAVTWMDNPIEVYVNDSVWVHGPIDDRCPAKPEEEGMMINISIGYHYPPI CLGRAPGCLMPAVQNWLVEVPTVSPISRFTYNMVSGMSLRPRVNYLQDFSYQRS LKFRPKGKPCPKEIPKESKNTEVLVWEECVANSVVILQNNEFGTIIDWAPRGQF YHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPRP KIISPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSLTVPL QSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGV WIPVSMDRPWEASPSIHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTAMAAVA GVALHSFVQSVNFVNDWQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLM SLEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLKE QIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCLF CLLLVCRFTQQLRRDSYHRERAMMTMVVLSKRKGGNVGKSKRDQIVTVSV	59
	HPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEQMKLPSTKKAEPPTWAQLKKL TQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTNWAYVPFP PLIRAVTWMDNPIEVYVNDSVWVHGPIDDRCPAKPEEEGMMINISIGYHYPPIC LGRAPGCLMPAVQNWLVEVPTVSPISRFTYNMVSGMSLRPRVNYLQDFSYQRSL KFRPKGKPCPKEIPKESKNTEVLVWEECVANSVVILQNNEFGTIIDWAPRGQFY HNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPRPK IISPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSLTVPLQ SCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGVW IPVSMDRPWEASPSIHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTAMAAVAG VALHSFVQSVNFVNDWQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLMS LEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLKEQ IFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCLFC LLLVCRFTQQLRRDSYHRERAMMTMVVLSKRKGGNVGKSKRDQIVTVSV	60
	MNPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLK KLTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTYWAYVP	61

	FPPLIRAVTWMDNPTEVYVNDSVWVPGPIDDRCPAKPEEEGMMINISIGYHYPP ICLGRAPGCLMPAVQNWLVEVPTVSPICRFTYHMVSGMSLRPRVNYLQDFSYQR SLKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWAPRGQ FYHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPR PKIVSPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTIDLNSSLTVP LQSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREG VWIPVSMDRPWEASPSVHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAV AGVALHSSVQSVNFVNDWQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRL MSLEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLK EQIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCL FCLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV;	
hENVK 2	NPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLKK LTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTYWAYVPF PPLIRAVTWMDNPTEVYVNDSVWVPGPIDDRCPAKPEEEGMMINISIGYHYPPI CLGRAPGCLMPAVQNWLVEVPTVSPICRFTYHMVSGMSLRPRVNYLQDFSYQRS LKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWAPRGQF YHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPRP KIVSPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTIDLNSSLTVPL QSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGV WIPVSMDRPWEASPSVHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAVA GVALHSSVQSVNFVNDWQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLM SLEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLKE QIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCLF CLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV	62
hENVK 3	MNPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLK KLTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTYWAYVP FPPLIRAVTWMDNPIEVYVNDSVWVPGPTDDHCPAKPEEEGMMINISIGYRYPP ICLGRAPGCLMPAVQNWLVEVPTVSPISRFTYHMVSGMSLRPRVNYLQDFSYQR SFKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWAPRGQ FYHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPR PKIISPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSVTVP LQSCIKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREG VWIPVSMDRPWETSPSIHTLTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAV AGVALHSSVQSVNFVNDWQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRL MSLEHRFQLQCDWNTSDFSITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLK EQIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCL FCLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV	63
	NPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLKK LTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTYWAYVPF PPLIRAVTWMDNPIEVYVNDSVWVPGPTDDHCPAKPEEEGMMINISIGYRYPPI CLGRAPGCLMPAVQNWLVEVPTVSPISRFTYHMVSGMSLRPRVNYLQDFSYQRS FKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWAPRGQF YHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPRP KIISPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSVTVPL QSCIKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGV WIPVSMDRPWETSPSIHTLTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAVA GVALHSSVQSVNFVNDWQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLM SLEHRFQLQCDWNTSDFSITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLKE QIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCLF CLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV	64
hENVK 4	MNPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLK KLTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTNWAYVP FPPLIRAVTWMDNPIEVYVNDSVWVPGPIDDRCPAKPEEEGMMINISIGYRYPI CLGRAPGCLMPAVQNWLVEVPIVSPICRFTYHMVSGMSLRPRVNYLQDFSYQRS LKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWTPQGQF YHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPRP KIISPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSLTLPL QSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGV	65

	WIPVSMDRPWEASPSIHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAVA GVALHSSVQSVNFVNDGQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLM SLEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLKE QIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCLF CLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV	
	NPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLKK LTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTNWAYVPF PPLIRAVTWMDNPIEVYVNDSVWVPGPIDDRCPAKPEEEGMMINISIGYRYPIC LGRAPGCLMPAVQNWLVEVPIVSPICRFTYHMVSGMSLRPRVNYLQDFSYQRSL KFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWTPQGQFY HNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPRPK IISPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSLTLPLQ SCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGVW IPVSMDRPWEASPSIHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAVAG VALHSSVQSVNFVNDGQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLMS LEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLKEQ IFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCLFC LLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV	66
hENVK 5	MNPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLK KLTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTYWAYVP FPPLIRAVTWMDNPIEIYVNDSVWVPGPTDDCCPAKPEEEGMMINISIGYRYPP ICLGRAPGCLMPAVQNWLVEVPTVSPISRFTYHMVSGMSLRPRVNYLQDFSYQR SLKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTLIDWAPRGQ FYHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTAR PKIISPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTIDLNSSLTVP LQSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREG VWIPVSMDRPWEASPSVHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAV AGVALHSSVQSVNFVNDWQNNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRL MSLEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRCHLQGREDNLTLDISKLK EQIFEASKAHLNLVPGTEAIAGVADGLANLNTVTWVKTIGSTTIINLILILVCL FCLLLVYRCTQQLRRDSDHRERAMMTMVVLSKRKGGNVGKSKRDQIVTVSV	67
	NPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLKK LTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTYWAYVPF PPLIRAVTWMDNPIEIYVNDSVWVPGPTDDCCPAKPEEEGMMINISIGYRYPPI CLGRAPGCLMPAVQNWLVEVPTVSPISRFTYHMVSGMSLRPRVNYLQDFSYQRS LKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTLIDWAPRGQF YHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTARP KIISPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTIDLNSSLTVPL QSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGV WIPVSMDRPWEASPSVHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAVA GVALHSSVQSVNFVNDWQNNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLM SLEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRCHLQGREDNLTLDISKLKE QIFEASKAHLNLVPGTEAIAGVADGLANLNTVTWVKTIGSTTIINLILILVCLF CLLLVYRCTQQLRRDSDHRERAMMTMVVLSKRKGGNVGKSKRDQIVTVSV	68
hENVK 6	MNPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLK KLTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAVANYTNWAYVP FPPLIRAVTWMDNPIEVYVNDSVWVPGPIDDRCPAKPEEEGMMINISIGYRYPP ICLGRAPGCLMPAVQNWLVEVPTVSPISRFTYHMVSGMSLRPRVNYLQDFSYQR SLKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWAPRGQ FYHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKRISTPR PKIVSPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSLTLP LQSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREG VWIPVSMDRPWEASPSVHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAV AGVALHSSVQSVNFVNDGQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRL MSLEHRFQLQCDWNTSDFCITPQIYNDSEHHWDMVRRHLQGREDNLTLDISKLK EQIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCL FCLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV;	69

	NPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLKK LTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAVANYTNWAYVPF PPLIRAVTWMDNPIEVYVNDSVWVPGPIDDRCPAKPEEEGMMINISIGYRYPPI CLGRAPGCLMPAVQNWLVEVPTVSPISRFTYHMVSGMSLRPRVNYLQDFSYQRS LKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWAPRGQF YHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKRISTPRP KIVSPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSLTLPL QSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGV WIPVSMDRPWEASPSVHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAVA GVALHSSVQSVNFVNDGQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLM SLEHRFQLQCDWNTSDFCITPQIYNDSEHHWDMVRRHLQGREDNLTLDISKLKE QIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCLF CLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV	70
hENVFRD	MGLLLLVLILTPSLAAYRHPDFPLLEKAQQLLQSTGSPYSTNCWLCTSSSTETP GTAYPASPREWTSIEAELHISYRWDPNLKGLMRPANSLLSTVKQDFPDIRQKPP IFGPIFTNINLMGIAPICVMAKRKNGTNVGTLPSTVCNVTFTVDSNQQTYQTYT HNQFRHQPRFPKPPNITFPQGTLLDKSSRFCQGRPSSCSTRNFWFRPADYNQCL QISNLSSTAEWVLLDQTRNSLFWENKTKGANQSQTPCVQVLAGMTIATSYLGIS AVSEFFGTSLTPLFHFHISTCLKTQGAFYICGQSIHQCLPSNWTGTCTIGYVTP DIFIAPGNLSLPIPIYGNSPLPRVRRAIHFIPLLAGLGILAGTGTGIAGITKAS LTYSQLSKEIANNIDTMAKALTTMQEQIDSLAAVVLQNRRGLDMLTAAQGGICL ALDEKCCFWVNQSGKVQDNIRQLLNQASSLRERATQGWLNWEGTWKWFSWVLPL TGPLVSLLLLLLFGPCLLNLITQFVSSRLQAIKLQTNLSAGRHPRNIQESPF;	71
	GLLLLVLILTPSLAAYRHPDFPLLEKAQQLLQSTGSPYSTNCWLCTSSSTETPG TAYPASPREWTSIEAELHISYRWDPNLKGLMRPANSLLSTVKQDFPDIRQKPPI FGPIFTNINLMGIAPICVMAKRKNGTNVGTLPSTVCNVTFTVDSNQQTYQTYTH NQFRHQPRFPKPPNITFPQGTLLDKSSRFCQGRPSSCSTRNFWFRPADYNQCLQ ISNLSSTAEWVLLDQTRNSLFWENKTKGANQSQTPCVQVLAGMTIATSYLGISA VSEFFGTSLTPLFHFHISTCLKTQGAFYICGQSIHQCLPSNWTGTCTIGYVTPD IFIAPGNLSLPIPIYGNSPLPRVRRAIHFIPLLAGLGILAGTGTGIAGITKASL TYSQLSKEIANNIDTMAKALTTMQEQIDSLAAVVLQNRRGLDMLTAAQGGICLA LDEKCCFWVNQSGKVQDNIRQLLNQASSLRERATQGWLNWEGTWKWFSWVLPLT GPLVSLLLLLLFGPCLLNLITQFVSSRLQAIKLQTNLSAGRHPRNIQESPF	72
hENVR	MLGMNMLLITLFLLLPLSMLKGEPWEGCLHCTHTTWSGNIMTKTLLYHTYYECA GTCLGTCTHNQTTYSVCDPGRGQPYVCYDPKSSPGTWFEIHVGSKEGDLLNQTK VFPSGKDVVSLYFDVCQIVSMGSLFPVIFSSMEYYSSCHKNRYAHPACSTDSPV TTCWDCTTWSTNQQSLGPIMLTKIPLEPDCKTSTCNSVNLTILEPDQPIWTTGL KAPLGARVSGEEIGPGAYVYLYIIKKTRTRSTQQFRVFESFYEHVNQKLPEPPP LASNLFAQLAENIASSLHVASCYVCGGMNMGDQWPWEARELMPQDNFTLTASSL EPAPSSQSIWFLKTSIIGKFCIARWGKAFTDPVGELTCLGQQYYNETLGKTLWR GKSNNSESPHPSPFSRFPSLNHSWYQLEAPNTWQAPSGLYWICGPQAYRQLPAK WSGACVLGTIRPSFFLMPLKQGEALGYPIYDETKRKSKRGITIGDWKDNEWPPE RIIQYYGPATWAEDGMWGYRTPVYMLNRIIRLQAVLEIITNETAGALNLLAQQA TKMRNVIYQNRLALDYLLAQEEGVCGKFNLTNCCLELDDEGKVIKEITAKIQKL AHIPVQTWKG;	73
	LGMNMLLITLFLLLPLSMLKGEPWEGCLHCTHTTWSGNIMTKTLLYHTYYECAG TCLGTCTHNQTTYSVCDPGRGQPYVCYDPKSSPGTWFEIHVGSKEGDLLNQTKV FPSGKDVVSLYFDVCQIVSMGSLFPVIFSSMEYYSSCHKNRYAHPACSTDSPVT TCWDCTTWSTNQQSLGPIMLTKIPLEPDCKTSTCNSVNLTILEPDQPIWTTGLK APLGARVSGEEIGPGAYVYLYIIKKTRTRSTQQFRVFESFYEHVNQKLPEPPPL ASNLFAQLAENIASSLHVASCYVCGGMNMGDQWPWEARELMPQDNFTLTASSLE PAPSSQSIWFLKTSIIGKFCIARWGKAFTDPVGELTCLGQQYYNETLGKTLWRG KSNNSESPHPSPFSRFPSLNHSWYQLEAPNTWQAPSGLYWICGPQAYRQLPAKW SGACVLGTIRPSFFLMPLKQGEALGYPIYDETKRKSKRGITIGDWKDNEWPPER IIQYYGPATWAEDGMWGYRTPVYMLNRIIRLQAVLEIITNETAGALNLLAQQAT KMRNVIYQNRLALDYLLAQEEGVCGKFNLTNCCLELDDEGKVIKEITAKIQKLA HIPVQTWKG	74

hENVR(b)	MDPLHTIEKVPARRNIHDRGHQGHRMGDGTPGRPKISVQQMTRFSLIIFFLSAP FVVNASTSNVFLQWAHSYADGLQQGDPCWVCGSLPVTNTMELPWWVSPLQGKDW VFFQSFIGDLKQWTGAQMTGVTRKNISEWPINKTLNEPGHDKPFSVNETRDKVI AFAIPLLDTKVFVQTSRPQNTQYRNGFLQIWDGFIWLTATKGHLSQIAPLCWEQ RNHSLDNWPNTTRVMGWIPPGQCRHTILLQQRDLFATDWSQQPGLNWYAPNGTQ WLCSPNLWPWLPSGWLGCCTLGIPWAQGRWVKTMEVYPYLPHVVNQGTRAIVHR NDHLPTIFMPSVGLGTVIQHIEALANFTQRALNDSLQSISLMNAEVYYMHEDIL QNRMALDILTAAEGGTCALIKTECCVYIPNNSRNISLALEDTCRQIQVISSSAL SLHDWIASQFSGRPSWWQKILIVLATLWSVGIALCCGLYFCRMFSQHIPQTHSI IFQQELPLSPPSQEHYQSQRDIFHSNAP	75
	DPLHTIEKVPARRNIHDRGHQGHRMGDGTPGRPKISVQQMTRFSLIIFFLSAPF VVNASTSNVFLQWAHSYADGLQQGDPCWVCGSLPVTNTMELPWWVSPLQGKDWV FFQSFIGDLKQWTGAQMTGVTRKNISEWPINKTLNEPGHDKPFSVNETRDKVIA FAIPLLDTKVFVQTSRPQNTQYRNGFLQIWDGFIWLTATKGHLSQIAPLCWEQR NHSLDNWPNTTRVMGWIPPGQCRHTILLQQRDLFATDWSQQPGLNWYAPNGTQW LCSPNLWPWLPSGWLGCCTLGIPWAQGRWVKTMEVYPYLPHVVNQGTRAIVHRN DHLPTIFMPSVGLGTVIQHIEALANFTQRALNDSLQSISLMNAEVYYMHEDILQ NRMALDILTAAEGGTCALIKTECCVYIPNNSRNISLALEDTCRQIQVISSSALS LHDWIASQFSGRPSWWQKILIVLATLWSVGIALCCGLYFCRMFSQHIPQTHSII FQQELPLSPPSQEHYQSQRDIFHSNAP	76
hENVF(c)1	MARPSPLCLLLLLTLLTPIVPSNSLLTEPPFRWRFYLHETWTQGNRLSTVTLAT VDCQPHGCQAQVTFNFTSFKSVLRGWSNPTICFVYDQTHSNCRDYWVDTNGGCP YAYCRMHVTQLHTAKKLQHTYRLTSDGRTTYFLTIPDPWDSRWVSGVTGRLYRW PTDSYPVGKLRIFLTYIRVIPQVLSNLKDQADNIKHQEEVINTLVQSHPKADMV TYDDKAEAGPFSWITLVRHGARLVNMAGLVNLSHCFLCTALSQPPLVAVPLPQA FNTSGNHTAHPSGVFSEQVPLFRDPLQPQFPFCYTTPNSSWCNQTYSGSLSNLS APAGGYFWCNFTLTKHLNISSNNTLSRNLCLPISLVPRLTLYSEAELSSLVNPP MRQKRAVFPPLVIGVSLTSSLVASGLGTGAIVHFISSSQDLSIKLQMAIEASAE SLASLQRQITSVAKVAMQNRRALDLLTADKGGTCMFLGEECCYYINESGLVETS LLTLDKIRDGLHRPSSTPNYGGGWWQSPLTTWIIPFISPILIICLLLLIAPCVL KFIKNRISEVSRVTVNQMLLHPYSRLPTSEDHYDDALTQQEAAR	77
	ARPSPLCLLLLLTLLTPIVPSNSLLTEPPFRWRFYLHETWTQGNRLSTVTLATV DCQPHGCQAQVTFNFTSFKSVLRGWSNPTICFVYDQTHSNCRDYWVDTNGGCPY AYCRMHVTQLHTAKKLQHTYRLTSDGRTTYFLTIPDPWDSRWVSGVTGRLYRWP TDSYPVGKLRIFLTYIRVIPQVLSNLKDQADNIKHQEEVINTLVQSHPKADMVT YDDKAEAGPFSWITLVRHGARLVNMAGLVNLSHCFLCTALSQPPLVAVPLPQAF NTSGNHTAHPSGVFSEQVPLFRDPLQPQFPFCYTTPNSSWCNQTYSGSLSNLSA PAGGYFWCNFTLTKHLNISSNNTLSRNLCLPISLVPRLTLYSEAELSSLVNPPM RQKRAVFPPLVIGVSLTSSLVASGLGTGAIVHFISSSQDLSIKLQMAIEASAES LASLQRQITSVAKVAMQNRRALDLLTADKGGTCMFLGEECCYYINESGLVETSL LTLDKIRDGLHRPSSTPNYGGGWWQSPLTTWIIPFISPILIICLLLLIAPCVLK FIKNRISEVSRVTVNQMLLHPYSRLPTSEDHYDDALTQQEAAR	78
hENVF(c)2	MNSPCDRLQQFIQVLLEESWSFPSFANTLHWPENLLSYIDELVWQGSLQNFHQH EVRFDKPPLRLPLTGFSSLTENWSSRQAVSSRLVATAASPPAGCQAPIAFLGLK FSSLGPARKNPALCFLYDQSNSKCNTSWVKENVGCPWHWCNIHEALIRTEKGSD PMFYVNTSTGGRDGFNGFNLQISDPWDPRWASGVDGGLYEHKTFMYPVAKIRIA RTLKTTVTGLSDLASSIQSAEKELTSQLQPAADQAKSSRFSWLTLISEGAQLLQ STGVQNLSHCFLCAALRRPPLVAVPLPTPFNYTINSSTPIPPVPKGQVPLFSDP IRHKFPFCYSTPNASWCNQTRMLTSTPAPPRGYFWCNSTLTKVLNSTGNHTLCL PISLIPGLTLYSQDELSHLLAWTEPRPQNKSKWAIFLPLVLGISLASSLVASGL GKGALTHSIQTSQDLSTHLQLAIEASAESLDSLQRQITTVAQVAAQNRQALDLL MAEKGRTCLFLQEECCYYLNESGVVENSLQTLKKKKSSKRS	79
	NSPCDRLQQFIQVLLEESWSFPSFANTLHWPENLLSYIDELVWQGSLQNFHQHE VRFDKPPLRLPLTGFSSLTENWSSRQAVSSRLVATAASPPAGCQAPIAFLGLKF SSLGPARKNPALCFLYDQSNSKCNTSWVKENVGCPWHWCNIHEALIRTEKGSDP MFYVNTSTGGRDGFNGFNLQISDPWDPRWASGVDGGLYEHKTFMYPVAKIRIAR TLKTTVTGLSDLASSIQSAEKELTSQLQPAADQAKSSRFSWLTLISEGAQLLQS TGVQNLSHCFLCAALRRPPLVAVPLPTPFNYTINSSTPIPPVPKGQVPLFSDPI	80

	RHKFPFCYSTPNASWCNQTRMLTSTPAPPRGYFWCNSTLTKVLNSTGNHTLCLP ISLIPGLTLYSQDELSHLLAWTEPRPQNKSKWAIFLPLVLGISLASSLVASGLG KGALTHSIQTSQDLSTHLQLAIEASAESLDSLQRQITTVAQVAAQNRQALDLLM AEKGRTCLFLQEECCYYLNESGVVENSLQTLKKKKSSKRS	
hENVK$_c$ on	MNPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLK KLTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTYWAYVP FPPLIRAVTWMDNPIEVYVNDSVWVPGPIDDRCPAKPEEEGMMINISIGYRYPP ICLGRAPGCLMPAVQNWLVEVPTVSPISRFTYHMVSGMSLRPRVNYLQDFSYQR SLKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWAPRGQ FYHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPR PKIVSPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSLTVP LQSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREG VWIPVSMDRPWEASPSVHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAV AGVALHSSVQSVNFVNDWQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRL MSLEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLK EQIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCL FCLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV	81
	NPSEMQRKAPPRRRRHRNRAPLTHKMNKMVTSEEQMKLPSTKKAEPPTWAQLKK LTQLATKYLENTKVTQTPESMLLAALMIVSMVVSLPMPAGAAAANYTYWAYVPF PPLIRAVTWMDNPIEVYVNDSVWVPGPIDDRCPAKPEEEGMMINISIGYRYPPI CLGRAPGCLMPAVQNWLVEVPTVSPISRFTYHMVSGMSLRPRVNYLQDFSYQRS LKFRPKGKPCPKEIPKESKNTEVLVWEECVANSAVILQNNEFGTIIDWAPRGQF YHNCSGQTQSCPSAQVSPAVDSDLTESLDKHKHKKLQSFYPWEWGEKGISTPRP KIVSPVSGPEHPELWRLTVASHHIRIWSGNQTLETRDRKPFYTVDLNSSLTVPL QSCVKPPYMLVVGNIVIKPDSQTITCENCRLLTCIDSTFNWQHRILLVRAREGV WIPVSMDRPWEASPSVHILTEVLKGVLNRSKRFIFTLIAVIMGLIAVTATAAVA GVALHSSVQSVNFVNDWQKNSTRLWNSQSSIDQKLANQINDLRQTVIWMGDRLM SLEHRFQLQCDWNTSDFCITPQIYNESEHHWDMVRRHLQGREDNLTLDISKLKE QIFEASKAHLNLVPGTEAIAGVADGLANLNPVTWVKTIGSTTIINLILILVCLF CLLLVCRCTQQLRRDSDHRERAMMTMAVLSKRKGGNVGKSKRDQIVTVSV	82

PLASMA MEMBRANE RECRUITMENT ELEMENT

[0094] In some aspects, the lipid delivery particle provided herein comprises a plasma membrane recruitment element. The lipid delivery particle disclosed herein can comprise a membrane. In some cases, the membrane encapsulates a payload. In some cases, the lipid delivery particle comprises a plasma membrane recruitment element, for example, inside the cavity of the lipid delivery particle. The plasma membrane recruitment element can localize itself to the membrane of the lipid delivery particles. The plasma membrane recruitment element can be utilized to recruit a component (e.g., a payload) to the membrane of the lipid delivery particles via forming a chimeric protein of the plasma membrane recruitment element and a component to be localized to the membrane or other mechanisms of attachment. In some cases, the membrane encapsulates a protein core. In some cases, at least a portion of the plasma membrane recruitment element forms the basic structure of the lipid delivery particle, such as a portion of the protein core inside the lipid delivery particle. In some cases, at least a portion of the plasma membrane recruitment element binds to the membrane of the lipid delivery particle from the inside.

[0095] The plasma membrane recruitment element can play a role in the assembly of the lipid delivery particle, such as packing various components (e.g., a payload) into the lipid delivery particles. The plasma membrane recruitment element can direct budding of the lipid delivery particles from a producer cell. In

some cases, expressing plasma membrane recruitment element alone or together with an envelope protein disclosed herein in a producer cell can lead to formation of the lipid delivery particle.

[0096] In some cases, the plasma membrane recruitment element has a viral origin. For instance, the plasma membrane recruitment element comprises a retroviral gag protein, e.g., a retroviral polyprotein that comprises one or more of a matrix (MA) polypeptide, an RNA-binding phosphoprotein polypeptide, a capsid (CA) polypeptide, or a nucleocapsid (NC) polypeptide. The plasma membrane recruitment element can comprise HIV gag or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a gag from murine leukemia virus (MLV) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a gag from Moloney murine leukemia virus (MMLV) or a biologically active mutant thereof. In some cases, the plasma membrane recruitment element forms structural protein that forms the protein core of the lipid delivery particles described herein. The plasma membrane recruitment element can comprise Respiratory syncytial virus (RSV) M or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Human Papillomavirus (HPV) L1 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise HPV L2 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Hepatitis B virus (HBV) core protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Hepatitis C virus (HCV) core protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise hepatitis E virus (HeV) M protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Chikungunya virus (CHIKV) C-E3-E2-6k-E1 or a biologically active mutant thereof. The plasma membrane recruitment element can comprise RSV NP or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Human metapneumovirus (HMPV) M or a biologically active mutant thereof. The plasma membrane can comprise a glycoprotein from a flavivirus. The flavivirus can comprise Chikungunya virus, Zika virus, Dengue virus, or West Niles virus. The plasma membrane recruitment element can comprise Zika virus (ZIKV) C or a biologically active mutant thereof. The plasma membrane recruitment element can comprise ZIKV prM/M or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Dengaue virus (DENV) C-prM or a biologically active mutant thereof. The plasma membrane recruitment element can comprise West Nile Virus (WNV) prME protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise WNV CprME protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Filovirus VP40 or Z protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Baculovirus P1 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Rotavirus VP7 or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Rotavirus VP2 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Rotavirus VP6 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Porcine Circovirus Type 2 (PCV2) capsid or a biologically active mutant thereof. The plasma membrane recruitment element can

comprise baculovirus VP2 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise baculovirus VP5 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise baculovirus VP3 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise or baculovirus VP7 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Ebola nucleocapsid or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Parovirus VP1 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Parovirus VP2 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Newcastle disease virus (NDV) M protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Human polyomavirus 2 (JCPyV) VP1 protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise Human parainfluenza virus type 3 (HPIV3) M protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise HPIV3N protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise or Mumps virus (MuV) M proteins or a biologically active mutant thereof. The plasma membrane recruitment element can comprise SARS M protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise SARS E protein or a biologically active mutant thereof. The plasma membrane recruitment element can comprise SARS N protein or a biologically active mutant thereof.

[0097] In some cases, the plasma membrane recruitment element is a mammalian protein or part thereof. For example, the plasma membrane recruitment element can include a pleckstrin homology (PH) domain or a transmembrane domain of a mammalian protein, such as a mouse protein or a human protein. In some cases, the plasma membrane recruitment element has a human origin. Utilizing the plasma membrane recruitment element of a human origin in the lipid delivery particle can give rise to reduced immunogenicity for administration to a human subject. The plasma membrane recruitment element can include a gag from human endogenous retrovirus, such as Human Endogenous Retrovirus K (e.g., HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV- K11p22, and HERV-K12q13) and Human Endogenous Retrovirus-W (HERV-W) or a biologically active mutant thereof. The plasma membrane recruitment element can include a hGAGKcon or a biologically active mutant thereof. The plasma membrane recruitment element can include an endogenous gag of a mammal (e.g., human) from retrotransposons (e.g., Arc from vertebrate lineage of Ty3/gypsy retrotransposon), which are also ancestral to retroviruses. In some cases, the plasma membrane recruitment element comprises a portion from human Arc.

[0098] The plasma membrane recruitment element can include a pleckstrin homology (PH) domain from a mammalian protein or a biologically active mutant thereof. The plasma membrane recruitment element can include a pleckstrin homology (PH) domain from a human protein or a biologically active mutant thereof. The PH domains can play a role in protein–membrane interactions via binding to phosphatidylinositol phosphate (PIP), for example PIP2 or PIP3, or other lipids or proteins within the membrane of the lipid delivery particles. PH domains with different sequences can have varied affinities

and selectivity when binding different PIPs. The plasma membrane recruitment element can include a PH domain of phospholipase Cδ1 (e.g., human phospholipase Cδ1) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of Akt1 (e.g., human Akt1) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a mutant PH domain of human Akt1 with E17K substitution or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of 3-phosphoinositide-dependent protein kinase 1 (e.g., human 3-phosphoinositide-dependent protein kinase 1) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of Dapp1 (e.g., human Dapp1) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of Grp1 (e.g., mouse Grp1) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of human Grp1 or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of OSBP (e.g., human OSBP) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of Btk1 (e.g., human Btk1) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of FAPP1 (e.g., human FAPP1) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of CERT (e.g., human CERT) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of PKD (e.g., human PKD) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of PHLPP1 (e.g., human PHLPP1) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of SWAP70 (e.g., human SWAP70) or a biologically active mutant thereof. The plasma membrane recruitment element can comprise a PH domain of MAPKAP1 (e.g., human MAPKAP1) or a biologically active mutant thereof.

[0099] The plasma membrane recruitment element can also include a membrane protein (e.g., a human membrane protein), a transmembrane domain thereof, or a biologically active mutant thereof. For example, the transmembrane domain of a human protein can be a tetraspanin or a biologically active mutant thereof. In some cases, the plasma membrane recruitment element comprises a transmembrane domain of human CD9 or a biologically active mutant thereof. In some cases, the plasma membrane recruitment element comprises a transmembrane domain of human CD47 or a biologically active mutant thereof. In some cases, the plasma membrane recruitment element comprises a transmembrane domain of human CD63 or a biologically active mutant thereof. In some cases, the plasma membrane recruitment element comprises a transmembrane domain of human CD81, or a biologically active mutant thereof.

[0100] The plasma membrane recruitment element can comprise a retroviral gag or a biologically active mutant thereof. The mutant of a retroviral gag can include only a portion of the retroviral gag. The plasma membrane recruitment element can include a gag of an alpha retrovirus or a biologically active mutant thereof. The plasma membrane recruitment element can a beta retrovirus or biologically active mutant thereof. The plasma membrane recruitment element can include a gamma retrovirus or biologically active mutant thereof. The plasma membrane recruitment element can include a delta retrovirus or biologically

active mutant thereof. The plasma membrane recruitment element can include or biologically active mutant thereof. The plasma membrane recruitment element can include an epsilon retrovirus or biologically active mutant thereof. The plasma membrane recruitment element can include a spumavirus or biologically active mutant thereof. The retroviral gag can include a gag of HIV (e.g., HIV-1), a gag of murine leukemia virus (MLV), a gag of Moloney murine leukemia virus (MMLV), a gag of Simian immunodeficiency virus (SIV), a gag of Rous sarcoma virus (RSV), a gag of human T-cell leukemia virus type-1 (HTLV), or a gag of bovine leukemia virus (BLV), or a biologically active mutant thereof. The plasma membrane recruitment element can include a gag of HIV (e.g., HIV-1) or a biologically active mutant thereof. The plasma membrane recruitment element can include a gag of MLV or a biologically active mutant thereof. The plasma membrane recruitment element can include a gag of RSV or a biologically active mutant thereof. The plasma membrane recruitment element can include a gag of Friend murine leukemia virus (FMLV) or biologically active mutant thereof.

[0101] In some cases, the plasma membrane recruitment element comprises one or more of the sequences set forth in Table 4 with at least one amino acid substitution, deletion, or insertion. For instance, N-terminal methionine can be absent from the plasma membrane recruitment element of the lipid delivery particle provided herein relative to the wild-type viral plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises one or more of the sequences set forth in Table 4 and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0102] In some cases, the plasma membrane recruitment element comprises any one of the sequences set forth in Table 4 with at least one amino acid substitution, deletion, or insertion. For instance, N-terminal methionine can be absent from the plasma membrane recruitment element of the lipid delivery particle provided herein relative to the wild-type viral plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises any one of the sequences set forth in Table 4 and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0103] In some cases, the plasma membrane recruitment element comprises the sequences set forth in Table 4 with a further truncation on the N-terminus. For example, for those amino acid sequences start with a N-terminal methionine, the N-terminal methionine can be absent. In some cases, the plasma membrane recruitment element comprises the sequences set forth in Table 4 with a further truncation on the C-terminus. In some cases, the plasma membrane recruitment element comprises the sequences set forth in Table 4 with one amino acid substitution. In some cases, the plasma membrane recruitment element comprises the sequences set forth in Table 4 with two or more amino acid substitutions. In some cases, the plasma membrane recruitment element comprises the sequences set forth in Table 4 and a heterologous peptide sequence fused to the N-terminal or C-terminal.

[0104] In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in Table 4. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set

forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 50% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 60% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 70% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 75% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 80% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 85% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 90% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 95% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 96% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 97% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 98% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48. In some cases, the plasma membrane recruitment element comprises an amino acid sequence that has at least about 99% sequence identity to a sequence set forth in any one of SEQ ID NOs: 1-48.

Table 4. Exemplary plasma membrane recruitment elements and their sequences

Plasma membrane recruitment element	Amino Acid Sequences	SEQ ID NO:
hGAGKcon*	MGQTKSKIKSKYASYLSFIKILLKRGGVKVSTKNLIKLFQIIEQFCPWFP EQGTLDLKDWKRIGKELKQAGRKGNIIPLTVWNDWAIIKAALEPFQTEED SVSVSDAPGSCIIDCNENTRKKSQKETEGLHCEYVAEPVMAQSTQNVDYN QLQEVIYPETLKLEGKGPELVGPSESKPRGTSPLPAGQVPVTLQPQKQVK ENKTQPPVAYQYWPPAELQYRPPPESQYGYPGMPPAPQGRAPYPQPPTRR LNPTAPPSRQGSELHEIIDKSRKEGDTEAWQFPVTLEPMPPGEGAQEGEP PTVEARYKSFSIKMLKDMKEGVKQYGPNSPYMRTLLDSIAHGHRLIPYDW EILAKSSLSPSQFLQFKTWWIDGVQEQVRRNRAANPPVNIDADQLLGIGQ NWSTISQQALMQNEAIEQVRAICLRAWEKIQDPGSTCPSFNTVRQGSKEP YPDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVP AGSDVISEYVKACDGIGGAMHKAMLMAQAITGVVLGGQVRTFGGKCYNCG	1

	QIGHLKKNCPVLNKQNITIQATTTGREPPDLCPRCKKGKHWASQCRSKFD KNGQPLSGNEQRGQPQAPQQTGAFPIQPFVPQGFQGQQPPLSQVFQGISQ LPQYNNCPPPQAAVQQ	
	GQTKSKIKSKYASYLSFIKILLKRGGVKVSTKNLIKLFQIIEQFCPWFPE QGTLDLKDWKRIGKELKQAGRKGNIIPLTVWNDWAIIKAALEPFQTEEDS VSVSDAPGSCIIDCNENTRKKSQKETEGLHCEYVAEPVMAQSTQNVDYNQ LQEVIYPETLKLEGKGPELVGPSESKPRGTSPLPAGQVPVTLQPQKQVKE NKTQPPVAYQYWPPAELQYRPPPESQYGYPGMPPAPQGRAPYPQPPTRRL NPTAPPSRQGSELHEIIDKSRKEGDTEAWQFPVTLEPMPPGEGAQEGEPP TVEARYKSFSIKMLKDMKEGVKQYGPNSPYMRTLLDSIAHGHRLIPYDWE ILAKSSLSPSQFLQFKTWWIDGVQEQVRRNRAANPPVNIDADQLLGIGQN WSTISQQALMQNEAIEQVRAICLRAWEKIQDPGSTCPSFNTVRQGSKEPY PDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPA GSDVISEYVKACDGIGGAMHKAMLMAQAITGVVLGGQVRTFGGKCYNCGQ IGHLKKNCPVLNKQNITIQATTTGREPPDLCPRCKKGKHWASQCRSKFDK NGQPLSGNEQRGQPQAPQQTGAFPIQPFVPQGFQGQQPPLSQVFQGISQL PQYNNCPPPQAAVQQ	2
Human Arc	MELDHRTSGGLHAYPGPRGGQVAKPNVILQIGKCRAEMLEHVRRTHRHLL AEVSKQVERELKGLHRSVGKLESNLDGYVPTSDSQRWKKSIKACLCRCQE TIANLERWVKREMHVWREVFYRLERWADRLESTGGKYPVGSESARHTVSV GVGGPESYCHEADGYDYTVSPYAITPPPAAGELPGQEPAEAQQYQPWVPG EDGQPSPGVDTQIFEDPREFLSHLEEYLRQVGGSEEYWLSQIQNHMNGPA KKWWEFKQGSVKNWVEFKKEFLQYSEGTLSREAIQRELDLPQKQGEPLDQ FLWRKRDLYQTLYVDADEEEIIQYVVGTLQPKLKRFLRHPLPKTLEQLIQ RGMEVQDDLEQAAEPAGPHLPVEDEAETLTPAPNSESVASDRTQPE	3
	ELDHRTSGGLHAYPGPRGGQVAKPNVILQIGKCRAEMLEHVRRTHRHLLA EVSKQVERELKGLHRSVGKLESNLDGYVPTSDSQRWKKSIKACLCRCQET IANLERWVKREMHVWREVFYRLERWADRLESTGGKYPVGSESARHTVSVG VGGPESYCHEADGYDYTVSPYAITPPPAAGELPGQEPAEAQQYQPWVPGE DGQPSPGVDTQIFEDPREFLSHLEEYLRQVGGSEEYWLSQIQNHMNGPAK KWWEFKQGSVKNWVEFKKEFLQYSEGTLSREAIQRELDLPQKQGEPLDQF LWRKRDLYQTLYVDADEEEIIQYVVGTLQPKLKRFLRHPLPKTLEQLIQR GMEVQDDLEQAAEPAGPHLPVEDEAETLTPAPNSESVASDRTQPE	4
Pleckstrin homology domain of human phospholipase Cδ1 (hPLCδ1)	MDSGRDFLTLHGLQDDEDLQALLKGSQLLKVKSSSWRRERFYKLQEDCKT IWQESRKVMRTPESQLFSIEDIQEVRMGHRTEGLEKFARDVPEDRCFSIV FKDQRNTLDLIAPSPADAQHWVLGLHKIIHHSGSMDQRQKLQHWIHSCLR KADKNKDNKMSFKELQNFLKELNIQ	5
	DSGRDFLTLHGLQDDEDLQALLKGSQLLKVKSSSWRRERFYKLQEDCKTI WQESRKVMRTPESQLFSIEDIQEVRMGHRTEGLEKFARDVPEDRCFSIVF KDQRNTLDLIAPSPADAQHWVLGLHKIIHHSGSMDQRQKLQHWIHSCLRK ADKNKDNKMSFKELQNFLKELNIQ	6
Pleckstrin homology domain of human Akt1 (hAkt1)	MSDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERPQDVDQREA PLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREEWT TAIQTVADGLKKQEEEEMDFRSGSPSDNSGAEEMEVSLAKPKHRVTMNEF EYLKLLGKGTFGKVDPPV	7
	SDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERPQDVDQREAP LNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREEWTT AIQTVADGLKKQEEEEMDFRSGSPSDNSGAEEMEVSLAKPKHRVTMNEFE YLKLLGKGTFGKVDPPV	8
	MSDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERPQDVDQREA PLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREEWT TAIQTVADGLKKQEEEEMDFRSGSPSDNSGAEEMEVSLAKPKHRVTMNEF EYLKLLGKGTFGKVDPPVV	9
	SDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERPQDVDQREAP LNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREEWTT AIQTVADGLKKQEEEEMDFRSGSPSDNSGAEEMEVSLAKPKHRVTMNEFE YLKLLGKGTFGKVDPPVV	10

Mutant Pleckstrin homology domain of human Akt1 with E17K substitution (hAkt1E17K)	MSDVAIVKEGWLHKRGKYIKTWRPRYFLLKNDGTFIGYKERPQDVDQREA PLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREEWT TAIQTVADGLKKQEEEEMDFRSGSPSDNSGAEEMEVSLAKPKHRVTMNEF EYLKLLGKGTFGKVDPPV	11
	SDVAIVKEGWLHKRGKYIKTWRPRYFLLKNDGTFIGYKERPQDVDQREAP LNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREEWTT AIQTVADGLKKQEEEEMDFRSGSPSDNSGAEEMEVSLAKPKHRVTMNEFE YLKLLGKGTFGKVDPPV	12
Pleckstrin homology domain of human 3-phosphoinositide-dependent protein kinase 1 (hPDPK1)	MKMGPVDKRKGLFARRRQLLLTEGPHLYYVDPVNKVLKGEIPWSQELRPE AKNFKTFFVHTPNRTYYLMDPSGNAHKWCRKIQEVWRQRYQSH	13
	KMGPVDKRKGLFARRRQLLLTEGPHLYYVDPVNKVLKGEIPWSQELRPEA KNFKTFFVHTPNRTYYLMDPSGNAHKWCRKIQEVWRQRYQSH	14
Human CD9	MSPVKGGTKCIKYLLFGFNFIFWLAGIAVLAIGLWLRFDSQTKSIFEQET NNNNSSFYTGVYILIGAGALMMLVGFLGCCGAVQESQCMLGLFFGFLLVI FAIEIAAAIWGYSHKDEVIKEVQEFYKDTYNKLKTKDEPQRETLKAIHYA LNCCGLAGGVEQFISDICPKKDVLETFTVKSCPDAIKEVFDNKFHIIGAV GIGIAVVMIFGMIFSMILCCAIRRNREMV	15
	SPVKGGTKCIKYLLFGFNFIFWLAGIAVLAIGLWLRFDSQTKSIFEQETN NNNSSFYTGVYILIGAGALMMLVGFLGCCGAVQESQCMLGLFFGFLLVIF AIEIAAAIWGYSHKDEVIKEVQEFYKDTYNKLKTKDEPQRETLKAIHYAL NCCGLAGGVEQFISDICPKKDVLETFTVKSCPDAIKEVFDNKFHIIGAVG IGIAVVMIFGMIFSMILCCAIRRNREMV	16
Human CD47	MWPLVAALLLGSACCGSAQLLFNKTKSVEFTFCNDTVVIPCFVTNMEAQN TTEVYVKWKFKGRDIYTFDGALNKSTVPTDFSSAKIEVSQLLKGDASLKM DKSDAVSHTGNYTCEVTELTREGETIIELKYRVVSWFSPNENILIVIFPI FAILLFWGQFGIKTLKYRSGGMDEKTIALLVAGLVITVIVIVGAILFVPG EYSLKNATGLGLIVTSTGILILLHYYVFSTAIGLTSFVIAILVIQVIAYI LAVVGLSLCIAACIPMHGPLLISGLSILALAQLLGLVYMKFVE	17
	WPLVAALLLGSACCGSAQLLFNKTKSVEFTFCNDTVVIPCFVTNMEAQNT TEVYVKWKFKGRDIYTFDGALNKSTVPTDFSSAKIEVSQLLKGDASLKMD KSDAVSHTGNYTCEVTELTREGETIIELKYRVVSWFSPNENILIVIFPIF AILLFWGQFGIKTLKYRSGGMDEKTIALLVAGLVITVIVIVGAILFVPGE YSLKNATGLGLIVTSTGILILLHYYVFSTAIGLTSFVIAILVIQVIAYIL AVVGLSLCIAACIPMHGPLLISGLSILALAQLLGLVYMKFVE	18
Human CD63	MAVEGGMKCVKFLLYVLLLAFCACAVGLIAVGVGAQLVLSQTIIQGATPG SLLPVVIIAVGVFLFLVAFVGCCGACKENYCLMITFAIFLSLIMLVEVAA AIAGYVFRDKVMSEFNNNFRQQMENYPKNNHTASILDRMQADFKCCGAAN YTDWEKIPSMSKNRVPDSCCINVTVGCGINFNEKAIHKEGCVEKIGGWLR KNVLVVAAAALGIAFVEVLGIVFACCLVKSIRSGYEVM	19
	AVEGGMKCVKFLLYVLLLAFCACAVGLIAVGVGAQLVLSQTIIQGATPGS LLPVVIIAVGVFLFLVAFVGCCGACKENYCLMITFAIFLSLIMLVEVAAA IAGYVFRDKVMSEFNNNFRQQMENYPKNNHTASILDRMQADFKCCGAANY TDWEKIPSMSKNRVPDSCCINVTVGCGINFNEKAIHKEGCVEKIGGWLRK NVLVVAAAALGIAFVEVLGIVFACCLVKSIRSGYEVM	20
Human CD81	MGVEGCTKCIKYLLFVFNFVFWLAGGVILGVALWLRHDPQTTNLLYLELG DKPAPNTFYVGIYILIAVGAVMMFVGFLGCYGAIQESQCLLGTFFTCLVI LFACEVAAGIWGFVNKDQIAKDVKQFYDQALQQAVVDDDANNAKAVVKTF HETLDCCGSSTLTALTTSVLKNNLCPSGSNIISNLFKEDCHQKIDDLFSG KLYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	21
	GVEGCTKCIKYLLFVFNFVFWLAGGVILGVALWLRHDPQTTNLLYLELGD KPAPNTFYVGIYILIAVGAVMMFVGFLGCYGAIQESQCLLGTFFTCLVIL FACEVAAGIWGFVNKDQIAKDVKQFYDQALQQAVVDDDANNAKAVVKTFH	22

	ETLDCCGSSTLTALTTSVLKNNLCPSGSNIISNLFKEDCHQKIDDLFSGK LYLIGIAAIVVAVIMIFEMILSMVLCCGIRNSSVY	
Pleckstrin homology domain of Human Dapp1	MQTGRTEDDLVPTAPSLGTKEGYLTKQGGLVKTWKTRWFTLHRNELKYFK DQMSPEPIRILDLTECSAVQFDYSQERVNCFCLVFPFRTFYLCAKTGVEA DEWIKILRWKLSQIRKQLNQGEGTIR	23
	QTGRTEDDLVPTAPSLGTKEGYLTKQGGLVKTWKTRWFTLHRNELKYFKD QMSPEPIRILDLTECSAVQFDYSQERVNCFCLVFPFRTFYLCAKTGVEAD EWIKILRWKLSQIRKQLNQGEGTIR	24
Pleckstrin homology domain of Mouse Grp1	MPFKIPEDDGNDLTHTFFNPDREGWLLKLGGRVKTWKRRWFILTDNCLYY FEYTTDKEPRGIIPLENLSIREVEDPRKPNCFELYNPSHKGQVIKACKTE ADGRVVEGNHVVYRISAPSPEEKEEWMKSIKASISRDPFYDMLATRKRRI ANKK	25
	PFKIPEDDGNDLTHTFFNPDREGWLLKLGGRVKTWKRRWFILTDNCLYYF EYTTDKEPRGIIPLENLSIREVEDPRKPNCFELYNPSHKGQVIKACKTEA DGRVVEGNHVVYRISAPSPEEKEEWMKSIKASISRDPFYDMLATRKRRIA NKK	26
Pleckstrin homology domain of Human Grp1	MNPDREGWLLKLGGRVKTWKRRWFILTDNCLYYFEYTTDKEPRGIIPLEN LSIREVEDPRKPNCFELYNPSHKGQVIKACKTEADGRVVEGNHVVYRISA PSPEEKEEWMKSIKASISPFKIPEDDGNDLTHTFFNPDREGWLLKLGGRV KTWKRRWFILTDNCLYYFEYTTDKEPRGIIPLENLSIREVEDPRKPNCFE LYNPSHKGQVIKACKTEADGRVVEGNHVVYRISAPSPEEKEEWMKSIKAS ISRDPFYDMLATRKRRIANKK	27
	NPDREGWLLKLGGRVKTWKRRWFILTDNCLYYFEYTTDKEPRGIIPLENL SIREVEDPRKPNCFELYNPSHKGQVIKACKTEADGRVVEGNHVVYRISAP SPEEKEEWMKSIKASISPFKIPEDDGNDLTHTFFNPDREGWLLKLGGRVK TWKRRWFILTDNCLYYFEYTTDKEPRGIIPLENLSIREVEDPRKPNCFEL YNPSHKGQVIKACKTEADGRVVEGNHVVYRISAPSPEEKEEWMKSIKASI SRDPFYDMLATRKRRIANKK	28
Pleckstrin homology domain of Human OSBP	MGSGSAREGWLFKWTNYIKGYQRRWFVLSNGLLSYYRSKAEMRHTCRGTI NLATANITVEDSCNFIISNGGAQTYHLKASSEVERQRWVTALELAKAKAV K	29
	GSGSAREGWLFKWTNYIKGYQRRWFVLSNGLLSYYRSKAEMRHTCRGTIN LATANITVEDSCNFIISNGGAQTYHLKASSEVERQRWVTALELAKAKAVK	30
	SGSAREGWLFKWTNYIKGYQRRWFVLSNGLLSYYRSKAEMRHTCRGTINL ATANITVEDSCNFIISNGGAQTYHLKASSEVERQRWVTALELAKAKAVK	31
Pleckstrin homology domain of Human Btk1	MAAVILESIFLKRSQQKKKTSPLNFKKRLFLLTVHKLSYYEYDFERGRRG SKKGSIDVEKITCVETVVPEKNPPPERQIPRRGEESSEMEQISIIERFPY PFQVVYDEGPLYVFSPTEELRKRWIHQLKNVIRYNSDLVQKYHPCFWIDG QYLCCSQTAKNAMGCQILENRNGSLKP	32
	AAVILESIFLKRSQQKKKTSPLNFKKRLFLLTVHKLSYYEYDFERGRRGS KKGSIDVEKITCVETVVPEKNPPPERQIPRRGEESSEMEQISIIERFPYP FQVVYDEGPLYVFSPTEELRKRWIHQLKNVIRYNSDLVQKYHPCFWIDGQ YLCCSQTAKNAMGCQILENRNGSLKP	33
Pleckstrin homology domain of Human FAPP1	MEGVLYKWTNYLTGWQPRWFVLDNGILSYYDSQDDVCKGSKGSIKMAVCE IKVHSADNTRMELIIPGEQHFYMKAVNAAERQRWLVALGSSKACLTDT	34
	EGVLYKWTNYLTGWQPRWFVLDNGILSYYDSQDDVCKGSKGSIKMAVCEI KVHSADNTRMELIIPGEQHFYMKAVNAAERQRWLVALGSSKACLTDT	35
Pleckstrin homology domain of Human CERT	MSDNQSWNSSGSEEDPETESGPPVERCGVLSKWTNYIHGWQDRWVVLKNN ALSYYKSEDETEYGCRGSICLSKAVITPHDFDECRFDISVNDSVWYLRAQ DPDHRQQWIDAIEQHKTESGYG	36
	SDNQSWNSSGSEEDPETESGPPVERCGVLSKWTNYIHGWQDRWVVLKNNA LSYYKSEDETEYGCRGSICLSKAVITPHDFDECRFDISVNDSVWYLRAQD PDHRQQWIDAIEQHKTESGYG	37
	MPVERCGVLSKWTNYIHGWQDRWVVLKNNALSYYKSEDETEYGCRGSICL SKAVITPHDFDECRFDISVNDSVWYLRAQDPDHRQQWIDAIEQHKT	38

	PVERCGVLSKWTNYIHGWQDRWVVLKNNALSYYKSEDETEYGCRGSICLS KAVITPHDFDECRFDISVNDSVWYLRAQDPDHRQQWIDAIEQHKT	39
Pleckstrin homology domain of Human PKD	MGTVMKEGWMVHYTSKDTLRKRHYWRLDSKCITLFQNDTGSRYYKEIPLS EILSLEPVKTSALIPNGANPHCFEITTANVVYYVGENVVNPSSPSPNNSV LTSGVGADVARMWEIAIQHALM	40
	GTVMKEGWMVHYTSKDTLRKRHYWRLDSKCITLFQNDTGSRYYKEIPLSE ILSLEPVKTSALIPNGANPHCFEITTANVVYYVGENVVNPSSPSPNNSVL TSGVGADVARMWEIAIQHALM	41
	TVMKEGWMVHYTSKDTLRKRHYWRLDSKCITLFQNDTGSRYYKEIPLSEI LSLEPVKTSALIPNGANPHCFEITTANVVYYVGENVVNPSSPSPNNSVLT SGVGADVARMWEIAIQHALM	42
Pleckstrin homology domain of Human PHLPP1	MRIQLSGMYNVRKGKMQLPVNRWTRRQVILCGTCLIVSSVKDSLTGKMHV LPLIGGKVEEVKKHQHCLAFSSSGPQSQTYYICFDTFTEYLRWLRQVSKV AS	43
	RIQLSGMYNVRKGKMQLPVNRWTRRQVILCGTCLIVSSVKDSLTGKMHVL PLIGGKVEEVKKHQHCLAFSSSGPQSQTYYICFDTFTEYLRWLRQVSKVA S	44
Pleckstrin homology domain of Human SWAP70	MDVLKQGYMMKKGHRRKNWTERWFVLKPNIISYYVSEDLKDKKGDILLDE NCCVESLPDKDGKKCLFLVKCFDKTFEISASDKKKKQEWIQAIHSTIH	45
	DVLKQGYMMKKGHRRKNWTERWFVLKPNIISYYVSEDLKDKKGDILLDEN CCVESLPDKDGKKCLFLVKCFDKTFEISASDKKKKQEWIQAIHSTIH	46
Pleckstrin homology domain of Human MAPKAP1	MDMLSSHHYKSFKVSMIHRLRFTTDVQLGISGDKVEIDPVTNQKASTKFW IKQKPISIDSDLLCACDLAEEKSPSHAIFKLTYLSNHDYKHLYFESDAAT VNEIVLKVNYILES	47
	DMLSSHHYKSFKVSMIHRLRFTTDVQLGISGDKVEIDPVTNQKASTKFWI KQKPISIDSDLLCACDLAEEKSPSHAIFKLTYLSNHDYKHLYFESDAATV NEIVLKVNYILES	48

[0105] *hGAGKcon is a consensus sequence from ten proviral GAG sequences. The GAG sequences used to derive this consensus GAG sequence are from the following HERVs: HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV- K11p22, and HERV-K12q13.

[0106] In some cases, the lipid delivery particle disclosed herein comprises a protein core that is composed of at least a structural protein of a viral origin, for instance, a retroviral gag protein. In some of these cases, the lipid delivery particle comprises a retroviral gag-pro-pol polyprotein, *e.g.*, a gag-pro-pol poly protein from HIV, MMLV, or FMLV, which can help assemble a protein core of the lipid delivery particle. In some of these cases, some of the gag-pro-pol polyprotein is cleaved, *e.g.*, by pro (protease) present freely or in the gag-pro-pol polyprotein. Without wishing to be bound by any particular theory, the cleavage by pro can be inefficient, and the resultant cleavage products can include gag polyprotein, gag-pro polyprotein, free pro, and free pol (polymerase). In some cases, a retroviral gag polyprotein can be further cleaved into MA, CA, NC, and other small fragments, if any. In some other cases, the lipid delivery particle comprises a retroviral gag-pro polyprotein without the pol component, and the gag-pro polyprotein can help form a protein core of the lipid delivery particle. The gag-pro can also be cleaved by pro, in some cases, inefficiently, into separate gag and pro proteins. In some cases, there can be different plasma membrane recruitment elements in a lipid delivery particle. For instance, a gag-pro or gag-pro-pol polyprotein from one species of virus (*e.g.*, a retrovirus, *e.g.*, a HIV) can help assemble form a protein core of the lipid delivery particle, while a chimeric protein in the lipid delivery particle, discussed *infra*, can comprise a payload fused with a gag protein from a different species of virus (*e.g.*, an MMLV), or

from a HERV, or a PH domain or transmembrane domain of a huma protein (*e.g.*, a PH domain of human Akt1 with E17K substitution

Mutant gag polyprotein

[0107] In some aspects, disclosed herein is a recombinant protein comprising a plasma membrane recruitment element comprising a mutant gag polyprotein. Also disclosed herein is a lipid delivery particle comprising a plasma membrane recruitment element comprising a mutant gag polyprotein. The mutant gag polyprotein is a mutant of a corresponding wild-type gag polyprotein. Relative to a wild-type gag polyprotein, a mutant gag polyprotein comprises an amino acid insertion, an amino acid deleteion, an amino acid substituion or any combinations thereof. In some cases, a mutant gag polyprotein comprises at least about 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, or 98% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 40% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 45% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 50% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 55% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 60% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 65% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 70% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 75% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 80% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 85% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 90% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 91% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 92% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 93% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 94% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 95% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 96% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 97% identity to a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises at least about 98% identity to a corresponding wild-type gag polyprotein.

[0108] A wild-type gag polyprotein can comprise various domains, such as a matrix domain, an RNA-binding phosphoprotein, a capsid (including a major homology region), nucleocapsid, a particle budding

motif (also termed as "budding domain" or "late domain"), a spacer peptide, a gag-endogenous protease cleavage sequence. A gag-endogenous protease cleavage sequence is the cleavage sequence homologous to a mutant gag polyprotein described herein, *e.g.*, the gag-endogenous protease cleavage sequence is naturally present in the wild-type version of the mutant gag polyprotein. For example, a gag-endogenous protease cleavage sequence for MMLV gag includes MSKLLATW.

[0109] In some cases, the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a retrovirus. In some cases, the retrovirus is an endogenous retrovirus. In some cases, the mutant gag polyprotein is a mutant of a retroviral gag polyprotein. The mutant of a retroviral gag protein can include only a portion of the wild-type retroviral gag protein. In some cases, the wild type retroviral gag protein is endogenous. In some cases, the retroviral gag protein can comprise a retroviral nucleocapsid domain and/or a retroviral matrix domain. In some cases, the retroviral gag protein can be a gag homology protein. In some cases, the gag homology protein can be Arc protein (e.g, Arc1), Asprv1, a Sushi-Class protein, a SCAN protein, or a PNMA protein. In some cases, the gag homology protein can be ZCC18, ZCH12, PNM8B, PNM6A, PNMA6E_i2, PMA6F, PMAGE, PNMA1, PNMA2, PNM8A, PNMA3, PNMA4, PNMA5, PNMA6, PNMA7, PNMA1, MOAP1, or CCD8. In some cases, the Gag-homology protein is an Arc protein, e.g., hARC or dARC1. In some cases, the Gag-homology protein can comprise ASPRV1. In some cases, the Gag-homology protein is PEG10, RTL3, RTL10, or RTL1. In some cases, the Gag Homology protein is a SCAN protein, for example, PGBD1. In some cases, the PEG10 Gag homology protein is PEG10_i6 or PEG10_i2. In some cases, the gag homology protein can be Arc protein (e.g, Arc1), Asprv1, PNMA1, PNMA3, PNMA4, PNMA5, PNMA6, PNMA7, PEG10, RTL1, MOAP1, or ZCCHC12.

[0110] The plasma membrane recruitment element can include a mutant of a wild-type gag of an alpha retrovirus. The plasma membrane recruitment element can include a mutant of a wild-type gag of a beta retrovirus. The plasma membrane recruitment element can include a mutant of a wild-type gag of a gamma retrovirus. The plasma membrane recruitment element can include a mutant of a wild-type gag of a delta retrovirus. The plasma membrane recruitment element can include a mutant of a wild-type gag of an epsilon retrovirus. The plasma membrane recruitment element can include a mutant of a wild-type gag of a spumavirus. The retroviral gag can include a mutant of a wild-type gag of HIV (*e.g.*, HIV-1), a mutant of a wild-type gag of murine leukemia virus (MLV), a mutant of a wild-type gag of Moloney murine leukemia virus (MMLV), a mutant of a wild-type gag of Simian immunodeficiency virus (SIV), a mutant of a wild-type gag of Rous sarcoma virus (RSV), a mutant of a wild-type gag of human T-cell leukemia virus type-1 (HTLV), or a mutant of a wild-type gag of bovine leukemia virus (BLV). The plasma membrane recruitment element can include a mutant of a wild-type gag of HIV (*e.g.*, HIV-1). The plasma membrane recruitment element can include a mutant of a wild-type gag of MLV. The plasma membrane recruitment element can include a mutant of a wild-type gag of MMLV. The plasma membrane recruitment element can include a mutant of a wild-type gag of RSV. The plasma membrane recruitment element can include a mutant of a wild-type gag of Friend murine leukemia virus (FMLV). The plasma membrane recruitment element can include a mutant of a wild-type gag of Rous

Sarcoma Virus. The plasma membrane recruitment element can include a mutant of a wild-type gag of Avian Leukosis Virus. The plasma membrane recruitment element can include a mutant of a wild-type gag of Avian Myeloblastosis Virus. The plasma membrane recruitment element can include a mutant of a wild-type gag of Avian Myeloblastosis Virus. The plasma membrane recruitment element can include a mutant of a wild-type gag of Human T cell Leukemia Virus-1. The plasma membrane recruitment element can include a mutant of a wild-type gag of Mouse Mammary Tumor Virus. The plasma membrane recruitment element can include a mutant of a wild-type gag of Jaagsiekte sheep retrovirus. The plasma membrane recruitment element can include a mutant of a wild-type gag of Mason-Pfizer Monkey Virus. In some cases, a wild-type gag polyprotein comprises an amino acid sequence selected from any one of sequence set forth in Table 15. In some cases, a wild-type gag polyprotein comprises an amino acid sequence selected from any one of SEQ ID Nos 285-298.

[0111] In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 50% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 60% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 70% sequence identity to any one of sequence set forth in **Table 15.** In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 75% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 75% sequence identity to any one of sequence set forth in **Table 15.** In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 80% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 85% sequence identity to any one of sequence set forth in **Table 15.** In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 90% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 95% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 96% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 97% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 98% sequence identity to any one of sequence set forth in **Table 15**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 99% sequence identity to any one of sequence set forth in **Table 15**.

[0112] In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag

polyprotein comprises an amino acid sequence that has at least about 50% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 60% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 70% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298.** In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 75% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 75% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298.** In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 80% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 85% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298.** In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 90% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 95% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 96% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 97% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 98% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises an amino acid sequence that has at least about 99% sequence identity to any one of sequence set forth in **SEQ ID NO: 285-298**. In some cases, the mutant gag polyprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, or 99% of the entire amino acid sequence of the wild type gag polyprotein that comprises an amino acid sequence selected from **Table 15**. In some cases, the mutant gag polyprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, or 99% of the entire amino acid sequence of the wild type gag polyprotein that comprises an amino acid sequence set forth in any one of SEQ ID NO: **285-298.** In some cases, the mutant gag polyprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, or 99% of the entire amino acid sequence of the wild type gag polyprotein that comprises an amino acid sequence selected from **Table 15**. In some cases, the mutant gag polyprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9 ,10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more mutations (e.g., amino acid deletions, insertion and/or substitutions) as compared to a wild-type polyprotein. In some cases, the mutant gag-polyprotein comprises a truncation (e.g., at the N-terminus and/or at the C-terminus) of at least about 1, 2, 2, 3, 4, 5, 6, 7, 8, 9 ,10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more contiguous amino acid residues as compared to the wild type polyprotein.

[0113] In some cases, the mutant gag polyprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9 ,10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more mutations (e.g., amino acid deletions, insertion and/or substitutions) as compared to a wild-type polyprotein that comprises an amino acid sequence selected from **Table 15**. In some cases, the mutant gag-polyprotein comprises a truncation (e.g., at the N-terminus and/or at the C-terminus) of at least about 1, 2, 2, 3, 4, 5, 6, 7, 8, 9 ,10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more contiguous amino acid residues as compared to the wild type polyprotein that comprises an amino acid sequence set forth in any one of SEQ ID NO: **285-298**.

[0114] The plasma membrane recruitment element can comprise a mutant of HIV gag. The plasma membrane recruitment element can comprise a mutant of a gag from murine leukemia virus (MLV). The plasma membrane recruitment element can comprise a mutant of a gag from Moloney murine leukemia virus (MMLV).

[0115] The plasma membrane recruitment element can comprise a mutant of Respiratory syncytial virus (RSV) M. The plasma membrane recruitment element can comprise a mutant of Human Papillomavirus (HPV) L1 protein. The plasma membrane recruitment element can comprise a mutant of HPV L2 protein. The plasma membrane recruitment element can comprise a mutant of Hepatitis B virus (HBV) core protein. The plasma membrane recruitment element can comprise a mutant of Hepatitis C virus (HCV) core protein. The plasma membrane recruitment element can comprise a mutant of hepatitis E virus (HeV) M protein. The plasma membrane recruitment element can comprise a mutant of Chikungunya virus (CHIKV) C-E3-E2-6k-E1. The plasma membrane recruitment element can comprise a mutant of RSV NP. The plasma membrane recruitment element can comprise a mutant of Human metapneumovirus (HMPV) M. The plasma membrane recruitment element can comprise a mutant of Influenza M1. The plasma membrane recruitment element can comprise a mutant of Zika virus (ZIKV) C. The plasma membrane recruitment element can comprise a mutant of ZIKV prM/M. The plasma membrane recruitment element can comprise a mutant of Dengaue virus (DENV) C-prM. The plasma membrane recruitment element can comprise a mutant of West Nile Virus (WNV) prME protein. The plasma membrane recruitment element can comprise a mutant of WNV CprME protein. The plasma membrane recruitment element can comprise a mutant of Filovirus VP40 or Z protein. The plasma membrane recruitment element can comprise a mutant of Baculovirus P1 protein. The plasma membrane recruitment element can comprise a mutant of Rotavirus VP7. The plasma membrane recruitment element can comprise a mutant of Rotavirus VP2 protein. The plasma membrane recruitment element can comprise a mutant of Rotavirus VP6 protein. The plasma membrane recruitment element can comprise a mutant of Porcine Circovirus Type 2 (PCV2) capsid. The plasma membrane recruitment element can comprise a mutant of baculovirus VP2 protein. The plasma membrane recruitment element can comprise a mutant of baculovirus VP5 protein. The plasma membrane recruitment element can comprise a mutant of baculovirus VP3 protein. The plasma membrane recruitment element can comprise a mutant of or baculovirus VP7 protein. The plasma membrane recruitment element can comprise a mutant of Ebola nucleocapsid. The plasma membrane recruitment element can comprise a mutant of Parovirus VP1 protein. The plasma membrane recruitment element can comprise a mutant of Parovirus VP2 protein. The

plasma membrane recruitment element can comprise a mutant of Newcastle disease virus (NDV) M protein. The plasma membrane recruitment element can comprise a mutant of Nipah virus (NIV) M protein. The plasma membrane recruitment element can comprise a mutant of Human polyomavirus 2 (JCPyV) VP1 protein. The plasma membrane recruitment element can comprise a mutant of Human parainfluenza virus type 3 (HPIV3) M protein. The plasma membrane recruitment element can comprise a mutant of HPIV3N protein. The plasma membrane recruitment element can comprise a mutant of or Mumps virus (MuV) M proteins. The plasma membrane recruitment element can comprise a mutant of SARS M protein. The plasma membrane recruitment element can comprise a mutant of SARS E protein. The plasma membrane recruitment element can comprise a mutant of SARS N protein.

[0116] In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that lacks at least a fragment of a matrix protein as compared to a wild-type gag polyprotein. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that lacks at least a fragment of a RNA-binding phosphoprotein as compared to a wild-type gag polyprotein, for example, MMLV gag. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that lacks at least a fragment of at least a fragment of a capsid protein as compared to a wild-type gag polyprotein. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that lacks at least a fragment of a gag-endogenous protease cleavage sequence as compared to a wild-type gag polyprotein. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that lacks a gag-endogenous protease cleavage sequence as compared to a wild-type gag polyprotein. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that lacks at least a fragment of a gag-endogenous protease cleavage sequence as compared to a wild-type gag polyprotein. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that comprises a mutant gag-endogenous protease cleavage sequence as compared to a wild-type polyprotein. In some cases, the mutant gag-endogenous protease clevage sequence comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9 ,10, 20, 30, 40, 50, 60, 70 , 80, 90 , 100 or more mutations (e.g. amino acid deletions, insertion and/or substitutions) as compared to a wild-type polyprotein. In some cases, the mutant gag-endogenous protease clevage sequence comprises a truncation (e.g., at the N-terminus and/or at the C-terminus) of at least about 1, 2, 2, 3, 4, 5, 6, 7, 8, 9 ,10, 20, 30, 40, 50, 60, 70 , 80, 90 , 100 or more contiguous amino acid residues as compared to a wild type polyprotein. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that comprises a mutant gag-endogenous protease cleavage sequence as compared to a wild-type polyprotein, wherein the mutant gag-endogenous protease cleavage sequence cannot be recognized or cleaved by the gag-endogenous protease. In some cases, the mutant gag-endogenous protease cleavage sequence is recognized or cleaved by a different protease than the gag-endogenous protease that recognizes the corresponding wild type gag-endogenous protease cleavage sequence. In some cases, the mutant gag-endogenous protease cleavage sequence exhibits improved clevage (higher cleavage efficiency) relative to that by corresponding wild type gag-endogenous protease cleavage sequence. In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that comprises (e.g., at least

one, 2, 3, 4, 5 or more) exogenous protease cleavage sequences as compared to a wild-type polyprotein. In some cases, an exogenous protease cleavage sequence is a protease cleavage sequence that does not naturally occur in the corresponding wild type polyprotein sequence. In some cases, an exogenous protease cleavage sequence links one or more domains of the mutant gag polyprotein.

[0117] In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that lacks at least a fragment of a nucleocapsid protein as compared to a wild-type gag polyprotein.

[0118] In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein, for example, a mutant of wild-type HIV gag, a mutant of wild-type MMLV gag, a mutant of wild-type RSV gag, and a mutant of wild-type HERV gag.

[0119] In some cases, the plasma membrane recruitment element comprises a full-length capsid protein (i.e., the capsid protein of the wild-type gag). In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein comprising a fragment of a capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 20% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 25% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 30% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 35% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 40% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 45% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 50% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 55% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 60% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 65% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 70% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 75% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 80% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 85% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a

mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 90% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 91% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 92% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 93% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 94% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 95% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 96% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 97% identity to the capsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a capsid protein comprising at least about 98% identity to the capsid protein of a corresponding wild-type gag polyprotein.

[0120] In some cases, the plasma membrane recruitment element comprises a full-length matrix protein (i.e., the matrix protein of the wild-type gag). In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein comprising a fragment of a matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 20% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 25% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 30% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 35% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 40% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 45% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 50% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 55% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 60% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 65% identity to the matrix

protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 70% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 75% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 80% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 85% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 90% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 91% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 92% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 93% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 94% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 95% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 96% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 97% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a matrix protein comprising at least about 98% identity to the matrix protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein lacks the matrix protein of a corresponding wild-type gag polyprotein.

[0121] In some cases, the plasma membrane recruitment element comprises a full-length nucleocapsid protein (i.e., the nucleocapsid protein of the wild-type gag). In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein comprising a fragment of a nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 20% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 25% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 30% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 35% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment

of a nucleocapsid protein comprising at least about 40% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 45% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 50% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 55% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 60% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 65% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 70% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 75% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 80% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 85% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 90% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 91% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 92% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 93% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 94% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 95% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 96% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 97% identity to the nucleocapsid protein of a corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein comprises a fragment of a nucleocapsid protein comprising at least about 98% identity to the nucleocapsid protein of a

corresponding wild-type gag polyprotein. In some cases, a mutant gag polyprotein lacks the nucleocapsid protein of a corresponding wild-type gag polyprotein.

[0122] In some cases, the plasma membrane recruitment element comprises heterologous sequence. In some cases, the heterologous sequence is fused to a fragment of the matrix protein, such as the N-terminal of the fragment of the matrix protein. In some cases, the heterologous sequence is fused to a fragment of the capsid protein, such as the N-terminal of the fragment of the capsid protein. In some cases, the heterologous sequence is fused to a matrix protein or a fragment thereof. In some cases, the heterologous sequence is fused to a nucleocapsid protein or a fragment thereof. In some cases, the heterologous sequence is fused to a particle budding motif or a fragment thereof (*e.g.,* a late domain of RSV). In some cases, the heterologous sequence is a pleckstrin homology (PH) domain or a mutant thereof, such as those listed in **Table 4**. In some cases, the PH domain is a human PH domain. In some cases, the fragment of the matrix protein lacks a N-terminal myristoylation motif, a N-terminal glycine, a highly basic region (HBR), a N-terminal fragment, or any combinations thereof. In some cases, the plasma membrane recruitment element comprises at least a portion of a nucleocapsid protein. In some cases, the plasma membrane recruitment element comprises two or more particle budding motifs described herein. In some cases, at least one of the two or more particle budding motifs is endogenous. In some cases, at least one of the two or more particle budding motifs is heterologous, such as RSV P2B or a mutant thereof. In some cases, at least one of the two or more particle budding motifs comprises a PTAP motif, a PPPY motif, a PPXY motif, a YXXL motif, a YPXnL motif, or any combinations thereof, and wherein n is an integer from 1 to 5. In some cases, at least one of the two or more particle budding motifs comprises a sequence listed in **Table 5**. In some cases, the plasma membrane recruitment element comprises comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV and comprises at least a portion of a P6 domain. In some cases, the plasma membrane recruitment element comprises at least a N-terminal fragment of the P6 domain. In some cases, the plasma membrane recruitment element comprises at least a C-terminal fragment of the P6 domain. In some cases, the plasma membrane recruitment element comprises two spacer peptides (*e.g.,* P2 domain, P1 domain, or both). In some cases, the plasma membrane recruitment element is fused to the post-translational modification motif as described herein. In some cases, the post-translational modification motif is fused to the N-terminus of the plasma membrane recruitment element. In some cases, the post-translational modification motif is fused to the C-terminus of the plasma membrane recruitment element. In some cases, the post-translational modification motif is a myristoylation motif. In some cases, the post-translational modification motif is an acetylation motif. In some cases, the post-translational modification motif is an isoprenylation motif. In some cases, the post-translational modification motif is a palmitoylation motif. In some cases, the post-translational modification motif is a farnesylation motif. In some cases, the plasma membrane recruitment element is fused to the membrane penetrating peptide. In some cases, the membrane penetrating peptide is linked to the plasma membrane recruitment element. In some cases, the membrane penetrating peptide connects the plasma membrane recruitment element and a payload. In some cases, the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in **Table 6**.

[0123] In some cases, the plamamembrane recruitment element comprises a mutant gag polyprotein of a wild-type Rous Sarcoma Virus (RSV) gag polyprotein. In some cases, the plamamembrane recruitment element lacks a capsid protein of the RSV gag. In some cases, the plamamembrane recruitment element lacks a nucleocapsid protein of the RSV gag. In some cases, the plamamembrane recruitment element comprises at least a portion of the matrix protein of the RSV gag. In some cases, the plasma membrane recruitment element comprises a matrix protein of the RSV gag and a late domain of the RSV gag. In some cases, the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid protein of the RSV. In some cases, the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid protein of the RSV arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of the nucleocapsid protein of the RSV gag. In some cases, the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of the nucleocapsid protein of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element further comprises a N-terminal myristoylation motif. In some cases, the plasma membrane recruitment element comprises a matrix protein of the RSV gag and a late domain of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element consists of a matrix protein of the RSV gag and a late domain of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of a full-length nucleocapsid of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element consists of a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of a full-length nucleocapsid of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of a full-length nucleocapsid of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element consists of a myr group of the RSV gag, a late domain of the RSV gag, and a fragment of a full-length nucleocapsid of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a myr group of the RSV gag, a late domain of the RSV gag, and a fragment of a full-length nucleocapsid of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element consists of a myr group of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element

comprises a myr group of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid of the RSV gag arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element.In some cases, a plasma membrane recruitment element is linked to a payload (*e.g.,* a base editor), for example, via a cleavable linker, which forms a chimeric protein descried herein. In some cases, a plasma membrane recruitment element is linked to a protease, for example, with or without a cleavable linker. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) includes any one of those described in **Table 10A or Table 10B** with at least one amino acid substitution, deletion, or insertion. For example, for those amino acid sequences start with a N-terminal methionine, the N-terminal methionine can be absent. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) includes any one of those described in **Table 10A or Table 10B** and a heterologous peptide sequence (*e.g.,* post-translational modification motif) fused to the N-terminal or C-terminal. The payload in some of the exemplary sequences in **Table 10A and Table 10B** can be replaced with any desired therapeutic molecule (*e.g.,* a prime editor, an antibody, etc).

[0124] In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 50% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 60% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 70% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 75% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 80% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 85% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.,* a base editor) comprises an amino acid sequence that has at least about 90% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element

with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 95% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 96% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 97% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 98% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 99% sequence identity to any one of sequence set forth in **Table 10A or Table 10B**. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to any one of sequence set forth Table 10A. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to any one of sequence set forth Table 10B. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in any one of **SEQ ID NOs:** 194-233. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in any one of **SEQ ID NOs:** 234-263. In some cases, the plasma membrane recruitment element with or without a payload (*e.g.*, a base editor) comprises an amino acid sequence that has at least about 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in any one of **SEQ ID NOs:** 194-263.

Table 15 Exemplary wild type gag polyprotein and the corresponding amino acid sequences

Description	**Sequence**	**SEQ ID NO**
Alpharetroviral Gag protein sequences		
Rous Sarcoma Virus >sp|P03322|GAG_RSVP Gag polyprotein	MEAVIKVISSACKTYCGKTSPSKKEIGAMLSLLQKEGLL MSPSDLYSPGSWDPITAALSQRAMILGKSGELKTWGLV LGALKAAREEQVTSEQAKFWLGLGGGRVSPPGPECIEKP ATERRIDKGEEVGETTVQRDAKMAPEETATPKTVGTSC YHCGTAIGCNCATASAPPPPYVGSGLYPSLAGVGEQQG	285

OS=Rous sarcoma virus subgroup C (strain Prague) OX=11888 GN=gag PE=1 SV=1	QGGDTPPGAEQSRAEPGHAGQAPGPALTDWARVREEL ASTGPPVVAMPVVIKTEGPAWTPLEPKLITRLADTVRTK GLRSPITMAEVEALMSSPLLPHDVTNLMRVILGPAPYAL WMDAWGVQLQTVIAAATRDPRHPANGQGRGERTNLN RLKGLADGMVGNPQGQAALLRPGELVAITASALQAFRE VARLAEPAGPWADIMQGPSESFVDFANRLIKAVEGSDLP PSARAPVIIDCFRQKSQPDIQQLIRTAPSTLTTPGEIIKYVL DRQKTAPLTDQGIAAAMSSAIQPLIMAVVNRERDGQTG SGGRARGLCYTCGSPGHYQAQCPKKRKSGNSRERCQLC NGMGHNAKQCRKRDGNQGQRPGKGLSSGPWPGPEPPA VSLAMTMEHKDRPLVRVILTNTGSHPVKQRSVYITALL DSGADITIISEEDWPTDWPVMEAANPQIHGIGGGIPMRKS RDMIELGVINRDGSLERPLLLFPAVAMVRGSILGRDCLQ GLGLRLTNL	
Rous Sarcoma Virus >sp|P03322|GAG_RSVP Gag polyprotein OS=Rous sarcoma virus subgroup C (strain Prague) OX=11888 GN=gag PE=1 SV=1	EAVIKVISSACKTYCGKTSPSKKEIGAMLSLLQKEGLLM SPSDLYSPGSWDPITAALSQRAMILGKSGELKTWGLVLG ALKAAREEQVTSEQAKFWLGLGGGRVSPPGPECIEKPAT ERRIDKGEEVGETTVQRDAKMAPEETATPKTVGTSCYH CGTAIGCNCATASAPPPPYVGSGLYPSLAGVGEQQGQG GDTPPGAEQSRAEPGHAGQAPGPALTDWARVREELAST GPPVVAMPVVIKTEGPAWTPLEPKLITRLADTVRTKGLR SPITMAEVEALMSSPLLPHDVTNLMRVILGPAPYALWM DAWGVQLQTVIAAATRDPRHPANGQGRGERTNLNRLK GLADGMVGNPQGQAALLRPGELVAITASALQAFREVAR LAEPAGPWADIMQGPSESFVDFANRLIKAVEGSDLPPSA RAPVIIDCFRQKSQPDIQQLIRTAPSTLTTPGEIIKYVLDR QKTAPLTDQGIAAAMSSAIQPLIMAVVNRERDGQTGSG GRARGLCYTCGSPGHYQAQCPKKRKSGNSRERCQLCN GMGHNAKQCRKRDGNQGQRPGKGLSSGPWPGPEPPAV SLAMTMEHKDRPLVRVILTNTGSHPVKQRSVYITALLDS GADITIISEEDWPTDWPVMEAANPQIHGIGGGIPMRKSR DMIELGVINRDGSLERPLLLFPAVAMVRGSILGRDCLQG LGLRLTNL	286
Avian Leukosis Virus tr|Q7SQ99|Q7SQ99_ALV Gag protein	MEAVIKVISSACKTYCGKTSPSKKEIGAMLSLLQKEGLL MSPSDLYSPGSWDPITAALSQRAMVLGKSGELKTWGLV LGALKAAREEQVTSEQAKFWLGLGGGRVSPPGPESIEKP ATERRVDKGEEVGETTVQRDAKMAPEETATPKTVGTSC YHCGTAIGCNCATASAPPPPYVGSGLYPSLAGVGEQQG	287

OS=Avian leukosis virus OX=11864 GN=gag PE=4 SV=1	QGGDTPRGAEQPRAEPGHAGQAPGPALTDWARVREEL ASTGPPVVAMPVVIKTEGPAWTPLEPKLITRLADTVRTK GLRSPITMAEVEALMSSPLLPHDVTNLMRVILGPAPYAL WMDAWGVQLQTVIAAATRDPRHPANGQGRGERTNLD RLKGLADGMVGNPQGQAALLRPGELVAITASALQAFRE VARLAEPAGPWADITQGPSESFVDFANRLIKAVEGSDLP PTARAPVIIDCFRQKSQPDIQQLIRAAPSTLTTPGEIIKYVL DRQKTAPLTDQGIAAAMSSAIQPLVMAVVNRERDGQTG PGGRARGLCYTCGSPGHYQAQCPKKRKSGNSRERCQLC DGMGHNAKQCRRRDGNQGQRPGRGLSSGPWPVSEQPA VSLAMTMEHKDRPLVRVILTNTGSHPVKQRSVYITALL DSGADITIISEEDWPTDWPVVDTANPQIHGIGGGIPMRKS RDMIELGVINRDGSLERPLLLFPAVAMVRGSILGRDCLQ GLGLRLTNL	
Avian Leukosis Virus tr|Q7SQ99|Q7SQ99_ALV Gag protein OS=Avian leukosis virus OX=11864 GN=gag PE=4 SV=1	EAVIKVISSACKTYCGKTSPSKKEIGAMLSLLQKEGLLM SPSDLYSPGSWDPITAALSQRAMVLGKSGELKTWGLVL GALKAAREEQVTSEQAKFWLGLGGGRVSPPGPESIEKPA TERRVDKGEEVGETTVQRDAKMAPEETATPKTVGTSCY HCGTAIGCNCATASAPPPPYVGSGLYPSLAGVGEQQGQ GGDTPRGAEQPRAEPGHAGQAPGPALTDWARVREELAS TGPPVVAMPVVIKTEGPAWTPLEPKLITRLADTVRTKGL RSPITMAEVEALMSSPLLPHDVTNLMRVILGPAPYALW MDAWGVQLQTVIAAATRDPRHPANGQGRGERTNLDRL KGLADGMVGNPQGQAALLRPGELVAITASALQAFREVA RLAEPAGPWADITQGPSESFVDFANRLIKAVEGSDLPPT ARAPVIIDCFRQKSQPDIQQLIRAAPSTLTTPGEIIKYVLD RQKTAPLTDQGIAAAMSSAIQPLVMAVVNRERDGQTGP GGRARGLCYTCGSPGHYQAQCPKKRKSGNSRERCQLC DGMGHNAKQCRRRDGNQGQRPGRGLSSGPWPVSEQPA VSLAMTMEHKDRPLVRVILTNTGSHPVKQRSVYITALL DSGADITIISEEDWPTDWPVVDTANPQIHGIGGGIPMRKS RDMIELGVINRDGSLERPLLLFPAVAMVRGSILGRDCLQ GLGLRLTNL	288
Avian Myeloblastosis Virus >AAB31928.1 polyprotein I	MEAVIKVISSACKTYCGKTSPSKKEIGAMLSLLQKEGLL MSPSDLYSPGSWDPITAALSQRAMVLGKSGELKTWGLV LGALKAAREEQVTSEQAKFWLGLGGGRVSPPGPECIEKP ATERRTDKGEEVGETTAQRDAKMAPEETATPKTVGTSC YHCGTAIGCSCATASAPPPPYVGSGLYPSLAGVGEQQGQ	289

[Avian myeloblastosis virus]	EGDTPGGAEQPRGEPRHAGLAPKAALTDWARVREELAS TGPPVVAMPVVIKTEGPAWTPLEPKWITRLADTVRTKG LRSPITMAEVEALMSSPLLPHDVTNLMRVILGPAPYALW MDAWGVQLQTVIAAATRDPRHPANGQGRGERTNLNRL KGLADGMVGNPQGQAALLRPGELVAITAAALQAFREV ARLAEPAGPWADITQGPSEPFVDFANRLIKAVEGSDLPP SARAPVIIDCFRQKSQPDIQQLIRAAPSTLTTPGEIIKYVL DRQKTAPLTDQGIAAAMSSAIQPLVMAVVNRERDGQTG SGGRARGLCYTCGSPGHYQAQCPKKRKSGNSRERCQLC DGMGHNAKQCRKRDGNQGQRPGRGLSSGPWPVSEPPA VSLAMTMEHKDRPLVRVILTNTGSHPVKQRSVYITALL DSGADITIISEEDWPADWPVMEAANPQIHGIGGGIPMRK SRDMIEVGVINRDGSLERPLLLFPAVAMVRGSILGRDCL QGLGLRLTNL	
Avian Myeloblastosis Virus >AAB31928.1 polyprotein I [Avian myeloblastosis virus]	EAVIKVISSACKTYCGKTSPSKKEIGAMLSLLQKEGLLM SPSDLYSPGSWDPITAALSQRAMVLGKSGELKTWGLVL GALKAAREEQVTSEQAKFWLGLGGGRVSPPGPECIEKP ATERRTDKGEEVGETTAQRDAKMAPEETATPKTVGTSC YHCGTAIGCSCATASAPPPPYVGSGLYPSLAGVGEQQGQ EGDTPGGAEQPRGEPRHAGLAPKAALTDWARVREELAS TGPPVVAMPVVIKTEGPAWTPLEPKWITRLADTVRTKG LRSPITMAEVEALMSSPLLPHDVTNLMRVILGPAPYALW MDAWGVQLQTVIAAATRDPRHPANGQGRGERTNLNRL KGLADGMVGNPQGQAALLRPGELVAITAAALQAFREV ARLAEPAGPWADITQGPSEPFVDFANRLIKAVEGSDLPP SARAPVIIDCFRQKSQPDIQQLIRAAPSTLTTPGEIIKYVL DRQKTAPLTDQGIAAAMSSAIQPLVMAVVNRERDGQTG SGGRARGLCYTCGSPGHYQAQCPKKRKSGNSRERCQLC DGMGHNAKQCRKRDGNQGQRPGRGLSSGPWPVSEPPA VSLAMTMEHKDRPLVRVILTNTGSHPVKQRSVYITALL DSGADITIISEEDWPADWPVMEAANPQIHGIGGGIPMRK SRDMIEVGVINRDGSLERPLLLFPAVAMVRGSILGRDCL QGLGLRLTNL	290
retroviral Gag proteins		
Deltaretrovirus: Human T cell Leukemia Virus-1	MGQIFSRSASPIPRPPRGLAAHHWLNFLQAAYRLEPGPSS YDFHQLKKFLKIALETPARICPINYSLLASLLPKGYPGRV NEILHILIQTQAQIPSRPAPPPPSSPTHDPPDSDPQIPPP	291

>sp|P03345|GAG_HTL1A Gag polyprotein OS=Human T-cell leukemia virus 1 (strain Japan ATK-1 subtype A) OX=11926 GN=gag PE=1 SV=3	YVEPTAPQVLPVMHPHGAPPNHRPWQMKDLQAIKQEV SQAAPGSPQFMQTIRLAVQQFDPTAKDLQDLLQYLCSSL VASLHHQQLDSLISEAETRGITGYNPLAGPLRVQANNPQ QQGLRREYQQLWLAAFAALPGSAKDPSWASILQGLEEP YHAFVERLNIALDNGLPEGTPKDPILRSLAYSNANKECQ KLLQARGHTNSPLGDMLRACQTWTPKDKTKVLVVQPK KPPPNQPCFRCGKAGHWSRDCTQPRPPPGPCPLCQDPTH WKRDCPRLKPTIPEPEPEEDALLLDLPADIPHPKNSIGGE V	
Deltaretrovirus: Human T cell Leukemia Virus-1 >sp|P03345|GAG_HTL1A Gag polyprotein OS=Human T-cell leukemia virus 1 (strain Japan ATK-1 subtype A) OX=11926 GN=gag PE=1 SV=3	GQIFSRSASPIPRPPRGLAAHHWLNFLQAAYRLEPGPSSY DFHQLKKFLKIALETPARICPINYSLLASLLPKGYPGRVN EILHILIQTQAQIPSRPAPPPPSSPTHDPPDSDPQIPPP YVEPTAPQVLPVMHPHGAPPNHRPWQMKDLQAIKQEV SQAAPGSPQFMQTIRLAVQQFDPTAKDLQDLLQYLCSSL VASLHHQQLDSLISEAETRGITGYNPLAGPLRVQANNPQ QQGLRREYQQLWLAAFAALPGSAKDPSWASILQGLEEP YHAFVERLNIALDNGLPEGTPKDPILRSLAYSNANKECQ KLLQARGHTNSPLGDMLRACQTWTPKDKTKVLVVQPK KPPPNQPCFRCGKAGHWSRDCTQPRPPPGPCPLCQDPTH WKRDCPRLKPTIPEPEPEEDALLLDLPADIPHPKNSIGGE V	292
Betaretrovirus: Mouse Mammary Tumor Virus >tr|Q9WJP5|Q9WJP5_MMTV Pr77 OS=Mouse mammary tumor virus OX=11757 GN=gag PE=4 SV=2	MGVSGSKGQKLFVSVLQRLLSERGLHVKESSAIEFYQFL IKVSPWFPEEGGLNLQDWKRVGREMKRYAAEHGTDSIP KQAYPIWLQLREILTEQSDLVLLSAEAKSVTEEELEEGLT GLLSTSSQEKTYGTRGTAYAEIDTEVDKLSEHIYDEPYEE KEKADKNEEKDHVRKIKKVVQRKENSEGKRKEKDSKA FLATDWNDDDLSPEDWDDLEEQAAHYHDDDELILPVK RKVVKKKPQALRRKPLPPVGFAGAMAEAREKGDLTFTF PVVFMGESDEDDTPVWEPLPLKTLKELQSAVRTMGPSA PYTLQVVDMVASQWLTPSDWHQTARATLSPGDYVLWR TEYEEKSKEMVQKAAGKRKGKVSLDMLLGTGQFLSPSS QIKLSKDVLKDVTTNAVLAWRAIPPPGVKKTVLAGLKQ GNEESYETFISRLEEAVYRMMPRGEGSDILIKQLAWENA	293

	NSLCQDLIRPIRKTGTIQDYIRACLDASPAVVQGMAYAA AMRGQKYSTFVKQTYGGGKGGQGAEGPVCFSCGKTGH IRKDCKDEKGSKRAPPGLCPRCKKGYHWKSECKSKFDK DGNPLPPLETNAENSKNL	
Betaretrovirus: Mouse Mammary Tumor Virus >tr|Q9WJP5|Q9WJP5_MMTV Pr77 OS=Mouse mammary tumor virus OX=11757 GN=gag PE=4 SV=2	GVSGSKGQKLFVSVLQRLLSERGLHVKESSAIEFYQFLIK VSPWFPEEGGLNLQDWKRVGREMKRYAAEHGTDSIPK QAYPIWLQLREILTEQSDLVLLSAEAKSVTEEELEEGLTG LLSTSSQEKTYGTRGTAYAEIDTEVDKLSEHIYDEPYEEK EKADKNEEKDHVRKIKKVVQRKENSEGKRKEKDSKAF LATDWNDDDLSPEDWDDLEEQAAHYHDDDELILPVKR KVVKKKPQALRRKPLPPVGFAGAMAEAREKGDLTFTFP VVFMGESDEDDTPVWEPLPLKTLKELQSAVRTMGPSAP YTLQVVDMVASQWLTPSDWHQTARATLSPGDYVLWR TEYEEKSKEMVQKAAGKRKGKVSLDMLLGTGQFLSPSS QIKLSKDVLKDVTTNAVLAWRAIPPPGVKKTVLAGLKQ GNEESYETFISRLEEAVYRMMPRGEGSDILIKQLAWENA NSLCQDLIRPIRKTGTIQDYIRACLDASPAVVQGMAYAA AMRGQKYSTFVKQTYGGGKGGQGAEGPVCFSCGKTGH IRKDCKDEKGSKRAPPGLCPRCKKGYHWKSECKSKFDK DGNPLPPLETNAENSKNL	294
Betaretrovirus: Jaagsiekte sheep retrovirus >sp|P31622|GAG_JSRV Gag polyprotein OS=Sheep pulmonary adenomatosis virus OX=11746 GN=gag PE=1 SV=1	MGHTHSRQLFVHMLSVMLKHRGITVSKTKLINFLSFIEE VCPWFPREGTVNLETWKKVGEQIRTHYTLHGPEKVPVE TLSFWTLIRDCLDFDNDELKRLGNLLKQEEDPLHTPDSV PSYDPPPPPPSLKMHPSDNDDSLSSTDEAELDEEAAKY HQEDWGFLAQEKGALTSKDELVECFKNLTIALQNAGIQ LPSNNNTFPSAPPFPPAYTPTVMAGLDPPPGFPPPSKHMS PLQKALRQAQRLGEVVSDFSLAFPVFENNNQRYYESLPF KQLKELKIACSQYGPTAPFTIAMIESLGTQALPPNDWKQ TARACLSGGDYLLWKSEFFEQCARIADVNRQQGIQTSY EMLIGEGPYQATDTQLNFLPGAYAQISNAARQAWKKLP SSSTKTEDLSKVRQGPDEPYQDFVARLLDTIGK IMSDEKAGMVLAKQLAFENANSACQAALRPYRKKGDL SDFIRICADIGPSYMQGIAMAAALQGKSIKEVLFQQQAR NKKGLQKSGNSGCFVCGQPGHRAAVCPQKHQTSVNTP NLCPRCKKGKHWARDCRSKTDVQGNPLPPVSGNWVRG QPLAPKQCYGATLQVPKEPLQTSVEPQEAARDWTSVPP PIQY	295

Betaretrovirus: Jaagsiekte sheep retrovirus >sp|P31622|GAG_JSRV Gag polyprotein OS=Sheep pulmonary adenomatosis virus OX=11746 GN=gag PE=1 SV=1	GHTHSRQLFVHMLSVMLKHRGITVSKTKLINFLSFIEEV CPWFPREGTVNLETWKKVGEQIRTHYTLHGPEKVPVET LSFWTLIRDCLDFDNDELKRLGNLLKQEEDPLHTPDSVP SYDPPPPPPPSLKMHPSDNDDSLSSTDEAELDEEAAKYH QEDWGFLAQEKGALTSKDELVECFKNLTIALQNAGIQLP SNNNTFPSAPPFPPAYTPTVMAGLDPPPGFPPPSKHMSPL QKALRQAQRLGEVVSDFSLAFPVFENNNQRYYESLPFK QLKELKIACSQYGPTAPFTIAMIESLGTQALPPNDWKQT ARACLSGGDYLLWKSEFFEQCARIADVNRQQGIQTSYE MLIGEGPYQATDTQLNFLPGAYAQISNAARQAWKKLPS SSTKTEDLSKVRQGPDEPYQDFVARLLDTIGK IMSDEKAGMVLAKQLAFENANSACQAALRPYRKKGDL SDFIRICADIGPSYMQGIAMAAALQGKSIKEVLFQQQAR NKKGLQKSGNSGCFVCGQPGHRAAVCPQKHQTSVNTP NLCPRCKKGKHWARDCRSKTDVQGNPLPPVSGNWVRG QPLAPKQCYGATLQVPKEPLQTSVEPQEAARDWTSVPP PIQY	296
Betaretrovirus: Mason-Pfizer Monkey Virus >sp|P07567|GAG_MPMV Gag polyprotein OS=Mason-Pfizer monkey virus OX=11855 GN=gag PE=1 SV=3	MGQELSQHERYVEQLKQALKTRGVKVKYADLLKFFDF VKDTCPWFPQEGTIDIKRWRRVGDCFQDYYNTFGPEKV PVTAFSYWNLIKELIDKKEVNPQVMAAVAQTEEILKSNS QTDLTKTSQNPDLDLISLDSDDEGAKSSSLQDKGLSSTK KPKRFPVLLTAQTSKDPEDPNPSEVDWDGLEDEAAKYH NPDWPPFLTRPPPYNKATPSAPTVMAVVNPKEELKEKIA QLEEQIKLEELHQALISKLQKLKTGNETVTHPDTAGGLS RTPHWPGQHIPKGKCCASREKEEQIPKDIFPVTETVDGQ GQAWRHHNGFDFAVIKELKTAASQYGATAPYTLAIVES VADNWLTPTDWNTLVRAVLSGGDHLLWKSEFFENCRD TAKRNQQAGNGWDFDMLTGSGNYSSTDAQMQYDPGL FAQIQAAATKAWRKLPVKGDPGASLTGVKQGPDEPFAD FVHRLITTAGRIFGSAEAGVDYVKQLAYENANPACQAAI RPYRKKTDLTGYIRLCSDIGPSYQQGLAMAAAFSGQTV KDFLNNKNKEKGGCCFKCGKKGHFAKNCHEHAHNNAE PKVPGLCPRCKRGKHWANECKSKTDNQGNPIPPHQGNG WRGQPQAPKQAYGAVSFVPANKNNPFQSLPEPPQEVQD WTSVPPPTQY	297
Betaretrovirus: Mason-Pfizer Monkey Virus	GQELSQHERYVEQLKQALKTRGVKVKYADLLKFFDFV KDTCPWFPQEGTIDIKRWRRVGDCFQDYYNTFGPEKVP VTAFSYWNLIKELIDKKEVNPQVMAAVAQTEEILKSNSQ	298

>sp|P07567|GAG_MPMV Gag polyprotein OS=Mason-Pfizer monkey virus OX=11855 GN=gag PE=1 SV=3	TDLTKTSQNPDLDLISLDSDDEGAKSSSLQDKGLSSTKK PKRFPVLLTAQTSKDPEDPNPSEVDWDGLEDEAAKYHN PDWPPFLTRPPPYNKATPSAPTVMAVVNPKEELKEKIAQ LEEQIKLEELHQALISKLQKLKTGNETVTHPDTAGGLSR TPHWPGQHIPKGKCCASREKEEQIPKDIFPVTETVDGQG QAWRHHNGFDFAVIKELKTAASQYGATAPYTLAIVESV ADNWLTPTDWNTLVRAVLSGGDHLLWKSEFFENCRDT AKRNQQAGNGWDFDMLTGSGNYSSTDAQMQYDPGLF AQIQAAATKAWRKLPVKGDPGASLTGVKQGPDEPFADF VHRLITTAGRIFGSAEAGVDYVKQLAYENANPACQAAI RPYRKKTDLTGYIRLCSDIGPSYQQGLAMAAAFSGQTV KDFLNNKNKEKGGCCFKCGKKGHFAKNCHEHAHNNAE PKVPGLCPRCKRGKHWANECKSKTDNQGNPIPPHQGNG WRGQPQAPKQAYGAVSFVPANKNNPFQSLPEPPQEVQD WTSVPPPTQY	

Mutant of an HIV Gag polyprotein

[0125] In some cases, the lipid delivery particle comprises a plasma membrane recruitment element comprising a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV, such as HIV-1. In some cases, the plasma membrane recruitment element is fused to the cleavable linker. In some cases, the plasma membrane recruitment element is fused to the membrane penetrating peptide. In some cases, the plasma membrane recruitment element is fused to the post-translational modification motif. In some cases, the lipid delivery particle further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof. Functions of various domains of HIV-1 gag are described in Accola MA *et al.*, J Virol. 2000 Jun;74(12):5395-402 and Montagna C *et al.*, Mol Ther Nucleic Acids. 2018 Sep 7;12:453-462., each of which are incorporated herein by reference in its entirety.

[0126] In some cases, the plasma membrane recruitment element comprises at least a fragment of matrix protein of an HIV gag, such as a N-terminal fragment of the matrix protein of the HIV gag and a pleckstrin homology (PH) domain (*e.g.,* a human PH domain or those listed in **Table 4**) or a mutant thereof. In some cases, the plasma membrane recruitment element comprises at least a fragment of capsid protein of the HIV gag, such as a full-length capsid protein of the HIV gag and a C-terminal fragment of capsid protein of the HIV gag. In some cases, the plasma membrane recruitment element comprises a spacer peptide of the HIV gag, such as a P2 domain of the HIV gag and a P1 domain of the HIV gag, or both.

[0127] In some cases, the plasma membrane recruitment element comprises a heterologous domain. In some cases, the heterologous domain can perform protein-protein interactions. In some cases, the heterologous domain comprises a multimerization motif. In some cases, the multimerization motif forms

parallel homodimers, such as a coiled-coil. In some cases, the multimerization motif forms parallel heterodimers (*e.g.*, dDZF1 and dDZF2). In some cases, the multimerization motif forms dimers, trimers, tetramers, or other oligomers. In some cases, the coiled-coil is a leucine zipper (LZ), such as a GCN4 leucine zipper or a mutant thereof. In some cases, the plasma membrane recruitment element comprises a leucine zipper and lacks nucleocapsid protein of the HIV gag. In some cases, the plasma membrane recruitment element comprises a full-length nucleocapsid protein of the HIV gag or a fragment thereof.

[0128] In some cases, the plasma membrane recruitment element comprises a particle budding motif. In some cases, the plasma membrane recruitment element comprises two or more particle budding motifs. In some cases, the plasma membrane recruitment element comprises one, two, or three particle budding motifs. In some cases, at least one of the particle budding motifs is a particle budding motif of the HIV gag, for example, a N-terminal fragment of the P6 domain of the HIV gag, a PTAP motif, or a full-length P6 domain of the HIV gag. In some cases, at least one of the particle budding motifs is a heterologous particle budding motif, for example, RSV P2B or a mutant thereof or a sequence listed in Table 5.

[0129] In some cases, the plasma membrane recruitment element lacks at least a C-terminal fragment of matrix protein of the HIV gag. In some cases, the plasma membrane recruitment element lacks at least a spacer peptide of the HIV gag. In some cases, the plasma membrane recruitment element lacks at least a fragment of the P6 domain of the HIV gag. In some cases, the plasma membrane recruitment element lacks at least a fragment of the P6 domain of the HIV gag. In some cases, the plasma membrane recruitment element lacks at least a fragment of capsid protein of the HIV gag, such as lacking a N-terminal fragment or a C-terminal fragment. In some cases, the plasma membrane recruitment element lacks at least a fragment or all of the nucleocapsid protein of the HIV gag. In some cases, the plasma membrane recruitment element lacks a P1 domain domain of the HIV gag. In some cases, the plasma membrane recruitment element lacks a P2 domain domain of the HIV. In some cases, the plasma membrane recruitment element lacks a P1 domain and a P2 domain domain of the HIV gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HIV gag and a fragment of the capsid protein of the HIV gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HIV gag, a fragment of the capsid protein of the HIV gag, and at least a fragment of the nucleocapsid protein of the HIV gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HIV gag, a fragment of the capsid protein of the HIV gag, at least a fragment of the nucleocapsid protein of the HIV gag, and a P1 domain domain of the HIV gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HIV gag, a fragment of the capsid protein of the HIV gag, at least a fragment of the nucleocapsid protein of the HIV gag, and a P2 domain domain of the HIV gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HIV gag, a fragment of the capsid protein of the HIV gag, at least a fragment of the nucleocapsid protein of the HIV gag, a P1 domain and a P2 domain domain of the HIV gag. In some cases, the plasma membrane recruitment element further lacks a HIV gag endogenous protease cleavage sequence or comprises a mutant HIV gag endogenous protease cleavage sequence that cannot be cleaved by a HIV protease.

[0130] In some cases, the plasma membrane recruitment element lacks a matrix protein of the HIV gag. In some cases, the plasma membrane recruitment element lacks a nucleocapsid protein of the HIV gag. In some cases, the plasma membrane recruitment element lacks a P6 domain of the HIV gag. In some cases, the plasma membrane recruitment element lacks a matrix protein of the HIV gag and a nucleocapsid protein of the HIV gag. In some cases, the plasma membrane recruitment element lacks a P2 domain of the HIV gag, a P1 domain of the HIV gag, or both. In some cases, the plasma membrane recruitment element lacks a matrix protein of the HIV gag, a P2 domain of the HIV gag, a nucleocapsid protein of the HIV gag, a P1 domain of the HIV gag, and a P6 domain of the HIV gag. In some cases, the plasma membrane recruitment element comprises a N-terminal N-terminal myristoylation motif, the full-length capsid protein of the HIV gag or a fragment thereof, the multimerization motif (optionally a DZF), and a heterologous particle budding motif (optionally a late domain of RSV) arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, a dDZF1, and a late domain of RSV) arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, a dDZF2, and a late domain of RSV) arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

[0131] In some cases, the plasma membrane recruitment element comprises

(a) the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof;

(b) the full-length capsid protein of the HIV gag or a fragment thereof;

(c) the multimerization motif (*e.g.,* leucine zipper) or the full-length nucleocapsid protein of the HIV gag or a fragment thereof; and

(d) the particle budding motif.

In some cases, the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element further comprises the P2 domain of the HIV gag located at a position between (b) and (c).

[0132] In some cases, the plasma membrane recruitment element comprises the following configurations arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment:

1) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

2) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;
3) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;
4) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag.
5) the N-terminal fragment of the matrix protein of the HIV gag, a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;
6) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag.
7) the N-terminal fragment of the matrix protein of the HIV gag, a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;
8) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;
9) the N-terminal fragment of the matrix protein of the HIV gag, C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;
10) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);
11) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);
12) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);
13) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV

gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5).

14) the N-terminal fragment of the matrix protein of the HIV gag, a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

15) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5).

16) the N-terminal fragment of the matrix protein of the HIV gag, a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

17) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

18) the N-terminal fragment of the matrix protein of the HIV gag, C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

19) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

20) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

21) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and P6 domain of the HIV gag;

22) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag.

23) the N-terminal fragment of the matrix protein of the HIV gag, a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

24) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag.

25) the N-terminal fragment of the matrix protein of the HIV gag, a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

26) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and P6 domain of the HIV gag;

27) the N-terminal fragment of the matrix protein of the HIV gag, C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and P6 domain of the HIV gag;

28) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

29) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

30) the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

31) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5).

32) the N-terminal fragment of the matrix protein of the HIV gag, a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

33) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5).

34) the N-terminal fragment of the matrix protein of the HIV gag, a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

35) the N-terminal fragment of the matrix protein of the HIV gag, a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

36) the N-terminal fragment of the matrix protein of the HIV gag, C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

37) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

38) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

39) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

40) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag.

41) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

42) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag.

43) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

44) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the

HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

45) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

46) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

47) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

48) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

49) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5).

50) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

51) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5).

52) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

53) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

54) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

55) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

56) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

57) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and P6 domain of the HIV gag;

58) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag.

59) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

60) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag.

61) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

62) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the

HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and P6 domain of the HIV gag;

63) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and P6 domain of the HIV gag;

64) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

65) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

66) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

67) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5).

68) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

69) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5).

70) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

71) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

72) the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif (*e.g.,* RSV P2B or a sequence selected from Table 5), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), and a second particle budding domain (*e.g.,* a sequence selected from Table 5);

73) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

74) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

75) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

76) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag.

77) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

78) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag.

79) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

80) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

81) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.,* leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

82) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.,* RSV P2B or a sequence selected from Table 5);

83) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

84) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

85) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5).

86) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

87) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5).

88) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

89) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

90) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

91) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

92) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

93) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and P6 domain of the HIV gag;

94) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag.

95) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

96) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag.

97) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

98) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and P6 domain of the HIV gag;

99) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and P6 domain of the HIV gag;

100) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

101) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

102) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

103) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5).

104) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

105) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5).

106) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

107) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

108) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

109) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

110) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

111) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

112) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag.

113) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-

terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

114) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag.

115) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and P6 domain of the HIV gag;

116) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

117) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and P6 domain of the HIV gag;

118) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

119) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a heterologous particle budding domain (*e.g.*, RSV P2B or a sequence selected from Table 5);

120) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

121) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5).

122) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

123) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5).

124) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

125) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

126) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), P1 domain of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

127) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

128) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

129) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and P6 domain of the HIV gag;

130) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag.

131) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

132) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag.

133) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and P6 domain of the HIV gag;

134) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and P6 domain of the HIV gag;

135) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and P6 domain of the HIV gag;

136) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

137) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

138) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), the full-length capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif

(*e.g.*, leucine zipper), and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

139) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5).

140) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, full-length nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

141) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5).

142) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a fragment of nucleocapsid protein of the HIV gag, and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

143) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), a N-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

144) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a first particle budding motif (*e.g.*, RSV P2B or a sequence selected from Table 5), C-terminal fragment of capsid protein of the HIV gag, P2 domain of the HIV gag, a multimerization motif (*e.g.*, leucine zipper), and a second particle budding domain (*e.g.*, a sequence selected from Table 5);

145) an HIV Gag myristoylation motif, a full-length capsid protein of the HIV gag or a fragment thereof, dDZF1, a particle budding domain (*e.g.*, RSV late domains);

146) an HIV Gag myristoylation motif, a full-length capsid protein of the HIV gag or a fragment thereof, dDZF2, a particle budding domain (*e.g.*, RSV late domains);

[0133] In some cases, each of the configurations 1) to 144) listed in the preceding paragraph independently lacks a HIV gag endogenous protease cleavage sequence. In some cases, each of the

configurations 1) to 144) listed above independently comprises a mutant HIV gag endogenous protease cleavage sequence that cannot be recognized and cleaved by an HIV protease. In some cases, in any one of configurations 1) to 144) listed above, the C-terminal fragment of capsid protein of the HIV gag comprises the major homology region (MHR). In some cases, each of the configurations 1) to 144) listed above is fused to a membrane penetrating peptide (*e.g.,* a sequence selected from Table 6). In some cases, each of the configurations 1) to 144) listed above is fused to a post-translational modification motif on the N-terminus or the C-terminus (*e.g.,* a sequence selected from Table 7). In some cases, the plasma membrane recruitment element comprises one, two, or three particle budding motif, each of which is selected from a sequence listed in Table 5. In some cases, in any one of the configurations 1) to 72) listed above, a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**) is fused the N-terminal of the fragment of the matrix protein, wherein the fragment of the matrix protein (a) lacks a N-terminal myristoylation motif, a N-terminal glycine, a highly basic region (HBR), a N-terminal fragment, or any combinations thereof or (b) comprises a mutated myr receptor by the amino acid substitution G2A on the matrix protein. In some cases, the plasma membrane recruitment element consists essentially of the domains in each of the configurations 1) to 144) listed in the preceding paragraph. In some cases, the plasma membrane recruitment element consists of the domains in each of the configurations 1) to 144) listed in the preceding paragraph.

Mutant of an MMLV Gag polyprotein

[0134] In some cases, the lipid delivery particle comprises a plasma membrane recruitment element comprising a mutant gag polyprotein that is not from HIV. In some cases, the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of MMLV. In some cases, the plasma membrane recruitment element is fused to the cleavable linker. In some cases, the plasma membrane recruitment element is fused to the membrane penetrating peptide. In some cases, the plasma membrane recruitment element is fused to the post-translational modification motif. In some cases, the lipid delivery particle further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof.

[0135] In some cases, the plasma membrane recruitment element comprises at least a fragment of matrix protein of an MMLV gag, such as a N-terminal fragment of the matrix protein of the MMLV gag and a pleckstrin homology (PH) domain (*e.g.,* a human PH domain or those listed in **Table 4**) or a mutant thereof. In some cases, the plasma membrane recruitment element comprises at least a fragment of capsid protein of the MMLV gag, such as a full-length capsid protein of the MMLV gag and a C-terminal fragment of capsid protein of the MMLV gag. In some cases, the plasma membrane recruitment element comprises P12 domain of the MMLV gag or a fragment thereof. In some cases, a fragment of the P12 domain of the MMLV gag is fused to a particle budding motif (*e.g.,* a sequence selected from Table 5). In some cases, the plasma membrane recruitment element lacks at least a C-terminal fragment of matrix protein of the MMLV gag. In some cases, the plasma membrane recruitment element lacks at least a fragment of the P12 domain of the MMLV gag. In some cases, the plasma membrane recruitment element

lacks at least a fragment of the P12 domain of the MMLV gag. In some cases, the plasma membrane recruitment element lacks at least a fragment of capsid protein of the MMLV gag, such as lacking a N-terminal fragment or a C-terminal fragment. In some cases, the plasma membrane recruitment element lacks at least a fragment or all of the nucleocapsid protein of the MMLV gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the MMLV gag and a fragment of the capsid protein of the MMLV gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the MMLV gag, a fragment of the capsid protein of the MMLV gag, and at least a fragment of the nucleocapsid protein of the MMLV gag. In some cases, the plasma membrane recruitment element further lacks a MMLV gag endogenous protease cleavage sequence or comprises a mutant MMLV gag endogenous protease cleavage sequence that cannot be cleaved by a MMLV protease.

[0136] In some cases, the plasma membrane recruitment element comprises a heterologous domain. In some cases, the heterologous domain comprises a multimerization motif. In some cases, the multimerization motif forms parallel homodimers, such as a coiled-coil. In some cases, the multimerization motif forms parallel heterodimers (*e.g.,* dDZF1 and dDZF2). In some cases, the multimerization motif forms dimers, trimers, tetramers, or other oligomers. In some cases, the coiled-coil is a leucine zipper (LZ), such as a GCN4 leucine zipper or a mutant thereof. In some cases, the plasma membrane recruitment element comprises a leucine zipper and lacks nucleocapsid protein of the MMLV gag. In some cases, the plasma membrane recruitment element comprises a full-length nucleocapsid protein of the MMLV gag or a fragment thereof.

[0137] In some cases, the plasma membrane recruitment element comprises a particle budding motif. In some cases, the plasma membrane recruitment element comprises two or more particle budding motifs. In some cases, the plasma membrane recruitment element comprises one, two, or three particle budding motifs. In some cases, at least one of the particle budding motifs is a particle budding motif of the MMLV gag, for example, a N-terminal fragment of the P12 domain of the MMLV gag, a PSAP motif, a LYPAL motif, a PPPY motif, or a full-length P12 domain of the MMLV gag. In some cases, at least one of the particle budding motifs is a heterologous particle budding motif, for example, RSV P2B or a mutant thereof or a sequence listed in Table 5.

[0138] In some cases, the plasma membrane recruitment element comprises

(a) a matrix protein of the MMLV gag (optionally full-length matrix protein of the MMLV gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the MMLV gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof;

(b) a capsid protein of the MMLV gag or a mutant thereof, optionally wherein the capsid protein of the MMLV gag or a mutant thereof is a full-length capsid protein of the MMLV gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the MMLV gag;

(c) heterologous domain, optionally wherein the heterologous domain comprises a coiled-coil (optionally a leucine zipper); and

(d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the MMLV gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5.

[0139] In some cases, the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element further comprises a P12 domain of the MMLV gag or a mutant thereof located between (a) and (b). In some cases, the P12 domain of the MMLV gag or a mutant thereof is a full-length P12 domain of the MMLV gag, a N-terminal fragment of the full-length P12 domain of the MMLV gag, a C-terminal fragment of the full-length P12 domain of the MMLV gag, or a fragment of the full-length P12 domain of the MMLV gag fused to a heterologous particle budding motif. In some cases, the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5.

[0140] In some cases, the plasma membrane recruitment element comprises the following configurations arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment:

1) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
2) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
3) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
4) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), the full-length capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
5) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
6) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
7) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

8) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
9) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
10) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
11) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
12) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;
13) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
14) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
15) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
16) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), the full-length capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
17) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
18) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

19) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
20) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
21) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
22) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
23) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
24) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;
25) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a leucine zipper;
26) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a leucine zipper;
27) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a leucine zipper;
28) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), the full-length capsid protein of the MMLV gag, and a leucine zipper;
29) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;
30) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;
31) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

32) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

33) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

34) the N-terminal fragment of the matrix protein of the MMLV gag, a fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

35) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

36) the N-terminal fragment of the matrix protein of the MMLV gag, a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

37) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

38) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

39) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

40) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

41) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

42) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

43) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

44) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

45) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

46) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

47) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

48) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

49) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

50) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

51) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

52) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

53) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

54) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

55) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

56) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

57) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

58) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

59) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

60) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

61) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

62) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

63) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

64) the N-terminal fragment of the matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

65) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

66) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

67) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

68) the N-terminal fragment of the matrix protein of the MMLV gag, a C-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

69) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

70) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

71) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

72) the N-terminal fragment of the matrix protein of the MMLV gag, a N-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

73) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

74) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

75) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

76) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), the full-length capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

77) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

78) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

79) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

80) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

81) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

82) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

83) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

84) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the MMLV gag, and the full-length nucleocapsid protein of the MMLV gag;

85) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

86) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

87) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

88) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), the full-length capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

89) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

90) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

91) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

92) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.*, a

sequence selected from Table 5), a C-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

93) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

94) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

95) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

96) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the MMLV gag, and a fragment of the nucleocapsid protein of the MMLV gag;

97) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a leucine zipper;

98) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a leucine zipper;

99) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, the full-length capsid protein of the MMLV gag, and a leucine zipper;

100) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), the full-length capsid protein of the MMLV gag, and a leucine zipper;

101) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

102) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

103) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, a C-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

104) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

105) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

106) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

107) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of P12 domain of the HIV gag, a N-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

108) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P12 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the MMLV gag, and a leucine zipper;

109) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

110) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

111) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

112) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

113) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

114) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

115) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

116) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

117) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

118) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

119) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

120) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, the full-length nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

121) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

122) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

123) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

124) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

125) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, a fragment of the

nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

126) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

127) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

128) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

129) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

130) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

131) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

132) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, a fragment of the nucleocapsid protein of the MMLV gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

133) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

134) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

135) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

136) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

137) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

138) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

139) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

140) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

141) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

142) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

143) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

144) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the MMLV gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

[0141] In some cases, each of the configurations 1) to 144) listed in the preceding paragraph independently lacks a MMLV gag endogenous protease cleavage sequence. In some cases, each of the configurations 1) to 144) listed above independently comprises a mutant MMLV gag endogenous protease cleavage sequence that cannot be recognized and cleaved by an MMLV protease. In some cases, in any one of configurations 1) to 144) listed above, the C-terminal fragment of capsid protein of the HIV gag comprises the major homology region (MHR). In some cases, each of the configurations 1) to 144) listed above is fused to a membrane penetrating peptide (*e.g.*, a sequence selected from Table 6). In some cases, each of the configurations 1) to 144) listed above is fused to a post-translational modification motif

on the N-terminus or the C-terminus (*e.g.,* a sequence selected from Table 7). In some cases, the plasma membrane recruitment element comprises one, two, or three particle budding motif, each of which is selected from a sequence listed in Table 5. In some cases, in any one of the configurations 1) to 72) listed above, a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**) is fused the N-terminal of the fragment of the matrix protein, wherein the fragment of the matrix protein lacks a N-terminal myristoylation motif, a N-terminal glycine, a highly basic region (HBR), a N-terminal fragment, or any combinations thereof. In some cases, the plasma membrane recruitment element consists essentially of the domains in each of the configurations 1) to 144) listed in the preceding paragraph. In some cases, the plasma membrane recruitment element consists of the domains in each of the configurations 1) to 144) listed in the preceding paragraph.

Mutant of a HERV Gag polyprotein

[0142] The plasma membrane recruitment element can include a mutant of a wild-type gag from human endogenous retrovirus, such as Human Endogenous Retrovirus K (*e.g.,* HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV- K11p22, and HERV-K12q13) and Human Endogenous Retrovirus-W. The plasma membrane recruitment element can include a mutant $hGAGK_{con}$. In some cases, the plasma membrane recruitment element is fused to the cleavable linker. In some cases, the plasma membrane recruitment element is fused to the membrane penetrating peptide. In some cases, the plasma membrane recruitment element is fused to the post-translational modification motif. In some cases, the lipid delivery particle further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof.

[0143] In some cases, the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of hGAGKcon. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of the hGAGKcon gag, a full-length capsid protein of the hGAGKcon gag or a fragment thereof, a multimerization motif (optionally a DZF), and a particle budding motif (optionally a late domain of RSV) arranged in order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag and a full-length capsid protein of the hGAGKcon gag. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag and a fragment of a full-length capsid protein of the hGAGKcon gag. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag, a full-length capsid protein of the hGAGKcon gag or a fragment thereof and a multimerization motif (optionally a DZF, such as dDZF1 or dDZF2). In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag, a full-length capsid protein of the hGAGKcon gag or a fragment thereof, a multimerization motif (optionally a DZF, such as dDZF1 or dDZF2) and a particle budding motif (optionally a late domain of RSV). In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation

motif of an HIV gag, a full-length capsid protein of the hGAGKcon gag or a fragment thereof, a multimerization motif (optionally a DZF, such as dDZF1 or dDZF2) and a particle budding motif (optionally a late domain of RSV) arranged in an order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag, a full-length capsid protein of the hGAGKcon gag, a dDZF1, and a particle budding motif (optionally a late domain of RSV) arranged in an order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag, a full-length capsid protein of the hGAGKcon gag, a dDZF2, and a particle budding motif (optionally a late domain of RSV) arranged in an order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag, a fragment of a full-length capsid protein of the hGAGKcon gag, a dDZF1, and a particle budding motif (optionally a late domain of RSV) arranged in an order from N-terminus to C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag, a fragment of a full-length capsid protein of the hGAGKcon gag, a dDZF2, and a particle budding motif (optionally a late domain of RSV) arranged in an order from N-terminus to C-terminus of the plasma membrane recruitment element.

[0144] In some cases, the plasma membrane recruitment element comprises a mutant of a wilt-type gag polyprotein of HERVK-113. In some cases, the plasma membrane recruitment element comprises at least a fragment of matrix protein of an HERVK-113 gag, such as a N-terminal fragment of the matrix protein of the HERVK-113 gag and a pleckstrin homology (PH) domain (*e.g.,* a human PH domain or those listed in **Table 4**) or a mutant thereof. In some cases, the plasma membrane recruitment element comprises at least a fragment of capsid protein of the HERVK-113 gag, such as a full-length capsid protein of the HERVK-113 gag and a C-terminal fragment of capsid protein of the HERVK-113 gag. In some cases, the plasma membrane recruitment element comprises P15 domain of the HERVK-113 gag or a fragment thereof. In some cases, a fragment of the P15 domain of the HERVK-113 gag is fused to a particle budding motif (*e.g.,* a sequence selected from **Table 5**). In some cases, the plasma membrane recruitment element lacks at least a C-terminal fragment of matrix protein of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks at least a spacer peptide of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks at least a fragment of the P15 domain of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks at least a fragment of the P15 domain of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks at least a fragment of capsid protein of the HERVK-113 gag, such as lacking a N-terminal fragment or a C-terminal fragment. In some cases, the plasma membrane recruitment element lacks at least a fragment or all of the nucleocapsid protein of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks a QP1 domain of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks a QP2 domain of the HERVK-113. In some cases, the plasma membrane recruitment element lacks a QP1 and a QP2 domain of the HERVK-113 gag. In some cases, the plasma

membrane recruitment element lacks a C-terminal fragment of the HERVK-113 gag and the spacer peptide of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HERVK-113 gag, the spacer peptide of the HERVK-113 gag, and a fragment of the capsid protein of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HERVK-113 gag, the spacer peptide of the HERVK-113 gag, a fragment of the capsid protein of the HERVK-113 gag, and at least a fragment of the nucleocapsid protein of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HERVK-113 gag, the spacer peptide of the HERVK-113 gag, a fragment of the capsid protein of the HERVK-113 gag, at least a fragment of the nucleocapsid protein of the HERVK-113 gag, and a QP1 domain of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HERVK-113 gag, the spacer peptide of the HERVK-113 gag, a fragment of the capsid protein of the HERVK-113 gag, at least a fragment of the nucleocapsid protein of the HERVK-113 gag, and a QP2 domain of the HERVK-113 gag. In some cases, the plasma membrane recruitment element lacks a C-terminal fragment of the HERVK-113 gag, the spacer peptide of the HERVK-113 gag, a fragment of the capsid protein of the HERVK-113 gag, at least a fragment of the nucleocapsid protein of the HERVK-113 gag, a QP1 and a QP2 domain of the HERVK-113 gag. In some cases, the plasma membrane recruitment element further lacks a HERVK-113 gag endogenous protease cleavage sequence or comprises a mutant HERVK-113 gag endogenous protease cleavage sequence that cannot be cleaved by a HERVK-113 protease.

[0145] In some cases, the plasma membrane recruitment element comprises a heterologous domain. In some cases, the heterologous domain comprises a multimerization motif. In some cases, the multimerization motif parallel homodimers, such as a coiled-coil. In some cases, the multimerization motif forms parallel heterodimers (*e.g.,* dDZF1 and dDZF2). In some cases, the multimerization motif forms dimers, trimers, tetramers, or other oligomers. In some cases, the multimerization motif is a leucine zipper oligomerization motif. The leucine zipper oligomerization motif can comprise a series of leucines spaced at intervals of every seventh amino acid along an α-helix. In some cases, a leucine zipper oligomerization motif can mediate dimerization or oligomerization. In some cases, the coiled-coil is a leucine zipper oligomerization motif (*e.g.,* a GCN4 leucine zipper or a mutant thereof). Upon dimerization, the leucine zipper oligomerization motif can form a parallel-coiled coil. *e.g.,*Without wishing to be bound by a theory there, the GCN4 leucine zipper can be used to induce multimerization that can assist in assembly of the lipid delivery particles described herein. In some cases, the plasma membrane recruitment element comprises a leucine zipper and lacks nucleocapsid protein of the HERVK-113 gag, and n is an integer from 1 to 5. In some cases, the plasma membrane recruitment element comprises a full-length nucleocapsid protein of the HERVK-113 gag or a fragment thereof.

[0146] In some cases, the plasma membrane recruitment element comprises a particle budding motif. In some cases, the plasma membrane recruitment element comprises two or more particle budding motifs. In some cases, the plasma membrane recruitment element comprises one, two, or three particle budding motifs. In some cases, at least one of the particle budding motifs is a particle budding motif of the

HERVK-113 gag, for example, a N-terminal fragment of the P15 domain of the HERVK-113 gag, a C-terminal fragment of the P15 domain of the HERVK-113 gag, a YPXnL motif, a PTAP motif, or a full-length P15 domain of the HERVK-113 gag. In some cases, at least one of the particle budding motifs is a heterologous particle budding motif, for example, RSV P2B or a mutant thereof or a sequence listed in Table 5.

[0147] In some cases, the plasma membrane recruitment element comprises (a) a matrix protein of the HERV-K113 gag (optionally full-length matrix protein of the HERV-K113 gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the HERV-K113 gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof; (b) a capsid protein of the HERV-K113 gag or a mutant thereof, optionally wherein the capsid protein of the HERV-K113 gag or a mutant thereof is a full-length capsid protein of the HERV-K113 gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the HERV-K113 gag; (c) heterologous domain, optionally wherein the heterologous domain comprises a coiled-coil (optionally a leucine zipper); and (d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the HERV-K113 gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5); (e) an optional QP1 domain of the HERV-K113 gag; and (f) an optional QP2 domain of the HERV-K113 gag; In some cases, (a)-(f) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element. In some cases, the plasma membrane recruitment element further comprises a P15 domain of the HERV-K113 gag or a mutant thereof. In some cases, the P15 domain of the HERV-K113 gag or a mutant thereof is a full-length P15 domain of the HERV-K113 gag, a N-terminal fragment of the full-length P15 domain of the HERV-K113 gag, a C-terminal fragment of the full-length P15 domain of the HERV-K113 gag, or a fragment of the full-length P15 domain of the HERV-K113 gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5).

[0148] In some cases, the plasma membrane recruitment element comprises the following configurations arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment:

1) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
2) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
3) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

4) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), the full-length capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
5) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
6) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
7) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
8) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
9) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
10) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
11) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
12) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;
13) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;
14) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

15) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

16) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), the full-length capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

17) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

18) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

19) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

20) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

21) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

22) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

23) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

24) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

25) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a leucine zipper;

26) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a leucine zipper;

27) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a leucine zipper;

28) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), the full-length capsid protein of the HERVK-113 gag, and a leucine zipper;

29) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

30) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

31) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

32) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

33) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

34) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

35) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

36) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.,* a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

37) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

38) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

39) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

40) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

41) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

42) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

43) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

44) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

45) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

46) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

47) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

48) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

49) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

50) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

51) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

52) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

53) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

54) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

55) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

56) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

57) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

58) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

59) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

60) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

61) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

62) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

63) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

64) the N-terminal fragment of the matrix protein of the HERVK-113 gag, the full-length capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

65) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

66) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

67) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

68) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

69) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

70) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

71) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

72) the N-terminal fragment of the matrix protein of the HERVK-113 gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.,* a sequence selected from Table 5);

73) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

74) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

75) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, the full-length

capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

76) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), the full-length capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

77) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

78) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

79) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

80) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

81) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

82) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

83) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

84) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the HERVK-113 gag, and the full-length nucleocapsid protein of the HERVK-113 gag;

85) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

86) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

87) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

88) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), the full-length capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

89) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

90) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

91) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

92) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

93) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

94) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

95) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

96) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a

sequence selected from Table 5), a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a fragment of the nucleocapsid protein of the HERVK-113 gag;

97) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a leucine zipper;

98) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a leucine zipper;

99) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, the full-length capsid protein of the HERVK-113 gag, and a leucine zipper;

100) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), the full-length capsid protein of the HERVK-113 gag, and a leucine zipper;

101) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

102) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

103) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

104) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a C-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

105) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

106) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

107) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment or a C-terminal fragment of P15 domain of the HIV gag, a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

108) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a fusion of a fragment of P15 domain of the HIV gag and a particle budding motif (*e.g.*, a sequence selected from Table 5), a N-terminal fragment of the capsid protein of the HERVK-113 gag, and a leucine zipper;

109) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

110) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

111) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

112) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

113) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

114) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

115) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

116) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

117) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length

nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

118) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

119) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

120) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, the full-length nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

121) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

122) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

123) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

124) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

125) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

126) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

127) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

128) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

129) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

130) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

131) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

132) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, a fragment of the nucleocapsid protein of the HERVK-113 gag, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

133) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

134) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

135) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

136) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), the full-length capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

137) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

138) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

139) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

140) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a C-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

141) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

142) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

143) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

144) a pleckstrin homology (PH) domain or a mutant thereof (*e.g.*, a sequence selected from **Table 4**), a N-terminal fragment of the capsid protein of the HERVK-113 gag, a leucine zipper, and a particle budding motif (*e.g.*, a sequence selected from Table 5);

[0149] In some cases, each of the configurations 1) to 144) listed in the preceding paragraph independently comprises a QP1 domain at the C-terminus of the plasma membrane recruitment element. In some cases, each of the configurations 1) to 144) listed above independently comprises a QP2 domain at the C-terminus of the plasma membrane recruitment element. In some cases, each of the configurations 1) to 144) listed above independently comprises a QP1 and a QP2 domain at the C-terminus of the plasma membrane recruitment element. In some cases, each of the configurations 1) to 144) listed above independently lacks a HERVK-113 gag endogenous protease cleavage sequence. In some cases, each of the configurations 1) to 144) listed above independently comprises a mutant HERVK-113 gag endogenous protease cleavage sequence that cannot be recognized and cleaved by an HERVK-113 protease. In some cases, in any one of configurations 1) to 144) listed above, the C-terminal fragment of capsid protein of the HIV gag comprises the major homology region (MHR). In some cases, each of the configurations 1) to 144) listed above is fused to a membrane penetrating peptide (*e.g.*, a sequence selected from Table 6). In some cases, each of the configurations 1) to 144) listed above is fused to a post-translational modification motif on the N-terminus or the C-terminus (*e.g.*, a sequence selected from

Table 7). In some cases, the plasma membrane recruitment element comprises one, two, or three particle budding motif, each of which is selected from a sequence listed in Table 5. In some cases, in any one of the configurations 1) to 72) listed above, a pleckstrin homology (PH) domain or a mutant thereof (*e.g.,* a sequence selected from **Table 4)** is fused the N-terminal of the fragment of the matrix protein, wherein the fragment of the matrix protein lacks a N-terminal myristoylation motif, a N-terminal glycine, a highly basic region (HBR), a N-terminal fragment, or any combinations thereof. In some cases, the plasma membrane recruitment element consists essentially of the domains in each of the configurations 1) to 144) listed in the preceding paragraph. In some cases, the plasma membrane recruitment element consists of the domains in each of the configurations 1) to 144) listed in the preceding paragraph.

CHIMERIC PROTEIN

[0150] In aspects, the present disclosure provides a chimeric protein comprising a plasma membrane recruitment element described herein (*e.g.*, a mutant gag polyprotein) and a payload that is a protein or a fragment thereof. In some aspects, the lipid delivery particle comprises a chimeric protein comprising a plasma membrane recruitment element and a payload that is a protein or a fragment thereof. In some cases, the plasma membrane recruitment element and the payload are fused directly in the chimeric protein. In other cases, the plasma membrane recruitment element (*e.g.*, a mutant gag polyprotein) and the payload are fused indirectly via a linker. In some cases, the linker between the plasma membrane recruitment element (*e.g.*, a mutant gag polyprotein) and the payload is a cleavable linker that is recognized by a protease.

[0151] The chimeric protein (*e.g.*, comprising a gag protein) can form at least part of a protein core of the lipid delivery particle. A lipid delivery particle can comprise two or more chimeric proteins. The chimeric protein can include a structural protein. The structural protein can comprise a plasma membrane recruitment element (*e.g.*, retroviral gag protein). The plasma membrane recruitment element can be fused to a payload. In some cases, the two or more chimeric proteins comprise the same structural protein. In some cases, the two or more chimeric proteins comprise different structural proteins. In some cases, the two or more chimeric proteins comprise different payloads. In some cases, the chimeric protein comprises a payload that comprises a nucleic acid-binding moiety. In some cases, the payload further comprises a guide nucleic acid molecule that forms a ribonucleoprotein complex with the nucleic acid-binding moiety. In some cases, the chimeric protein is suitable for delivery by a lipid delivery particle disclosed herein.

[0152] In some cases, the lipid delivery particle of the present disclosure further comprises a protease that recognizes the cleavable linker in the chimeric protein and cuts the chimeric protein at the cleavable linker. In some cases, the protease is fused to a plasma membrane recruitment element described herein (*e.g,* a wild-type gag polyprotein, a mutant gag polyprotein described herein, a PH domain, or a fusion of PH-mutant gag polyprotein) with or without a cleavable linker. In some cases, the protease is encoded by a *pro* gene that is from the same source as the mutant gag polyprotein and can recognize and cleave a gag-endogenous protease cleavage sequence. In some cases, the protease is a heterologous protease that is from a different source from the mutant gag polyprotein. As a result of the cleavage at the cleavable linker by the protease, the payload can be separated from the plasma membrane recruitment element. In

some cases, the payload is present as a "free" entity separate from the plasma membrane recruitment element. For instance, the payload can be free and present within an inside of the lipid delivery particle (e.g., within an inside of a protein core of the lipid delivery particle). In some cases, the protease is part of a second chimeric protein comprising a second plasma membrane recruitment element and the protease, where the second plasma membrane recruitment element can be either different from or same as the plasma membrane recruitment element that is fused with the payload.

[0153] In some cases, the chimeric protein disclosed herein also comprises one or more non-cleavable linkers that operably link components together. The non-cleavable linker can be any suitable linker sequence that is used for chimeric protein construction, such as peptide linkers that consist of glycine (Gly) and serine (Ser) residues. In some embodiments, the non-cleavable linker comprises an amino acid sequence selected from the group consisting of: (GS)x (SEQ ID NO: 564), (GGS)x (SEQ ID NO: 565), (GGGGS)x (SEQ ID NO: 566), (GGSG)x (SEQ ID NO: 567), and (SGGG)x (SEQ ID NO: 568), and wherein x is an integer from 1 to 50.

[0154] In some cases, the chimeric protein of the present disclosure comprises a nuclear export signal (NES) sequence that can direct transport of the chimeric protein out of the nucleus of a cell, *e.g.*, a producer cell.

[0155] In some cases, the chimeric protein disclosed herein has one of the following configurations of components positioned in an order from N-terminus to C-terminus:

[0156] [plasma membrane recruitment element]-[cleavable linker]-[payload];

[0157] [plasma membrane recruitment element]-[n * NES]-[cleavable linker]-[payload];

[0158] [plasma membrane recruitment element]-[cleavable linker]-[payload]-[n * NES];

[0159] [plasma membrane recruitment element]-[cleavable linker]-[n * NES]-[payload];

[0160] [plasma membrane recruitment element]-[cleavable linker 1]-[payload]-[cleavable linker 2]-[n * NES];

[0161] [payload]-[cleavable linker]-[n * NES]-[plasma membrane recruitment element];

[0162] [payload]-[n * NES]-[cleavable linker]-[plasma membrane recruitment element];

[0163] [n * NES]-[payload]-[cleavable linker]-[plasma membrane recruitment element];

[0164] [n * NES]-[cleavable linker 1]-[payload]-[cleavable linker 2]-[plasma membrane recruitment element]; and

[0165] [payload]-[cleavable linker]-[plasma membrane recruitment element];

[0166] wherein n is an integer in the range of from 1 to 10, and denotes the number of repeats of the NES sequence. Non-cleavable linker sequence can be present or absent in any of the foregoing configurations between any two neighboring components. As provided herein, the payload sequence in the chimeric protein can have one or more NLS sequences, at its N-terminus, C-terminus, or both.

[0167] [n * NES]-[cleavable linker 1]-[payload]-[cleavable linker 2]-[plasma membrane recruitment element]; and

[0168] [payload]-[cleavable linker]-[plasma membrane recruitment element];

[0169] wherein n is an integer in the range of from 1 to 10, and denotes the number of repeats of the NES sequence. Non-cleavable linker sequence can be present or absent in any of the foregoing configurations between any two neighboring components. As provided herein, the payload sequence in the chimeric protein can have one or more NLS sequences, at its N-terminus, C-terminus, or both.

Nuclear Export Signal

[0170] Direction of nuclear transport within the cell can be governed by nuclear targeting signals within payload proteins or coupled to (*e.g.*, fused with) the payload proteins. As used herein, the term "nuclear export signal" refers to a sequence of amino acids that targets a payload protein for export from the nucleus. In some cases, a nuclear export signal (NES) is a short target peptide sequence containing four hydrophobic residues. These residues target the protein for export from the nucleus to the cytoplasm through the nuclear pore complex. A chimeric protein provided herein can comprise 1 NES, 2 NESs, 3 NESs, 4 NESs, 5 NESs, 6 NESs, 7 NESs, 8 NESs, 9 NESs, or 10 NESs. In some cases, the NES is located at the N-terminus, C-terminus, or in an internal region of the chimeric protein. In some cases, a NES is coupled between the plasma membrane recruitment element and the payload in the chimeric protein. In some cases, there is a cleavable linker between the plasma membrane recruitment element and the payload in the chimeric protein, and one or more NESs present on the same of the cleavable linker as the plasma membrane recruitment element.

[0171] In some cases, the NES sequence that is used in the chimeric protein comprises LQLPPLERLTL (SEQ ID NO: 403) derived from HIV-1 Rev protein, or any of the sequences having at least 80% identity thereto. In some cases, the NES sequence comprises NELALKLAGLDI (SEQ ID NO: 416) or LALKLAGLDI (SEQ ID NO: 352) derived from PKIα, or any of the sequences having at least 80% identity thereto. In some cases, the NES sequence that is used in the chimeric protein comprises an amino acid sequence as set forth in **Table 8**. In some cases, the NES sequence comprises any one of the sequences set forth in **Table 8**. In some cases, the NES sequence comprises one or more of the sequences set forth in **Table 8**. In some cases, the NES sequence comprises more than one, more than two, more than three, more than four, more than five, more than six, more than seven, more than eight, more than nine, or more than ten of the sequences set forth in **Table 8**. In some cases, the NES sequences comprises multiple sequences set forth in **Table 8**.

[0172] In some cases, the NES sequence comprises an amino acid sequence having 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to any one of sequences listed in **Table 8**. In some cases, the NES sequence comprises an amino acid sequence having 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to any sequence set forth in **SEQ ID NOs: 352-453**. In some cases, the NES sequence comprises an amino acid sequence set forth in **SEQ ID NOs: 352-453.** In some cases, the NES sequence described herein comprises a sequence with greater than 80% sequence identity to any sequence listed in **Table 8**. The transport of payload proteins within a cell is enabled through both NES and nuclear export receptors. In some cases, the NES described herein is associated with a nuclear export receptor (*e.g.,* CRM-1). In some cases, the NES may be conditionally active or inactive. In some cases, the NES sequence disclosed herein comprises a sequence such as those

described in T la Cour, et al., Nucleic Acids Res. 2003;31(1):393-396; and Xu D, et al. *Mol Biol Cell.* 2012 Sep;23(18):3673-6, each of which is incorporated herein by reference in its entirety. Any of the NES sequences described in the NES sequence database (NESdb©; prodata.swmed.edu/LRNes) or (NESbase; services.healthtech.dtu.dk/datasets/NESbase-1.0) can be used in a chimeric protein disclosed herein, *e.g.*, for the purpose of packaging a payload into the molecular assembly, *e.g.*, the lipid delivery particle.

[0173] In some cases, a chimeric protein disclosed herein include a nuclear export sequence (NES). In some cases, the NES facilitates localization of the chimeric protein in the cytosol of a target cell relative to the nucleus.

[0174] In some cases, a chimeric protein disclosed herein includes at least one NES sequences, such as, 2 or more, 3 or more, 4 or more, or 5 or more NES sequences. In some cases, one or more NES sequences (2 or more, 3 or more, 4 or more, or 5 or more NES sequences) are positioned at or near (*e.g.*, within 50 amino acids of) the N-terminus and/or the C- terminus of the chimeric protein. In some cases, the chimeric protein disclosed herein comprises only one NES sequence. In some cases, the chimeric protein disclosed herein comprises two NES sequences. In some cases, the chimeric protein disclosed herein comprises three NES sequences. In some cases, one or more NES sequences (2 or more, 3 or more, 4 or more, or 5 or more NES sequences) are positioned at or near (*e.g.*, within 50 amino acids of) the N-terminus of the chimeric protein. In some cases, one or more NES sequences (2 or more, 3 or more, 4 or more, or 5 or more NES sequences) are positioned at or near (*e.g.*, within 50 amino acids of) the C-terminus of the chimeric protein. In some cases, one or more NES sequences (3 or more, 4 or more, or 5 or more NES sequences) are positioned at or near (*e.g.*, within 50 amino acids of) both the N-terminus and the C-terminus of the chimeric protein. In some cases, an NES sequence is positioned at the N-terminus and an NES sequence is positioned at the C-terminus of the chimeric protein.

[0175] In some cases, a payload is a protein that is delivered as part of the chimeric protein disclosed herein, *e.g.*, operably linked to a structural protein (*e.g.*, human endogenous retroviral structural protein or a Plasma membrane recruitment element). In some embodiments, the one or more NES sequences are positioned at or near the one or both ends of the payload protein sequence inside the chimeric protein. For example, in some cases, one or more NES sequences (2 or more, 3 or more, 4 or more, or 5 or more NES sequences) are positioned at or near (*e.g.*, within 50 amino acids of) the N-terminus and/or the C-terminus of the payload protein sequence. In some cases, one or more NES sequences (2 or more, 3 or more, 4 or more, or 5 or more NES sequences) are positioned at or near (*e.g.*, within 50 amino acids of) the N-terminus of the payload protein sequence. In some cases, one or more NES sequences (2 or more, 3 or more, 4 or more, or 5 or more NES sequences) are positioned at or near (*e.g.*, within 50 amino acids of) the C-terminus of the payload protein sequence. In some cases, one or more NES sequences (3 or more, 4 or more, or 5 or more NES sequences) are positioned at or near (*e.g.*, within 50 amino acids of) both the N-terminus and the C-terminus of the payload protein sequence. In some cases, an NES sequence is positioned at the N-terminus and an NES sequence is positioned at the C-terminus of the payload protein sequence. In some cases, the chimeric protein disclosed herein comprises only one NES sequence. In

some cases, the chimeric protein comprises only one NES sequence, and the NES sequence is positioned at or near (*e.g.*, within 50 amino acids of) the N-terminus of the payload protein.

[0176] In eukaryotic cells, transport of proteins between the nucleus and the cytoplasm can be mediated by transport factors in the karyopherin-β family, which are also known as importins and exportins. The direction of nuclear–cytoplasmic transport can be dictated by nuclear targeting signals within the payload proteins. Nuclear export sequences (NESs) can direct export of proteins from the nucleus to the cytoplasm. NESs can bind directly to the export karyopherin CRM1 (also known as exportin 1), which can escort payload proteins through the nuclear pore complex.

Table 8. Exemplary nuclear export signals and their sequences

NES sequence	Protein from which NES can be derived	SEQ ID NO:
LALKLAGLDI	PKIα	352
AAEPVILDLRDLFQL	Dab1	353
AGVEAIIRILQQLLF	Vpr	354
AHWMRQLVSFQKLKL	Tbx5	355
AKIIPYSGLLLVITV	RSV M	356
ANMRIQDLKVSLKPL	MK5	357
AQLQNLTKRIDSLPL	APC protein	358
ATMRVDYEQIKIKKI	MK5	359
ATRELDELMASLSDF	Paxillin	360
CAFLSVKKQFEELTL	Survivin	361
DELLQVLRMMVGVNI	CHP1	362
DHAEKVAEKLEALSV	RanBP1	363
DMDFLRNLFSQTLSL	SIRT2	364
DTVLDILRDFFELRL	Topo IIα	365
DVKEEMTSALATMRV	MK2	366
EAINKLENNLRELQI	c-Abl	367
EAINKLESNLRELQI	c-Abl	368
EAIQDLCLAVEEVSL	NPM mutA	369
EESYDLTSHLARLGV	LEI	370
EESYTLNSDLARLGV	LEI	371
EFSLPTHHTVRLIRV	N protein	372
EGCVSNLMV	p28GANK	373
EIVRDIKEKLCYVAL	Actin	374
ENFEILMKLKESLEL	p73	375
EQLLEIVHDLENLSL	Hst2	376
ERFEMFRELNEALEL	p53	377
ESSAEDLRTLQQLFL	E7	378
FETVYELTKMCTIR	Smad1	379
FETVYELTKMCTIRM	Smad1	380
FNATAVVRHMRKLQL	CaMKIα	381
GIQQAHAEQLANMRI	MK5	382
GNYKKPKLGGSGLALKLAGLDL	Human FGF1 + GGSG (SEQ ID NO: 540) + Protein Kinase Inhibitor α NES	383
GNYKKPKLGGSGLQLPPLERLTL	Human FGF1 + GGSG (SEQ ID NO: 540) + HIV REV NES	384
GNYKKPKLGGSGLSAQLYSSLSLD	Human FGF1 + HTLV 1 Rex Protein NES	385
GNYKKPKLGGSGLTDWARVREEL	Human FGF1 + GGSG (SEQ ID NO: 540) + RSV gag NES	386

GNYKKPKLGGSGQLVEELLKIICAFQL	Human FGF1 + BRCA1 NES	387
GNYKKPKLGGSGVKGVGTMVMELIRMI	Human FGF1 + Influenza A NP NES	388
GNYKKPKLGNYKKPKL	Human FGF1 (2x sequence)	389
GNYKKPKLGNYKKPKLGNYKKPKL	Human FGF1 (3x sequence)	390
ISFTEFVKVLEKVDV	CHP1g	391
ISPEHVIQALESLGF	NC2β	392
IVLNQLCVRFFGLDL	nsP2	393
KKRKKKRK	RSV gag (2x sequence)	394
KKRKKKRKKKRK	RSV gag (3x sequence)	395
KKRKKKRKKKRKKKRK	RSV gag (4x sequence)	396
KQVLWDRTFSLFQQL	Stat1	397
KVYPIILRLGSNLSL	ORF-9b	398
LALKLAGLDL	Protein Kinase Inhibitor α	399
LEPLKKLECLKSLDL	APRIL	400
LINRNGELKLANFGL	Cdk5-p27	401
LQGEEFVCLKSIILL	ERα	402
LQLPPLERLTL	HIV REV (NES)	403
LQSEEVHWLHLDMGV	FAK1	404
LQVRKYSLDLASLIL	FAK1	405
LRSEEVHWLHVDMGV	FAK1	406
LSAQLYSSLSLD	HTLV 1 Rex Protein	407
LSSHFQELSI	ADAR1	408
LTDWARVREEL	RSV gag	409
MEELSQALASSFSV	Snurportin	410
MEGCVSNLMV	p28GANK	411
MESAITLWQFLLQL	Net	412
MNFKELKDFLKELNI	PLC-δ1	413
MSSGYYLGEILRLAL	Hxk2	414
NDENEHQLSLRTVSL	NPM	415
NELALKLAGLDI	PKIα	416
NHRMKNLREISQLGI	Gal3	417
NHRVKKLNEISKLGI	Gal3	418
NSVNEILSEFYYVRL	Top2	419
NVMKYFTDLFDYLPL	PP2ACα	420
PAAKRVKLDGGSGLALKLAGLDL	C Myc + GGSG (SEQ ID NO: 540) + Protein Kinase Inhibitor α NES	421
PAAKRVKLDGGSGLQLPPLERLTL	C Myc + GGSG (SEQ ID NO: 540) + HIV REV NES	422
PAAKRVKLDGGSGLTDWARVREEL	C Myc + GGSG (SEQ ID NO: 540) + RSV gag NES	423
PAAKRVKLDLSAQLYSSLSLD	C Myc + HTLV 1 Rex Protein NES	424
PAAKRVKLDQLVEELLKIICAFQL	C Myc + BRCA1 NES	425
PAAKRVKLDVKGVGTMVMELIRMI	C Myc + Influenza A NP NES	426
PKYSDIDVDGLCSEL	Yap1p	427
PLQLPPLERLTL	HIV-REV	428
PSAHEITGLADSLQL	Oct-6	429
PSVQELTEQIHRLLM	mPER2	430
QARFILEKIDGKIII	Topo IIαg	431
QLVEELLKIICAFQL	BRCA1	432
QSTHVDIRTLEDLLM	E7	433
QVKFIKMIIEKELTV	Top2	434
RQERKRPLLDLHIEL	FLIP-L	435

RRIYDITNVLEGIGL	E2F4	436
SDQKQEQLLLKKMYL	Stat1	437
SGIFGLVTNLEELEV	STRADα	438
SGKASSSLGLQDFDL	λPKC	439
SLGGFEITPPVVLRL	NPM	440
STNGSLAAEFRHLQL	Stat1	441
SVMLAVQEGIDLLTF	E1A	442
TEKHLQKYLRQDLRL	DcpS	443
TGVEALIRILQQLLF	VPR protein	444
THYGQKAILFLPLPV	FGF-1	445
TNLEALQKKLEELEL	MAPKK1/MEK1	446
VDLACTPTDVRDVDI	Cyclin D1	447
VKGVGTMVMELIRMI	Influenza A NP	448
VPKELMQQIENFEKI	Hxk2	449
VRLHDVLHSDKKLTL	Cdk5-p27	450
YAGFSLPHAILRIDL	Actin	451
YGEKTTQRDLTELEI	p38	452
YQNIELITFINALKL	BPV E1	453

Nuclear Localization Signal

[0177] In some instances, a payload described herein comprises one or more nuclear localization sequences (NLS). As used herein, the term "nuclear localization signal" refers to a sequence of amino acids that targets a payload *(e.g.*, a protein or a short polypeptide), which the NLS is present within or coupled to, to localize to the nucleus. In some cases, an NLS facilitates the import of a polypeptide comprising an NLS into the cell nucleus. A polypeptide can comprise 1 NLS, 2 NLSs, 3 NLSs, 4 NLSs, 5 NLSs, 6 NLSs, 7 NLSs, 8 NLSs, 9 NLSs, or 10 NLSs. In some cases, the NLS is located at the N-terminus, C-terminus, or in an internal region of the polypeptide. In some cases, a NLS is coupled to a nucleic acid binding domain described elsewhere herein. In some cases, a NLS is coupled to a nucleic acid modifying domain described elsewhere herein. In some cases, a NLS is coupled to a guidable polypeptide domain, a deaminase domain, or a reverse transcriptase domain. In some cases, a NLS is covalently linked to a nucleic acid binding domain described elsewhere herein. In some cases, a NLS is covalently linked to a nucleic acid modifying domain described elsewhere herein. In some cases, a NLS is covalently linked to a guidable polypeptide domain, a deaminase domain, or a reverse transcriptase domain. In some cases, a nucleic acid binding domain does not comprise an NLS. In some cases, a nucleic acid binding domain does not comprise an NLS. In some cases, a guidable polypeptide domain, a deaminase domain, or a reverse transcriptase domain does not comprise an NLS. Examples of NLS are provided in **Table 9** below.

[0178] In some cases, the NLS comprises an amino acid sequence as set forth in **Table 9**. In some cases, the NLS comprises any one of the sequences set forth in **Table 9**. In some cases, the NLS comprises one or more of the sequences set forth in **Table 9**. In some cases, the NLS comprises more than one of the sequences set forth in **Table 9**. In some cases, the NLS comprises multiple sequences set forth in **Table 9.** In some cases, NLS sequence can comprise an amino acid sequence having 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to any sequence listed in **Table 9**. In some cases, the NLS sequence described herein can comprise a sequence with greater than 80% sequence

identity to any sequence listed in **Table 9**. In some cases, the NLS sequence can comprise an amino acid sequence having 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to any sequence set forth in **SEQ ID NOs: 454-477 or 541-559.** In some cases, the NLS sequence can comprise an amino acid sequence set forth in **SEQ ID NOs: 454-477 or 541-559.**

[0179] In some cases, a chimeric protein disclosed herein includes a nuclear localization sequence (NLS). In some cases, the NLS facilitates delivery of the chimeric protein, or a payload released from the chimeric protein (for instance, released from the chimeric protein following cleavage of a cleavable linker), into the nucleus of a target cell.

[0180] In some cases, a payload is a protein and is delivered as part of the chimeric protein disclosed herein, *e.g.*, operably linked to a structural protein (*e.g.*, plasma membrane recruitment element). In some embodiments, the one or more NLS sequences are positioned at or near the one or both ends of the payload protein sequence of the chimeric protein. In some cases, a chimeric protein includes (*e.g.*, is fused to) between 2 and 5 NLS sequences (*e.g.*, 2-4, or 2-3 NLSs). Examples of NLS sequences include an NLS sequence derived from: the NLS of the SV40 virus large T-antigen, having the amino acid sequence PKKKRKV (SEQ ID NO: 468); the NLS from nucleoplasmin (*e.g.*, the nucleoplasmin bipartite NLS with the sequence KRPAATKKAGQAKKKK (SEQ ID NO: 460); the c-myc NLS having the amino acid sequence PAAKRVKLD (SEQ ID NO: 467) or RQRRNELKRSP (SEQ ID NO: 541); the hRNPAl M9 NLS having the sequence NQSSNFGPMKGGNFGGRSSGPYGGGGQYFAKPRNQGGY (SEQ ID NO: 542); the sequence RMRIZFKNKGKDTAELRRRRVEVSVELRKAKKDEQILKRRNV (SEQ ID NO: 543) of the IBB domain from importin-alpha; the sequences VSRKRPRP (SEQ ID NO: 477) and PPKKARED (SEQ ID NO: 544) of the myoma T protein; the sequence PQPKKKPL (SEQ ID NO: 545) of human p53; the sequence SALIKKKKKMAP (SEQ ID NO: 546) of mouse c-abl IV; the sequences DRLRR (SEQ ID NO: 547) and PKQKKRK (SEQ ID NO: 548) of the influenza virus NS1; the sequence RKLKKKIKKL (SEQ ID NO: 549) of the Hepatitis virus delta antigen; the sequence REKKKFLKRR (SEQ ID NO: 550) of the mouse Mxl protein; the sequence KRKGDE VDGVDEV AKKKS KK (SEQ ID NO: 551) of the human poly(ADP-ribose) polymerase; and the sequence RKCLQAGMNLEARKTKK (SEQ ID NO: 552) of the steroid hormone receptors (human) glucocorticoid, and sequences having at least 80% identity to the foregoing. In some cases, an NLS comprises the amino acid sequence MDSLLMNRRKFLY QFKNVRWAKGRRETYLC (SEQ ID NO: 553).

[0181] Other examples of an NLS sequence include KRTADGSEFESPKKKRKV (SEQ ID NO: 462), KKTELQTTNAENKTKKL (SEQ ID NO: 554), KRGINDRNFWRGENGRKTR (SEQ ID NO: 555), RKSGKIAAIVVKRPRK (SEQ ID NO: 556), and MDSLLMNRRKFLYQFKNVRWAKGRRETYLC (SEQ ID NO: 463), SPKKKRKVEAS (SEQ ID NO: 557), encoded by AGCCCCAAGAAgAAGAGaAAGGTGGAGGCCAGC (SEQ ID NO: 558), GPKKKRKVAAA (SEQ ID NO: 559), as well as any of those described in Cokol *et al.*, *EMBO Rep.*, 2000, 1(5): 411-415 and Freitas *et al.*, *Current Genomics*, 2009, 10(8): 550-7; Lu, J., et la., *Cell Commun Signal* 19, 60 (2021); international publication no. WO/2001/038547, each of which is incorporated herein by reference in its entirety, and sequences having at least 80% identity to the foregoing.

[0182] In some embodiments, the chimeric protein comprises one NES sequence and two NLS sequences. In some cases of these embodiments, the NES sequence, NLS sequences, and the payload protein sequence are positioned in an order from N-terminus to C-terminus as follows: NES-NLS-payload protein-NLS. In some embodiments, the chimeric protein comprises two or more NES sequences and two NLS sequences. In some cases of these embodiments, the NES sequences, NLS sequences, and the payload protein sequence are positioned in an order from N-terminus to C-terminus as follows: n X NES (n >=2)-NLS-payload protein-NLS.

Table 9. Exemplary NLS sequences

Amino Acid Sequence	Protein from which NLS can be derived	SEQ ID NO:
AVKRPAATKKAGQAKKKKLD	NUCLEOPLASMIN	454
EGAPPAKRAR	HEPATITIS D VIRUS ANTIGEN	455
GNYKKPKL	Human FGF1	456
KGINDRNFWRGENGRRTR	Influenza A NP	457
KKRK	RSVgag	458
KLKIKRPVK	TUS-PROTEIN	459
KRPAATKKAGQAKKKK	Nucleoplasmin	460
KRTADGSEFEPKKKRKV	Plasma Derived Variant	461
KRTADGSEFESPKKKRKV	BIPARTITE SV40	462
MDSLLMNRRKFLYQFKNVRWAKGRRETYLC	AID	463
DSLLMNRRKFLYQFKNVRWAKGRRETYLC	AID	464
MKRTADGSEFESPKKKRKV	BIPARTITE SV40	465
MSRRRKANPTKLSENAKKLAKEVEN	EGL-13	466
PAAKRVKLD	C-MYC	467
PKKKRKV	Simian Virus	468
PKKKRKVEDPYC	SV40LargeTAntigen	469
PKKKRKVPKKKRKV	Simian Virus (2x sequence)	470
PKKKRKVPKKKRKVPKKKRKV	Simian Virus (3x sequence)	471
PKTRRQRTRRARRNRPPT	HTLV Rex Protein	472
PPQPKKKPLDGE	MURINE P53	473
SGGSKRTADGSEFEPKKKRKV	PE1 AND PE2	474
TKGTKRSYEQM	Influenza A NP	475
TKGTKRSYEQMTKGTKRSYEQM	Influenza A NP(2x sequence)	476
VSRKRPRP	POLYOMA LARGE T-AG	477
RQRRNELKRSP	C-MYC	541
NQSSNFGPMKGGNFGGRSSGPYGGGGQYFAKPR NQGGY	hRNPAl M9	542
RMRIZFKNKGKDTAELRRRRVEVSVELRKAKKD EQILKRRNV	Importin-alpha	543
PPKKARED	Myoma T	544
PQPKKKPL	Human p53	545
SALIKKKKKMAP	Mouse c-abl IV	546
DRLRR	Influenza virus NS1	547
PKQKKRK	Influenza virus NS1	548
RKLKKKIKKL	Hepatitis virus delta antigen	549
REKKKFLKRR	Mouse Mxl protein	550
KRKGDEVDGVDEVAKKKSKK	Human poly(ADP-ribose) polymerase	551
RKCLQAGMNLEARKTKK	Glucocorticoid receptor	552

MDSLLMNRRKFLYQFKNVRWAKGRRETYLC	Activation-induced Cytidine Deaminase	553
KKTELQTTNAENKTKKL	Kanadaptin	554
KRGINDRNFWRGENGRKTR	Influenza A nucleoprotein	555
RKSGKIAAIVVKRPRK	Tight junction protein ZO-2	556
SPKKKRKVEAS	Cas9	557
AGCCCCAAGAAgAAGAGaAAGGTGGAGGCCAGC	Cas9	558
GPKKKRKVAAA	Cas9	559

Cleavable Linker

[0183] In some cases, the chimeric protein comprises a cleavable linker in between two or more components. For instance, the chimeric protein can comprise a cleavable linker between a payload protein sequence and a plasma membrane recruitment element sequence (e.g., retroviral gag protein sequence). In some cases, the cleavable linker separates the plasma membrane recruitment element sequence from a NLS sequence, and/or a NES sequence at its N-terminus or C-terminus. The cleavable linker can separate the payload protein sequence from the plasma membrane recruitment element sequence, NLS sequence, and/or NES sequence at its N-terminus or C-terminus. Examples of cleavable linker sequences that can be used in the chimeric protein include TSTLLMENSS (SEQ ID NO: 560), PRSSLYPALTP (SEQ ID NO: 561), VQALVLTQ (SEQ ID NO: 562), and PLQVLTLNIERR (SEQ ID NO: 563), and sequences having at least 80% identity to any one of the foregoing.

PAYLOAD

[0184] A payload in a lipid delivery particle of the present disclosure can comprise a protein, a polypeptide, a nucleic acid (e.g., DNA or RNA), or any combinations thereof.

[0185] The payload can be a part of the chimeric protein disclosed herein or can comprise a part of the chimeric protein disclosed herein. Alternatively or additionally, the payload can include an entity in the lipid delivery particle separate from the chimeric protein disclosed herein. For instance, in some cases, the payload is a protein or polypeptide coupled to a plasma membrane recruitment element. In some cases, the payload comprises a first moiety (e.g., a nucleic acid-binding protein) that is fused to a plasma membrane recruitment element, and further comprises a second moiety that is coupled to the first moiety via covalent or non-covalent interaction. For instance, the first moiety can be a nucleic acid binding protein that is fused with the plasma membrane recruitment element, and the second moiety can be a nucleic acid molecule that binds to the nucleic acid binding protein.

[0186] In some cases, a payload is directly packaged within the lipid delivery particles and delivered into a target cell in its free form. In some cases, a payload can be fused to a plasma membrane recruitment element (e.g., pleckstrin homology domain) and form a chimeric protein as part of the lipid delivery particles, and then delivered into the target cell. In some cases, the plasma membrane recruitment element (e.g., pleckstrin homology domain) forms at least part of a protein core of the lipid delivery particle. In some embodiments, the payload in its free form or as part of a chimeric protein is within the inside cavity of the protein core of the lipid delivery particles disclosed herein. In some cases, the payload in its free form derives from a cleavage of the chimeric protein comprising the payload.

[0187] In some cases, a lipid delivery particle can deliver more than one payload. Each of the payloads can independently comprise nucleic acid-binding moiety, a nucleic acid-modifying moiety, a fusion protein, or a nucleic acid, or any combinations thereof.

[0188] In some embodiments, the plasma membrane recruitment element and the payload are coupled via any suitable method. Covalent coupling between the plasma membrane recruitment element and a payload peptide can include inteins that can form peptide bonds, direct protein-protein chimeras generated from a single reading frame. In some cases, nucleic acids base pairing to other nucleic acids via hydrogen bonding interactions (*e.g.,* DNA/RNA, DNA/DNA, or RNA/RNA hybrids), protein-protein binding, or protein-nucleic acid molecule binding can be involved for the coupling between the plasma membrane recruitment element and the payload. Examples of protein-nucleic acid molecule binding include an RNA binding protein (RBP) and an RBP binding sequence (*e.g.,* an RNA) that binds to the RBP. In some embodiments, each of the plasma membrane recruitment element and the payload is fused to a heterologous sequence, and the two heterologous sequences dimerize or multimerize with or without the need for a chemical compound to induce the protein-protein binding, such as a single-stranded nucleic acid sequence or protein dimerization domains). In some embodiments, each of the plasma membrane recruitment element and the payload is fused to one member of a pair of binding partners (*e.g.,* antibody and its target antigen). In some embodiments, the plasma membrane recruitment element is fused to an RBP and the payload is fused to a RBP binding sequence. Examples of suitable protein domains or nucleic acid molecules for forming the non-covalent connections include single chain variable fragments, nanobodies, affibodies, DmrA/DmrB/DmrC, FKBP/FRB, dDZFs, Leucine zippers, proteins that bind to DNA and/or RNA, optogenetic protein domains that can dimerize or multimerize in the presence of certain light wavelengths, proteins with quaternary structural interactions, and/or naturally reconstituting split proteins. Examples of RBPs and their RBP binding sequences that can be used include a sequence having at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in in **Table 13**.

[0189] Examples of RBPs and their RBP binding sequences that can be used include a sequence having at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a sequence set forth in any one of **SEQ ID NOs: 478-513**. In some cases, the RBP comprises an amino acid sequence as set forth in **Table 13**. In some cases, the RBP comprises any one of the sequences set forth in **Table 13**. In some cases, the RBP comprises one or more of the sequences set forth in **Table 13**. In some cases, the RBP comprises more than one of the sequences set forth in **Table 13**. In some cases, the RBP comprises multiple sequences set forth in **Table 13.** In some cases, the RBP binding sequence comprises an amino acid sequence as set forth in **Table 13**. In some cases, the RBP binding sequence comprises any one of the sequences set forth in **Table 13**. In some cases, the RBP binding sequence comprises one or more of the sequences set forth in **Table 13**. In some cases, the RBP binding sequence comprises more than one of the sequences set forth in **Table 13**. In some cases, the RBP binding sequence comprises multiple sequences set forth in **Table 13.**

Table 13. Exemplary RNA binding proteins (RBP) and corresponding RBP binding sequences

RBP	RBP Amino Acid Sequence	SEQ ID NO:	RBP binding sequence	SEQ ID NO:
MS2 (N55K)	MASNFTQFVLVDNGGTGDVTVAPSNFANGIAEWISSNSRSQAYKVTCSVRQSSAQKRKYTIKVEVPKVATQTVGGVELPVAAWRSYLNMELTIPIFATNSDCELIVKAMQGLLKDGNPIPSAIAANSGIY	478	GGGAGCACAUGAGGAUCACCCAUGUGCGACUCCCACAGUCACUGGGGAGUCUUCCC	502
	ASNFTQFVLVDNGGTGDVTVAPSNFANGIAEWISSNSRSQAYKVTCSVRQSSAQKRKYTIKVEVPKVATQTVGGVELPVAAWRSYLNMELTIPIFATNSDCELIVKAMQGLLKDGNPIPSAIAANSGIY	479		
Com	MGKSIRCKNCNKLLFKADSFDHIEIRCPRCKRHIIMLNACEHPTEKHCGKREKITHSDETVRY	480	CUGAAUGCCUGCGAGCAUC	503
	GKSIRCKNCNKLLFKADSFDHIEIRCPRCKRHIIMLNACEHPTEKHCGKREKITHSDETVRY	481		
PP7	MAKTIVLAVGEATRTLTEIQSTADRQIFEEKVGPLVGRLRLTASLRQNGAKTAYRVNLKLDQADVVDASTSVAGELPKVRYTQVWSHDVTIVANSTEASRKSLYDLTKSLVATSQVEDLVVNLVPLGRSLE	482	GGAGCAGACGAUAUGGCGUCGCUCCGGCC	504
	AKTIVLAVGEATRTLTEIQSTADRQIFEEKVGPLVGRLRLTASLRQNGAKTAYRVNLKLDQADVVDASTSVAGELPKVRYTQVWSHDVTIVANSTEASRKSLYDLTKSLVATSQVEDLVVNLVPLGRSLE	483		
TAT BP6.7	MAVPETRPNHTIYINNLNSKIKKDELKKSLYAIFSQFGQILDILVPRQRTPRGQAFVIFKEVSSATNALRSMQGFPFYDKPMRIQYAKTDKRIPAKMKGTFV	484	GGCCAGAUCUGAGCCUGGGAGCUCUCUGGCC	505
	AVPETRPNHTIYINNLNSKIKKDELKKSLYAIFSQFGQILDILVPRQRTPRGQAFVIFKEVSSATNALRSMQGFPFYDKPMRIQYAKTDKRIPAKMKGTFV	485		
SLBP	MADFETDESVLMRRQKQINYGKNTIAYDRYIKEVPRHLRQPGIHPKTPNKFKKYSRRSWDQQIKLWKVALHFWD	486	CAAACAAACAAACCAAAGGCUCUUCUCAGAGCCACCCA	506
	ADFETDESVLMRRQKQINYGKNTIAYDRYIKEVPRHLRQPGIHPKTPNKFKKYSRRSWDQQIKLWKVALHFWD	487		
L7Ae	MYVRFEVPEDMQNEALSLLEKVRESGKVKKGTNETTKAVERGLAKLVYIAEDVDPPEIVAHLPLLCEEKNVPYIYVKSKNDLGRAVGIEVPCASAAIINEGELRKELGSLVEKIKGLQK	488	GGGCGUGAUCCGAAAGGUGACCC	507
	YVRFEVPEDMQNEALSLLEKVRESGKVKKGTNETTKAVERGLAKLVYIAEDVDPPEIVAHLPLLCEEKNVPYIYVKSKNDLGRAVGIEVPCASAAIINEGELRKELGSLVEKIKGLQK	489		
Csy4 (H29A)	MGDHYLDIRLRPDPEFPPAQLMSVLFGKLAQALVAQGGDRIGVSFPDLDESRSRLGERLRIHASADDLRALLARPWLEGLRDHLQFGEPAVVPHPTPYRQVSRVQAKSNPERLRRRLMRRHDLSEEEARKRIPDTVARALDLPFVTLRSQSTGQHFRLFIRHGPLQVTAEEGGFTCYGLSKGGFVPWF	490	GUUCACUGCCGUAUAGGCAGCUAAGAAA	508
	GDHYLDIRLRPDPEFPPAQLMSVLFGKLAQALVAQGGDRIGVSFPDLDESRSRLGERLRIHASADDLRALLARPWLEGLRDHLQFGEPAVVPHPTPYRQVSRVQAKSNPERLRRRLMRRHDLSEEEARKRIPDTVARALDLPFVTLRSQSTGQHFRLFIRHGPLQVTAEEGGFTCYGLSKGGFVPWF	491		
Lambda N	MDAQTRRRERRAEKQAQWKAANPLLVGVSAKPVNRPILSLNRKPKSRVESALNPIDLTVLAEYHKQIESNLQRIERKNQRTWYSKPGERGITCSGRQKIKGKSIPLI	492	GGAUCCGGGCCCUGAAGAAG	509

	DAQTRRRERRAEKQAQWKAANPLLVGVSAKPVNRPILSL NRKPKSRVESALNPIDLTVLAEYHKQIESNLQRIERKNQ RTWYSKPGERGITCSGRQKIKGKSIPLI	493	GGCCCUUUCC UUU	
Lamb da N (non anti-termin ating)	MDAQTRRRERRAEERAQWKAAN	494	GCCCUGAAAA AGGGC	510
	DAQTRRRERRAEERAQWKAAN	495		
HTLV -1 Rex	MPKTRRRPRRSQRKRP	496	UAGGCGACGG UACGCAAGUA CUCUUGCGCC GGCCUA	511
	PKTRRRPRRSQRKRP	497		
HIV-1 REV	MTRQARRNRRRRWRERQR	498	GGCUGGACUC GUACUUCGGU ACUGGAGAAA CAGCC	512
	TRQARRNRRRRWRERQR	499		
U1A (U1hp II)	MHTIYINNLNEKIKKDELKKSLYAIFSQFGQILDILVSR SLKMRGQAFVIFKEVSSATNALRSMQGFPFYDKPMRIQY ART	500	AGCUUAUCCA UUGCACUCCG GAUGAGCU	513
	HTIYINNLNEKIKKDELKKSLYAIFSQFGQILDILVSRS LKMRGQAFVIFKEVSSATNALRSMQGFPFYDKPMRIQYA RT	501		

Nucleic acid binding domains and nucleic acid modifying domains

[0190] In some cases, the payload comprises a nucleic acid-binding moiety, a nucleic acid-modifying moiety, a fusion protein, or a nucleic acid. In some cases, the payload comprises a nucleic acid-binding domain, *e.g.,* a DNA-binding protein domain or polypeptide or an RNA-binding domain or polypeptide *e.g.,* an RNA-binding protein (RBP). A nucleic acid-binding moiety can be capable of binding a nucleic acid. A nucleic acid-binding domain can bind to a nucleic acid in a nonspecific or a site-specific manner.

[0191] In some cases, the nucleic acid-binding moiety binds to a nucleic acid in a site-specific manner. For example, a nucleic acid-binding moiety can comprise an aptamer binding domain that selectively binds to a specific target. In some cases, a nucleic acid-binding moiety recognizes a specific recognition sequence in the target nucleic acid. In some cases, a nucleic acid-binding moiety comprises an aptamer binding domain. In some cases, a nucleic acid binding moiety selectively binds to a sequence or a structural element in a nucleic acid molecule. In some cases, an RNA-binding domain selectively binds to a specific sequence motif in an RNA molecule. In some cases, a nucleic acid-binding moiety selectively binds to a structural element in a nucleic acid molecule. For example, a nucleic acid-binding domain can bind to a stem-loop in a nucleic acid molecule.

[0192] In some cases, a nucleic acid-binding moiety is or comprises a guidable polypeptide domain, a transcriptional regulatory domain, or a nucleic acid-modifying domain. A guidable polypeptide domain can be capable of binding to a polynucleotide (*e.g.,* an RNA guide) that can direct the guidable polypeptide domain a target site. In some cases, the guidable polypeptide domain forms a complex with the RNA guide and recognizes the target sequence through DNA-RNA base pairing. In some cases, a nucleic-acid binding moiety is or comprises a transcriptional regulatory domain. In other cases, a nucleic-binding moiety can help recruit a transcriptional repressor or activator to a target site. In some cases, a nucleic acid-binding moiety is or comprises a nucleic acid-modifying moiety. In some cases, the present

disclosure uses nucleic acid-binding moieties to recruit a nucleic acid-modifying moiety to a target site. In some cases, a nucleic-acid binding moiety comprises catalytic activity. In other cases, a nucleic acid-binding moiety is catalytically inactive. In some cases, a nucleic-acid binding moiety comprising catalytic activity is modified to have a reduced level of activity compared to its wild-type counterpart.

[0193] In some cases, the payload in the present disclosure comprises a nucleic acid modifying domain. A nucleic acid-modifying domain can comprise a polypeptide domain, a nucleic acid or a combination thereof (*e.g.,* a ribonucleoprotein complex). A nucleic acid-modifying domain can be capable of modifying nucleic acid, such as cleaving double-stranded nucleic acid; nicking a single-stranded nucleic acid; introducing a mutation, deletion, or insertion in a nucleic acid; methylating or demethylating a nucleic acid, or altering the structure of DNA (*e.g.,* changing chromatin structure through modifying histones). For example, a nucleic acid modifying domain can comprise a nuclease domain, a nickase domain, a deaminase domain, a polymerase, reverse transcriptase domain, a recombinase domain, a transposase domain, or an epigenetic modifying domain. A nuclease domain can be capable of cleaving phosphodiester bonds between nucleotides in nucleic acids. A nuclease domain can comprise an exonuclease (*e.g.,* a nuclease capable of cleaving nucleic acids from the ends) or an endonuclease (*e.g.,* a nuclease capable of cleaving nucleic acids in the middle). In some cases, a nucleic acid modifying effector or nucleic acid binding domain is a nickase, which can be capable of cleaving a single-strand in a double-stranded DNA. Nucleic acid modifying domains can be useful for gene editing, or for regulating, activating, or inhibiting gene expression.

Guidable polypeptide domain

[0194] In some cases, the payload in the present disclosure comprises a guidable polypeptide domain (*e.g.,* a CRISPR-Cas protein domain). In some cases, a guidable polypeptide domain is capable of binding to a polynucleotide (*e.g.,* a RNA guide) that directs it to a target site. In some cases, the guidable polypeptide domain forms a complex with the polynucleotide and recognizes the target sequence through DNA-RNA base pairing. In some cases, a guidable polypeptide domain is a CRISPR/CRISPR-associated (Cas) domain. A CRISPR domain can be a natural or an engineered domain. A Cas protein or domain can be derived from a CRISPR system or share structural and/or functional similarities to a protein involved in a CRISPR system.

[0195] In some cases, the guidable polypeptide domain is any suitable nuclease, e.g., a CRISPR-associated (Cas) protein or a Cas nuclease which functions in a non-naturally occurring CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas (CRISPR-associated) system. In bacteria, this system can provide adaptive immunity against foreign DNA (Barrangou, R., *et al*, "CRISPR provides acquired resistance against viruses in prokaryotes," Science (2007) 315: 1709-1712; Makarova, K.S., *et al*, "Evolution and classification of the CRISPR-Cas systems," Nat Rev Microbiol (2011) 9:467-477; Garneau, J. E., *et al*, "The CRISPR/Cas bacterial immune system cleaves bacteriophage and plasmid DNA," Nature (2010) 468:67-71 ; Sapranauskas, R., *et al*, "The Streptococcus thermophilus CRISPR/Cas system provides immunity in Escherichia coli," Nucleic Acids Res (2011) 39: 9275-9282).

[0196] Suitable nucleases include CRISPR-associated (Cas) proteins or Cas nucleases including type I CRISPR-associated (Cas) polypeptides, type II CRISPR-associated (Cas) polypeptides (*e.g.*, Cas9 or Cas14), type III CRISPR-associated (Cas) polypeptides, type IV CRISPR-associated (Cas) polypeptides, type V CRISPR-associated (Cas) polypeptides (*e.g.*, Cpf1/Cas12a, C2c1, or c2c3), and type VI CRISPR-associated (Cas) polypeptides (*e.g.*, C2c2/Cas13a, Cas13b, Cas13c, Cas13d).

[0197] A CRISPR system is a system encoding DNA sequence arrays known as clustered regularly interspaced short palindromic repeats (CRISPRs), which can be found in microbial genomes or phage genomes. In some cases, CRISPR systems comprise genes encoding CRISPR-associated (Cas) proteins and/or small RNA guide molecules (*e.g.,* crRNA or tracrRNA) that assemble with the CRISPR domain. In some cases, the CRISPR-Cas domain forms a complex with one or more RNA guide molecules to form an effector ribonucleoprotein complex. The effector ribonucleoprotein complex can recognize a target sequence through sequence specific DNA-RNA base pairing with a spacer sequence in the RNA guide. In some cases, target recognition activates one or more nuclease domains (*e.g.,* a RuvC domain or HNH domain) in the CRISPR domain to make a double-stranded cut at the target DNA. A CRISPR-Cas domain complexed with an RNA guide can be capable of inactivating target gene through a gene knockout. In some cases, the CRISPR domain is used to enable gene insertion and/or deletion, which can inactivate, modify, or restore the gene's function.

[0198] One or more components of a CRISPR/Cas system (*e.g.*, modified and/or unmodified) delivered by the lipid delivery particles disclosed herein can be utilized as a genome engineering tool in a wide variety of organisms including diverse mammals, animals, plants, and yeast. A CRISPR/Cas system can comprise a guide nucleic acid such as a guide RNA (gRNA) complexed with a Cas protein for targeted regulation of gene expression and/or activity or nucleic acid editing. An RNA-guided Cas protein (*e.g.*, a Cas nuclease such as a Cas9 nuclease) can specifically bind a target polynucleotide (*e.g.*, DNA) in a sequence-dependent manner. The Cas protein, if possessing nuclease activity, can cleave the DNA (Gasiunas, G., *et al*, "Cas9-crRNA ribonucleoprotein complex mediates specific DNA cleavage for adaptive immunity in bacteria," Proc Natl Acad Sci USA (2012) 109: E2579-E2 86; Jinek, M., *et al*, "A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity," Science (2012) 337:816-821; Sternberg, S. H., *et al*, "DNA interrogation by the CRISPR RNA-guided endonuclease Cas9," Nature (2014) 507:62; Deltcheva, E., *et al*, "CRISPR RNA maturation by trans-encoded small RNA and host factor RNase III," Nature (201 1) 471 :602-607), and has been widely used for programmable genome editing in a variety of organisms and model systems (Cong, L., *et al*, "Multiplex genome engineering using CRISPR Cas systems," Science (2013) 339:819-823; Jiang, W., *et al*, "RNA-guided editing of bacterial genomes using CRISPR-Cas systems," Nat. Biotechnol. (2013) 31: 233-239; Sander, J. D. & Joung, J. K, "CRISPR-Cas systems for editing, regulating and targeting genomes," Nature Biotechnol. (2014) 32:347-355).

[0199] In some cases, the Cas protein is mutated and/or modified to yield a nuclease deficient protein or a protein with decreased nuclease activity relative to a wild-type Cas protein. A nuclease deficient protein can retain the ability to bind DNA but can lack or have reduced nucleic acid cleavage activity. A protein

encoded by a donor sequence comprises a Cas nuclease (*e.g.*, retaining wild-type nuclease activity, having reduced nuclease activity, and/or lacking nuclease activity) can function in a CRISPR/Cas system to regulate the level and/or activity of a target gene or protein (*e.g.*, decrease, increase, or elimination). The Cas protein can bind to a target polynucleotide and prevent transcription by physical obstruction or edit a nucleic acid sequence to yield non-functional gene products. In some cases, the Cas protein cleaves both strands of DNA. In some cases, the Cas protein cleaves one strand of DNA.

[0200] In some embodiments, the nuclease is a Cas protein that forms a complex with a guide nucleic acid, such as a guide RNA (gRNA). In some embodiments, the donor sequence disclosed herein encodes a Cas protein that forms a complex with a single guide nucleic acid, such as a single guide RNA (sgRNA). In some embodiments, the donor sequence disclosed herein encodes a Cas protein that forms a complex with two separate RNA molecules of a dual guide nucleic acid (dgRNA). In some embodiments, the donor sequence in the lipid delivery particles disclosed herein comprises or encodes an RNA-binding protein (RBP) optionally complexed with a guide nucleic acid, such as a guide RNA (*e.g.*, sgRNA, dgRNA), which is able to form a complex with a Cas protein. In some embodiments, the gRNA comprises a scaffolding sequences that tethers the gRNA to the Cas protein. In some embodiments, the gRNA comprises a scaffolding sequence and a spacer sequence that directs the Cas protein to a specific locus. In some embodiments, the scaffolding sequence is configured to bind to the positively charged groves in the Cas9 protein. In some embodiments, the scaffolding sequence is configured to bind to the Cas protein in the payload. In some cases, Cas undergoes a conformational change when the gRNA binds to the target locus. In some cases, the conformational change in Cas shifts the molecule from an inactive, non-DNA binding conformation into an active DNA-binding conformation. In some cases, the Cas protein undergoes a confirmational change if the spacer sequence has sufficient homology to the sequence at the target locus. In some embodiments, gRNAs can be modified. Exemplary modifications to the gRNA are provided in United States Patent Number 11,479,767 B2, United States Patent Application Publication Number US2020/0339980 A1, and United States Patent Application Publication Number US2021/0079389 A1, each of which is incorporated herein by reference in its entirety.

[0201] One or more components of any suitable CRISPR/Cas system can be delivered by the lipid delivery particle described in the present disclosure. A CRISPR/Cas system can be referred to using a variety of naming systems. Exemplary naming systems are provided in Makarova, K.S. *et al*, "An updated evolutionary classification of CRISPR-Cas systems," Nat Rev Microbiol (2015) 13:722-736 and Shmakov, S. *et al*, "Discovery and Functional Characterization of Diverse Class 2 CRISPR-Cas Systems," Mol Cell (2015) 60:1-13. A CRISPR/Cas system can be a type I, a type II, a type III, a type IV, a type V, a type VI system, or any other suitable CRISPR/Cas system. A CRISPR/Cas system as used herein can be a Class 1, Class 2, or any other suitably classified CRISPR/Cas system. Class 1 or Class 2 determination can be based upon the genes encoding the effector module. Class 1 systems generally have a multi-subunit crRNA-effector complex, whereas Class 2 systems generally have a single protein, such as Cas9, Cpf1, C2c1, C2c2, C2c3, or a crRNA-effector complex. A Class 1 CRISPR/Cas system can use a complex of multiple Cas proteins to effect regulation. A Class 1 CRISPR/Cas system can comprise, for

example, type I (*e.g.*, I, IA, IB, IC, ID, IE, IF, IU), type III (*e.g.*, III, IIIA, IIIB, IIIC, IIID), and type IV (*e.g.*, IV, IVA, IVB) CRISPR/Cas type. A Class 2 CRISPR/Cas system can use a single large Cas protein to effect regulation. A Class 2 CRISPR/Cas systems can comprise, for example, type II (*e.g.*, II, IIA, IIB) and type V CRISPR/Cas type. CRISPR systems can be complementary to each other, and/or can lend functional units in trans to facilitate CRISPR locus targeting. Examples of Cas proteins that can be used as part of the CRISPR systems described herein include c2c1, Cas13a (formerly C2c2), Cas13b, Cas13c, Cas13d, c2c3, Cas1, Cas1B, Cas2, Cas3, Cas4, Cas5, Cas5e (CasD), Cas6, Cas6e, Cas6f, Cas7, Cas8a, Cas8al, Cas8a2, Cas8b, Cas8c, Cas9 (Csnl or Csxl2), Cas10, Cas10d, Cas14, Cas10, Cas10d, CasF, CasG, CasH, Cas12a (formerly Cpf1), Csy1, Csy2, Csy3, Cse1 (CasA), Cse2 (CasB), Cse3 (CasE), Cse4 (CasC), Csc1, Csc2, Csa5, Csn2, Csm2, Csm3, Csm4, Csm5, Csm6, Cmr1, Cmr3, Cmr4, Cmr5, Cmr6, Csb1, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CasX, Csx3, Csx1, Csx15, Csf1, Csf2, Csf3, Csf4, and Cul966, and homologs or modified versions thereof. Examples of mutant Cas9 proteins or Cas9 variants include SpG, SpCas9-NG. Cas9-NRNH, SpG, SpRY, Cas9-VQR, Cas9-EQR, SaCas9-KKH, Nme2Cas9, eNme2-C, eNme2-C.NR, eNme2-T.1, eNme2-T.2, SpRY, eSpCas9(1.1), SpCas9-HF1, nSpCas9, eSpCas9, Sniper-Cas9, HypaCas9, evoCas9, Cas9TX, HscCas9-v1.2, superFi-Cas9, efSaCas9, SaCas9-HF, Cas9-HF, Cas mini, SaCas9, SpCas9(H840A), dSpCas9, SpCas9(N863A), SpCas9(D839A), SpCas9(H983A), as well as others described in Chuang CK *et al.*, *Int J Mol Sci.* 2021 Sep 13;22(18):9872 and Li, T. et al., *Sig Transduct Target Ther* **8**, 36 (2023), each of which is incorporated herein by reference in its entirety.

[0202] A CRISPR system can comprise single subunit or multi-subunit effectors. In some cases, a CRISPR system is a Class 1 CRISPR system. A Class 1 CRISPR system can be a type I, type III, or a type IV system. A Class 1 type I CRISPR system can comprise a multi-subunit effector. In some cases, a Class 1 type I CRISPR system comprises a protein or domain in the Cascade-Cas3 protein complex. A Class 1 type I CRISPR system can comprise a Cas6, Cas7, Cas5, Cas11, Cas8, or Cas3 domain. A Class 1 type III CRISPR system can comprise a multi-subunit effector. In some cases, a Class 1 type III CRISPR system comprises a Csm complex or a Cmr complex. In some cases, a Class 1 type III CRISPR system comprises a Cas6, a Cas7 (Csm3 or Cmr4), a Cas7-related (Csm5, Cmr1, or Cmr6), a Cas5 (e.g., Csm4 or Cmr5), a Cas11 (e.g., Csm2 or Cmr3), or a Cas10 (e.g., Csm1 or Cmr2) domain. A Class 1 type IV CRISPR system can comprise a Cas6, a Cas7, a Cas5, a Cas11, a Cas8 (e.g., Csf1), or a DinG or CysH domain. In some cases, a CRISPR system comprises Cmr1, Cmr3, Cmr4, Cmr5, or Cmr6. In some cases, a CRISPR system comprises Csb1, Csb2, or Csb3. A CRISPR system can comprise Csf1, Csf2, Csf3, or Csf4. A CRISPR system can comprise Csn2, Csm2, Csm3, Csm4, Csm5, or Csm6. A CRISPR system can comprise Csc1 or Csc2. A CRISPR system can comprise Cas1, Cas1B, Cas2, or Cas4. A CRISPR system can comprise Csy1, Csy2, or Csy3. A CRISPR system can comprise Cse1 or Cse2. A CRISPR system can comprise Csn2. A CRISPR system can comprise CsaX, Csx1, Csx3, Csx10, Csx14, Csx15, Csx16, or Csx17. In some cases, a CRISPR system comprises a modified version of any one of the foregoing Cas proteins. In some cases, a modified version of the foregoing Cas protein comprises a nickase mutation. In some cases, the nickase mutation corresponds to the D10A mutation of the wild type

Cas9 protein. In some cases, the nickase mutation corresponds to the H840A mutation of the wild type Cas9 protein. In some cases, the nickase mutation occurs in the RuvC domain of the wild type Cas9 protein. In some cases, the nickase mutation occurs in the HNH domain of the wild type Cas9 protein. In some cases the RuvC domain can be mutated to prevent cleavage of the non-target DNA strand. In some cases the HNH domain can be mutated to prevent cleavage of the target DNA strand. In some cases, a modified version of the foregoing Cas protein comprises one or more mutations that disrupt cleavage activity. In some cases, a Cas protein with disrupted cleavage activity is catalytically inactive or catalytically dead. In some cases, the catalytically dead mutations occur in the RuvC domain and the HNH domain of the wild type Cas9 protein. In some cases, the catalytically inactive mutations correspond to the D10A mutation and the H840A mutation of the wild type Cas9 protein.

[0203] In some cases, a CRISPR system is a Class 2 CRISPR system. A Class 2 CRISPR system can be a Class 2 type II CRISPR system, a Class 2 type V CRISPR system, or a Class 2 type VI CRISPR system. A Class 2 type II CRISPR system can comprise a Cas9 domain (also known as Csn1 and Csx12). A Cas9 domain can be a SpyCas9, a GeoCas9, a SauCas9, a KhuCas9, a AinCas9, an FmaCas9, a SgaCas9, a ScCas9, a SauriCas9 domain. A Cas9 domain can be a hyperactive Cas9 domain. A Class 2 type V CRISPR system can comprise a Cas12 domain. A Cas12 domain can be a Cas12a, a Cas12b, a Cas12b1, a Cas12c, a Cas12d, a Cas12e, a Cas12f, a Cas12g, a Cas12h, a Cas12i, a Cas12j, a Cas12k, a Cas12l, or a Cas12m domain. A Class 2 type VI CRISPR system can comprise a Cas13 domain.

[0204] In some cases, a CRISPR system comprises a circularly permuted Cas9.

[0205] In some cases, a CRISPR system comprises CjCas9, Cas13a, Cas13b, Cas13c, or Cas13d. In some cases, a CRISPR system comprises Cas14, xCas9, or SpCas9-NG.

[0206] In some cases, a CRISPR-Cas domain comprises one or more subdomains. For example, a Cas9 domain can comprise a Rec1, a Rec2, a Rec3, a RuvC, an HNH, or a Wedge/PAM-interacting domain. A Cas12 domain can comprise a Rec1, Rec2, a crRNA oligonucleotide binding domain (OBD), a Nuc domain, a PAM-interacting (PI) domain, or a RuvC domain. In some cases, the RuvC domain comprises nuclease activity. In some cases, the HNH domain comprises nuclease activity. The PAM-interacting domain can bind to a protospacer adjacent motif (PAM) sequence that is next to a target sequence in a target nucleic acid molecule. PAM recognition can help activate a nuclease domain to make a cut at the target sequence. In some cases, a CRISPR protein or domain is an engineered or mutated variant of a protein involved in a CRISPR system. An engineered or mutated CRISPR domain can comprise a truncation, a deletion of a part of one or more domains or subdomains, or a mutation of an active site (*e.g.,* a RuvC active site or HNH active site). In some cases, a CRISPR domain with a mutation of one or more active sites is catalytically inactive (*e.g.,* dCas9). In some cases, a CRISPR domain with one or more mutated active sites comprises less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, less than 5%, or less than 1% of the nuclease activity of its wildtype counterpart. For example, a dCas9 can result from the point mutations D10A in the RuvC domain and the point mutation H840A in the HNH domain. In other cases, a mutation can result in a CRISPR nickase. A nickase can generate nick or a single-stranded cut. A nickase can

generate a nick in the strand complementary to the RNA guide (*e.g.*, the targeting strand) or in the strand on the non-targeting strand. For example, a RuvC mutation D10A in a Cas9 domain can produce a Cas9 nickase domain that nicks the targeting strand. An HNH mutation H840A in a Cas9 domain can produce a Cas9 nickase domain that nicks the non-targeting strand.

[0207] A Cas protein can comprise one or more domains. Examples of domains include, guide nucleic acid recognition and/or binding domain, nuclease domains (*e.g.*, DNase or RNase domains, RuvC, HNH), DNA binding domain, RNA binding domain, helicase domains, protein-protein interaction domains, and dimerization domains. A guide nucleic acid recognition and/or binding domain can interact with a guide nucleic acid. A nuclease domain can comprise catalytic activity for nucleic acid cleavage. A nuclease domain can lack catalytic activity to prevent nucleic acid cleavage. A Cas protein can be a chimeric Cas protein that is fused to other proteins or polypeptides. A Cas protein can be a chimera of various Cas proteins, for example, comprising domains from different Cas proteins.

[0208] In some cases, a CRISPR system comprises an Argonaute (Ago) domain.

[0209] Another example of a Cas protein that can be used as part of the prime editor includes Cas14. A Cas14 protein or polypeptide (also termed as "CasZ" protein or polypeptide) can bind and/or modify (*e.g.*, cleave, nick, methylate, demethylate, etc.) a target nucleic acid and/or a polypeptide associated with target nucleic acid (*e.g.*, methylation or acetylation of a histone tail) (*e.g.*, in some cases the CasZ protein includes a chimeric partner with an activity, and in some cases the CasZ protein provides nuclease activity). In some cases, the Cas14 protein or polypeptide is a naturally occurring protein (*e.g.*, naturally occurs in prokaryotic cells) (*e.g.*, a CasZ protein). In other cases, the Cas14 protein or polypeptide not a naturally occurring polypeptide (*e.g.*, the Cas14 protein is a variant Cas14 protein, a chimeric protein, and the like). A Cas14 protein includes 3 partial RuvC domains (RuvC-I, RuvC-II, and RuvC-III, also referred to herein as subdomains) that are not contiguous with respect to the primary amino acid sequence of the Cas14 protein but form a RuvC domain once the protein is produced and folds. A naturally occurring Cas14 protein functions as an endonuclease that catalyzes cleavage at a specific sequence in a targeted nucleic acid (*e.g.*, a double stranded DNA (dsDNA)). The sequence specificity is provided by the associated guide RNA, which hybridizes to a target sequence within the target DNA. The naturally occurring Cas14 guide RNA is a crRNA, where the crRNA includes (i) a guide sequence that hybridizes to a target sequence in the target DNA and (ii) a protein binding segment that binds to the Cas14 protein. Examples of Cas14 proteins include those described U.S. Patent Publication Nos. US20200172886 and US20210214697, Harrington LB *et al.*, *Science*. 2018 Nov 16;362(6416):839-842; Aquino-Jarquin G. *Nanomedicine*. 2019 Jun;18:428-431; each of which is incorporated herein by reference in its entirety. In some cases, the donor sequence disclosed herein encodes Cas14 polypeptide or a nucleic acid molecule encoding Cas14 polypeptide. In some cases, the donor sequence disclosed herein encodes Cas14a polypeptide. In some cases, the donor sequence disclosed herein encodes Cas14b polypeptide. In some cases, the donor sequence disclosed herein encodes Cas14c polypeptide.

[0210] A Cas protein can be from any suitable organism. Examples include Streptococcus pyogenes, Streptococcus thermophilus, Streptococcus sp., Staphylococcus aureus, Nocardiopsis dassonvillei,

Streptomyces pristinae spiralis, Streptomyces viridochromo genes, Streptomyces viridochromogenes, Streptosporangium roseum, Streptosporangium roseum, AlicyclobacHlus acidocaldarius, Bacillus pseudomycoides, Bacillus selenitireducens, Exiguobacterium sibiricum, Lactobacillus delbrueckii, Lactobacillus salivarius, Microscilla marina, Burkholderiales bacterium, Polaromonas naphthalenivorans, Polaromonas sp., Crocosphaera watsonii, Cyanothece sp., Microcystis aeruginosa, Pseudomonas aeruginosa, Synechococcus sp., Acetohalobium arabaticum, Ammonifex degensii, Caldicelulosiruptor becscii, Candidatus Desulforudis, Clostridium botulinum, Clostridium difficile, Finegoldia magna, Natranaerobius thermophilus, Pelotomaculum thermopropionicum, Acidithiobacillus caldus, Acidithiobacillus ferrooxidans, Allochromatium vinosum, Marinobacter sp., Nitrosococcus halophilus, Nitrosococcus watsoni, Pseudoalteromonas haloplanktis, Ktedonobacter racemifer, Methanohalobium evestigatum, Anabaena variabilis, Nodularia spumigena, Nostoc sp., Arthrospira maxima, Arthrospira platensis, Arthrospira sp., Lyngbya sp., Microcoleus chthonoplastes, Oscillatoria sp., Petrotoga mobilis, Thermosipho africanus, Acaryochloris marina, Leptotrichia shahii, Leptotrichia wadeii, Leptotrichia wadeii F0279, Rhodobacter capsulatus SB1003, Rhodobacter capsulatus R121, Rhodobacter capsulatus DE442, Lachnospiraceae bacterium NK4A179, Lachnospiraceae bacterium MA2020, Clostridium aminophilum DSM 10710, Paludibacter propionicigenes WB4, Carnobacterium gallinarum DMS4847, Carnobacterium gallinarum DSM4847, and Francisella novicida. In some aspects, the organism is Streptococcus pyogenes (S. pyogenes). In some aspects, the organism is Staphylococcus aureus (S. aureus). In some aspects, the organism is Streptococcus thermophilus (S. thermophilus).

[0211] A Cas protein can be derived from a variety of bacterial species including Veillonella atypical, Fusobacterium nucleatum, Filifactor alocis, Solobacterium moorei, Coprococcus catus, Treponema denticola, Peptoniphilus duerdenii, Catenibacterium mitsuokai, Streptococcus mutans, Listeria innocua, Listeria seeligeri, Listeria weihenstephanensis FSL R90317, Listeria weihenstephanensis FSL M60635, Staphylococcus pseudintermedius, Acidaminococcus intestine, Olsenella uli, Oenococcus kitaharae, Bifidobacterium bifidum, Lactobacillus rhamnosus, Lactobacillus gasseri, Finegoldia magna, Mycoplasma mobile, Mycoplasma gallisepticum, Mycoplasma ovipneumoniae, Mycoplasma canis, Mycoplasma synoviae, Eubacterium rectale, Streptococcus thermophilus, Eubacterium dolichum, Lactobacillus coryniformis subsp. Torquens, Ilyobacter polytropus, Ruminococcus albus, Akkermansia muciniphila, Acidothermus cellulolyticus, Bifidobacterium longum, Bifidobacterium dentium, Corynebacterium diphtheria, Elusimicrobium minutum, Nitratifractor salsuginis, Sphaerochaeta globus, Fibrobacter succinogenes subsp. Succinogenes, Bacteroides fragilis, Capnocytophaga ochracea, Rhodopseudomonas palustris, Prevotella micans, Prevotella ruminicola, Flavobacterium columnare, Aminomonas paucivorans, Rhodospirillum rubrum, Candidatus Puniceispirillum marinum, Verminephrobacter eiseniae, Ralstonia syzygii, Dinoroseobacter shibae, Azospirillum, Nitrobacter hamburgensis, Bradyrhizobium, Wolinella succinogenes, Campylobacter jejuni subsp. Jejuni, Helicobacter mustelae, Bacillus cereus, Acidovorax ebreus, Clostridium perfringens, Parvibaculum lavamentivorans, Roseburia intestinalis, Neisseria meningitidis, Pasteurella multocida subsp. Multocida,

Sutterella wadsworthensis, proteobacterium, Legionella pneumophila, Parasutterella excrementihominis, Wolinella succinogenes, and Francisella novicida.

[0212] A Cas protein as disclosed herein can be a wildtype or a modified form of a Cas protein. A Cas protein can be an active variant, inactive variant, or fragment of a wild type or modified Cas protein. A Cas protein can comprise an amino acid change such as a deletion, insertion, substitution, variant, mutation, fusion, chimera, or any combination thereof relative to a wild-type version of the Cas protein. A Cas protein can be a polypeptide with at least about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity or sequence similarity to a wild type exemplary Cas protein. A Cas protein can be a polypeptide with at most about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% sequence identity and/or sequence similarity to a wild type exemplary Cas protein. Variants or fragments can comprise at least about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity or sequence similarity to a wild type or modified Cas protein or a portion thereof. Variants or fragments can be targeted to a nucleic acid locus in complex with a guide nucleic acid while lacking nucleic acid cleavage activity.

[0213] A Cas protein can comprise one or more nuclease domains, such as DNase domains. For example, a Cas9 protein can comprise a RuvC-like nuclease domain and/or an HNH-like nuclease domain. The RuvC and HNH domains can each cut a different strand of double-stranded DNA to make a double-stranded break in the DNA. A Cas protein can comprise only one nuclease domain (*e.g.*, Cpf1 comprises RuvC domain but lacks HNH domain).

[0214] A Cas protein can comprise an amino acid sequence having at least about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity or sequence similarity to a nuclease domain (*e.g.*, RuvC domain, HNH domain) of a wild-type Cas protein.

[0215] A Cas protein can be modified to optimize regulation of gene expression. A Cas protein can be modified to increase or decrease nucleic acid binding affinity, nucleic acid binding specificity, and/or enzymatic activity. Cas proteins can also be modified to change any other activity or property of the protein, such as stability. For example, one or more nuclease domains of the Cas protein can be modified, deleted, or inactivated, or a Cas protein can be truncated to remove domains that are not essential for the function of the protein or to optimize (*e.g.*, enhance or reduce) the activity of the Cas protein for regulating gene expression.

[0216] In some embodiments, the prime editor delivered by the lipid delivery particles of the present disclosure contain a nuclease-null DNA binding protein derived from a DNA nuclease that can induce transcriptional activation or repression of a target DNA sequence. In some embodiments, the donor sequence encodes a nuclease-null RNA binding protein derived from an RNA nuclease that can induce transcriptional activation or repression of a target RNA sequence. For example, a doner sequence can encode a Cas protein which lacks cleavage activity.

[0217] A Cas protein can be a chimeric protein. For example, a Cas protein can be fused to a heterologous functional domain. A heterologous functional domain can comprise a cleavage domain, an epigenetic modification domain, a transcriptional activation domain, or a transcriptional repressor domain. A Cas protein can also be fused to a heterologous polypeptide providing increased or decreased stability. The fused domain or heterologous polypeptide can be located at the N-terminus, the C-terminus, or internally within the Cas protein.

[0218] The regulation of genes can be of any gene of interest. It is contemplated that genetic homologues of a gene described herein are covered. For example, a gene can exhibit a certain identity and/or homology to genes disclosed herein. Therefore, it is contemplated that a gene that exhibits or exhibits about 50%, 55%, 60%, 65%,70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% homology (at the nucleic acid or protein level) can be modified. It is also contemplated that a gene that exhibits or exhibits about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity (at the nucleic acid or protein level) can be modified.

[0219] A Cas protein can be provided in any form. For example, a Cas protein can be provided in the form of a protein, such as a Cas protein alone or complexed with a guide nucleic acid. A Cas protein can be provided in the form of a nucleic acid encoding the Cas protein, such as an RNA (*e.g.*, messenger RNA (mRNA)) or DNA.

[0220] The nucleic acid encoding the Cas protein that is part of the prime editor can be codon optimized for efficient translation into protein in a particular cell or organism.

[0221] In some embodiments, a Cas protein is a dead Cas protein. A dead Cas protein can be a protein that lacks nucleic acid cleavage activity.

[0222] A Cas protein can comprise a modified form of a wild type Cas protein. The modified form of the wild type Cas protein can comprise an amino acid change (*e.g.*, deletion, insertion, or substitution) that reduces the nucleic acid-cleaving activity of the Cas protein. For example, the modified form of the Cas protein can have less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, less than 5%, or less than 1% of the nucleic acid-cleaving activity of the wild-type Cas protein (*e.g.*, Cas9 from S. pyogenes). The modified form of Cas protein can have no substantial nucleic acid-cleaving activity. When a Cas protein is a modified form that has no substantial nucleic acid-cleaving activity, it can be referred to as enzymatically inactive and/or "dead" (abbreviated by "d"). A dead Cas protein (*e.g.*, dCas, dCas9) can bind to a target polynucleotide but may not cleave the target polynucleotide. In some aspects, a dead Cas protein is a dead Cas9 protein.

[0223] A dCas9 polypeptide can associate with a guide nucleic acid molecule (*e.g.*, PEgRNA) to activate or repress transcription of target DNA. Guide nucleic acid molecules can be introduced into cells expressing the engineered chimeric receptor polypeptide. In some cases, such cells contain one or more different guide nucleic acid molecules that target the same nucleic acid. In other cases, the guide nucleic acid molecules target different nucleic acids in the cell. The nucleic acids targeted by the guide nucleic acid molecule can be any that are expressed in a cell such as an immune cell. The nucleic acids targeted

can be a gene involved in immune cell regulation. In some embodiments, the nucleic acid is associated with cancer. The nucleic acid associated with cancer can be a cell cycle gene, cell response gene, apoptosis gene, or phagocytosis gene. The recombinant guide nucleic acid molecule can be recognized by a CRISPR protein, a nuclease-null CRISPR protein, variants thereof, derivatives thereof, or fragments thereof.

[0224] Enzymatically inactive can refer to a polypeptide that can bind to a nucleic acid sequence in a polynucleotide in a sequence-specific manner, but may not cleave a target polynucleotide. An enzymatically inactive site-directed polypeptide can comprise an enzymatically inactive domain (*e.g.*, nuclease domain). Enzymatically inactive can refer to no activity. Enzymatically inactive can refer to substantially no activity. Enzymatically inactive can refer to essentially no activity. Enzymatically inactive can refer to an activity less than 1%, less than 2%, less than 3%, less than 4%, less than 5%, less than 6%, less than 7%, less than 8%, less than 9%, or less than 10% activity compared to a wild-type exemplary activity (*e.g.*, nucleic acid cleaving activity, wild-type Cas9 activity).

[0225] One or a plurality of the nuclease domains (*e.g.*, RuvC, HNH) of a Cas protein can be deleted or mutated so that they are no longer functional or comprise reduced nuclease activity (*e.g.*, deactivated or dead Cas, i.e., "dCas"). For example, in a Cas protein comprising at least two nuclease domains (*e.g.*, Cas9), if one of the nuclease domains is deleted or mutated, the resulting Cas protein, known as a nickase, can generate a single-strand break at a CRISPR RNA (crRNA) recognition sequence within a double-stranded DNA but not a double-strand break. Such a nickase can cleave the complementary strand or the non-complementary strand, but may not cleave both. If all of the nuclease domains of a Cas protein (*e.g.*, both RuvC and HNH nuclease domains in a Cas9 protein; RuvC nuclease domain in a Cpf1 protein) are deleted or mutated, the resulting Cas protein can have a reduced or no ability to cleave both strands of a double-stranded DNA. An example of a mutation that can convert a Cas9 protein into a nickase is a D10A (aspartate to alanine at position 10 of Cas9) mutation in the RuvC domain of Cas9 from S. pyogenes. H939A (histidine to alanine at amino acid position 839) or H840A (histidine to alanine at amino acid position 840) in the HNH domain of Cas9 from S. pyogenes can convert the Cas9 into a nickase. An example of a mutation that can convert a Cas9 protein into a dead Cas9 is a D10A (aspartate to alanine at position 10 of Cas9) mutation in the RuvC domain and H939A (histidine to alanine at amino acid position 839) or H840A (histidine to alanine at amino acid position 840) in the HNH domain of Cas9 from S. pyogenes.

[0226] A dead Cas protein can comprise one or more mutations relative to a wild-type version of the protein. The mutation can result in less than 90%, less than 80%, less than 70%, less than 60%, less than 50%, less than 40%, less than 30%, less than 20%, less than 10%, less than 5%, or less than 1% of the nucleic acid-cleaving activity in one or more of the plurality of nucleic acid-cleaving domains of the wild-type Cas protein. The mutation can result in one or more of the plurality of nucleic acid-cleaving domains retaining the ability to cleave the complementary strand of the target nucleic acid but reducing its ability to cleave the non-complementary strand of the target nucleic acid. The mutation can result in one or more of the plurality of nucleic acid-cleaving domains retaining the ability to cleave the non-complementary

strand of the target nucleic acid but reducing its ability to cleave the complementary strand of the target nucleic acid. The mutation can result in one or more of the plurality of nucleic acid-cleaving domains lacking the ability to cleave the complementary strand and the non-complementary strand of the target nucleic acid. The residues to be mutated in a nuclease domain can correspond to one or more catalytic residues of the nuclease. For example, residues in the wild type exemplary *S. pyogenes* Cas9 polypeptide such as Asp10, His840, Asn854 and Asn856 can be mutated to inactivate one or more of the plurality of nucleic acid-cleaving domains (*e.g.*, nuclease domains). The residues to be mutated in a nuclease domain of a Cas protein can correspond to residues Asp10, His840, Asn854 and Asn856 in the wild type *S. pyogenes* Cas9 polypeptide, for example, as determined by sequence and/or structural alignment.

[0227] As examples, residues D10, G12, G17, E762, H840, N854, N863, H982, H983, A984, D986, and/or A987 (or the corresponding mutations of any of the Cas proteins) can be mutated. For example, *e.g.*, D10A, G12A, G17A, E762A, H840A, N854A, N863A, H982A, H983A, A984A, and/or D986A. Mutations other than alanine substitutions can be suitable.

[0228] A D10A mutation can be combined with one or more of H840A, N854A, or N856A mutations to produce a Cas9 protein substantially lacking DNA cleavage activity (*e.g.*, a dead Cas9 protein). A H840A mutation can be combined with one or more of D10A, N854A, or N856A mutations to produce a site-directed polypeptide substantially lacking DNA cleavage activity. A N854A mutation can be combined with one or more of H840A, D10A, or N856A mutations to produce a site-directed polypeptide substantially lacking DNA cleavage activity. A N856A mutation can be combined with one or more of H840A, N854A, or D10A mutations to produce a site-directed polypeptide substantially lacking DNA cleavage activity.

[0229] In some cases, a dCas9 can be fused to other proteins. In some cases, dCas9 can be fused to SunTag, KRAB, VPS4, P3000, VPR, VP64, V64-p65-Rta, VP160, VP192, HDAC1, DNMT3A, TET1, SPH, KRAB-MeCP2, epigenetic regulators, or other proteins. In some cases, a dCas9 fusion comprises a ZIM3 KRAB-Cas9 fusion. In some cases, a Cas9 fusion can be a paired dCas9 system. In some cases, the dCas9 can be part of a SAM system or REDMAP system. Examples of Cas9 variants and fusion proteins can be found in Li, T. et al., *Sig Transduct Target Ther* 8, 36 (2023), which is incorporated in its entirety.

[0230] In some embodiments, a Cas protein is a Class 2 Cas protein. In some embodiments, a Cas protein is a type II Cas protein. In some embodiments, the Cas protein is a Cas9 protein, a modified version of a Cas9 protein, or derived from a Cas9 protein. For example, a Cas9 protein lacking cleavage activity. In some embodiments, the Cas9 protein is a Cas9 protein from *S. pyogenes* (*e.g.*, SwissProt accession number Q99ZW2). In some embodiments, the Cas9 protein is a Cas9 from *S.aureus* (*e.g.*, SwissProt accession number J7RUA5). In some embodiments, the Cas9 protein is a modified version of a Cas9 protein from *S. pyogenes* or *S. Aureus*. In some embodiments, the Cas9 protein is derived from a Cas9 protein from *S. pyogenes* or *S. Aureus*. For example, a *S. pyogenes* or *S. Aureus* Cas9 protein lacking cleavage activity.

[0231] Cas9 can generally refer to a polypeptide with at least about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% sequence identity and/or sequence similarity to a wild type exemplary Cas9

polypeptide (*e.g.*, Cas9 from *S. pyogenes*). Cas9 can refer to a polypeptide with at most about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% sequence identity and/or sequence similarity to a wild type exemplary Cas9 polypeptide (*e.g.*, from *S. pyogenes*). Cas9 can refer to the wildtype or a modified form of the Cas9 protein that can comprise an amino acid change such as a deletion, insertion, substitution, variant, mutation, fusion, chimera, or any combination thereof.

[0232] In some embodiments, a guidable polypeptide domain is a Cas9 or variant thereof. In some embodiments, the Cas9 or variant thereof is a nuclease active Cas9 domain, a nuclease inactive Cas9 domain, or a Cas9 nickase domain or a variant thereof. In some embodiments, a guidable polypeptide domain is Cas9, Cas12e, Cas12d, Cas12a, Casl2bl, Cas13a, Cas12c, or Argonaute (Ago domain), any of which optionally has a nickase activity. In some embodiments, a guidable polypeptide domain comprises an amino acid sequence at least 80%, 85%, 90%, 95%, or 99% identical to any one of sequences listed in **Table 14** below. In some embodiments, a guidable polypeptide domain comprises an amino acid sequence at least 80%, 85%, 90%, 95%, or 99% identical to any one of sequences set forth in **SEQ ID NOs: 264-284**. In some cases, a guidable polypeptide domain is a Cas9 H840A nickase. In some cases, a guidable polypeptide domain is Cas9 D10A nickase. Cas9-H840A. In some cases, a guidable polypeptide domain is a Cas12a/b nickase.

Table 14. Exemplary guidable polypeptide domain sequences

Description	SEQ ID NO:	Sequence
AsCas12 a (Previously known as Cpfl) *Acidaminococcus sp. (strain BV3L6)* UniProtKB U2UMQ6	264	MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKE LKPIIDRIYKTYADQCLQLVQLDWENLSAAIDSYRKEKTEETRNALIEE QATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLKQLG TVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQD NFPKFKENCHIFTRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFPF YNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHI IASLPHRFIPLFKQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNE NVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNALYER RISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSE ILSHAHAALDQPLPTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDESN EVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPT LASGWDVNKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSE GFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTTPILLSNNFIEPLE ITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSK YTKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISFQRIAEKEIMDAV ETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLNGQ AELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHR LSHDLSDEARALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLNYQAA NSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRS LNTIQQFDYQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIV DLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQFEKMLIDKLNCLVLK DYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTG FVDPFVWKTIKNHESRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQR GLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHRFTGRYRDL YPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQM RNSNAATGEDYINSPVRDLNGVCFDSRFQNPEWPMDADANGAYHIALKG QLLLNHLKESKDLKLQNGISNQDWLAYIQELRN
AsCas12a nickase (*e.g.*, R1226A)	265	MTQFEGFTNLYQVSKTLRFELIPQGKTLKHIQEQGFIEEDKARNDHYKE LKPIIDRIYKTYADQCLQLVQLDWENLSAAIDSYRKEKTEETRNALIEE QATYRNAIHDYFIGRTDNLTDAINKRHAEIYKGLFKAELFNGKVLKQLG TVTTTEHENALLRSFDKFTTYFSGFYENRKNVFSAEDISTAIPHRIVQD NFPKFKENCHIFTRLITAVPSLREHFENVKKAIGIFVSTSIEEVFSFPF

		YNQLLTQTQIDLYNQLLGGISREAGTEKIKGLNEVLNLAIQKNDETAHI IASLPHRFIPLFKQILSDRNTLSFILEEFKSDEEVIQSFCKYKTLLRNE NVLETAEALFNELNSIDLTHIFISHKKLETISSALCDHWDTLRNALYER RISELTGKITKSAKEKVQRSLKHEDINLQEIISAAGKELSEAFKQKTSE ILSHAHAALDQPLPTTLKKQEEKEILKSQLDSLLGLYHLLDWFAVDESN EVDPEFSARLTGIKLEMEPSLSFYNKARNYATKKPYSVEKFKLNFQMPT LASGWDVNKEKNNGAILFVKNGLYYLGIMPKQKGRYKALSFEPTEKTSE GFDKMYYDYFPDAAKMIPKCSTQLKAVTAHFQTHTTPILLSNNFIEPLE ITKEIYDLNNPEKEPKKFQTAYAKKTGDQKGYREALCKWIDFTRDFLSK YTKTTSIDLSSLRPSSQYKDLGEYYAELNPLLYHISFQRIAEKEIMDAV ETGKLYLFQIYNKDFAKGHHGKPNLHTLYWTGLFSPENLAKTSIKLNGQ AELFYRPKSRMKRMAHRLGEKMLNKKLKDQKTPIPDTLYQELYDYVNHR LSHDLSDEARALLPNVITKEVSHEIIKDRRFTSDKFFFHVPITLNYQAA NSPSKFNQRVNAYLKEHPETPIIGIDRGERNLIYITVIDSTGKILEQRS LNTIQQFDYQKKLDNREKERVAARQAWSVVGTIKDLKQGYLSQVIHEIV DLMIHYQAVVVLENLNFGFKSKRTGIAEKAVYQQFEKMLIDKLNCLVLK DYPAEKVGGVLNPYQLTDQFTSFAKMGTQSGFLFYVPAPYTSKIDPLTG FVDPFVWKTIKNHESRKHFLEGFDFLHYDVKTGDFILHFKMNRNLSFQR GLPGFMPAWDIVFEKNETQFDAKGTPFIAGKRIVPVIENHRFTGRYRDL YPANELIALLEEKGIVFRDGSNILPKLLENDDSHAIDTMVALIRSVLQM ANSNAATGEDYINSPVRDLNGVCFDSRFQNPEWPMDADANGAYHIALKG QLLLNHLKESKDLKLQNGISNQDWLAYIQELRN
BhCas12b *B. hisashii* 1108 AA 130.4 kDa	266	MATRSFILKIEPNEEVKKGLWKTHEVLNHGIAYYMNILKLIRQEAIYEH HEQDPKNPKKVSKAEIQAELWDFVLKMQKCNSFTHEVDKDEVFNILREL YEELVPSSVEKKGEANQLSNKFLYPLVDPNSQSGKGTASSGRKPRWYNL KIAGDPSWEEEKKKWEEDKKKDPLAKILGKLAEYGLIPLFIPYTDSNEP IVKEIKWMEKSRNQSVRRLDKDMFIQALERFLSWESWNLKVKEEYEKVE KEYKTLEERIKEDIQALKALEQYEKERQEQLLRDTLNTNEYRLSKRGLR GWREIIQKWLKMDENEPSEKYLEVFKDYQRKHPREAGDYSVYEFLSKKE NHFIWRNHPEYPYLYATFCEIDKKKKDAKQQATFTLADPINHPLWVRFE ERSGSNLNKYRILTEQLHTEKLKKKLTVQLDRLIYPTESGGWEEKGKVD IVLLPSRQFYNQIFLDIEEKGKHAFTYKDESIKFPLKGTLGGARVQFDR DHLRRYPHKVESGNVGRIYFNMTVNIEPTESPVSKSLKIHRDDFPKVVN FKPKELTEWIKDSKGKKLKSGIESLEIGLRVMSIDLGQRQAAAASIFEV VDQKPDIEGKLFFPIKGTELYAVHRASFNIKLPGETLVKSREVLRKARE DNLKLMNQKLNFLRNVLHFQQFEDITEREKRVTKWISRQENSDVPLVYQ DELIQIRELMYKPYKDWVAFLKQLHKRLEVEIGKEVKHWRKSLSDGRKG LYGISLKNIDEIDRTRKFLLRWSLRPTEPGEVRRLEPGQRFAIDQLNHL NALKEDRLKKMANTIIMHALGYCYDVRKKKWQAKNPACQIILFEDLSNY NPYEERSRFENSKLMKWSRREIPRQVALQGEIYGLQVGEVGAQFSSRFH AKTGSPGIRCSVVTKEKLQDNRFFKNLQREGRLTLDKIAVLKEGDLYPD KGGEKFISLSKDRKCVTTHADINAAQNLQKRFWTRTHGFYKVYCKAYQV DGQTVYIPESKDQKQKIIEEFGEGYFILKDGVYEWVNAGKLKIKKGSSK QSSSELVDSDILKDSFDLASELKGEKLMLYRDPSGNVFPSDKWMAAGVF FGKLERILISKLTNQYSISTIEDDSSKQSM
LbaCas12a *L. bacterium* 1228 AA 143.9 kDa	267	MSKLEKFTNCYSLSKTLRFKAIPVGKTQENIDNKRLLVEDEKRAEDYKG VKKLLDRYYLSFINDVLHSIKLKNLNNYISLFRKKTRTEKENKELENLE INLRKEIAKAFKGNEGYKSLFKKDIIETILPEFLDDKDEIALVNSFNGF TTAFTGFFDNRENMFSEEAKSTSIAFRCINENLTRYISNMDIFEKVDAI FDKHEVQEIKEKILNSDYDVEDFFEGEFFNFVLTQEGIDVYNAIIGGFV TESGEKIKGLNEYINLYNQKTKQKLPKFKPLYKQVLSDRESLSFYGEGY TSDEEVLEVFRNTLNKNSEIFSSIKKLEKLFKNFDEYSSAGIFVKNGPA ISTISKDIFGEWNVIRDKWNAEYDDIHLKKKAVVTEKYEDDRRKSFKKI GSFSLEQLQEYADADLSVVEKLKEIIIQKVDEIYKVYGSSEKLFDADFV LEKSLKKNDAVVAIMKDLLDSVKSFENYIKAFFGEGKETNRDESFYGDF VLAYDILLKVDHIYDAIRNYVTQKPYSKDKFKLYFQNPQFMGGWDKDKE TDYRATILRYGSKYYLAIMDKKYAKCLQKIDKDDVNGNYEKINYKLLPG PNKMLPKVFFSKKWMAYYNPSEDIQKIYKNGTFKKGDMFNLNDCHKLID FFKDSISRYPKWSNAYDFNFSETEKYKDIAGFYREVEEQGYKVSFESAS KKEVDKLVEEGKLYMFQIYNKDFSDKSHGTPNLHTMYFKLLFDENNHGQ IRLSGGAELFMRRASLKKEELVVHPANSPIANKNPDNPKKTTTLSYDVY KDKRFSEDQYELHIPIAINKCPKNIFKINTEVRVLLKHDDNPYVIGIDR

		GERNLLYIVVVDGKGNIVEQYSLNEIINNFNGIRIKTDYHSLLDKKEKE RFEARQNWTSIENIKELKAGYISQVVHKICELVEKYDAVIALEDLNSGF KNSRVKVEKQVYQKFEKMLIDKLNYMVDKKSNPCATGGALKGYQITNKF ESFKSMSTQNGFIFYIPAWLTSKIDPSTGFVNLLKTKYTSIADSKKFIS SFDRIMYVPEEDLFEFALDYKNFSRTDADYIKKWKLYSYGNRIRIFRNP KKNNVFDWEEVCLTSAYKELFNKYGINYQQGDIRALLCEQSDKAFYSSF MALMSLMLQMRNSITGRTDVDFLISPVKNSDGIFYDSRNYEAQENAILP KNADANGAYNIARKVLWAIGQFKKAEDEKLDKVKIAISNKEWLEYAQTS VKH
Cas9 nickase (Met minus) *Streptococcus pyogenes* Q99ZW2 Cas9 with R863A	268	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGA LLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFH RLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDK ADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFE ENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSL GLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKN LSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLP EKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKL NREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEK ILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSF IERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFL SGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNA SLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKT YAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDG FANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKG ILQTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRIE EGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLS DYDVDHIVPQSFLKDDSIDNKVLTRSDKNAGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVA QILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINNY HHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIG KATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRD FATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDP KKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKN PIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNEL ALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISE FSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD
dead Cas9 or dCas9 *Streptococcus pyogenes* Q99ZW2 Cas9 with D10X and H810X Where "X" is any amino acid	269	MDKKYSIGLXIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIG ALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFF HRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLF EENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALS LGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAK NLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQL PEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVK LNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIE KILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQS FIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAF LSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLK TYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSD GFANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKK GILQTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRI EEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRL SDYDVDXIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNY WRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHV AQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINN YHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGR DFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWD PKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEK NPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNE

		LALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQIS EFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAA FKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD
LfCas9 *Lactobacillus fermentum* wild type GenBank: SNX31424.11	270	MKEYHIGLDIGTSSIGWAVTDSQFKLMRIKGKTAIGVRLFEEGKTAAER RTFRTTRRRLKRRKWRLHYLDEIFAPHLQEVDENFLRRLKQSNIHPEDP TKNQAFIGKLLFPDLLKKNERGYPTLIKMRDELPVEQRAHYPVMNIYKL REAMINEDRQFDLREVYLAVHHIVKYRGHFLNNASVDKFKVGRIDFDKS FNVLNEAYEELQNGEGSFTIEPSKVEKIGQLLLDTKMRKLDRQKAVAKL LEVKVADKEETKRNKQIATAMSKLVLGYKADFATVAMANGNEWKIDLSS ETSEDEIEKFREELSDAQNDILTEITSLFSQIMLNEIVPNGMSISESMM DRYWTHERQLAEVKEYLATQPASARKEFDQVYNKYIGQAPKERGFDLEK GLKKILSKKENWKEIDELLKAGDFLPKQRTSANGVIPHQMHQQELDRII EKQAKYYPWLATENPATGERDRHQAKYELDQLVSFRIPYYVGPLVTPEV QKATSGAKFAWAKRKEDGEITPWNLWDKIDRAESAEAFIKRMTVKDTYL LNEDVLPANSLLYQKYNVLNELNNVRVNGRRLSVGIKQDIYTELFKKKK TVKASDVASLVMAKTRGVNKPSVEGLSDPKKFNSNLATYLDLKSIVGDK VDDNRYQTDLENIIEWRSVFEDGEIFADKLTEVEWLTDEQRSALVKKRY KGWGRLSKKLLTGIVDENGQRIIDLMWNTDQNFKEIVDQPVFKEQIDQL NQKAITNDGMTLRERVESVLDDAYTSPQNKKAIWQVVRVVEDIVKAVGN APKSISIEFARNEGNKGEITRSRRTQLQKLFEDQAHELVKDTSLTEELE KAPDLSDRYYFYFTQGGKDMYTGDPINFDEISTKYDIDHILPQSFVKDN SLDNRVLTSRKENNKKSDQVPAKLYAAKMKPYWNQLLKQGLITQRKFEN LTKDVDQNIKYRSLGFVKRQLVETRQVIKLTANILGSMYQEAGTEIIET RAGLTKQLREEFDLPKVREVNDYHHAVDAYLTTFAGQYLNRRYPKLRSF FVYGEYMKFKHGSDLKLRNFNFFHELMEGDKSQGKVVDQQTGELITTRD EVAKSFDRLLNMKYMLVSKEVHDRSDQLYGATIVTAKESGKLTSPIEIK KNRLVDLYGAYTNGTSAFMTIIKFTGNKPKYKVIGIPTTSAASLKRAGK PGSESYNQELHRIIKSNPKVKKGFEIVVPHVSYGQLIVDGDCKFTLASP TVQHPATQLVLSKKSLETISSGYKILKDKPAIANERLIRVFDEVVGQMN RYFTIFDQRSNRQKVADARDKFLSLPTESKYEGAKKVQVGKTEVITNLL MGLHANATQGDLKVLGLATFGFFQSTTGLSLSEDTMIVYQSPTGLFERR ICLKDI
SaCas9 *Staphylococcus aureus* wild type GenBank: AYD60528.1	271	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIG ALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFF HRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLF EENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALS LGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAK NLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQL PEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVK LNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIE KILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQS FIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAF LSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLK TYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSD GFANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKK GILQTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRI EEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRL SDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNY WRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHV AQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINN YHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGR DFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWD PKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEK NPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNE LALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQIS EFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAA FKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD

LcCas9 *Lactobacillus crispatus* NCBI Reference Sequence: WP_133478044.1 Wild type	272	MKIKNYNLALTPSTSAVGHVEVDDDLNILEPVHHQKAIGVAKFGEGETA EARRLARSARRTTKRRANRINHYFNEIMKPEIDKVDPLMFDRIKQAGLS PLDERKEFRTVIFDRPNIASYYHNQFPTIWHLQKYLMITDEKADIRLIY WALHSLLKHRGHFFNTTPMSQFKPGKLNLKDDMLALDDYNDLEGLSFAV ANSPEIEKVIKDRSMHKKEKIAELKKLIVNDVPDKDLAKRNNKIITQIV NAIMGNSFHLNFIFDMDLDKLTSKAWSFKLDDPELDTKFDAISGSMTDN QIGIFETLQKIYSAISLLDILNGSSNVVDAKNALYDKHKRDLNLYFKFL NTLPDEIAKTLKAGYTLYIGNRKKDLLAARKLLKVNVAKNFSQDDFYKL INKELKSIDKQGLQTRFSEKVGELVAQNNFLPVQRSSDNVFIPYQLNAI TFNKILENQGKYYDFLVKPNPAKKDRKNAPYELSQLMQFTIPYYVGPLV TPEEQVKSGIPKTSRFAWMVRKDNGAITPWNFYDKVDIEATADKFIKRS IAKDSYLLSELVLPKHSLLYEKYEVFNELSNVSLDGKKLSGGVKQILFN EVFKKTNKVNTSRILKALAKHNIPGSKITGLSNPEEFTSSLQTYNAWKK YFPNQIDNFAYQQDLEKMIEWSTVFEDHKILAKKLDEIEWLDDDQKKFV ANTRLRGWGRLSKRLLTGLKDNYGKSIMQRLETTKANFQQIVYKPEFRE QIDKISQAAAKNQSLEDILANSYTSPSNRKAIRKTMSVVDEYIKLNHGK EPDKIFLMFQRSEQEKGKQTEARSKQLNRILSQLKADKSANKLFSKQLA DEFSNAIKKSKYKLNDKQYFYFQQLGRDALTGEVIDYDELYKYTVLHII PRSKLTDDSQNNKVLTKYKIVDGSVALKFGNSYSDALGMPIKAFWTELN RLKLIPKGKLLNLTTDFSTLNKYQRDGYIARQLVETQQIVKLLATIMQS RFKHTKIIEVRNSQVANIRYQFDYFRIKNLNEYYRGFDAYLAAVVGTYL YKVYPKARRLFVYGQYLKPKKTNQENQDMHLDSEKKSQGFNFLWNLLYG KQDQIFVNGTDVIAFNRKDLITKMNTVYNYKSQKISLAIDYHNGAMFKA TLFPRNDRDTAKTRKLIPKKKDYDTDIYGGYTSNVDGYMLLAEIIKRDG NKQYGFYGVPSRLVSELDTLKKTRYTEYEEKLKEIIKPELGVDLKKIKK IKILKNKVPFNQVIIDKGSKFFITSTSYRWNYRQLILSAESQQTLMDLV VDPDFSNHKARKDARKNADERLIKVYEEILYQVKNYMPMFVELHRCYEK LVDAQKTFKSLKISDKAMVLNQILILLHSNATSPVLEKLGYHTRFTLGK KHNLISENAVLVTQSITGLKENHVSIKQML
StCas9 *Streptococcus thermophilus* UniProtKB/Swiss-Prot: G3ECR1.2 Wild type	273	MLFNKCIIISINLDFSNKEKCMTKPYSIGLDIGTNSVGWAVITDNYKVP SKKMKVLGNTSKKYIKKNLLGVLLFDSGITAEGRRLKRTARRRYTRRRN RILYLQEIFSTEMATLDDAFFQRLDDSFLVPDDKRDSKYPIFGNLVEEK VYHDEFPTIYHLRKYLADSTKKADLRLVYLALAHMIKYRGHFLIEGEFN SKNNDIQKNFQDFLDTYNAIFESDLSLENSKQLEEIVKDKISKLEKKDR ILKLFPGEKNSGIFSEFLKLIVGNQADFRKCFNLDEKASLHFSKESYDE DLETLLGYIGDDYSDVFLKAKKLYDAILLSGFLTVTDNETEAPLSSAMI KRYNEHKEDLALLKEYIRNISLKTYNEVFKDDTKNGYAGYIDGKTNQED FYVYLKNLLAEFEGADYFLEKIDREDFLRKQRTFDNGSIPYQIHLQEMR AILDKQAKFYPFLAKNKERIEKILTFRIPYYVGPLARGNSDFAWSIRKR NEKITPWNFEDVIDKESSAEAFINRMTSFDLYLPEEKVLPKHSLLYETF NVYNELTKVRFIAESMRDYQFLDSKQKKDIVRLYFKDKRKVTDKDIIEY LHAIYGYDGIELKGIEKQFNSSLSTYHDLLNIINDKEFLDDSSNEAIIE EIIHTLTIFEDREMIKQRLSKFENIFDKSVLKKLSRRHYTGWGKLSAKL INGIRDEKSGNTILDYLIDDGISNRNFMQLIHDDALSFKKKIQKAQIIG DEDKGNIKEVVKSLPGSPAIKKGILQSIKIVDELVKVMGGRKPESIVVE MARENQYTNQGKSNSQQRLKRLEKSLKELGSKILKENIPAKLSKIDNNA LQNDRLYLYYLQNGKDMYTGDDLDIDRLSNYDIDHIIPQAFLKDNSIDN KVLVSSASNRGKSDDFPSLEVVKKRKTFWYQLLKSKLISQRKFDNLTKA ERGGLLPEDKAGFIQRQLVETRQITKHVARLLDEKFNNKKDENNRAVRT VKIITLKSTLVSQFRKDFELYKVREINDFHHAHDAYLNAVIASALLKKY PKLEPEFVYGDYPKYNSFRERKSATEKVYFYSNIMNIFKKSISLADGRV IERPLIEVNEETGESVWNKESDLATVRRVLSYPQVNVVKKVEEQNHGLD RGKPKGLFNANLSSKPKPNSNENLVGAKEYLDPKKYGGYAGISNSFAVL VKGTIEKGAKKKITNVLEFQGISILDRINYRKDKLNFLLEKGYKDIELI IELPKYSLFELSDGSRRMLASILSTNNKRGEIHKGNQIFLSQKFVKLLY HAKRISNTINENHRKYVENHKKEFEELFYYILEFNENYVGAKKNGKLLN SAFQSWQNHSIDELCSSFIGPTGSERKGLFELTSRGSAADFEFLGVKIP RYRDYTPSSLLKDATLIHQSVTGLYETRIDLAKLGEG
PdCas9 *Pedicoccus damnosus* NCBI Reference	274	MTNEKYSIGLDIGTSSIGFAVVNDNNRVIRVKGKNAIGVRLFDEGKAAA DRRSFRTTRRSFRTTRRRLSRRRWRLKLLREIFDAYITPVDEAFFIRLK ESNLSPKDSKKQYSGDILFNDRSDKDFYEKYPTIYHLRNALMTEHRKFD VREIYLAIHHIMKFRGHFLNATPANNFKVGRLNLEEKFEELNDIYQRVF

Sequence: WP_062913273.1 Wild type		PDESIEFRTDNLEQIKEVLLDNKRSRADRQRTLVSDIYQSSEDKDIEKR NKAVATEILKASLGNKAKLNVITNVEVDKEAAKEWSITFDSESIDDDLA KIEGQMTDDGHEIIEVLRSLYSGITLSAIVPENHTLSQSMVAKYDLHKD HLKLFKKLINGMTDTKKAKNLRAAYDGYIDGVKGKVLPQEDFYKQVQVN LDDSAEANEIQTYIDQDIFMPKQRTKANGSIPHQLQQQELDQIIENQKA YYPWLAELNPNPDKKRQQLAKYKLDELVTFRVPYYVGPMITAKDQKNQS GAEFAWMIRKEPGNITPWNFDQKVDRMATANQFIKRMTTTDTYLLGEDV LPAQSLLYQKFEVLNELNKIRIDHKPISIEQKQQIFNDLFKQFKNVTIK HLQDYLVSQGQYSKRPLIEGLADEKRFNSSLSTYSDLCGIFGAKLVEEN DRQEDLEKIIEWSTIFEDKKIYRAKLNDLTWLTDDQKEKLATKRYQGWG RLSRKLLVGLKNSEHRNIMDILWITNENFMQIQAEPDFAKLVTDANKGM LEKTDSQDVINDLYTSPQNKKAIRQILLVVHDIQNAMHGQAPAKIHVEF ARGEERNPRRSVQRQRQVEAAYEKVSNELVSAKVRQEFKEAINNKRDFK DRLFLYFMQGGIDIYTGKQLNIDQLSSYQIDHILPQAFVKDDSLTNRVL TNENQVKADSVPIDIFGKKMLSVWGRMKDQGLISKGKYRNLTMNPENIS AHTENGFINRQLVETRQVIKLAVNILADEYGDSTQIISVKADLSHQMRE DFELLKNRDVNDYHHAFDAYLAAFIGNYLLKRYPKLESYFVYGDFKKFT QKETKMRRFNFIYDLKHCDQVVNKETGEILWTKDEDIKYIRHLFAYKKI LVSHEVREKRGALYNQTIYKAKDDKGSGQESKKLIRIKDDKETKIYGGY SGKSLAYMTIVQITKKNKVSYRVIGIPTLALARLNKLENDSTENNGELY KIIKPQFTHYKVDKKNGEIIETTDDFKIVVSKVRFQQLIDDAGQFFMLA SDTYKNNAQQLVISNNALKAINNTNITDCPRDDLERLDNLRLDSAFDEI VKKMDKYFSAYDANNFREKIRNSNLIFYQLPVEDQWENNKITELGKRTV LTRILQGLHANATTTDMSIFKIKTPFGQLRQRSGISLSENAQLIYQSPT GLFERRVQLNKIK
EcCas9 *Enterococcus cecorum* NCBI Reference Sequence: WP_047338501.1 Wild type	275	RRKQRIQILQELLGEEVLKTDPGFFHRMKESRYVVEDKRTLDGKQVELP YALFVDKDYTDKEYYKQFPTINHLIVYLMTTSDTPDIRLVYLALHYYMK NRGNFLHSGDINNVKDINDILEQLDNVLETFLDGWNLKLKSYVEDIKNI YNRDLGRGERKKAFVNTLGAKTKAEKAFCSLISGGSTNLAELFDDSSLK EIETPKIEFASSSLEDKIDGIQEALEDRFAVIEAAKRLYDWKTLTDILG DSSSLAEARVNSYQMHHEQLLELKSLVKEYLDRKVFQEVFVSLNVANNY PAYIGHTKINGKKKELEVKRTKRNDFYSYVKKQVIEPIKKKVSDEAVLT KLSEIESLIEVDKYLPLQVNSDNGVIPYQVKLNELTRIFDNLENRIPVL RENRDKIIKTFKFRIPYYVGSLNGVVKNGKCTNWMVRKEEGKIYPWNFE DKVDLEASAEQFIRRMTNKCTYLVNEDVLPKYSLLYSKYLVLSELNNLR IDGRPLDVKIKQDIYENVFKKNRKVTLKKIKKYLLKEGIITDDDELSGL ADDVKSSLTAYRDFKEKLGHLDLSEAQMENIILNITLFGDDKKLLKKRL AALYPFIDDKSLNRIATLNYRDWGRLSERFLSGITSVDQETGELRTIIQ CMYETQANLMQLLAEPYHFVEAIEKENPKVDLESISYRIVNDLYVSPAV KRQIWQTLLVIKDIKQVMKHDPERIFIEMAREKQESKKTKSRKQVLSEV YKKAKEYEHLFEKLNSLTEEQLRSKKIYLYFTQLGKCMYSGEPIDFENL VSANSNYDIDHIYPQSKTIDDSFNNIVLVKKSLNAYKSNHYPIDKNIRD NEKVKTLWNTLVSKGLITKEKYERLIRSTPFSDEELAGFIARQLVETRQ STKAVAEILSNWFPESEIVYSKAKNVSNFRQDFEILKVRELNDCHHAHD AYLNIVVGNAYHTKFTNSPYRFIKNKANQEYNLRKLLQKVNKIESNGVV AWVGQSENNPGTIATVKKVIRRNTVLISRMVKEVDGQLFDLTLMKKGKG QVPIKSSDERLTDISKYGGYNKATGAYFTFVKSKKRGKVVRSFEYVPLH LSKQFENNNELLKEYIEKDRGLTDVEILIPKVLINSLFRYNGSLVRITG RGDTRLLLVHEQPLYVSNSFVQQLKSVSSYKLKKSENDNAKLTKTATEK LSNIDELYDGLLRKLDLPIYSYWFSSIKEYLVESRTKYIKLSIEEKALV IFEILHLFQSDAQVPNLKILGLSTKPSRIRIQKNLKDTDKMSIIHQSPS GIFEHEIELTSL
AhCas9 *Anaerostipes hadrus* NCBI Reference Sequence: WP_044924278.1 Wild type	276	MQNGFLGITVSSEQVGWAVTNPKYELERASRKDLWGVRLFDKAETAEDR RMFRTNRRLNQRKKNRIHYLRDIFHEEVNQKDPNFFQQLDESNFCEDDR TVEFNFDTNLYKNQFPTVYHLRKYLMETKDKPDIRLVYLAFSKFMKNRG HFLYKGNLGEVMDFENSMKGFCESLEKFNIDFPTLSDEQVKEVRDILCD HKIAKTVKKKNIITITKVKSKTAKAWIGLFCGCSVPVKVLFQDIDEEIV TDPEKISFEDASYDDYIANIEKGVGIYYEAIVSAKMLFDWSILNEILGD HQLLSDAMIAEYNKHHDDLKRLQKIIKGTGSRELYQDIFINDVSGNYVC YVGHAKTMSSADQKQFYTFLKNRLKNVNGISSEDAEWIDTEIKNGTLLP KQTKRDNSVIPHQLQLREFELILDNMQEMYPFLKENREKLLKIFNFVIP YYVGPLKGVVRKGESTNWMVPKKDGVIHPWNFDEMVDKEASAECFISRM

		TGNCSYLFNEKVLPKNSLLYETFEVLNELNPLKINGEPISVELKQRIYE QLFLTGKKVTKKSLTKYLIKNGYDKDIELSGIDNEFHSNLKSHIDFEDY DNLSDEEVEQIILRITVFEDKQLLKDYLNREFVKLSEDERKQICSLSYK GWGNLSEMLLNGITVTDSNGVEVSVMDMLWNTNLNLMQILSKKYGYKAE IEHYNKEHEKTIYNREDLMDYLNIPPAQRRKVNQLITIVKSLKKTYGVP NKIFFKISREHQDDPKRTSSRKEQLKYLYKSLKSEDEKHLMKELDELND HELSNDKVYLYFLQKGRCIYSGKKLNLSRLRKSNYQNDIDYIYPLSAVN DRSMNNKVLTGIQENRADKYTYFPVDSEIQKKMKGFWMELVLQGFMTKE KYFRLSRENDFSKSELVSFIEREISDNQQSGRMIASVLQYYFPESKIVF VKEKLISSFKRDFHLISSYGHNHLQAAKDAYITIVVGNVYHTKFTMDPA IYFKNHKRKDYDLNRLFLENISRDGQIAWESGPYGSIQTVRKEYAQNHI AVTKRVVEVKGGLFKQMPLKKGHGEYPLKTNDPRFGNIAQYGGYTNVTG SYFVLVESMEKGKKRISLEYVPVYLHERLEDDPGHKLLKEYLVDHRKLN HPKILLAKVRKNSLLKIDGFYYRLNGRSGNALILTNAVELIMDDWQTKT ANKISGYMKRRAIDKKARVYQNEFHIQELEQLYDFYLDKLKNGVYKNRK NNQAELIHNEKEQFMELKTEDQCVLLTEIKKLFVCSPMQADLTLIGGSK HTGMIAMSSNVTKADFAVIAEDPLGLRNKVIYSHKGEK
KvCas9 *Kandleria vitulina* NCBI Reference Sequence: WP_031589969.1 Wild type	277	MSQNNNKIYNIGLDIGDASVGWAVVDEHYNLLKRHGKHMWGSRLFTQAN TAVERRSSRSTRRRYNKRRERIRLLREIMEDMVLDVDPTFFIRLANVSF LDQEDKKDYLKENYHSNYNLFIDKDFNDKTYYDKYPTIYHLRKHLCESK EKEDPRLIYLALHHIVKYRGNFLYEGQKFSMDVSNIEDKMIDVLRQFNE INLFEYVEDRKKIDEVLNVLKEPLSKKHKAEKAFALFDTTKDNKAAYKE LCAALAGNKFNVTKMLKEAELHDEDEKDISFKFSDATFDDAFVEKQPLL GDCVEFIDLLHDIYSWVELQNILGSAHTSEPSISAAMIQRYEDHKNDLK LLKDVIRKYLPKKYFEVFRDEKSKKNNYCNYINHPSKTPVDEFYKYIKK LIEKIDDPDVKTILNKIELESFMLKQNSRTNGAVPYQMQLDELNKILEN QSVYYSDLKDNEDKIRSILTFRIPYYFGPLNITKDRQFDWIIKKEGKEN ERILPWNANEIVDVDKTADEFIKRMRNFCTYFPDEPVMAKNSLTVSKYE VLNEINKLRINDHLIKRDMKDKMLHTLFMDHKSISANAMKKWLVKNQYF SNTDDIKIEGFQKENACSTSLTPWIDFTKIFGKINESNYDFIEKIIYDV TVFEDKKILRRRLKKEYDLDEEKIKKILKLKYSGWSRLSKKLLSGIKTK YKDSTRTPETVLEVMERTNMNLMQVINDEKLGFKKTIDDANSTSVSGKF SAEVQELAGSPAIKRGIWQALLIVDEIKKIMKHEPAHVYIEFARNEDEK ERKDSFVNQMLKLYKDYDFEDETEKEANKHLKGEDAKSKIRSERLKLYY TQMGKCMYTGKSLDIDRLDTYQVDHIVPQSLLKDDSIDNKVLVLSSENQ RKLDDLVIPSSIRNKMYGFWEKLFNNKIISPKKFYSLIKTEFNEKDQER FINRQIVETRQITKHVAQIIDNHYENTKVVTVRADLSHQFRERYHIYKN RDINDFHHAHDAYIATILGTYIGHRFESLDAKYIYGEYKRIFRNQKNKG KEMKKNNDGFILNSMRNIYADKDTGEIVWDPNYIDRIKKCFYYKDCFVT KKLEENNGTFFNVTVLPNDTNSDKDNTLATVPVNKYRSNVNKYGGFSGV NSFIVAIKGKKKKGKKVIEVNKLTGIPLMYKNADEEIKINYLKQAEDLE EVQIGKEILKNQLIEKDGGLYYIVAPTEIINAKQLILNESQTKLVCEIY KAMKYKNYDNLDSEKIIDLYRLLINKMELYYPEYRKQLVKKFEDRYEQL KVISIEEKCNIIKQILATLHCNSSIGKIMYSDFKISTTIGRLNGRTISL DDISFIAESPTGMYSKKYKL
EfCas9 *Enterococcus faecalis* NCBI Reference Sequence: WP_011644410.1 Wild type	278	MRLFEEGHTAEDRRLKRTARRRISRRRNRLRYLQAFFEEAMTDLDENFF ARLQESFLVPEDKKWHRHPIFAKLEDEVAYHETYPTIYHLRKKLADSSE QADLRLIYLALAHIVKYRGHFLIEGKLSTENTSVKDQFQQFMVIYNQTF VNGESRLVSAPLPESVLIEEELTEKASRTKKSEKVLQQFPQEKANGLFG QFLKLMVGNKADFKKVFGLEEEAKITYASESYEEDLEGILAKVGDEYSD VFLAAKNVYDAVELSTILADSDKKSHAKLSSSMIVRFTEHQEDLKKFKR FIRENCPDEYDNLFKNEQKDGYAGYIAHAGKVSQLKFYQYVKKIIQDIA GAEYFLEKIAQENFLRKQRTFDNGVIPHQIHLAELQAIIHRQAAYYPFL KENQEKIEQLVTFRIPYYVGPLSKGDASTFAWLKRQSEEPIRPWNLQET VDLDQSATAFIERMTNFDTYLPSEKVLPKHSLLYEKFMVFNELTKISYT DDRGIKANFSGKEKEKIFDYLFKTRRKVKKKDIIQFYRNEYNTEIVTLS GLEEDQFNASFSTYQDLLKCGLTRAELDHPDNAEKLEDIIKILTIFEDR QRIRTQLSTFKGQFSAEVLKKLERKHYTGWGRLSKKLINGIYDKESGKT ILDYLVKDDGVSKHYNRNFMQLINDSQLSFKNAIQKAQSSEHEETLSET VNELAGSPAIKKGIYQSLKIVDELVAIMGYAPKRIVVEMARENQTTSTG KRRSIQRLKIVEKAMAEIGSNLLKEQPTTNEQLRDTRLFLYYMQNGKDM

		YTGDELSLHRLSHYDIDHIIPQSFMKDDSLDNLVLVGSTENRGKSDDVP SKEVVKDMKAYWEKLYAAGLISQRKFQRLTKGEQGGLTLEDKAHFIQRQ LVETRQITKNVAGILDQRYNAKSKEKKVQIITLKASLTSQFRSIFGLYK VREVNDYHHGQDAYLNCVVATTLLKVYPNLAPEFVYGEYPKFQTFKENK ATAKAIIYTNLLRFFTEDEPRFTKDGEILWSNSYLKTIKKELNYHQMNI VKKVEVQKGGFSKESIKPKGPSNKLIPVKNGLDPQKYGGFDSPVVAYTV LFTHEKGKKPLIKQEILGITIMEKTRFEQNPILFLEEKGFLRPRVLMKL PKYTLYEFPEGRRRLLASAKEAQKGNQMVLPEHLLTLLYHAKQCLLPNQ SESLAYVEQHQPEFQEILERVVDFAEVHTLAKSKVQQIVKLFEANQTAD VKEIAASFIQLMQFNAMGAPSTFKFFQKDIERARYTSIKEIFDATIIYQ SPTGLYETRRKVVD
Staphylococcus aureus Cas9	279	KRNYILGLDIGITSVGYGIIDYETRDVIDAGVRLFKEANVENNEGRRSK RGARRLKRRRRHRIQRVKKLLFDYNLLTDHSELSGINPYEARVKGLSQK LSEEEFSAALLHLAKRRGVHNVNEVEEDTGNELSTKEQISRNSKALEEK YVAELQLERLKKDGEVRGSINRFKTSDYVKEAKQLLKVQKAYHQLDQSF IDTYIDLLETRRTYYEGPGEGSPFGWKDIKEWYEMLMGHCTYFPEELRS VKYAYNADLYNALNDLNNLVITRDENEKLEYYEKFQIIENVFKQKKKPT LKQIAKEILVNEEDIKGYRVTSTGKPEFTNLKVYHDIKDITARKEIIEN AELLDQIAKILTIYQSSEDIQEELTNLNSELTQEEIEQISNLKGYTGTH NLSLKAINLILDELWHTNDNQIAIFNRLKLVPKKVDLSQQKEIPTTLVD DFILSPVVKRSFIQSIKVINAIIKKYGLPNDIIIELAREKNSKDAQKMI NEMQKRNRQTNERIEEIIRTTGKENAKYLIEKIKLHDMQEGKCLYSLEA IPLEDLLNNPFNYEVDHIIPRSVSFDNSFNNKVLVKQEENSKKGNRTPF QYLSSSDSKISYETFKKHILNLAKGKGRISKTKKEYLLEERDINRFSVQ KDFINRNLVDTRYATRGLMNLLRSYFRVNNLDVKVKSINGGFTSFLRRK WKFKKERNKGYKHHAEDALIIANADFIFKEWKKLDKAKKVMENQMFEEK QAESMPEIETEQEYKEIFITPHQIKHIKDFKDYKYSHRVDKKPNRELIN DTLYSTRKDDKGNTLIVNNLNGLYDKDNDKLKKLINKSPEKLLMYHHDP QTYQKLKLIMEQYGDEKNPLYKYYEETGNYLTKYSKKDNGPVIKKIKYY GNKLNAHLDITDDYPNSRNKVVKLSLKPYRFDVYLDNGVYKFVTVKNLD VIKKENYYEVNSKCYEEAKKLKKISNQAEFIASFYNNDLIKINGELYRV IGVNNDLLNRIEVNMIDITYREYLENMNDKRPPRIIKTIASKTQSIKKY STDILGNLYEVKSKKHPQIIKKG
Geobacillus thermodenitrificans Cas9	280	MKYKIGLDIGITSIGWAVINLDIPRIEDLGVRIFDRAENPKTGESLALP RRLARSARRRLRRRKHRLERIRRLFVREGILTKEELNKLFEKKHEIDVW QLRVEALDRKLNNDELARILLHLAKRRGFRSNRKSERTNKENSTMLKHI EENQSILSSYRTVAEMVVKDPKFSLHKRNKEDNYTNTVARDDLEREIKL IFAKQREYGNIVCTEAFEHEYISIWASQRPFASKDDIEKKVGFCTFEPK EKRAPKATYTFQSFTVWEHINKLRLVSPGGIRALTDDERRLIYKQAFHK NKITFHDVRTLLNLPDDTRFKGLLYDRNTTLKENEKVRFLELGAYHKIR KAIDSVYGKGAAKSFRPIDFDTFGYALTMFKDDTDIRSYLRNEYEQNGK RMENLADKVYDEELIEELLNLSFSKFGHLSLKALRNILPYMEQGEVYST ACERAGYTFTGPKKKQKTVLLPNIPPIANPVVMRALTQARKVVNAIIKK YGSPVSIHIELARELSQSFDERRKMQKEQEGNRKKNETAIRQLVEYGLT LNPTGLDIVKFKLWSEQNGKCAYSLQPIEIERLLEPGYTEVDHVIPYSR SLDDSYTNKVLVLTKENREKGNRTPAEYLGLGSERWQQFETFVLTNKQF SKKKRDRLLRLHYDENEENEFKNRNLNDTRYISRFLANFIREHLKFADS DDKQKVYTVNGRITAHLRSRWNFNKNREESNLHHAVDAAIVACTTPSDI ARVTAFYQRREQNKELSKKTDPQFPQPWPHFADELQARLSKNPKESIKA LNLGNYDNEKLESLQPVFVSRMPKRSITGAAHQETLRRYIGIDERSGKI QTVVKKKLSEIQLDKTGHFPMYGKESDPRTYEAIRQRLLEHNNDPKKAF QEPLYKPKKNGELGPIIRTIKIIDTTNQVIPLNDGKTVAYNSNIVRVDV FEKDGKYYCVPIYTIDMMKGILPNKAIEPNKPYSEWKEMTEDYTFRFSL YPNDLIRIEFPREKTIKTAVGEEIKIKDLFAYYQTIDSSNGGLSLVSHD NNFSLRSIGSRTLKRFEKYQVDVLGNIYKVRGEKRVGVASSSHSKAGET IRPL
FnCas9 *Fusobaterium nucleatum* NCBI Reference	281	MKKQKFSDYYLGFDIGTNSVGWCVTDLDYNVLRFNKKDMWGSRLFEEAK TAAERRVQRNSRRRLKRRKWRLNLLEEIFSNEILKIDSNFFRRLKESSL WLEDKSSKEKFTLFNDDNYKDYDFYKQYPTIFHLRNELIKNPEKKDIRL VYLAIHSIFKSRGHFLFEGQNLKEIKNFETLYNNLIAFLEDNGINKIID KNNIEKLEKIVCDSKKGLKDKEKEFKEIFNSDKQLVAIFKLSVGSSVSL NDLFDTDEYKKGEVEKEKISFREQIYEDDKPIYYSILGEKIELLDIAKT

Sequence: WP_060798984.1		FYDFMVLNNILADSQYISEAKVKLYEEHKKDLKNLKYIIRKYNKGNYDK LFKDKNENNYSAYIGLNKEKSKKEVIEKSRLKIDDLIKNIKGYLPKVEE IEEKDKAIFNKILNKIELKTILPKQRISDNGTLPYQIHEAELEKILENQ SKYYDFLNYEENGIITKDKLLMTFKFRIPYYVGPLNSYHKDKGGNSWIV RKEEGKILPWNFEQKVDIEKSAEEFIKRMTNKCTYLNGEDVIPKDTFLY SEYVILNELNKVQVNDEFLNEENKRKIIDELFKENKKVSEKKFKEYLLV KQIVDGTIELKGVKDSFNSNYISYIRFKDIFGEKLNLDIYKEISEKSIL WKCLYGDDKKIFEKKIKNEYGDILTKDEIKKINTFKFNNWGRLSEKLLT GIEFINLETGECYSSVMDALRRTNYNLMELLSSKFTLQESINNENKEMN EASYRDLIEESYVSPSLKRAIFQTLKIYEEIRKITGRVPKKVFIEMARG GDESMKNKKIPARQEQLKKLYDSCGNDIANFSIDIKEMKNSLISYDNNS LRQKKLYLYYLQFGKCMYTGREIDLDRLLQNNDTYDIDHIYPRSKVIKD DSFDNLVLVLKNENAEKSNEYPVKKEIQEKMKSFWRFLKEKNFISDEKY KRLTGKDDFELRGFMARQLVNVRQTTKEVGKILQQIEPEIKIVYSKAEI ASSFREMFDFIKVRELNDTHHAKDAYLNIVAGNVYNTKFTEKPYRYLQE IKENYDVKKIYNYDIKNAWDKENSLEIVKKNMEKNTVNITRFIKEKKGQ LFDLNPIKKGETSNEIISIKPKVYNGKDDKLNEKYGYYKSLNPAYFLYV EHKEKNKRIKSFERVNLVDVNNIKDEKSLVKYLIENKKLVEPRVIKKVY KRQVILINDYPYSIVTLDSNKLMDFENLKPLFLENKYEKILKNVIKFLE DNQGKSEENYKFIYLKKKDRYEKNETLESVKDRYNLEFNEMYDKFLEKL DSKDYKNYMNNKKYQELLDVKEKFIKLNLFDKAFTLKSFLDLFNRKTMA DFSKVGLTKYLGKIQKISSNVLSKNELYLLEESVTGLFVKKIKL
SpCas9 *Streptococcus pyogenes* wild type Encoded product of SWBC2D7W014	282	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIG ALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFF HRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLF EENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALS LGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAK NLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQL PEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVK LNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIE KILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQS FIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAF LSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLK TYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSD GFANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKK GILQTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRI EEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRL SDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNY WRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHV AQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINN YHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGR DFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWD PKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEK NPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNE LALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQIS EFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAA FKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDGSPK KKRKVSSDYKDHDGDYKDHDIDYKDDDDKAAG
SpCas9 *Streptococcus pyogenes* M1 SwissProt Accession No.Q99ZW2 Wildtype	283	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIG ALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFF HRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLF EENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALS LGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAK NLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQL PEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVK LNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIE KILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQS FIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAF

		LSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLK TYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSD GFANRNFMQLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKK GILQTVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRI EEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRL SDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNY WRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHV AQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINN YHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGR DFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWD PKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEK NPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNE LALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQIS EFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAA FKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD
SpCas9 Streptococcus pyogenes MGAS1882 wildtype NC_017053.1	284	MDKKYSIGLDIGTNSVGWAVITDDYKVPSKKFKVLGNTDRHSIKKNLIG ALLFGSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFF HRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLADSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQIYNQLF EENPINASRVDAKAILSARLSKSRRLENLIAQLPGEKRNGLFGNLIALS LGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAK NLSDAILLSDILRVNSEITKAPLSASMIKRYDEHHQDLTLLKALVRQQL PEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVK LNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIE KILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQS FIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAF LSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGAYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDRGMIEERLK TYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSD GFANRNFMQLIHDDSLTFKEDIQKAQVSGQGHSLHEQIANLAGSPAIKK GILQTVKIVDELVKVMGHKPENIVIEMARENQTTQKGQKNSRERMKRIE EGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLS DYDVDHIVPQSFIKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVA QILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINNY HHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIG KATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRD FATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDP KKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKN PIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNEL ALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISE FSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD

Polymerase

[0233] In some cases, the payload in the present disclosure comprises a polymerase (*e.g.,* reverse transcriptase). A polymerase can comprise a natural or an engineered domain. A polymerase can be capable of synthesizing nucleic acids. A polymerase can be a DNA polymerase or an RNA polymerase. In some cases, a polymerase is a reverse transcriptase. A reverse transcriptase can synthesize DNA from deoxyribonucleotides. In some cases, a reverse transcriptase adds deoxyribonucleotides to the 3' end of a nucleic acid primer to synthesize DNA. In some cases, a reverse transcriptase uses an RNA template and uses base-pairing interactions to synthesize a DNA strand that is complementary to the RNA template. The reverse transcriptase domain can be a reverse transcriptase from any organism, phage, virus, or an

engineered or mutated variant. The reverse transcriptase domain can be a reverse transcriptase derived from or sharing structural or sequencing similarity to a reverse transcriptase in a CRISPR system. The reverse transcriptase can be an M-MLV or HIV reverse transcriptase. The reverse transcriptase can be a human LINE-1 reverse transcriptase or a group II intron reverse transcriptase. The reverse transcriptase can be a human endogenous retrovirus reverse transcriptase.

Transposase domain

[0234] In some cases, a nucleic-acid modifying effector or a nucleic acid-binding moiety comprises a transposase domain. A transposase domain can be a natural or an engineered domain. A transposase domain can be capable of aiding the translocation of a transposable element, a nucleic acid sequence that can change its position within a genome. In some cases, a transposase domain comprises a TnsA, a TnsB, a TnsC, or a TnsD domain. In some cases, a transposase domain comprises a TniQ domain. In some cases, a transposase domain is derived from or shares sequence or structural similarity with a transposase in a CRISPR system (*e.g.,* a CRISPR-associated transposase). In some cases, a transposase domain is derived from or share sequence or structural similarity with a transposase domain from a type I CRISPR-associated transposon (CAST) system. In some cases, transposase domain is derived from or share sequence or structural similarity with a transposase domain from a type V CRISPR-associated transposon (CAST) system. A transposase domain can be capable of binding to a guidable polypeptide domain. In some cases, a transposase domain is coupled to a guidable polypeptide domain. In some cases, a transposase domain is capable of binding to a type I CRISPR-Cas domain (*e.g.,* a Cascade domain, a Cas8 domain, or a Cas5 domain). In some cases, a transposase domain is capable of binding to a type V CRISPR-Cas domain (*e.g.,* a Cas12 domain). In some cases, a transposase domain is capable of mediating targeted insertion of a nucleic acid into a target nucleic acid. In some cases, a transposase domain is capable of mediating targeted insertion of a nucleic acid that is at least 5 kb, at least 6 kb, at least 7 kb, at least 8kb, at least 9kb, at least 10kb, at least 11kb, at least 12kb, at least 13kb, at least 14kb, or at least 15 kb into a target nucleic acid.

Transcriptional regulatory domain

[0235] In some cases, the payload comprises a transcriptional regulatory domain. A transcriptional regulatory domain can be a natural or an engineered domain. A transcriptional regulatory domain can be capable of regulating, activating, or inhibiting gene expression. For example, a transcriptional repressor can silence gene expression by binding to the promoter of a gene. A transcriptional activator can bind to enhancers or regulatory elements to activate expression of a gene. A transcriptional regulatory domain can comprise a transcription factor. A transcriptional regulatory domain can comprise a transcriptional activation domain or a transcriptional repression domain. For example, a transcriptional activation domain can be or comprise a CAP domain, a VP64 domain, a p65 domain, an Rta domain, a synergistic activation mediator (SAM) domain, a SunTag domain, a VPR domain, a DNA demethylase domain, a histone methyltransferase domain, a histone acetyltransferase domain, or a histone demethylase domain. A transcriptional repression domain can be or comprise a dCas9 domain, a KRAB domain, a Sin3 interacting domain (SID), or a MePC2 domain, a DNA methyltransferase domain, a histone deacetylase

domain, a histone methyltransferase domain, or a histone demethylase domain. In some cases, a transcriptional regulatory domain comprises an epigenetic modifying effector domain. For example, an epigenetic modifying effector can be a DNA methyltransferase, a DNA demethylase, a histone methyltransferase, a histone demethylase, a histone acetyltransferase, or a histone deacetylase domain. A DNA methyltransferase domain can be capable of methylating a nucleic acid. A DNA demethylase domain can be capable of demethylating a nucleic acid. A histone methyltransferase domain can be capable of methylating a histone. A histone demethylase domain can be capable of demethylating a histone. A histone acetyltransferase domain can be capable of adding an acetyl group to a histone. A histone deacetylase domain can be capable of removing an acetyl group from a histone.

Zinc finger domain

[0236] In some embodiments, the payload comprises a zinc finger domain. A zinc finger domain can be a natural or an engineered domain. A zinc finger domain can bind to a specific DNA sequence in a target nucleic acid. A zinc finger domain can comprise from 1 to 10, from 2 to 10, from 3 to 10, from 4 to 10, from 5 to 10, from 6 to 10, from 7 to 10, from 8 to 10, from 9 to 10 zinc fingers, from 1 to 8, from 2 to 8, from 3 to 8, from 4 to 8, from 5 to 8, from 6 to 8, from 7 to 8, from 8 to 8, from 9 to 8 zinc fingers. In some cases, a zinc finger domain comprises a two-handed zinc finger domain. A two handed zinc finger domain can comprise two clusters of zinc finger domains that are separated by intervening amino acids. A two handed zinc finger domain can bind to two noncontiguous target DNA sequences. In some cases, the spacing between the two noncontiguous target sequences comprises from 1 to 15, from 1 to 12, from 1 to 10, from 1 to 8, or from 1 to 5 nucleotides. For example, a two handed type of zinc finger binding protein can be SIP1. A cluster of zinc finger domains in a two handed zinc finger domain can be capable of binding to a unique target nucleic acid sequence.

TALE domain

[0237] In some embodiments, the payload comprises a TALE domain. A TALE domain can be a natural or an engineered domain. A TALE domain can bind to a specific DNA sequence. A TALE domain can comprise one or more effector domains. A TALE effector domain can comprise a central repeat domain comprising tandem repeats. A tandem repeat can comprise repeat variable residues (RVD). One or more RVDs can detect a specific DNA base. Different TALE effector domains may have a different number of repeats and a different order of their repeats. The C-terminal repeat is usually shorter in length (*e.g.,* about 20 amino acids). Sequential repeats and their RVDs can recognize sequential DNA bases.

[0238] A TALE domain described herein can be derived from a TALE effector from a bacterial species. The TALE domain can be engineered to target a given nucleic acid sequence based on their DNA base specificities. The TALE domain can be engineered to remove or add a TALE effector domain. In some cases, the TALE domain corresponds to a perfect match to a nucleic acid target sequence. In some cases, the TALE domain of an epigenetic effector corresponds to one or more mismatches to a target base in the target nucleic acid.

Fusion protein

[0239] In some cases, the payload in the present disclosure comprises a fusion protein. A fusion protein can comprise two or more polypeptide domains of any of the polypeptide domains described elsewhere herein. A fusion protein can be a natural or an engineered fusion protein. In some cases, the two or more polypeptide domains are coupled together. The two or more polypeptide domains can be coupled together directly or coupled together indirectly. For example, a first polypeptide domain can be coupled directly to a second polypeptide domain. Alternatively, the first polypeptide domain can be coupled indirectly to the second polypeptide domain by coupling with a third polypeptide domain that is coupled directly to the second polypeptide domain. In some cases, a first polypeptide domain is coupled to the N-terminus of a second polypeptide domain. In some cases, a first polypeptide domain is coupled to the C-terminus of a second polypeptide domain. In some cases, a first polypeptide domain is coupled to an internal component of a second polypeptide domain. In some cases, the two or more polypeptide domains are covalently linked. In some cases, the two or more polypeptide domains are noncovalently linked. In some cases, the two or more polypeptide domains are coupled together by a linker. For example, a linker may be a peptide linker. A linker can be a rigid linker, which helps maintain a fixed distance between the polypeptide domains that it links. A linker can be a flexible linker, which can allow some flexibility in movement of one polypeptide domain relative to the other polypeptide domain that it is linked to. In some cases, a linker is a cleavable linker. For example, a cleavable linker can comprise a disulfide bond. Alternatively, a cleavable linker can be an enzymatic cleavable linker, *e.g.,* a linker comprising a protease cleavage site.

[0240] The present disclosure provides fusion proteins comprising a guidable polypeptide domain (*e.g.,* a CRISPR domain). A fusion protein comprising a guidable polypeptide domain (*e.g.,* a CRISPR domain) can comprise one or more of a FokI domain, a deaminase domain, a reverse transcriptase domain, an RNA binding domain, a transcriptional regulatory domain, a plasma membrane recruitment domain, a transmembrane domain, a signaling domain, a receptor domain, a packaging domain, or a targeting domain.

[0241] In some cases, the present disclosure provides a fusion protein comprising a guidable polypeptide domain (*e.g.,* a CRISPR domain) coupled to a deaminase domain. A guidable polypeptide domain (*e.g.,* a CRISPR domain) coupled to a deaminase domain can be used for base editing. A base editor can be capable of editing a nucleic acid sequence in a target nucleic acid molecule. A base editor can be capable of enabling the generation of base conversions or point mutations in a target nucleic acid. For example, a cytosine base editor can comprise a guidable polypeptide domain (*e.g.,* a CRISPR domain) and a cytidine deaminase domain. An adenine base editor can comprise CRISPR domain and an adenosine deaminase domain. In some cases, a base editor enables the conversion of C to G, A to I, or C to U. A cytosine base editor can be capable of enabling the conversion of a C-G base pair to a T-A base pair. A glycosylase base editor can be capable of enabling the conversion of a G-C base pair to a C-G base pair or a G-T base pair. An adenine base editor can be capable of enabling the conversion of an A-T base pair to a G-C base pair. In some cases, a base editor comprises a catalytically inactive guidable polypeptide domain (*e.g.,* a

CRISPR domain) (*e.g.*, dCas9, dCas12a, or dCas13b). In other cases, the base editor comprises a guidable polypeptide nickase domain (*e.g.*, nCas9). In some cases, the base editor enables a base pair conversion without introducing a double-stranded break. In some cases, the base editor enables base pair conversions in a target window. In some cases, the base editor comprises a targeting window of from 1 to 20 bases, from 1 to 19 bases, from 1 to 18 bases, from 1 to 17 bases, from 1 to 16 bases, from 1 to 15 bases, from 1 to 14 bases, from 1 to 13 bases, from 1 to 12 bases, from 1 to 11 bases, from 1 to 10 bases, from 1 to 9 bases, from 1 to 8 bases, from 1 to 7 bases, from 1 to 6 bases, from 1 to 5 bases, from 1 to 4 bases, from 1 to 3 bases, or from 1 to 2 bases. In some cases, a base editor has a targeting window of from 3 to 10 bases, from 3 to 9 bases, from 3 to 8 bases, from 3 to 7 bases, from 3 to 6 bases, from 3 to 5 bases, or from 3 to 4 bases. In some cases, the guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to the N-terminus of a deaminase domain. In some cases, the guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to the C-terminus of a deaminase domain. In some cases, the guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to an internal component of a deaminase domain.

[0242] In some cases, the fusion protein comprises a guidable polypeptide domain (*e.g.*, a CRISPR domain) coupled to a reverse transcriptase domain. A guidable polypeptide domain (*e.g.*, a CRISPR domain) coupled to a reverse transcriptase can be capable of enabling prime editing. A prime editor can be capable of editing a nucleic acid sequence in a target nucleic acid molecule. A prime editor can be capable of mediating insertion or deletion of a nucleic acid sequence in a target nucleic acid molecule. In some cases, the prime editor enables a sequence insertion or sequence deletion without introducing a double-stranded break. In some cases, the prime editor introduces a nick at the target site. The prime editor can enable insertion of a template sequence in a target nucleic acid molecule. The template sequence can comprise the desired edit. In some cases, a prime editor reverse transcribes a template sequence to synthesize a complementary strand. In some cases, the synthesized complementary strand is inserted in the target nucleic acid molecule. In some cases, the prime editor uses a primer to carry out reverse transcription. The prime editor can nucleotides to the 3' end of a primer strand. In some cases, a primer strand is generated by nicking the target nucleic acid molecule. In some cases, nicking a strand of the target nucleic acid molecule produces a flap with a 3' OH group. In some cases, the prime editor uses the flap with the 3' OH group as the primer to carry out reverse transcription. In some cases, a guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to the N-terminus of a reverse transcriptase domain. In some cases, a guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to the C-terminus of a reverse transcriptase domain. In some cases, a guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to an internal component of a reverse transcriptase domain.

[0243] In some cases, the fusion protein comprises a guidable polypeptide domain (*e.g.*, a CRISPR domain) coupled to a transcriptional regulatory domain. In some cases, a guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to a transcriptional regulatory domain. In some cases, a guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to a transcriptional activation domain. In some cases, a guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to a transcriptional repression domain. In some cases, guidable polypeptide domain (*e.g.*, a CRISPR domain) is coupled to a

transcriptional regulatory domain. A guidable polypeptide domain (*e.g.,* a CRISPR domain) coupled to a transcriptional regulatory domain can be capable of enabling CRISPR interference (CRISPRi) or CRISPR activation (CRISPRa). In some cases, a guidable polypeptide domain (e.g., a CRISPR domain) can be coupled to a transcriptional regulatory domain such as P3000 or DNMT3. In some cases, a guidable polypeptide domain (*e.g.,* a CRISPR domain) is coupled to the C-terminus of a transcriptional regulatory domain. In some cases, a guidable polypeptide domain (*e.g.,* a CRISPR domain) is coupled to an internal component of a transcriptional regulatory domain. Any of the payloads described herein can further comprise a plasma membrane recruitment domain, transmembrane domain, a signaling domain, a receptor domain, a packaging domain, or a targeting domain. Any of payloads described herein can comprise or be engineered to comprise a protein tag, a peptide tag, or small molecule tag. For example, a payload can comprise a small nuclear localization signal (NLS), a nuclear export signal (NES), a cell penetrating peptide (CPP), a mitochondria penetrating peptide (MPP), a solubility tag, or a fluorescent tag.

Base editor

[0244] In some cases, the payload to be delivered by the lipid containing particles of the present disclosure comprises a nucleobase editor (also termed as "base editor") or one or more components of a nucleobase editing (also termed as "base editing") complex.

[0245] The term "base editor (BE), " or "nucleobase editor (NBE)," as used herein, can refer to an agent comprising a polypeptide that is capable of making a modification to a base (e.g., A, T, C, G, or U) within a nucleic acid sequence (e.g., DNA or RNA). In some embodiments, the base editor is capable of deaminating a base within a nucleic acid. In some embodiments, the base editor is capable of deaminating a base within a DNA molecule. In some embodiments, the base editor is capable of deaminating an adenosine (A) in DNA. In some embodiments, the base editor is capable of deaminating a cytosine (C) in DNA. In some embodiments, the base editor is capable of converting a guanine (G) in DNA through a glycoylase.

[0246] In some cases, the payload in the present disclosure comprises a deaminase domain. The deaminase domain can be a natural or an engineered domain. A deaminase domain can be capable of carrying out deamination reactions in DNA. A deaminase domain can be capable of enabling the generation of base conversions or point mutations in a target nucleic acid. For example, a deaminase domain can be a cytidine deaminase domain or an adenosine deaminase domain. A cytidine deaminase domain can be capable of converting cytosine to uracil. A cytidine deaminase domain can be capable of enabling the conversion of a C-G base pair to a T-A base pair. For example, a cytidine deaminase can be or comprise a APOBEC1 cytidine deaminase. An adenosine deaminase domain can be capable of converting an adenosine to hypoxanthine. An adenosine deaminase domain can be capable of converting an adenosine to an inosine. An adenosine deaminase can comprise TadA or a TadA mutant. In some embodiments, TadA comprises a monomer. In some embodiments, TadA comprises a heterodimer comrpsiing a wildtype TadA and a mutated Tad A. In some embodiments, TadA comprises a homodimer comprising two wildtype TadA domains or two mutated TadA domains. An adenosine deaminase domain can be capable of enabling the conversion of an A-T base pair to a G-C base pair. A deaminase domain

can be a mutated variant. In some cases, a deaminase domain enables the conversion of C to G, A to I, or C to U.

[0247] In some cases, the payload in the present disclosure comprises a glycosylase domain. The glycosylase domain can be a natural or an engineered domain. A glycosylase-based guanine base editor can be designed to remove G, and the AP site generated is repaired by translesion synthesis and/or DNA replication, leading to G-to-C or G-to-T conversion. A glycosylase domain can be capable of enabling the generation of base conversions or point mutations in a target nucleic acid. For example, a glycosylase domain can be a guanine glycosylase domain. Examples of glycosylase base edits can be found in Sun N, et al., Mol Ther. 2022 Jul 6;30(7):2452-2463 and Huawei Tong, et al., *National Science Review*, Volume 10, Issue 8, August 2023, each of which is incorporated in its entirety herein.

[0248] In some cases, the base editor disclosed herein comprises a deaminase or a functional domain thereof ("deaminase domain") that catalyzes deamination reaction.

[0249] The term "deaminase" or "deaminase domain," as used herein, refers to a protein or enzyme that catalyzes a deamination reaction. In some embodiments, the deaminase or deaminase domain is an adenosine deaminase, catalyzing the deamination of adenosine, converting it to the nucleoside hypoxanthine. In some embodiments, the deaminase or deaminase domain is a cytidine deaminase, catalyzing the hydrolytic deamination of cytidine or deoxycytidine to uridine or deoxyuridine, respectively. In some embodiments, the deaminase or deaminase domain is a cytidine deaminase domain, catalyzing the hydrolytic deamination of cytosine to uracil. In some embodiments, the deaminase or deaminase domain is a naturally-occurring deaminase from an organism, such as a human, chimpanzee, gorilla, monkey, cow, dog, rat, or mouse. In some embodiments, the deaminase or deaminase domain is a variant of a naturally-occurring deaminase from an organism, that does not occur in nature. For example, in some embodiments, the deaminase or deaminase domain is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75% at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 99.5% identical to a naturally-occurring deaminase from an organism.

[0250] As used herein, an "adenosine deaminase" is an enzyme that catalyzes the deamination of adenosine, converting it to the nucleoside hypoxanthine. Under standard Watson-Crick hydrogen bond pairing, an adenosine base hydrogen bonds to a thymine base (or a uracil in case of RNA).
When adenine is converted to hypoxanthine, the hypoxanthine undergoes hydrogen bond pairing with cytosine. Thus, a conversion of "A" to hypoxanthine by adenosine deaminase will cause the insertion of "C" instead of a "T" during cellular repair and/or replication processes. Since the cytosine "C" pairs with guanine "G", the adenosine deaminase in coordination with DNA replication causes the conversion of an A•T pairing to a C•G pairing in the double-stranded DNA molecule.

[0251] In some embodiments, the base editor is a chimeric protein comprising a nucleic acid programmable R/DNA binding protein (napR/DNAbp) fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase) domain. The term "nucleic acid programmable D/RNA binding protein (napR/DNAbp)" refers to any protein that can associate (e.g., form a complex) with one or more nucleic

acid molecules (i.e., which can broadly be referred to as a "napR/DNAbp-programming nucleic acid molecule" and includes, for example, guide RNA in the case of Cas systems) which direct or otherwise program the protein to localize to a specific target nucleotide sequence (e.g., a gene locus of a genome, or an RNA molecule) that is complementary to the one or more nucleic acid molecules (or a portion or region thereof) associated with the protein, thereby causing the protein to bind to the nucleotide sequence at the specific target site. This term napR/DNAbp embraces CRISPR Cas9 proteins, as well as Cas9 equivalents, homologs, orthologs, or paralogs, whether naturally occurring or non-naturally occurring (e.g., engineered or recombinant), and can include a Cas9 equivalent from any type of CRISPR system (e.g., type II, V, VI), including Cpf1 (a type-V CRISPR-Cas systems), C2c1 (a type V CRISPR-Cas system), C2c2 (a type VI CRISPR-Cas system) and C2c3 (a type V CRISPR-Cas system). Further Cas-equivalents are described in Makarova et al., "C2c2 is a single-component programmable RNA-guided RNA-targeting CRISPR effector," Science 2016; 353(6299), the contents of which are incorporated herein by reference. However, the nucleic acid programmable R/DNA binding protein (napR/DNAbp) that can be used in connection with this disclosure are not limited to CRISPR-Cas systems. The present disclosure embraces any such programmable protein, such as the Argonaute protein from Natronobacterium gregoryi (NgAgo) which can also be used for DNA-guided genome editing. NgAgo-guide DNA system does not require a PAM sequence or guide RNA molecules, which means genome editing can be performed simply by the expression of generic NgAgo protein and introduction of synthetic oligonucleotides on any genomic sequence. See Gao F, Shen X Z, Jiang F, Wu Y, Han C. DNA-guided genome editing using the Natronobacterium gregoryi Argonaute. Nat Biotechnol 2016; 34(7):768-73, which is incorporated herein by reference.

[0252] In some cases, the napR/DNAbp is derived from a nuclease disclosed herein, such as, Cas9 (e.g., dCas9 and nCas9), CasX, CasY, Cas14, Cpf1, C2c1, C2c2, C2c3, Argonaute protein, or a variant thereof. In some embodiments, the base editor comprises a Cas9 (e.g., dCas9 and nCas9), CasX, CasY, Cpf1, C2c1, C2c2, C2c3, or Argonaute protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a Cas9 nickase (nCas9) fused to an deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a CasX protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a nuclease-inactive Cas9 (dCas9) fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a CasY protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a Cas14 protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a Cpf1 protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a C2c1 protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a C2c2 protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments, the base editor comprises a C2c3 protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase). In some embodiments,

the base editor comprises an Argonaute protein fused to a deaminase (e.g., cytidine deaminase or adenosine deaminase).

[0253] In some embodiments, the adenosine deaminases provided herein are capable of deaminating adenosine. In some embodiments, the adenosine deaminases provided herein are capable of deaminating adenosine in a deoxyadenosine residue of DNA. The adenosine deaminase can be derived from any suitable organism (e.g., E. coli). In some embodiments, the adenosine deaminase is a naturally-occurring adenosine deaminase that includes one or more mutations corresponding to any of the mutations provided herein (e.g., mutations in ecTadA). One of skill in the art will be able to identify the corresponding residue in any homologous protein and in the respective encoding nucleic acid by methods well known in the art, e.g., by sequence alignment and determination of homologous residues. Accordingly, one of skill in the art would be able to generate mutations in any naturally-occurring adenosine deaminase (e.g., having homology to ecTadA) that corresponds to any of the mutations described herein, e.g., any of the mutations identified in ecTadA. In some embodiments, the adenosine deaminase is from a prokaryote. In some embodiments, the adenosine deaminase is from a bacterium. In some embodiments, the adenosine deaminase is from Escherichia coli, Staphylococcus aureus, Salmonella typhi, Shewanella putrefaciens, Haemophilus influenzae, Caulobacter crescentus, or Bacillus subtilis. In some embodiments, the adenosine deaminase is from E. coli.

[0254] In some cases, the deaminase domain of the base editor disclosed herein is derived from a cytidine deaminase. In some cases, the cytidine deaminase domain is derived from the apolipoprotein B mRNA-editing complex (APOBEC) family deaminase, such as APOBEC1 deaminase, APOBEC2 deaminase, APOBEC3A deaminase, APOBEC3B deaminase, APOBEC3C deaminase, APOBEC3D deaminase, APOBEC3F deaminase, APOBEC3G deaminase, or APOBEC3H deaminase. In some cases, the cytidine deaminase is a modification of an APOBEC family deaminase. In some cases, the cytidine deaminase is an evolved derivative of an APOBEC family deaminase. In some embodiments, the base editor comprises BE1, BE2, BE3, BE4, BE4max, or another base editor variant. In some embodiments, the base editor comprises BE4max (R33A) AUGI-hUNG complex (CGBE1).

[0255] In some embodiments, the base editor is fused to, or further comprises as part of a chimeric protein, an inhibitor of base excision repair, for example, a uracil clycosylase inhibitor (UGI) domain. In some embodiments, the base editor is fused to one, two, or three UGI domains. In some embodiments, the base editor is fused to one or more UGI domains. In some embodiments, a UGI domain reduces off target effects, specifically the conversion of C to G or C to A.

[0256] In some cases, the base editor disclosed herein is a chimeric protein that comprises a structure such as, NH2-[deaminase domain]-[napR/DNAbp]-[UGI domain]-COOH; NH2-[deaminase domain]-[napR/DNAbp]-[UGI]-[UGI]-COOH; NH2-[deaminase domain]-[napR/DNAbp]-[UGI]-COOH; NH2-[UGI]-[deaminase domain]-[napR/DNAbp]-COOH; NH2-[deaminase domain]-[UGI]-[napR/DNAbp]-COOH; NH2-[napR/DNAbp]-[UGI]-[deaminase domain]-COOH; or NH2-[napR/DNAbp]-[deaminase domain]-[UGI]–COOH; wherein each instance of"-" comprises an optional linker.

[0257] In some cases, the base editor is fused to, or further comprises as part of a chimeric protein, a uracil binding protein (UBP). The term "uracil binding protein" or "UBP," as used herein, refers to a protein that is capable of binding to uracil. In some embodiments, the uracil binding protein is a uracil modifying enzyme. In some embodiments, the uracil binding protein is a uracil base excision enzyme. In some embodiments, the uracil binding protein is a uracil DNA glycosylase (UDG). In some embodiments, a uracil binding protein binds uracil with an affinity that is at least 1%, 2%, 3%, 5%, 10%, 15%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or at least 95% of the affinity that a wild type UDG (e.g., a human UDG) binds to uracil. The term "base excision enzyme" or "BEE," as used herein, refers to a protein that is capable of removing a base (e.g., A, T, C, G, or U) from a nucleic acid molecule (e.g., DNA or RNA). In some embodiments, a BEE is capable of removing a cytosine from DNA. In some embodiments, a BEE is capable of removing a thymine from DNA. Exemplary BEEs include, without limitation UDG Tyr147Ala, and UDG Asn204Asp as described in Sang et al., "A Unique Uracil-DNA binding protein of the uracil DNA glycosylase superfamily," Nucleic Acids Research, Vol. 43, No. 17 2015; the entire contents of which are hereby incorporated by reference.

[0258] In some embodiments, the UBP is a uracil modifying enzyme. In some embodiments, the UBP is a uracil base excision enzyme. In some embodiments, the UBP is a uracil DNA glycosylase. In some embodiments, the UBP is any of the uracil binding proteins provided herein. For example, the UBP can be a UDG, a UdgX, a UdgX*, a UdgX_On, or a SMUG1. In some embodiments, the UBP comprises an amino acid sequence that is at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 99.5% identical to a uracil binding protein, a uracil base excision enzyme or a uracil DNA glycosylase (UDG) enzyme.

[0259] In some cases, the base editor is fused to, or comprises as a part of the chimeric protein, a nucleic acid polymerase domain (NAP). For instance, the nucleic acid polymerase domain is a eukaryotic nucleic acid polymerase domain. In some cases, the nucleic acid polymerase domain is a DNA polymerase domain. In some cases, the nucleic acid polymerase domain has translesion polymerase activity. In some cases, the nucleic acid polymerase domain is a translesion DNA polymerase. In some cases, the nucleic acid polymerase domain is from Rev7, Rev1 complex, polymerase iota, polymerase kappa, and polymerase eta. In some cases, the nucleic acid polymerase domain is selected from the group of eukaryotic polymerases consisting of alpha, beta, gamma, delta, epsilon, gamma, eta, iota, kappa, lambda, mu, and nu.

[0260] In some cases, the base editor disclosed herein is a chimeric protein that comprises a structure such as, NH2-[deaminase domain]-[napR/DNAbp domain]-[UBP]-[NAP]-COOH; NH2-[deaminase domain]-[napR/DNAbp]-[NAP]-[UBP]-COOH; NH2-[deaminase domain]-[NAP]-[napR/DNAbp]-[UBP]-COOH; or NH2-[NAP]-[deaminase domain]-[napR/DNAbp]-[UBP]-COOH; wherein each instance of"-" comprises an optional linker.

[0261] In some cases, the base editor disclosed herein is complexed with a napR/DNAbp-programming nucleic acid molecule. In some cases, the base editing system disclose herein comprises a base editor and a napR/DNAbp-programming nucleic acid molecule, e.g., the base editor complexed with the

napR/DNAbp-programming nucleic acid molecule. In some cases, the lipid containing particles of the present disclosure deliver a base editing system that comprises both a base editor and a napR/DNAbp-programming nucleic acid molecule, e.g., the base editor complexed with the napR/DNAbp-programming nucleic acid molecule. In some cases, a base editor is delivered separately from the napR/DNAbp-programming nucleic acid molecule through lipid containing particles disclosed herein, or together with other delivery methods, into a cell.

[0262] The term "napR/DNAbp-programming nucleic acid molecule" or equivalently "guide sequence" refers the one or more nucleic acid molecules which associate with and direct or otherwise program a napR/DNAbp protein to localize to a specific target nucleotide sequence (e.g., a gene locus of a genome) that is complementary to the one or more nucleic acid molecules (or a portion or region thereof) associated with the protein, thereby causing the napR/DNAbp protein to bind to the nucleotide sequence at the specific target site. An example is a guide RNA of a Cas protein of a CRISPR-Cas genome editing system.

[0263] Exemplary configurations, sequences, and mutations thereof for deaminase domains, napR/DNAbp domains, UGI domains, and whole base editor proteins, and exemplary configurations of a base editing system (e.g., comprising both a base editor and a napR/DNAbp-programming nucleic acid molecule) that can be delivered by a lipid containing particle disclosed herein include those described in U.S. Patent Publication Nos. US20170121693, US20180073012, US20180312828, US20180170984, US2020010835, US2020172931, US20210230577, US20210198330, US20210277379, US2020399626, US2021371858, US2021380955, US2021277379, US2021301274, US20220127622, US20220313799, US20230055682, US20230159913, US20230086199, US20220127622, US20220313799, US20230279373, US20230055682, each of which is incorporated herein by reference in its entirety. Exemplary configurations, sequences, and mutations thereof for deaminase domains, napR/DNAbp domains, UGI domains, and whole base editor proteins, that can be delivered by a lipid containing particle disclosed herein also include those described in Komor AC et al. Nature. 2016 May 19;533(7603):420-4; Kim YB et al. Nat Biotechnol. 2017 Apr;35(4):371-376; Rees HA et al. Nat Commun. 2017 Jun 6;8:15790; Newby GA et al. Mol Ther. 2021 Nov 3;29(11):3107-3124; Huang TP et al. Nat Protoc. 2021 Feb;16(2):1089-1128; Lapinaite A et al. Science. 2020 Jul 31;369(6503):566-571; Anzalone AV et al. Nat Biotechnol. 2020 Jul;38(7):824-844; Rees HA et al. Nat Rev Genet. 2018 Dec;19(12):770-788; Koblan LW et al. Nat Biotechnol. 2018 Oct;36(9):843-846; and Gaudelli NM et al. Nature. 2017 Nov 23;551(7681):464-471; each of which is incorporated herein by reference in its entirety.

Prime editor

[0264] In some cases, the lipid delivery particles disclosed herein is capable of delivering a payload, such as a prime editing system, or one or more components thereof, such as a ribonucleoprotein (RNP) complex, into a cell in vitro, ex vivo, or in vivo. In some embodiments, the prime editing system, or one or more components thereof, is within the inside cavity of the protein core of the lipid delivery particles disclosed herein.

[0265] Prime editing system is a 'search-and-replace' genome editing technology by which the genome of living organisms can be modified. The term "prime editing system" or "prime editor (PE)" refers the compositions involved in genome editing using target-primed reverse transcription (TPRT) describe herein, can comprise a nucleic acid-guided polypeptide, e.g., nucleic acid-guided polypeptide, a nucleic acid polymerase, chimeric proteins (e.g., comprising guidable polypeptide domain and reverse transcriptase), guide nucleic acid molecule (e.g., guide RNAs), and complexes comprising fusion proteins and guide RNAs, as well as accessory elements, such as second strand nicking components and 5' endogenous DNA flap removal endonucleases (e.g., FEN1) for helping to drive the prime editing process towards the edited product formation.

[0266] In some embodiments, the prime editing system disclosed herein comprises a ribonucleoprotein (RNP) complex. In some cases, the RNP complex comprises a prime editor and a guide nucleic acid molecule. In some cases, the prime editor is formed between one or more proteins and one or more polynucleotides. The prime editor can comprise a nucleic acid-guided polypeptide. The guidable polypeptide domain can comprise a nucleic acid-guided polypeptide, for example a nuclease (e.g., a Cas protein). For instance, the prime editor can comprise a fusion protein, comprising a nucleic acid programmable R/DNA binding protein (e.g., a nuclease, such as a Cas protein) and a nucleic acid polymerase (e.g., a reverse transcriptase or any suitable DNA polymerase). In some cases, the nucleic acid polymerase is coupled to the nucleic acid-guided polypeptide. In some cases, the guide nucleic acid molecule can comprise a guide nucleic acid molecule, e.g., a guide RNA. In some cases, the prime editor is operably linked to the guide nucleic acid molecule via a linker, forming the RNP complex. In some cases, the prime editor is directly linked to the guide nucleic acid molecule, forming the RNP complex.

[0267] In a specific instance, prime editing system comprises a fusion protein that comprises an engineered Cas9 nickase and a reverse transcriptase, and the fusion protein is paired with an engineered prime editing guide RNA (PEgRNA). In some cases, the PEgRNA can direct Cas9 to a target site within a host cell where the lipid delivery particles are delivered. In some cases, the peg RNA can encode the information for installing the desired edit. In some cases, the prime editing system can function through a multi-step process: 1) the Cas9 domain can bind and nick the target genomic DNA site, which is specified by a spacer sequence in the PEgRNA; 2) the reverse transcriptase can use the nicked genomic DNA as a primer to initiate synthesis of an edited DNA strand using an engineered extension on the PEgRNA as a template for reverse transcription, which can generate a single-stranded 3' flap containing the edited DNA sequence; 3) cellular DNA repair mechanism can resolve the 3' flap intermediate by the displacement of a 5' flap species that occurs via invasion by the edited 3' flap, excision of the 5' flap containing the original DNA sequence, and ligation of the new 3' flap to incorporate the edited DNA strand, forming a heteroduplex of one edited and one unedited strand; and 4) cellular DNA repair mechanism can replace the unedited strand within the heteroduplex using the edited strand as a template for repair, which completes this editing process. In some embodiments, the prime editing machinery edits a target DNA molecule. In some embodiments, the prime editing machinery edits a target RNA molecule. Examples of targeting RNA molecules using prime editing are described in international patent application

WO2021072328 and U.S. Patent Application number US20230357766, each of which is incorporated in its entirety. In other instances, a prime editing system is a multi-flap prime editing system that can simultaneously edit both DNA strands. For example, a dual-flap prime editing system comprises two PEgRNAs, which can be used to target opposite strands of a genomic site and direct the synthesis of two complementary 3' flaps containing edited DNA sequence. The pair of edited DNA strands (3' flaps) does not need to directly compete with 5' flaps in endogenous genomic DNA, as the complementary edited strand is available for hybridization instead. In this instance, both strands of the duplex are synthesized as edited DNA, the dual-flap prime editing system obviates the need for the replacement of the non-edited complementary DNA strand. Instead, cellular DNA repair machinery can only excise the paired 5' flaps (original genomic DNA) and ligate the paired 3' flaps into the locus.

[0268] In some embodiments, a prime editing system can be paired with a separate Cas9 nickase and a separate gRNA that nicks the DNA at a locus that is different than the locus targeted by the PEgRNA. In some embodiments, one or more prime editing systems can be paired, each targeting a different locus. In some cases, pairing of two prime editing systems, each of which targets a different locus on the same chromosome, can install large insertions, deletions, or modifications. In some cases, pairing of two prime editing systems, each of which targets a different locus, can install large structural modifications. In some embodiments, a prime editor can install up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 modifications. In some embodiments, a prime editor can install 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more modifications. In some embodiments, a prime editor can install up to about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, or about 100 modifications. In some embodiments, a prime editor can install more than about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, or about 100 modifications. In some cases, a prime editor can install more than 100 modifications. In some embodiments, more than one prime editor can be used to install mutations more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more modifications. In some embodiments, more than one prime editor can be used to install mutations more than about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, or about 100 modifications. In some embodiments, more than one prime editor can be used to install mutations more than about 1kb, 5kb, 10kb, 20kb, 30kb, 40kb, 50kb, 60kb, 70kb, 80kb, 90kb, or more.

[0269] Different variants of prime editors have been developed, such as prime editors (PE) PE1, PE2, PE3, PE4, or PE5, some of which are described in Liu, D. et al., Nature 2019, 576, 149-157 and Huang Z, Liu G. Front Bioeng Biotechnol. 2023;11:1039315, U.S. Patent Application numbers US20210292769, US20230090221, US2022078655, US20230220374, each of which is hereby incorporated by reference herein in its entirety. In some cases, the prime editor comprises a reverse transcriptase (RT) fused with Cas9 H 840A nickase (Cas9n (H840A)) and a prime-editing guide RNA (pegRNA). In some cases, the RT comprises an RNA-dependent DNA polymerase. In some cases, the RT comprises a protein derived from a retrovirus. In some embodiments, the RT comprises Moloney Murine Leukemia Virus (M-

MMLV) RT. In some embodiments, the RT comprises a RT from HFV, LtrA, HERV-Kcon, Tel4c, Marathon, Gst-IIC, MA-INT5, or another RT ortholog. In some cases, the RT is modified, mutated, truncated, or evolved. In some cases, the RT comprises a full length RT protein. In some cases, the RT comprises a truncated RT. In some cases, the RT is fused to the Cas protein. In some cases, the RT is fused to the Cas protein at the N terminus to the Cas protein. In some cases, the RT is fused to the Cas protein at the C terminus of the Cas protein. In some cases, the RT is fused to the Cas protein as an inlaid fusion. In some cases, the RT is untethered to the Cas protein. Examples of prime editing architecture are described in Grünewald, J., et al., Nat Biotechnol 41, 337–343 (2023) and Gao Z, et al., Mol Ther. 2022; 30(9):2942-2951, each of which is incorporated herein in its entirety.

[0270] In some cases, the prime editor comprises (a) a fusion protein having the following N-terminus to C-terminus structure: [NLS]-[Cas9(H840A)]- [linker]-[MMLV_RT(wt)] and (b) a PEgRNA. In some cases, the prime editor comprises (a) a fusion protein having the following N-terminus to C-terminus structure: [NLS]-[Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K) (W313F)] and (b) a PEgRNA. In some cases, the prime editor comprises (a) a fusion protein having the following N-terminus to C-terminus structure: [NLS]-[Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K) (W313F)]; (b) a PEgRNA; and (c) a nicking guide RNA that introduces a nick in the non-edited DNA strand. In some cases, the addition of nicking guide RNA increases the chances of the unedited strand to be repaired rather than the edited strand. In some cases, the prime editor comprises (a) a fusion protein having the following N-terminus to C-terminus structure: [NLS]-[Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K) (W313F)]; (b) a PEgRNA; and (c) a nicking guide RNA that is designed with a spacer that matches only the edited strand but not the original allele before editing, so that the nicking guide RNA is not introduced until after the desired edit is installed. In some cases, the prime editor comprises (a) a fusion protein having the following N-terminus to C-terminus structure: [NLS]-[Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K) (W313F)]; (b) a PEgRNA; and (c) evading specific DNA mismatch repair (MMR) protein, such as co-expression of a dominant negative MMR protein, such as MLH1dn (e.g., MLH1 Δ754-756). In some cases, the prime editor comprises (a) a fusion protein having the following N-terminus to C-terminus structure: [NLS]-[Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K) (W313F)]; (b) a PEgRNA; (c) a nicking guide RNA that introduces a nick in the non-edited DNA strand; and (d) evading specific DNA mismatch repair (MMR) protein, such as co-expression of a dominant negative MMR protein, such as MLH1dn (e.g., MLH1 Δ754-756). Evading MMR protein, such as by co-expression of MMR protein MLH1dn can increase efficiency of prime editing, as described in International Publication No., WO2023102538 and Chen et al., Cell Volume 184, Issue 22, 28 October 2021, Pages 5635-5652.e29, each of which is hereby incorporated by reference herein in its entirety. An exemplary sequence for MLH1dn (MLH1 Δ754-756) is:

MSFVAGVIRRLDETVVNRIAAGEVIQRPANAIKEMIENCLDAKSTSIQVIVKEGGLKLIQIQDNGT
GIRKEDLDIVCERFTTSKLQSFEDLASISTYGFRGEALASISHVAHVTITTKTADGKCAYRASYSD

GKLKAPPKPCAGNQGTQITVEDLFYNIATRRKALKNPSEEYGKILEVVGRYSVHNAGISFSVKKQ GETVADVRTLPNASTVDNIRSIFGNAVSRELIEIGCEDKTLAFKMNGYISNANYSVKKCIFLLFINH RLVESTSLRKAIETVYAAYLPKNTHPFLYLSLEISPQNVDVNVHPTKHEVHFLHEESILERVQQHI ESKLLGSNSSRMYFTQTLLPGLAGPSGEMVKSTTSLTSSSTSGSSDKVYAHQMVRTDSREQKLD AFLQPLSKPLSSQPQAIVTEDKTDISSGRARQQDEEMLELPAPAEVAAKNQSLEGDTTKGTSEMS EKRGPTSSNPRKRHREDSDVEMVEDDSRKEMTAACTPRRRIINLTSVLSLQEEINEQGHEVLREM LHNHSFVGCVNPQWALAQHQTKLYLLNTTKLSEELFYQILIYDFANFGVLRLSEPAPLFDLAMLA LDSPESGWTEEDGPKEGLAEYIVEFLKKKAEMLADYFSLEIDEEGNLIGLPLLIDNYVPPLEGLPIF ILRLATEVNWDEEKECFESLSKECAMFYSIRKQYISEESTLSGQQSEVPGSIPNSWKWTVEHIVYK ALRSHILPPKHFTEDGNILQLANLPDLYKVF. In some cases, other strategies for evading MMR protein can be adopted, such as installing silent mutations next to the desired edit or co-expressing an antibody targeting the MMR protein. In some cases, the foregoing prime editor comprises (a) a fusion protein having the following N-terminus to C-terminus structure: [bipartite NLSI-[Cas9(R221K)(N394K)(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)]-[bipartite NLS]-[NLS] instead. In some cases, the components in the foregoing prime editors are packaged in a single lipid delivery particle. In some cases, the components in the foregoing prime editors are packaged in two or more lipid deliver particles that are delivered to the recipient cell simultaneously. In some cases, the components in the foregoing prime editors are packaged in two or more lipid deliver particles that are delivered to the recipient cell sequentially.

[0271] In some cases, the prime editing system can comprise a flap endonuclease (e.g., FEN1 or variant thereof) that is delivered as a part of the lipid delivery particle (e.g., fused to a plasma membrane recruitment element as a chimeric protein). The flap endonuclease can comprise naturally occurring enzymes that process the removal of 5' flaps formed during cellular processes, including DNA replication. The flap endonuclease includes those described in Patel et al., Nucleic Acids Research, 2012, 40(10): 4507-4519 and Tsutakawa et al., Cell, 2011, 145(2): 198-211, each of which is incorporated herein by reference in its entirety.

[0272] Additional elements that can be delivered as a part of the prime editing system via the lipid delivery particles (e.g., fused to the nucleic acid-guided polypeptide, or fused to plasma membrane recruitment element) described herein include inhibitor of base repair (e.g., proteins that inhibit a nucleic acid repair enzyme, for example, a base excision repair enzyme), uracil glycosylase inhibitor domains (e.g., protein that inhibits a uracil-DNA glycosylase base-excision repair enzyme), epitope tags, and reporter gene sequences, including those described in International Publication No. WO2023205744, which is incorporated herein by reference in its entirety.

Epigenetic editor

[0273] In some cases, the payload to be delivered by the lipid containing particles of the present disclosure comprises an epigenetic editor or one or more components of an epigenetic editing complex (e.g., comprising an epigenetic editor and a nucleic acid molecule that guides the epigenetic editor to bind and/or modify one or more specific target sequences).

[0274] In some cases, the epigenetic editor or epigenetic editing complex disclosed herein has epigenetic activities, such as, methyltransferase activity, demethylase activity, dismutase activity, alkylation activity, depurination activity, oxidation activity, pyrimidine dimer forming activity, integrase activity, transposase activity, recombinase activity, polymerase activity, ligase activity, helicase activity, photolyase activity or glycosylase activity, acetyltransferase activity, deacetylase activity, kinase activity, phosphatase activity, ubiquitin ligase activity, deubiquitinating activity, adenylation activity, deadenylation activity, SUMOylating activity, deSUMOylating activity, ribosylation activity, deribosylation activity, myristoylation activity, remodelling activity, protease activity, oxidoreductase activity, transferase activity, hydrolase activity, lyase activity, isomerase activity, synthase activity, synthetase activity, or demyristoylation activity. In some cases, the epigenetic editor or epigenetic editing complex disclosed herein has a chromosome modification enzyme, or a functional domain that has the functional activity equivalent to a chromosome modification enzyme, such as a methylase, demethylase, acetylase, deacetylase, deaminase, phosphorylase, dephosphorylase, histone modifying enzyme, or nucleotide modifying enzyme. In some cases, the epigenetic editor or epigenetic editing complex disclosed herein has a histone modifying enzyme, or a functional domain that has the functional activity equivalent to a histone modifying enzyme. In some cases, the epigenetic editor or epigenetic editing complex disclosed herein has a nucleotide modifying enzyme, or a functional domain that has the functional activity equivalent to a nucleotide modifying enzyme.

[0275] In some embodiments, the epigenetic editor or epigenetic editing system comprises a protein domain that represses expression of the target gene. For example, the epigenetic editor or epigenetic editing system can comprise a functional domain derived from a zinc finger repressor protein. Sequences of exemplary functional domains of an epigenetic editor or epigenetic editing system that can reduce or silence target gene expression are provided can be found in PCT/US2021/030643 and Tycko et al. (Tycko J, DelRosso N, Hess GT, Aradhana, Banerjee A, Mukund A, Van MV, Ego BK, Yao D, Spees K, Suzuki P, Marinov GK, Kundaje A, Bassik MC, Bintu L. High-Throughput Discovery and Characterization of Human Transcriptional Effectors. Cell. 2020 Dec 23;183(7):2020-2035.e16. doi: 10.1016/j.cell.2020.11.024. Epub 2020 Dec 15. PMID: 33326746; PMCID: PMC8178797.), each of which is incorporated here by reference in its entirety.

[0276] In some embodiments, the epigenetic editor or epigenetic editing system makes an epigenetic modification at a target gene that activates expression of the target gene. In some embodiments, the epigenetic editor or epigenetic editing system modifies the chemical modification of DNA or histone residues associated with the DNA at a target gene harboring the target sequence, thereby activating or increasing expression of the target gene. In some embodiments, the epigenetic editor or epigenetic editing system comprises a DNA demethylase, a DNA dioxygenase, a DNA hydroxylase, or a histone demethylase domain.

Nucleic acids and polynucleotides

[0277] In some cases, the lipid delivery particle of the present disclosure comprises a payload comprising a nucleic acid. The nucleic acid as a payload can comprise or be composed of one or more

nucleotides. Nucleotides are referred to by their commonly accepted single-letter codes: A represents adenine, C represents cytosine, G represents guanine, T represents thymine, U represents uracil, I represents inosine. Unless otherwise indicated, nucleotide sequences are written from left to right in a 5' to 3' orientation. In some cases, the nucleic acid as a payload comprises a polynucleotide. The nucleic acid as a payload can comprise DNA or RNA. In some cases, the nucleic acid as a payload comprises or encodes a gene. The nucleic acid as a payload can comprise or encode any of the polynucleotides described elsewhere herein. The nucleic acid as a payload can be a vector encoding any of the polypeptide domains described elsewhere herein. In some cases, the nucleic acid as a payload is an engineered polynucleotide. In some cases, the payload does not comprise a repair template. In some cases, the double stranded break is repaired through non-homologous end joining.

[0278] In some cases, the payload comprises a repair template. The repair template can be double-stranded or single-stranded. The repair template can comprise a template sequence comprising a desired edit to be introduced in a target nucleic acid molecule. In some cases, the repair template is a homology-directed repair template. A homology-directed repair template can comprise a homology arm that is homologous to a sequence in the target nucleic acid. In some cases, the payload comprises a DNA-synthesis template comprising a DNA-synthesis template sequence. The DNA-synthesis template can comprise a desired edit to be introduced in a target nucleic acid molecule. The DNA-synthesis template can be a template for a DNA polymerase or a reverse transcriptase to carry out DNA synthesis. For example, in prime editing, a prime editor can use the DNA synthesis template sequence to synthesize a DNA strand that is complementary to the DNA synthesis template sequence. In some cases, the DNA strand is inserted into the target nucleic acid. In some cases, the nucleic acid comprising the DNA synthesis template sequence also comprises a primer-binding sequence. A primer-binding sequence can be complementary to a sequence in a primer strand to which a DNA polymerase or reverse transcriptase can add nucleotides. In some cases, the primer strand is part of a target nucleic acid molecule. A primer-binding sequence can be complementary to a sequence in the target nucleic acid.

[0279] In some cases, the payload comprises a double-stranded DNA containing a desired gene sequence to be inserted in the target nucleic acid molecule. In some cases, the double-stranded DNA is configured to couple to a transposase domain. In some cases, the payload is delivered in the same particle as the transposase domain. In some cases, the payload is delivered in a separate particle as the transposase domain.

[0280] In some cases, the payload comprises a polynucleotide that is configured to bind to a guidable polypeptide domain. In some cases, the polynucleotide directs a guidable polypeptide domain to a sequence in a target nucleic acid molecule. In some cases, the polynucleotide comprises a scaffold segment configured to bind to a guidable polypeptide domain (*e.g.,* Cas9 or Cas12). In some cases, polynucleotide comprises a spacer sequence that is complementary to a target sequence in the target nucleic acid molecule and is capable of hybridizing to the target sequence. The polynucleotide can be a natural molecule or an engineered or synthetic molecule. The polynucleotide can be derived or share sequence or structural similarities to CRISPR RNA (crRNA), a tracrRNA, or a scoutRNA encoded in a

CRISPR system. In some cases, the polynucleotide is engineered to be a single RNA guide (sgRNA) comprising elements of the crRNA and the tracrRNA. In some cases, the polynucleotide comprises a scaffold segment and a spacer sequence. The scaffold segment can be configured to bind to a guidable polypeptide domain. The scaffold segment can be specific to a specific type of guidable polypeptide (*e.g.*, Cas9 or Cas12). In some cases, the spacer sequence is programmed to be any sequence. In some cases, the spacer sequence is programmed to a sequence complementary to a target nucleic acid sequence.

[0281] In some cases, the payload comprises a polynucleotide that is a guide nucleic acid molecule for a prime editing system, *e.g.*, a prime editing guide RNA (PEgRNA). In some cases, the PEgRNA is capable of (i) identifying a target nucleotide sequence to be edited, and (ii) encoding new genetic information that replaces the targeted sequence. In some cases, a guide nucleic acid molecule for a prime editing system comprises two or more guide RNAs. In some cases, a guide nucleic acid molecule for a prime editing system comprises a nicking guide RNA. In some cases, a guide RNA comprises (A) a primer binding site, (B) a clamp segment, (C) a sequence encoding new genetic information that replaces the targeted sequence, (D) an aptamer, (E) spacer, or (F) scaffold, or any combinations thereof. In some cases, a guide RNA comprises a sequence encoding new genetic information that replaces the targeted sequence, a spacer, and scaffold. In some cases, a guide RNA comprises a spacer and scaffold. In some cases, the guide nucleic acid molecule is heterologous to the cell or host receiving the lipid delivery particle.

[0282] In some cases, the PEgRNA comprises an extended single guide RNA (sgRNA) containing a primer binding site (PBS) and a template sequence for nucleic acid polymerase (*e.g.*, reverse transcriptase or DNA polymerase). For example, a PEgRNA can comprise an architecture corresponding to 5′-[spacer]-[guide RNA core]-[extension arm]-3′. The spacer sequence can comprise about 20 nucleotides in length. The spacer sequence can bind to a protospacer in a target nucleic acid molecule. The spacer sequence can guide the nucleic acid-guided polypeptide (*e.g.*, Cas9) to the target nucleic acid molecule. The guide RNA core can be responsible for binding of the nucleic acid-guided polypeptide (*e.g.*, Cas9). The extension arm can comprise a primer binding site, an edit template, and a homology arm, in a 3′ to 5′ direction. The PEgRNA can further comprise, optionally, a 3’ end modifier region, 5’ end modifier region, a transcriptional signal at the 3’ end. The PEgRNA can optionally comprise a secondary structure, such as, hairpins, stem/loops, toe loops, RNA-binding protein recruitment domains (*e.g.*, the MS2 aptamer which recruits and binds to the MS2cp protein). In some cases, the PEgRNA comprises an aptamer and the prime editor further comprises an aptamer binding protein (*e.g.*, fused to Cas protein or reverse transcriptase). Guide RNAs including an aptamer include those described in International Publication No. WO2023205708, which is hereby incorporated herein by reference in its entirety. Homology arm can encode a portion of a resulting reverse transcriptase-encoded single strand DNA flap to be integrated into the target DNA site by replacing the endogenous strand. The portion of the single strand DNA flap encoded by the homology arm is complementary to the non-edited strand of the target DNA sequence, which facilitates the displacement of the endogenous strand and annealing of the single strand DNA flap in its place, thereby installing the edit. The edit template can comprise a sequence corresponding to new genetic information that replaces the targeted sequence, i.e., a single strand RNA of the PEgRNA that

codes for a complementary single strand DNA that is either the sense or the antisense strand of the new genetic information that replaces the targeted sequence and which is incorporated into the genomic DNA target locus through the prime editing process.

[0283] In some cases, during genome editing, the primer binding site allows the 3' end of the nicked DNA strand to hybridize to the PEgRNA, while the reverse transcriptase template serves as a template for the synthesis of edited genetic information. A prime editing system can allow DNA synthesis based on the reverse transcriptase template at a nick site a single 3' flap, which becomes integrated into a target nucleic acid on the same strand. In other embodiments, a prime editing system can be a multi-flap prime editing system that generate pairs or multiple pairs of 3' flaps on different strands, which form duplexes comprising desired edits and which become incorporated into target nucleic acid molecules, *e.g.*, at specific loci or edit sites in a genome. In some embodiments, the pairs or multiple pairs of 3' flaps form duplexes because they comprise reverse complementary sequences which anneal to one another once generated by the prime editors described herein. The duplexes can be incorporated into the target site by cell-driven mechanisms that naturally replace the endogenous duplex sequences located between adjacent nick sites. In certain embodiments, the new duplex sequences can be introduced at one or more locations (*e.g.*, at adjacent genomic loci or on two different chromosomal locations), and can comprise one or more sequences of interest, *e.g.*, protein-encoding sequence, peptide-encoding sequence, or RNA-encoding sequence.

[0284] In some cases, the payload comprises a polynucleotide comprising a scaffold segment, a spacer sequence, a DNA synthesis template, and a primer-binding sequence. In some cases, the scaffold segment and a spacer sequence are on a first nucleic acid molecule and the DNA synthesis template and the primer-binding sequence are on a second nucleic acid molecule.

[0285] In some cases, the guide RNA further comprises a clamp segment. In some cases, the guide RNA comprising, from 3' to 5', a primer binding site, a sequence encoding at least a portion of the first recombinase recognition sequence, a clamp segment, scaffold, and spacer. The clamp segment comprises a sequence that, after being reverse transcribed is at least partially complementary to a genomic site close to the primer binding site and where the spacer binds. Without wishing to be bound by a certain theory, the clamp segment can enhance integration efficiency of the new genetic material that replaces the target sequence at the double-stranded target DNA sequence relative to a guide RNA without the clamp segment. The clamp segment can allow for a reduced number of nucleotides in the primer binding site need to bind its genomic site and facilitate reverse transcription, which in turn enables design of a guide RNA that is shorter than conventional guide RNAs used for other gene editing methods. The clamp segment is described in International Publication No. WO2023215831, which is hereby incorporated herein by reference in its entirety.

[0286] In some cases, a guide RNA can complete the insertion of new genetic material that replaces the target sequence without another guide RNA when delivered to a cell together with a prime editor described herein. The guide RNA can complete the insertion of the new genetic material that replaces the

target sequence with a second guide RNA that is a nicking guide RNA when delivered together with a prime editor described herein.

[0287] In some cases, a guide RNA comprises two or more guide RNAs. In some cases, the two or more guide RNAs comprise a first guide RNA encoding at least a first portion of new genetic material that replaces the target sequence. In some cases, the two or more guide RNAs comprise a second guide RNA encoding at least a second portion of the new genetic material that replaces the target sequence. In some cases, the first guide RNA and the second guide RNA work in a pair and collectively encode the new genetic material that replaces the target sequence, thereby inserting the new genetic material that replaces the target sequence into the genome of a cell receiving the lipid delivery particles in a site-specific manner. In some cases, the first and the second portion of the new genetic material that replaces the target sequence have at least 6bp overlap. In some cases, the first portion of the new genetic material that replaces the target sequence is 46 bp. In some cases, the first portion of the new genetic material that replaces the target sequence is 42 bp. In some cases, the first portion or the second portion of the new genetic material that replaces the target sequence is 36 bp, 38 bp, 40 bp, 42 bp, 44 bp, or 46 bp. The first guide RNA comprises a first spacer. The second guide RNA comprises a second spacer. The first spacer and the second spacer bind to two genomic target sites that are within 5-100 bp from each other. When the two or more guide RNAs are delivered to a cell together with a prime editor, the double strand DNA between the two genomic target sites are deleted and the full sequence of the new genetic material that replaces the target sequence is inserted instead. The deletion can be mediated by the following steps: (a) reverse transcription of the sequence encoding the first portion of the new genetic material that replaces the target sequence in the first guide RNA and the sequence encoding the second portion of the new genetic material that replaces the target sequence in the second guide RNA, wherein the first and the second portion of the new genetic material that replaces the target sequence having at least 6bp overlap, (b) annealing of the two overlapped portion of the new genetic material that replaces the target sequence, (c) synthesis of the second strand comprising the full sequence of the new genetic material that replaces the target sequence, (d) excision of the original DNA sequence, and (e) ligation of the pair nicks. The mechanism, process, and components of this process include those described in International Publication Nos. WO2023122764, WO2023205710, and WO2023225670, each of which is hereby incorporated herein by reference in its entirety.

[0288] In some cases, the payload comprises a polypeptide domain described herein coupled to a polynucleotide domain described herein. In some cases, the payload comprises a polypeptide domain described herein complexed to a polynucleotide domain described herein. In some cases, the payload comprises a ribonucleoprotein. For example, the payload may comprise a guidable polypeptide domain complexed to a polynucleotide configured to bind to the guidable polypeptide domain (*e.g.*, Cas9 complexed with an RNA guide).

[0289] Any of the payloads described herein can further comprise a plasma membrane recruitment element, a transmembrane domain, a signaling domain, a receptor domain, a packaging domain, or a targeting domain. Any of payloads described herein can comprise or be engineered to comprise a protein

tag, a peptide tag, or small molecule tag. For example, a payload can comprise a nuclear localization signal (NLS), a nuclear export signal (NES), a cell penetrating peptide (CPP), a mitochondria penetrating peptide (MPP), a solubility tag, or a fluorescent tag, or any combination thereof.

Other Payloads

[0290] In some cases, the payload in the lipid delivery particle of the present disclosure comprises a recombinant protein. The payload can be a diagnostic imaging agent, such as a contrast agent. In some cases, the payload comprises a therapeutic agent, including, but not limited to, a nuclease, a recombinase, a growth factor, an antibody, a chimeric antigen receptor, a T cell receptor, a cytokine, a cytokine inhibitor or agonist, a transcription factor, an organelle, a nucleic acid molecule, a therapeutic DNA, a therapeutic RNA, a retrotransposon, a reverse transcriptase, an oligonucleotide, an aptazyme, an aptamer, or a ribozyme, a generic or specific kinase inhibitor, a small molecule drug, an immunomodulator, a tumor suppressor, a developmental regulator, a cancer vaccine, an anesthetic, an enzyme, a hormone, a ligand, a receptor, a T cell receptor, a transposon, a retrotransposon, a DNA polymerase, a RNA dependent DNA polymerase, a homing endonuclease, interferons, chemokines, insulin, growth factors, an antisense oligonucleotide, an RNAi, a shRNA, and any combination thereof. The payload can be a prophylactic agent. In some cases, the payload comprises a biomarker. The payload can also comprise an exogenous antigen or an enzyme. In some cases, the payload comprises a metabolite molecule. In some cases, the payload comprises a lipid molecule. In some cases, the payload comprises a structural protein. In some cases, the payload comprises a hormone or a hormonal protein.

Motifs and Modifications in Lipid Delivery Particles

[0291] In some aspects, provided herein are short polypeptide motifs and/or modifications that can be present within the chimeric protein or the plasma membrane recruitment element as described herein. Without wishing to be bound by a theory, the motifs in the chimeric proteins and/or modifications to the chimeric protein disclosed herein can enhance one or multiple characteristics of particle assembly and/or payload delivery, including, but not limited to, payload expression, payload stability, payload loading and offloading, particle formation and/or budding, and payload translocation to and from the nucleus.

Particle Budding Motif

[0292] A particle budding motif can be a short polypeptide fused to the payload or plasma membrane recruitment element. Without wishing to be bound by a theory, the particle budding motif as described herein can enhance the interaction with host factors that are responsible for the creation of lipid delivery particles. In some cases, the particle budding motif can be a PPXY, LPXY, PTAP, or YPXnL. In some cases, n is an integer from 1 to 5. The particle budding motif can comprise a late domain of a wild-type gag polyprotein from a retrovirus or human endogenous retroviral gag. For example, the particle budding motif includes an RSV P2B and its associated late domain. The particle budding motif can bind ESCRT complex (*e.g.*, NEDD4, TSG101, and Alix). For example, PPXY and LPXY can bind NEDD4, PTAP can

bind TSG101, YPXnL can bind Alix. In some cases, the particle budding motif promotes the efficiency of particle essembly or budding (*e.g.,* increase particle titer). In some cases, the particle budding motif increases the particle titer by at least 1-fold, at least 2-fold, at least 3-fold, at least 4-fold, or at least 5-fold. In some cases, the particle budding motif increase the particle titer by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%. The particle budding motif can comprise a late assembly (L) domain. L domains are conserved sequences that can engage the endosomal sorting complex required for transport (ESCRT) components to promote budding. The particle budding motif can be found in retroviral gag proteins which recruit members of the ESCRT complex (*e.g.,* TSG101, ALIX, NEDD4). The ESCRT complex is located on the cytoplasmic surface of the multivesicular body and can recognize ubiquitinated proteins into vesicles. The vesicles can then bud into the multivesicular body and can be released into the extracellular space. The ESCRT also plays a role in endolysosomal membrane and plasma membrane repair, neuronal pruning, nuclear envelope maintenance, and autophagy. The ESCRT complex comprises three complexes (ESCRT-I, ESCRT-II, ESCRT-III) which are active in the cytosol and the plasma membrane to assist in assembly and fission from the membrane.

[0293] The lipid delivery particle can comprise the particle budding motif as described herein. In some cases, the particle budding motif is linked to the C-terminus of the chimeric protein. In some cases, the particle budding motif is linked to the N-terminus of the chimeric protein. In some cases, the particle budding motif is linked to the payload. In some cases, the particle budding motif is linked to the N-terminus of the payload. In some cases, the particle budding motif is linked to the C-terminus of the payload. In some cases, the particle budding motif is linked to a plasma membrane recruitment element (*e.g.,* a mutant gag polyprotein or a PH domain). In some cases, the particle budding motif is linked to the N-termimuns of a plasma membrane recruitment element (*e.g.,* a mutant gag polyprotein or a PH domain). In some cases, the particle budding motif is linked to the C-termimuns of a plasma membrane recruitment element (*e.g.,* a mutant gag polyprotein or a PH domain). In some cases, the particle budding motif is linked between the payload and the plasma membrane recruitment element. In some cases, the particle budding motif is linked to a nuclear export signal domain. In some cases, the particle budding motif is linked to the N-terminus of a nuclear export signal domain. In some cases, the particle budding motif is linked to the C-terminus of a nuclear export signal domain. In some cases, the particle budding motif is linked to a non-endogenous cleavage site. In some cases, the particle budding motif is linked to the N-terminus of a non-endogenous cleavage site. In some cases, the particle budding motif is linked to the C-terminus of a non-endogenous cleavage site. In some cases, the particle budding motif is linked to a post-translational modification motif. In some cases, the particle budding motif is linked to the N-terminus of a post-translational modification motif. In some cases, the particle budding motif is linked to the C-terminus of a post-translational modification motif. In some cases, the particle budding motif is linked to a multimerization motif. In some cases, the particle budding motif is linked to the N-terminus of a multimerization motif. In some cases, the particle budding motif is linked to the C-terminus of a multimerization motif. In some cases, the particle budding motif is present as tandem repeats in the

chimeric protein. In some cases, the chimeric protein can comprise one, two, three, four, five, or more particle budding motifs. In some cases, flexible linkers can be present in-between the particle budding motifs. In some cases, a particle budding motif can have a linker to the N-terminus and/or the C-terminus.

[0294] In some cases, the particle budding motif is sourced from a virus. The virus can include, but is not limited to, HIV, EIAV, RSV, ALV, FUJSV, HTLV-1, MLV, MMLV, EBOV, HTLV-2, SRV-2, CHMP4A, AVISY, fMLV, influenza, zika virus, dengue virus, WNV, and Tupaia. In some cases, the particle budding motif comprises a sequence with at least 80% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 106-137. In some cases, the particle budding motif comprises a sequence with at least 90% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 106-137. In some cases, the particle budding motif comprises a sequence with at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 106-137. In some cases, the particle budding motif comprises a sequence as set forth in any one of SEQ ID NOs: 106-137. In some cases, the particle budding motif comprises any of the sequences or a minimal sequence drawn from any of the sequences as set forth in **Table 5.**

Table 5. Exemplary particle budding motif (BD) sequences

SEQ ID NO.	Amino Acid Sequence	Virus Source	Budding Motif
106	LQSRPEPTAPPEESFRFGEETTTPSQKQEPI DKELYPLASLRSLFGSDPSSQ	HIV Gag	PTAP/PPEE/L YPL
107	PIQQKSQHNKSVVQETPQTQNLYPDLSEIKK EYNVKEKDQVEDLNLDSLWE	EIAV Gag	LYPDL
108	GETTVQRDAKMAPEETATPKTVGGTSCYHCG TAIGCNCATASAPPPPYVGSGLYPSLAGV	RSV / FUJSV / ALV Gag	PPPY/LYPSL
109	PAPPPPSSPTHDPPDSDPQIPPPYVEPTAPQ VL	HTLV-1 Gag	PPPY/PTAP
110	LPPLPTAPVL	MLV Gag	PTAP
111	LPTAPPEYMEAIYPA	EBOV VP40	PTAP/PPEY
112	LVKNQVSPSAPAAPVPTPICPTTTPPPPPPP SPEAHVPPPYVEPTTTQCFPIL	HTLV-2 Gag	PSAP/PPPY
113	PDWPPFLSRPPPYNRTAATA	SRV-2 Gag	PPPY
114	LTRPPPYNKATPSAPTVMAVV	SRV-1 / MPMV Gag	PPPY/PSAP
115	MSGLGRLFGKGKKEKGPTPEEAIQKLKETEK ILIKKQEFLEQKIQQELQTAKKYGTKNKRAA LQALRRKKRFEQQLAQTDGTLSTLEFQREAI ENATTNAEVLRTMELAAQSMKKAYQDMDIDK VDELMTDITEQQEVAQQISDAISRPMGFGDD VDEDELLEELEELEQEELAQELLNVGDKEEE	CHMP4A W/ other motifs	PSAP/PPPY

	PSVKLPSVPSTHLPAGPAPKVDEDEEALKQL AEWVSGDGSGSGGVSAREPSAPSIPTPAYQS SPAGGHAPTPPPYAPRTMPPTK		
116	MSGLGRLFGKGKKEKGPTPEEAIQKLKETEK ILIKKQEFLEQKIQQELQTAKKYGTKNKRAA LQALRRKKRFEQQLAQTDGTLSTLEFQREAI ENATTNAEVLRTMELAAQSMKKAYQDMDIDK VDELMTDITEQQEVAQQISDAISRPMGFGDD VDEDELLEELEELEQEELAQELLNVGDKEEE PSVKLPSVPSTHLPAGPAPKVDEDEEALKQL AEWVS	CHMP4A	
117	GETTVQRDAKMAPEETATPKTVGGTSCYHCG TASGCNCATATASAPPPPYVGSGLCPSLAGV G	AVISY Gag	PPPY
118	GPVPTTSTLILPPEYSSWGYPYEAPPSYEQ	HUMAN ARRD1	PPEY/PPSY
119	LYPALTSPLNTKPRPQVLPDSGGPLIDLLTE DPPPY	fMLV Gag	LYPAL/PPPY
120	KQVKENKTQPPVAYQYWPPAELQYRPPPESQ YGYPGMPPAPQGRAPYPQPPTRRLNPTAPPS RQGSELHEIIDKSRK	kcon (HERV-K) Gag	PPPE/PPAP/PTAP
121	LQSRPEPTAPPEESFRFGEETTTPSQKQEPI DKELYPLASLRSLFGSDPSSQKMQIFVKTLT GKTITLEVEPSDTIENVKAKIQDKEGIPPDQ QRLIFAGKQLEDGRTLSDYNIQKESTLHLVL RLRGG	HIV Gag with Ubiquilated Lysine	PTAP/PPEE/LYPL
122	KVLLSRTALLPQPSAPSAPPVLPPSEEEESF PHPFPPPYNPPAPPESSLV	Tcon Gag	PPPY/PAPP
123	TPGANERKYNNYMYLICYGFVEDVERTPETG KRKKIRTIA	Nipah M protein	YMYL
124	GLGDRKDECSMYMFLLGVVEDSDPLGPPIG	Measles M Protein	YMFL
125	NNMDKAVKLYRKLKREITFHGAKEISLSYS	Influenza M protein	YRKL
126	YDQSGAASANKYRYMSLKQDHTVKEGTMDD	Sindbis Structural Polypro.	YMSL
127	KKDDPVGFPQGYQCLLKVIIQLEKKDPTKS	Tupaia M Protein	YQCL
128	ANLADVRSYCYLASVSDLSTGRFSITPSAP	WNV Genome Polyprotein	YCYL, PSAP
129	KRFSLGMLQGRGPLKLYMALVAFLRFLTIP	Dengue Genome Glycoprotein	YMAL
130	MAAEITRRGSAYYMYLDRSDAGKAISFATT	Zika Genome Polyprotein	YMYL

131	PNCFNSSINNIHEMEIQLKDALEKNQQWLVY DQQREVYVKGLLAKIFELEKKTETAAHSLPQ QTKKPESEGYLQEEKQKC	Human Cep55	
132	PPQPPLPETKEKEQAPPAPSSLYRTLSLHGS	Human Gag V	PPAP/LYRTL
133	KPPPYKPSAP	Basic PPPY + PSAP motif	PPPY/PSAP
134	LPTAPPEYMEAIYPAKMQIFVKTLTGKTITL EVEPSDTIENVKAKIQDKEGIPPDQQRLIFA GKQLEDGRTLSDYNIQKESTLHLVLRLRGG	EBOV VP40 W/ Ubiquitylated Lysine	PTAP/PPEY
135	LPTAPPEYMEAIYPALPTAPPEYMEAIYPAL PTAPPEYMEAIYPA	EBOV VP40 repeated	PTAP/PPEY
136	TVDISPDTVGTLSLIMLAQAQEVFFLKATRD KMKDAIIAKLANQAADYFGDAFKQCQYKDTL PKEVFPVLAAKHCIMQANAEYHQSILAKQQK KFGEEIARLQHAAELIKTVASRYDEYVNVKD FSDKINRALAAAKKDNDFIYHDRVPDLKDLD PIGKATLVKSTPVNVPISQKFTDLFEKMVPV SVQQSLAAYNQRKADLVNRSIAQMREATTLA GDGSGSGGVSAREPSAPSIPTPAYQSSPAGG HAPTPPPYAPRTMPPTK	Chimeric Alix Protein	
137	KPPPYK	Basic PPPY motif	PPPY

Membrane Penetrating Peptide

[0295] A membrane penetrating peptide (*e.g.*, a cell penetrating peptide) can be a short polypeptide fused to the payload or plasma membrane recruitment element that can facilitate protein translocation across a phospholipid bilayer.

[0296] In some cases, the membrane penetrating peptide is fewer than 40 amino acids. In some cases, the membrane penetrating peptide is fewer than 30 amino acids. In some cases, the membrane penetrating peptide is fewer than 20 amino acids. In some cases, the membrane penetrating peptide is about 40 amino acids. In some cases, the membrane penetrating peptide is about 35 amino acids. In some cases, the membrane penetrating peptide is about 30 amino acids. In some cases, the membrane penetrating peptide is about 25 amino acids. In some cases, the membrane penetrating peptide is about 20 amino acids.

[0297] In some cases, the membrane penetrating peptide promotes recruitment of the payload to the plasma membrane. In some cases, the membrane penetrating peptide increases the efficiency of particle assembly and/or budding. In some cases, the membrane penetrating peptide functions in a pH-inducible manner. In some cases, the pH that can modulate membrane penetrating activity of the membrane penetrating peptide is between 3 and 10, such as 3, 4, 5, 6, 7, 8, 9 or 10. Without wishing to be bound by a theory, membrane penetrating peptides facilitate payload translocation via penetration of the membrane, endocytotic-mediated entry, or translocation through a transitory structure.

[0298] Membrane penetrating peptides can have amino acid compositions that either contain a high relative abundance of positively charged amino acids such as lysine or arginine or have sequences that contain an alternating pattern of polar, charged amino acids and non-polar, hydrophobic amino acids, as described in Derakhshankhah and Jafari (2018) *Biomedicine and Pharmacotherapy* 108:1090-1096. Membrane penetrating peptides can also contain only apolar residues with low net charge or hydrophobic amino acid groups that are helpful for cellular uptake. As described herein, the membrane penetrating peptides can be cationic, amphipathic, or hydrophobic.

[0299] The chimeric protein can comprise the membrane penetrating peptide as described herein. In some cases, the membrane penetrating peptide is linked to the C-terminus of the chimeric protein. In some cases, the membrane penetrating peptide is linked to the N-terminus of the chimeric protein. In some cases, the membrane penetrating peptide is linked to the payload. In some cases, the membrane penetrating peptide is linked to a plasma membrane recruitment element (*e.g.,* a mutant gag polyprotein). In some cases, the membrane penetrating peptide is linked between the payload and the plasma membrane recruitment element. In some cases, the membrane penetrating peptide is present as tandem repeats in the chimeric protein.

[0300] In some cases, the membrane penetrating peptide comprises a sequence with at least 80% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 138-161. In some cases, the membrane penetrating peptide comprises a sequence with at least 90% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 138-161. In some cases, the membrane penetrating peptide comprises a sequence with at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 138-161. In some cases, the membrane penetrating peptide comprises a sequence as set forth in any one of SEQ ID NOs: 138-161. In some cases, the membrane penetrating peptide comprises a sequence as set forth in **Table 6.**

Table 6. Exemplary membrane penetrating peptide sequences

SEQ ID NO.	Name	Amino Acid Sequence
138	YTA2	YTAIAWVKAFIRKLRK
139	HIV-1 TAT	GRKKRRQRRRPPQ
140	Pep-c19	VVNKLIRNNKMNC
141	Vectofusin	KKALLHAALAHLLALAHHLLALLKKA
142	L17E	IWLTALKFLGKHAAKHEAKQQLSKL
143	PCV2 NLSa	MTYPRRRFRRRRHRPRS
144	9R	RRRRRRRRR
145	11R	RRRRRRRRRRR
146	Penetratin	RQIKIWFQNRRMKWKK

147	Pep-1a	KETWWETWWTEWSQPKKKRKV
148	Pep-1b	KETWETWWTEWSQPKKKRKV
149	MTD_1	AAAVPVLVAA
150	MTD_2	PLLLLLPAL
151	MTD_3	AVALVAVVAVA
152	MTD_4	LLAAAAALLLA
153	MTD_5	AVVVPALVLAAP
154	MTD_6	AVLPLLAVP
155	MTD_7	AVKKKPAAA
156	pVEC	LLIILRRRIRKQAHAHSK
157	TP10	AGYLLGKINLKALAALAKKIL
158	MITO1	KLAKLAKKLAKLAK
159	nCTRL	DLSLARLATARLAI
160	KALA	WEAKLAKALAKALAKHLAKALAKALKACEA
161	HIV-1 TATplus	YGRKKRRQRRR

Post-Translational Modifications Motif

[0301] A post-translational modification motif disclosed herein can be a short peptide present within the chimeric protein that leads the payload to be modified following translation (*e.g.,* a post-translational modification). In some cases, the post-translational modification motif is between about 10 and about 40 amino acids in length. Without wishing to be bound by a theory, the post-translational modification alters the payload in a way that can promote recruitment to the plasma membrane. In some cases, the post-translational modification motif, upon the corresponding post-translational modification to the chimeric protein, can alter localization of the payload. The post-translational modification can be a covalent modification of one or more amino acids within the chimeric protein following biosynthesis. The post-translational modification motif can promote plasma membrane localization of cytosolic proteins. The post-translational modification motif can be enzymatic. As described herein, a post-translational modification motif can be to one or more amino acids within the payload, the plasma membrane recruitment element, or both. In some cases, a post-translational modification comprises phosphorylation, glycosylation, ubiquitination, nitrosylation, methylation, lipidation, acetylation, or proteolysis. In some cases, a post-translational modification comprises geranylgeranylation, myristoylation, glypiation, isoprenylation, palmitoylation, or farnesylation. Acetylation can comprise transfer of an acetyl group to nitrogen. Myristoylation can comprise an attachment of a myristoyl group to a N-terminal glycine residue of a protein. Isoprenylation can comprise an attachement of a prenyl group (*e.g.,* a hydrophobic molecule) to a protein. Farnesylation can comprise an attachement of a farnesyl group to a C-terminal cysteine residue of a protein. Phosphorylation can comprise addition of a phosphate group and can occur on serine, threonine, or tyrosine residues. Glycosylation can comprise addition of a sugar moiety (*e.g.,*

monosaccharide, polysaccharide, oligosaccharide, or carbohydrate) to a residue. Ubiquitination can comprise the addition of a ubiquitin polypeptide to a lysine residue of a protein. Nitrosylation can comprise incorporation of a nitrosyl moiety of nitric oxide to a protein. Nitrosylation can occur on free cysteine residues to produce S-nitrothiols. Methylation can comprise the transfer of one-carbon methyl groups to a protein and can increase hydrophobicity of the protein. Lipidation can comprise incorporation of a lipid moiety to a protein. Proteolysis can comprise cleaving of peptide bonds of a protein and can assist antigen processing, apoptosis, surface protein shedding, and cell signaling. Geranylgeranylation can comprise attachment of at least one lipophilic geranylgeranyl isoprene unit from geranylgeranyl diphosphate to at least one cysteine residue. Glypiation can comprise covalent bonding of a glycosylphosphatidylinositol (GPI) anchor to a protein. Palmitoylation can comprise the attachment of at least one fatty acid (*e.g.,* palmitic acid) to a cysteine residue of a protein.

[0302] The chimeric protein can comprise the post-translational modification motif as described herein. In some cases, the post-translational modification motif is linked to the C-terminus of the chimeric protein. In some cases, the post-translational modification motif is linked to the N-terminus of the chimeric protein. In some cases, the post-translational modification motif is linked to the payload. In some cases, the post-translational modification motif is linked to a plasma membrane recruitment element (*e.g.,* a mutant gag polyprotein). In some cases, the post-translational modification motif is linked to both a payload and a plasma membrane recruitment element (*e.g.,* a mutant gag polyprotein). In some cases, the post-translational modification motif is linked to some other part(s) of the chimeric protein than a payload and a plasma membrane recruitment element (*e.g.,* a mutant gag polyprotein). In some cases, the post-translational modification motif is linked to some other part(s) of the chimeric protein besides a payload and a plasma membrane recruitment element (*e.g.,* a mutant gag polyprotein). In some cases, the post-translational modification motif is linked between the payload and the plasma membrane recruitment element. In some cases, the post-translational modification motif is linked to a nuclear export signal domain. In some cases, the post-translational modification motif is linked to a non-endogenous cleavage site. In some cases, the post-translational modification motif is linked to a particle budding motif sequence. In some cases, the post-translational modification motif is present as tandem repeats in the chimeric protein.

[0303] In some cases, the post-translational modification motif comprises a sequence with at least 80% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 162-191. In some cases, the post-translational modification motif comprises a sequence with at least 90% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 162-191. In some cases, the post-translational modification motif comprises a sequence with at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a sequence as set forth in any one of SEQ ID NOs: 162-191. In some cases, the post-translational modification motif comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 162-191, with at least one but not more than 8 nucleic acid differences. In some cases, the post-translational modification motif comprises a sequence as set

forth in any one of SEQ ID NOs: 162-191. In some cases, the post-translational modification motif comprises a sequence as set forth in **Table 7.**

Table 7. Exemplary post-translational modification motif sequences

SEQ ID NO.	SEQ Origin	Amino Acid Sequence	Post-Translational Modification	Location on PH-Freight
162	HIV1	MGARASVLSGGELDKWE	Myristoylation	N-terminal
163	HIV2	MGARGSVLSGKKTDELE	Myristoylation	N-terminal
164	MMTV	MGQKLFVSVLQRLLSER	Myristoylation	N-terminal
165	MPMV	MGQELSQHERYVEQLKQ	Myristoylation	N-terminal
166	HERVK	MGQTKSKIKSKYASYLS	Myristoylation	N-terminal
167	MoMuLV	MGQTVTTPLSLTLGHWK	Myristoylation	N-terminal
168	HTLV1	MGQIFSRSASPIPRPPR	Myristoylation	N-terminal
169	BLV	MGNSPSYNPPAGISPSD	Myristoylation	N-terminal
170	RSV	MEAVIKVISSACKTYCG	Acetylation	N-terminal
171	EIAV	MGDPLTWSKALKKLEKV	Acetylation	N-terminal
172	FV	MASGSNVEEYELDVEAL	Acetylation	N-terminal
173	Myr1	MGSSKSKPKDEAVIKVISSACKTYCG	Acetylation	N-terminal
174	HERVV1	MGNQSSVPQDSPLGCIL	Myristoylation	N-terminal
175	hYes	MGCIKSKENKSPAIKYR	Myristoylation	N-terminal
176	hSrc	MGSNKSKPKDASQRRR	Myristoylation	N-terminal
177	hLck	MGCGCSSHPEDDWMENI	Myristoylation	N-terminal
178	hFyn	MGCVQCKDKEATKLTEE	Myristoylation	N-terminal
179	hLyn	MGCIKSKGKDSLSDDGV	Myristoylation	N-terminal
180	hYrk	MGCVQCKDKEATKLTEE	Myristoylation	N-terminal
181	hBlk	MGLVSSKKPDKEKPIKE	Myristoylation	N-terminal
182	hHck	MGGRSSCEDPGCPRDEE	Myristoylation	N-terminal
183	hFgr	MGCVFCKKLEPVATAKE	Myristoylation	N-terminal
184	hArf	MGNIFANLFKGLFGKKE	Myristoylation	N-terminal
185	hFSP1	MGSQVSVESGALHVVIV	Myristoylation	N-terminal
186	hRhoB	CINCCKVL	isoprenylation and palmitoylation	C-terminal
187	hH-Ras	QHKLRKLNPPDESGPGCMSCKCVLS	isoprenylation	C-terminal

188	hN-Ras	QYRMKKLNSSDDGTQGCMGL PCVVM	isoprenylation	C-terminal
189	hK-Ras4a	QYRLKKISKEEKTPGCVKIK KCIIM	isoprenylation	C-terminal
190	hK-Ras4b	KHKEKMSKDGKKKKKKSKTK CVIM	isoprenylation	C-terminal
191	hH-Ras	LRSRAQASNSGCMSCKCVLS	farnesylation motif of HRAS	C-terminal

Multimerization Motif

[0304] The chimeric protein described herein can comprise a multimerization motif. In some cases, the multimerization motif can perform protein-protein interactions. In some cases, the multimerization motif forms a parallel homodimer, such as a coiled-coil. In some cases, the multimerization motif forms dimers, trimers, tetramers, or other oligomers. In some cases, the multimerization motif is a leucine zipper oligomerization motif. The leucine zipper oligomerization motif can comprise a series of leucines spaced at intervals of every seventh amino acid along an α-helix. In some cases, a leucine zipper oligomerization motif can mediate dimerization or oligomerization. In some cases, the coiled-coil is a leucine zipper oligomerization motif (*e.g.,* a GCN4 leucine zipper or a mutant thereof). Upon dimerization, the leucine zipper oligomerization motif can form a parallel-coiled coil. In some cases, the leucine zipper oligomerization motif (*e.g.,* the GCN4 leucine zipper motif). In some cases, the multimerization motif is synthetic. In some cases, the multimerization motif is a dimerization zinc-finger (DZF) motif, for example, dDZF1 and dDZF2. In some cases, the dDZF1 is an antiparallel heterodimerization domain 1 and binds to dDZF2. In some cases, the dDZF2 is an antiparallel heterodimerization domain 2 and binds to dDZF1. Details of synthetic multimerization motif, including DZFs, are described in Giesecke AV *et al.*, Mol Syst Biol. 2006 2: 2006.0011. Exemplary sequence for dDZF1 or antiparallel heterodimerization domain 1, which binds to dDZF2, can comprise: FKCEHCRILFLDHVMFTIHMGCHGFRDPFKCNMCGEKCDGPVGLFVHMARNAHGEKPFYCEHC EITFRDVVMYSLHKGYHGFRDPFECNICGYHSQDRYEFSSHIVRGEH (SEQ ID NO: 192). Exemplary dDZF2 or antiparallel heterodimerization domain 2, which binds to dDZF1, can include HHCQHCDMYFADNILYTIHMGCHSCDDVFKCNMCGEKCDGPVGLFVHMARNAHGEKPTKCVH CGIVFLDEVMYALHMSCHGFRDPFECNICGYHSQDRYEFSSHIVRGEH (SEQ ID NO: 193). Without wishing to be bound by a theory there, the multimerization motif (*e.g.,* GCN4 leucine zipper, dDZF1/2, or a mutant thereof) can be used to induce multimerization that can assist in assembly of the lipid delivery particles described herein. As such, it can complement removal of nucleic acid binding domains that are necessary for multimerization in a wild-type gag polyprotein.

[0305] In some cases, the multimerization motif (*e.g.,* a leucine zipper oligomerization motif) is linked to the C-terminus of the chimeric protein. In some cases, the multimerization motif (*e.g.,* a leucine zipper oligomerization motif) is linked to the N-terminus of the chimeric protein. In some cases, the

multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked to the payload. In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked to a plasma membrane recruitment element (*e.g.*, a mutant gag polyprotein). In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked to both a payload and a plasma membrane recruitment element (*e.g.*, a mutant gag polyprotein). In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked to some other part(s) of the chimeric protein than a payload and a plasma membrane recruitment element (*e.g.*, a mutant gag polyprotein). In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked to some other part(s) of the chimeric protein besides a payload and a plasma membrane recruitment element (*e.g.*, a mutant gag polyprotein). In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked between the payload and the plasma membrane recruitment element. In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked to a nuclear export signal domain. In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked to a heterlogous protease cleavage sequence. In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is linked to a particle budding motif sequence. In some cases, the multimerization motif (*e.g.*, a leucine zipper oligomerization motif) is present as tandem repeats in the chimeric protein.

[0306] In some cases, the chimeric protein comprising the plasma membrane recruitment element that comprises a mutant gag polyprotein and a payload comprises any one of the arrangements provided in **Table 11A** from the N-terminus to the C-terminus. Plasma membrane recruitment domain is abbreviated PMRE, particle budding motif is abbreviated BD, and a protease cleavage sitecleavable sequence is abbreviated CS.

Table 11A. Exemplary Construct Arrangement for Chimeric Protein with Budding Motif

	Arrangement with Added NES		**Arrangement with Added CS**
PMRE–BD–Payload	PMRE–BD–NES–Payload	PMRE–BD–Payload–NES	PMRE–BD–NES–CS–Payload
PMRE–Payload–BD	PMRE–NES–Payload–BD	PMRE–Payload–NES–BD	PMRE–NES–CS–Payload–BD
BD–Payload–PMRE	BD–NES–Payload–PMRE	BD–Payload–NES–PMRE	BD–NES–CS–Payload–PMRE
BD–PMRE–Payload	BD–PMRE–NES–Payload	BD–PMRE–Payload–NES	BD–PMRE–NES–CS–Payload
Payload–PMRE–BD	NES–Payload–PMRE–BD	Payload– NES–PMRE–BD	NES–CS–Payload–PMRE–BD
Payload–BD–PMRE	NES–Payload–BD–PMRE	NES–Payload–BD–PMRE	NES–CS–Payload–BD–PMRE

[0307] In some cases, the chimeric protein comprising the plasma membrane recruitment element that comprises a mutant gag polyprotein and a payload comprises any one of the arrangements provided in **Table 11B** from the N-terminus to the C-terminus. Plasma membrane recruitment domain is abbreviated PMRE , membrane penetrating peptide is abbreviated MPP, and a protease cleavage sequence is abbreviated CS.

Table 11B. Exemplary Construct Arrangement for Chimeric Protein with Membrane Penetrating Peptide

	Arrangement with Added NES		**Arrangement with Added CS**
PMRE–MPP–Payload	PMRE–MPP–NES–Payload	PMRE–MPP–Payload–NES	PMRE–MPP–NES–CS–Payload
PMRE–Payload–MPP	PMRE–NES–Payload–MPP	PMRE–Payload–NES–MPP	PMRE–NES–CS–Payload–MPP
MPP–Payload–PMRE	MPP–NES–Payload–PMRE	MPP–Payload–NES–PMRE	MPP–NES–CS–Payload–PMRE
MPP–PMRE–Payload	MPP–PMRE–NES–Payload	MPP–PMRE–Payload–NES	MPP–PMRE–NES–CS–Payload
Payload–PMRE–MPP	NES–Payload–PMRE–MPP	Payload– NES–PMRE–MPP	NES–CS–Payload–PMRE–MPP
Payload–MPP–PMRE	NES–Payload–MPP–PMRE	NES–Payload–MPP–PMRE	NES–CS–Payload–MPP–PMRE

[0308] In some cases, the chimeric protein comprising the plasma membrane recruitment element that comprises a mutant gag polyprotein and a payload comprises any one of the arrangements provided in **Table 11C** from the N-terminus to the C-terminus. Plasma membrane recruitment domain is abbreviated PMRE, post-translational modification motif is abbreviated PTM, and a protease cleavage sequence is abbreviated CS.

Table 11C. Exemplary Construct Arrangement for Chimeric Protein with Post-Translational Modification

	Arrangement with Added NES		**Arrangement with Added CS**
PMRE–PTM–Payload	PMRE–PTM–NES–Payload	PMRE–PTM–Payload–NES	PMRE–PTM–NES–CS–Payload
PMRE–Payload–PTM	PMRE–NES–Payload–PTM	PMRE–Payload–NES–PTM	PMRE–NES–CS–Payload–PTM
PTM–Payload–PMRE	PTM–NES–Payload–PMRE	PTM–Payload–NES–PMRE	PTM–NES–CS–Payload–PMRE
PTM–PMRE–Payload	PTM–PMRE–NES–Payload	PTM–PMRE–Payload–NES	PTM–PMRE–NES–CS–Payload
Payload–PMRE–PTM	NES–Payload–PMRE–PTM	Payload–NES–PMRE–PTM	NES–CS–Payload–PMRE–PTM
Payload–PTM–PMRE	NES–Payload–PTM–PMRE	NES–Payload–PTM–PMRE	NES–CS–Payload–PTM–PMRE

[0309] In some cases, the chimeric protein comprising the plasma membrane recruitment element that comprises a mutant gag polyprotein and a payload comprises any one of the arrangements provided in **Table 12** from the N-terminus to the C-terminus. Plasma membrane recruitment domain is abbreviated PMRE, particle budding motif is abbreviated BD, post-translational modification motif is abbreviated PTM, and a protease cleavage sequence is abbreviated CS.

Table 12. Exemplary Construct Arrangement for Chimeric Protein with Post-Translational Modification Motif and Particle Budding Motif

	Arrangement with Added NES		**Arrangement with Added CS**
PTM–PMRE–BD–Payload	PTM–PMRE–BD–NES–Payload	PTM–PMRE–BD–Payload–NES	PTM–PMRE–BD–NES–CS–Payload
PTM–BD–PMRE–Payload	PTM–BD–PMRE–NES–Payload	PTM–BD–PMRE–Payload–NES	PTM–BD–PMRE–NES–CS–Payload
PTM–BD–Payload–PMRE	PTM–BD–NES–Payload–PMRE	PTM–BD–Payload–NES–PMRE	PTM–BD–NES–CS–Payload–PMRE
PTM–Payload–BD–PMRE	PTM–NES–Payload–BD–PMRE	PTM–Payload–NES–BD–PMRE	PTM–NES–CS–Payload–BD–PMRE
Payload–BD–PMRE–PTM	NES–Payload–BD–PMRE–PTM	Payload–NES–BD–PMRE–PTM	NES–CS–Payload–BD–PMRE–PTM
Payload–PMRE–BD–PTM	NES–Payload–PMRE–BD–PTM	Payload–NES–PMRE–BD–PTM	NES–CS–Payload–PMRE–BD–PTM
PMRE–BD–Payload–PTM	PMRE–BD–NES–Payload–PTM	PMRE–BD–Payload–NES–PTM	PMRE–BD–NES–CS–Payload–PTM
BD–PMRE–Payload–PTM	BD–PMRE–NES–Payload–PTM	BD–PMRE–Payload–NES–PTM	BD–PMRE–NES–CS–Payload–PTM

COMPOSITIONS AND SYSTEMS

[0310] In aspects, also provided herein are nucliec acid molecules that encode one or more components of the lipid delivery particles of the present disclosure. For instance, a nucleic acid molecule encoding the chimeric protein or the plasma membrane recruitment element is provided. A nucleic acid molecule encoding the envelope protein is also provided. A nucleic acid molecule encoding the deficient retroviral integrase is also provided. In aspects, provided herein are compositions or systems that include nucleic acid molecules that encode one or more of the components of the lipid delivery particles of the present disclosure. In some cases, the sytem comprises a producer cell, a cell-free extract, or a cell lysate.

[0311] In some cases, the present disclosure features a nucleic acid comprising nucleotide sequences that encode plasma membrane recruitment element, chimeric protein, protease or other component of the lipid delivery particle disclosed herein.

[0312] In some aspects, disclosed herein is a composition comprising a first nucleic acid sequence encoding the recombinant protein of the present disclosure or the chimeric protein of the present disclosure. In some cases, the composition comprises a second nucleic acid sequence encoding an

envelope protein described herein. In some cases, the envelope protein is a retroviral envelope protein or a mutant thereof. In some cases, the envelope protein is an envelope protein from human endogenous retrovirus (HERV) or a mutant thereof. In some cases, the composition further comprises a third nucleic acid sequence encoding a second plasma membrane recruitment element. In some cases, the second plasma membrane recruitment element is the same as the plasma membrane recruitment element. In some cases, the second plasma membrane recruitment element is a retroviral gag or a mutant thereof, a HERV gag or a mutant thereof, a pleckstrin homology (PH) domain or a mutant thereof, or a membrane protein or a transmembrane domain thereof or a mutant thereof. In some cases, the composition further comprises fourth nucleic acid encoding a protease described herein (*e.g.,* heterologous or gag-engodenous proteases). In some cases, the protease is a retroviral protease. In some cases, the plasma membrane recruitment element is linked to the protease, for example, via a cleavable linker. In some cases, the second plasma membrane recruitment element is linked to the protease, for example, via a cleavable linker.

[0313] In some cases, the nucleic acid is an isolated nucleic acid or a non-naturally occurring nucleic acid. Non-naturally occurring nucleic acids are well known to those of skill in the art. In some cases, the nucleic acid is an in vitro transcribed nucleic acid. The term "isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell. In some cases, provided herein is an isolated nucleic acid molecule encoding a lipid delivery particle comprising a lipid membrane, a plasma membrane recruitment element, and a chimeric protein comprising a particle budding motif, a membrane penetrating peptide, and/or a post-translational modification motif. In some cases, provided herein is an isolated nucleic acid molecule encoding a chimeric protein comprising a particle budding motif, a membrane penetrating peptide, and/or a post-translational modification motif.

[0314] In some cases, the nucleic acid molecule is a recombinant nucleic acid molecule. In some cases, provided herein is a recombinant nucleic acid molecule encoding a lipid delivery particle comprising a lipid membrane, a plasma membrane recruitment element, and a chimeric protein comprising a particle budding motif, a membrane penetrating peptide, and/or a post-translational modification motif. In some cases, provided herein is a recombinant nucleic acid molecule encoding a chimeric protein comprising a particle budding motif, a membrane penetrating peptide, and/or a post-translational modification motif. In some instances, the recombinant nucleic acid further comprises a leader sequence. In some instances, the recombinant nucleic acid further comprises a promoter sequence. In some instances, the recombinant nucleic acid further comprises a sequence encoding a poly(A) tail. In some instances, the recombinant nucleic acid further comprises a 3'UTR sequence.

[0315] In some cases, the lipid delivery particle is encoded by a messenger RNA (mRNA). In one aspect the mRNA encoding the lipid delivery particle is introduced into a cell for production of a lipid delivery particles. In one embodiment, the in vitro transcribed RNA lipid delivery particle can be introduced to a

cell as a form of transient transfection. The RNA is produced by in vitro transcription using a polymerase chain reaction (PCR)-generated template. DNA of interest from any source can be directly converted by PCR into a template for in vitro mRNA synthesis using appropriate primers and RNA polymerase. The source of the DNA can be, for example, genomic DNA, plasmid DNA, phage DNA, cDNA, synthetic DNA sequence or any other appropriate source of DNA. The desired template for in vitro transcription is a lipid delivery particle of the present disclosure. In one embodiment, the DNA to be used for PCR contains an open reading frame. The DNA can be from a naturally occurring DNA sequence from the genome of an organism. In one embodiment, the nucleic acid can include some or all of the 5' and/or 3' untranslated regions (UTRs). The nucleic acid can include exons and introns.

[0316] In some cases, the chimeric protein described herein is encoded by a messenger RNA (mRNA). In one aspect the mRNA encoding the chimeric protein is introduced into a cell for production of a lipid delivery particles comprising the chimeric protein. In one embodiment, the in vitro transcribed RNA chimeric protein can be introduced to a cell as a form of transient transfection. The RNA is produced by in vitro transcription using a polymerase chain reaction (PCR)-generated template. DNA of interest from any source can be directly converted by PCR into a template for in vitro mRNA synthesis using appropriate primers and RNA polymerase. The source of the DNA can be, for example, genomic DNA, plasmid DNA, phage DNA, cDNA, synthetic DNA sequence or any other appropriate source of DNA. The desired template for in vitro transcription is a chimeric protein of the present disclosure. In one embodiment, the DNA to be used for PCR contains an open reading frame. The DNA can be from a naturally occurring DNA sequence from the genome of an organism. In one embodiment, the nucleic acid can include some or all of the 5' and/or 3' untranslated regions (UTRs). The nucleic acid can include exons and introns.

[0317] In another aspect, the application features producer cells and vectors containing the nucleic acids described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell.

[0318] The compositions or systems can be used for producing a lipid delivery particle of the present disclosure, for instance, by transfecting or otherwise delivering the nucleic acid molecules in the compositions or systems into a producer cell. The nucleic acid molecules can be expressed in the producer cell, the result of which assemble, package, and subsequently cause the producer cell to release the lipid delivery particle.

[0319] In some cases, a lipid delivery particle of the present disclosure facilitates gene editing efficiency greater than 40%, greater than 50%, greater than 60%, or more. In some cases, a lipid delivery particle of the present disclosure facilitates gene editing efficiency greater than 70%. In some cases, a lipid delivery particle of the present disclosure facilitates gene editing efficiency comprising 8-fold increase of base editing efficiency when compared to a conventional VLP (*e.g.*, the VLPs described in Mangeot, P. E. *et al.* Genome editing in primary cells and in vivo using viral-derived Nanoblades loaded with Cas9-sgRNA ribonucleoproteins. *Nat. Commun.* **10**, 45 (2019).). In some cases, a lipid delivery particle of the present disclosure facilitates gene editing efficiency comprising 8-fold increase of prime editing efficiency when

compared to a conventional VLP. In some cases, a lipid delivery particle of the present disclosure exhibits reduced immunogenicity in transduced target cells. In some cases, a lipid delivery particle of the present disclosure produces reduced off-target genome editing in target cells when delivering genome editing system into the target cells when compared to a conventional VLP. In some cases, a lipid delivery particle of the present disclosure leads to more than 100-fold reduction in Cas-independent off-target editing when compared to a conventional VLP. In some cases, a lipid delivery particle of the present disclosure leads to at least 10-fold, such as 12- to 900-fold, lower Cas-dependent off-target editing when compared to a conventional VLP.

VECTORS

[0320] In various aspects, the lipid delivery vesicles can be embodied as plasmid vectors useful for transient or permanent protein expression in mammalian cells.

[0321] Further provided herein are vectors comprising the compositions or nucleotide sequences encoding a lipid delivery particle or a chimeric protein described herein. In some cases, the vectors comprise nucleotides encoding a lipid delivery particle described herein. In some cases, the vectors comprise nucleotides encoding a chimeric protein described herein. The vectors include, but are not limited to, a virus, plasmid, cosmid, lambda phage or a yeast artificial chromosome (YAC).

[0322] Numerous vector systems can be employed. For example, one class of vectors utilizes DNA elements which are derived from animal viruses such as, for example, bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (Rous Sarcoma Virus, MMTV or MOMLV) or SV40 virus. Another class of vectors utilizes RNA elements derived from RNA viruses such as Semliki Forest virus, Eastern Equine Encephalitis virus and Flaviviruses. In some cases, the vector is selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector. In some cases, the vector further comprises a promoter. In some cases, the vector is an in vitro transcribed vector. In some cases, a nucleic acid sequence in the vector further comprises a poly(A) tail. In some cases, a nucleic acid sequence in the vector further comprises a 3'UTR.

[0323] Once the expression vector or DNA sequence containing the constructs has been prepared for expression, the expression vectors may be transfected or introduced into an appropriate host cell. Various techniques may be employed to achieve this, such as, for example, protoplast fusion, calcium phosphate precipitation, electroporation, retroviral transduction, viral transfection, gene gun, lipid based transfection or other conventional techniques. In the case of protoplast fusion, the cells are grown in media and screened for the appropriate activity.

[0324] Methods and conditions for culturing the resulting transfected cells and for recovering the antibody molecule produced are known to those skilled in the art, and may be varied or optimized depending upon the specific expression vector and mammalian host cell employed, based upon the present description.

CELLS

[0325] In another aspect, described herein are producer cells comprising the lipid delivery particles described herein. In some cases, the producer cells comprise a nucleic acid sequence encoding a lipid delivery particle described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell. The host cell can be a eukaryotic cell, *e.g.,* a mammalian cell, an insect cell, a yeast cell, or a prokaryotic cell, *e.g., E. coli*. For example, the mammalian cell can be a cultured cell or a cell line. Exemplary mammalian cells include lymphocytic cell lines (*e.g.,* NSO), Chinese hamster ovary cells (CHO), COS cells, oocyte cells, and cells from a transgenic animal, *e.g.,* mammary epithelial cell.

[0326] The disclosure also provides producer cells comprising a nucleic acid encoding a chimeric protein as described herein. In some cases, the producer cells are genetically engineered to comprise nucleic acids encoding the antibody molecule.

[0327] In some cases, the producer cells are genetically engineered by using an expression cassette. The phrase "expression cassette," refers to nucleotide sequences, which are capable of affecting expression of a gene in hosts compatible with such sequences. Such cassettes may include a promoter, an open reading frame with or without introns, and a termination signal. Additional factors necessary or helpful in effecting expression may also be used, such as, for example, an inducible promoter.

[0328] The present also provides producer cells comprising the vectors described herein.

[0329] The cell can be, but is not limited to, a eukaryotic cell, a bacterial cell, an insect cell, or a human cell. Suitable eukaryotic cells include, but are not limited to, Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells. Suitable insect cells include, but are not limited to, Sf9 cells.

[0330] Also provided herein are cells (*e.g.,* isolated cells, preferably mammalian, *e.g.,* human, cells) that express, *e.g.,* that have been induced to overexpress, components of the lipid delivery particles and/or chimeric proteins described herein (*e.g.,* over expressed from exogenous sources, such as plasmids or stably integrated transgenes), and a payload fused to a human endogenous GAG, a PH domain, or alternative plasma membrane recruitment element. In some cases, the cell overexpresses a chimeric protein with one, two, or all of: a particle budding motif, a membrane penetrating peptide, and/or a post-translational modification motif. In some cases, the cell does not express a gag protein except for gag proteins that are encoded in the human genome or gag proteins that are encoded by a consensus sequence that is derived from gag proteins found in the human genome (overexpressed from exogenous sources, such as plasmids or stably integrated transgenes). In some cases, the cells are primary or stable human cell lines, *e.g.,* Human Embryonic Kidney (HEK) 293 cells, HEK293 T cells, or BeWo cells.

METHODS OF MAKING

[0331] Producer cell lines can be generated by stably integrating genetic material with a gene of interest into a host cell line. In some cases, the genetic material is transiently expressed in a producer cell line. In some cases, the genetic material is expressed via viral methods. In some cases, the genetic material is

expressed via non-viral methods. In some cases, a producer cell line grows in a serum-free medium or in suspension. A producer cell line can be grown in serum-free medium and suspension simultaneously. In some cases, producer cell lines can be generated with adherent cells (*e.g.,* cells cultured in media and attached to a substrate).

[0332] Producer cell lines can be generated by stably integrating genetic material with a gene of interest into a host cell line. In some cases, the genetic material is transiently expressed in a producer cell line. In some cases, the genetic material is expressed via viral methods. In some cases, the genetic material is expressed via non-viral methods. In some cases, a producer cell line grows in a serum-free medium or in suspension. A producer cell line can be grown in serum-free medium and suspension simultaneously. In some cases, producer cell lines can be generated with adherent cells (*e.g.*, cells cultured in media and attached to a substrate).

[0333] Producer cells can be used to produce the lipid delivery particles described herein. In some cases, generating a producer cell line comprises transfecting cells (*e.g.*, cells of a mammalian cell type) with genetic material of the present disclosure, culturing the cells to produce the lipid delivery particles, obtaining a media from the mammalian cell producing the lipid delivery particles, collecting and filtering the harvested media, and, optionally, purifying the lipid delivery particles to retain structural integrity. In some cases, the method of producing the lipid delivery particle further comprises providing new media to promote transient production of the lipid delivery particles. In some cases, the mammalian cell type includes a HT1080 cell, a COS cell, a HeLa cell, a Chinese Hamster Ovary (CHO) cell, or a HEK 293 cell. HEK293 cells are cells derived from human embryonic kidney cells grown in tissue culture. In some cases, the HEK293 cell is a HEK293, 293E, 293T, 293F, 293FT, or 293T Gesicle cell. The producer cell line can be transformed with a viral vector or non-viral method in any number of means including calcium phosphate and the like.

[0334] Following transfection, the cells can be cultured under conditions for production of lipid delivery particles. Exemplary culturing conditions can include refeeding cells in appropriate media, addition of CO2, and humidity. In some cases, culturing conditions includes addition of antibiotics, anti-fungals, and/or growth factors. The medium can be harvested after 24, 48, 72, or 96 hours, or at any appropriate time point to allow sufficient production of the lipid delivery particles.

[0335] Optionally, the lipid delivery particles in the media can be isolated and collected using any number of techniques known in the art. In some cases, the lipid delivery particles are purified, wherein the lipid delivery particles are washed or resuspended in an appropriate buffer or media or at particular concentration.

[0336] In an aspect, disclosed herein are methods of manufacturing producer cell lines that comprise the lipid delivery particles of the present disclosure. Adherent cells can be first transfected to produce lipid delivery particles. In some cases, transfection occurs by the addition or expression of exogenous nucleic acid sequences via non-viral methods (*e.g.,* by electroporation, microinjection, or a chemical system such as DEAE-dextran or cationic polymers). In some cases, transfection occurs by the addition or expression of exogenous nucleic acid sequences via viral methods *(e.g.*, by infecting the cells with a viral vector,

such as an adenoviral vector, adeno-associate viral vector, a lentiviral vector, a herpes viral vector, or a HSV vector). In some cases, the cells are from a HEK293 cell line (*e.g.*, HEK293, 293E, or 293T). In some cases, to transfect DNA into the host cells, the cells are cultured in a medium. In some cases, cells can be cultured in the medium for 5, 10, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 hours. In some cases, cells can be cultured in the medium for between 10-20 hours. In some cases, cells can be cultured in the medium for 18 hours.

[0337] Following incorporation into the transfection medium, cells are transferred to a new solution. In some cases, the new solution is new media. In some cases, the new media promotes the production of the lipid delivery particles. In some cases, the cells incorporate into the new media for between 10-50 hours. In some cases, the cells incorporate into the new media for 10, 20, 30, 35, 40, 45, or 50 hours. In some cases, the cells incorporate into the new media for 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40 hours. The media can then be harvested. The harvested media can be filtered, and the lipid delivery particles can be collected. Filtration can comprise microfiltration and/or depth filtration. In some cases, the lipid delivery particles can undergo further purification and/or concentration methods that maintain the structural integrity of the particles.

[0338] In some aspects, provided herein is a method of loading a lipid delivery particle with components such as a payload. RNA and protein from a producer cell can get packaged and/or incorporated into lipid delivery vehicles of the present disclosure. In some cases, the components of the lipid delivery particles, such as a payload, is loaded via the packaging and assembly process of the lipid delivery particle. For instance, the payload can be a polypeptide or protein that is packaged into the lipid delivery particle as a part of a chimeric protein as disclosed herein.

[0339] In some cases, the payload is assembled into the lipid delivery particle as an independent entity, *e.g.*, not as a part of a chimeric protein. In other embodiments, the lipid delivery particle provided herein is loaded with a payload by utilizing any suitable method for delivering a biological or chemical payload through a lipid membrane, such as nucleofection, electroporation, lipid-based, polymer-based, or $CaCl_2$ transfection, sonication, freeze thaw, incubation at various temperatures, or heat shock of lipid delivery particles mixed with payload. In some cases, the nucleic acid molecules, such as a template RNA described herein, are loaded into the lipid delivery particle by direct loading, such as electroporation of the lipid delivery particle in vitro. In some cases, the nucleic acid molecules are loaded into the lipid delivery particle by binding to a nucleic acid binding protein (*e.g.*, Cas protein) that is part of the lipid delivery particle or is already loaded into the lipid delivery particle.

[0340] There can be more than one type of loading techniques utilized for loading payloads (*e.g.*, for loading more than one type of payloads) into the lipid delivery particle. For instance, in some cases, a first payload is a polypeptide that is assembled into the lipid delivery particle as a part of a chimeric protein, and a second payload is a separate protein or nucleic acid (RNA or DNA) that interacts with (*e.g.*, binds) the first payload, and thus is loaded into the lipid delivery particle via the interaction between the first payload and the second payload. Alternatively, the second payload can be loaded into the lipid delivery particle via a transfection-like technique or any other suitable method.

[0341] In aspects, also provided herein are methods of using a lipid delivery particle or pharmaceutical composition according to some embodiments of the present disclosure, comprising contacting a cell with the lipid delivery particle described herein. In some cases, the cell is a mammalian cell, such as a human cell. In some cases, the cell is within a subject in need of treatment for a disease or a condition. In some cases, contact comprising administering the lipid delivery particle described herein to the subject, such as via injections.

[0342] In aspects, also provided herein are methods of administering a lipid delivery particle, systems, or pharmaceutical compositions according to some embodiments of the present disclosure. In some cases, the method comprises administering the lipid delivery particle, system, or pharmaceutical composition described herein to a subject in need thereof, such as via injections.

[0343] In aspects, also provided herein are methods of producing a lipid delivery particle or pharmaceutical composition according to some embodiments of the present disclosure. In some cases, the method comprises contacting a producer cell with compositions described herein.

Methods of purification

[0344] In an aspect, described herein are methods of purifying lipid delivery particles. In some cases, the lipid delivery particles are produced from producer cell lines that are either transiently transfected with at least one plasmid or stably expressing constructs that have been integrated into the producer cell line genomic DNA. In some cases, the producer cell culture medium is harvested 24-, 48-, 72-, or 96-hours post-transfection. In some cases, the producer cell culture medium is harvested between 40- and 48-hours post-transfection. The harvested medium can undergo centrifugation steps to remove producer cell debris while maintaining the structural integrity of the lipid delivery particle. In some cases, during harvesting, the producer cell medium is centrifuged, *e.g.*, at 500g for 5 minutes. The clarified lipid delivery particle containing supernatant can then be collected and filtered. In some cases, the lipid delivery particles are further concentrated. In some cases, the lipid delivery particles are further concentrated by ultracentrifugation. In some cases, the lipid delivery particles are concentrated 50-fold, 100-fold, 200-fold, 500-fold, 1000-fold, 2000-fold, 3000-fold, or 5000-fold. In some cases, the concentrated lipid delivery particles are resuspended, *e.g.*, in cold PBS. In some cases, the concentrated lipid delivery particles are frozen, *e.g.*, frozen at a rate of -1°C/min and stored at -80°C.

[0345] In some cases, the purification methods can comprise chromatographic methods (*e.g.*, anion exchange chromatography), ultrafiltration methods (*e.g.*, tangential flow filtration), clarifying normal flow filtration, and/or sterilizing membrane filtration. Anion exchange chromatography can separate substances based on net-surface charge, using an ion-exchange resin. Tangential flow filtration can separate molecules using ultrafiltration membranes. In some cases, the membrane pore size used for tangential flow filtration can retain a biological product of a size less than 1000 kDa, less than 750 kDa, less than 500 kDa, less than 250 kDa, less than 200 kDa, less than 150 kDa, less than 100 kDa, or less than 50 kDa. Normal flow filtration assists in the clarification of biofluid by convecting the substance directly toward a membrane under an applied pressure. In some cases, normal flow filtration can comprise

a membrane pore size of greater than 0.1 μm, greater than 0.2 μm, greater than 0.3 μm, greater than 0.4 μm, greater than 0.5 μm, greater than 0.6 μm, greater than 0.7 μm, greater than 0.8 μm, greater than 0.9 μm, greater than 1.0 μm, greater than 1.5 μm, or greater than 2.0 μm. In some cases, normal flow filtration can comprise a membrane pore size of 0.2 μm, 0.45 μm, 0.8 μm, 1.2 μm, or 2.0 μm. Sterilizing membrane filtration can be used to sterilize heat-sensitive liquid without exposure to denaturing hear. In some cases, sterilizing membrane filtration can comprise a membrane pore size of about 0.1 μm, about 0.2 μm, about 0.3 μm, about 0.4 μm, or about 0.5 μm. In some cases, sterilizing membrane filtration can comprise a membrane pore size of about 0.2 μm or 0.22 μm.

PHARMACEUTICAL FORMULATIONS

[0346] In an aspect, disclosed herein is a pharmaceutical formulation comprising the composition disclosed herein and optionally further comprising a pharmaceutically acceptable carrier, excipient, or additive. The term "pharmaceutical formulation", as used herein, refers to a composition formulated for pharmaceutical use. The terms such as "excipient", "carrier", "pharmaceutically acceptable carrier" or the like are used interchangeably herein. Pharmaceutical formulations comprise an immunologically effective amount of one or more cells, vectors, lipid delivery particles, or compositions disclosed herein, and optionally one or more other components which are pharmaceutically acceptable. In some cases, the pharmaceutical formulation comprises additional agents, *e.g.,* for specific delivery, increasing half-life, or other therapeutic benefit. In some cases, the pharmaceutical formulation may comprise one or more of dimethylsulfoxide (DMSO), dextrose, water, succinate, poly I: poly C, poly-L-lysine, carboxymethylcellulose, and/or chloride.

[0347] As used herein, a "pharmaceutically acceptable carrier" is an agent that is compatible with the other ingredients of the formulation and not injurious to the tissue of the subject (*e.g.,* physiologically compatible, sterile, physiologic pH, etc.) In some cases, a pharmaceutically acceptable carrier comprises any vehicle, such as a liquid or solid filler, diluent, excipient, manufacturing aid (*e.g.,* lubricant, talc magnesium, calcium or zinc stearate, or steric acid), or solvent encapsulating material, involved in carrying or transporting the compound from one site (*e.g.,* the delivery site) of the body, to another site (*e.g.,* organ, tissue or portion of the body).

[0348] Some exemplary materials which can serve as pharmaceutically-acceptable carriers include: (1) sugars, such as lactose, glucose and sucrose; (2) starches, such as corn starch and potato starch; (3) cellulose, and its derivatives, such as sodium carboxymethyl cellulose, methylcellulose, ethyl cellulose, microcrystalline cellulose and cellulose acetate; (4) powdered tragacanthin; (5) malt; (6) gelatin; (7) lubricating agents, such as magnesium stearate, sodium lauryl sulfate and talc; (8) excipients, such as cocoa butter and suppository waxes; (9) oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; (10) glycols, such as propylene glycol; (11) polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol (PEG); (12) esters, such as ethyl oleate and ethyl laurate; (13) agar; (14) buffering agents, such as magnesium hydroxide and aluminum hydroxide; (15) alginic acid; (16) pyrogen-free water; (17) isotonic saline; (18) Ringer's solution; (19) ethyl alcohol; (20) pH buffered

solutions; (21) polyesters, polycarbonates and/or polyanhydrides; (22) bulking agents, such as polypeptides and amino acids (23) serum alcohols, such as ethanol; and (24) other non-toxic compatible substances employed in pharmaceutical formulations. Wetting agents, coloring agents, release agents, coating agents, sweetening agents, flavoring agents, perfuming agents, preservative and antioxidants can also be present in the formulation.

[0349] Pharmaceutical formulation disclosed herein can comprise one or more pH buffering compounds to maintain the pH of the formulation at a predetermined level that reflects physiological pH, such as in the range of about 5.0 to about 8.0. The pH of the pharmaceutical formulation can be about 4, about 5, about 6, about 7, about 8 or about 9. The pH buffering compound used in the aqueous liquid formulation can be an amino acid or mixture of amino acids, such as histidine or a mixture of amino acids such as histidine and glycine. The pH buffering compound can be an agent which does not chelate calcium ions. Exemplary pH buffering compounds include, imidazole and acetate ions. The pH buffering compound can be present in any amount suitable to maintain the pH of the formulation at a predetermined level.

[0350] The pharmaceutical formulations described herein can be prepared by any method known or hereafter developed in the art of pharmacology. In general, such preparatory methods include the step of bringing the active ingredient(s) into association with an excipient and/or one or more other accessory ingredients, and then, optionally, shaping and/or packaging the product into a desired single- or multi-dose unit. Pharmaceutical formulations can additionally comprise a pharmaceutically acceptable excipient, which, as used herein, includes any and all solvents, dispersion media, diluents, or other liquid vehicles, dispersion or suspension aids, surface active agents, isotonic agents, thickening or emulsifying agents, preservatives, solid binders, lubricants, and the like, as suited to the particular dosage form desired.

METHOD OF TREATMENT, PREVENTION, OR DIAGNOSIS

[0351] A lipid delivery particle provided herein can find use in a variety of fields and methods. In some cases, the lipid delivery particle of the present disclosure can be used to deliver one or more payloads, such as a ribonucleoprotein complex to a cell. In some cases, the target cells to which the lipid delivery particles are delivered are *in vitro* cells, *ex vivo* cells, or *in vivo* cells. The lipid delivery particles of the present disclosure can be applicable for delivery of freights into a variety of cell types, such as, animal cells, plant cells, bacteria cells, algal cells, or fungal cells.

[0352] In aspects, also provided herein are methods of treating a subject by administering a lipid delivery particle described herein, a system described herein, a composition described herein, or pharmaceutical composition according to some embodiments of the present disclosure.

[0353] In some cases, the present disclosure provides methods of treating, preventing, or diagnosing a condition, disease, or disorder. In some cases, a composition, kit, or method described herein can be used to treat, prevent, or diagnose a condition, disease, or disorder. The condition, disease, or disorder can comprise a cancer, an immune disorder, an autoimmune disorder, a metabolic disorder, a hormonal disorder, an inflammatory disorder, a developmental disorder, a reproductive disorder, an imprinting

disorder, a genetic disorder, a neurological disorder, or a neurodegenerative disorder. In some cases, the condition, disease, or disorder comprises a liver disorder, an eye disorder, a heart disorder, a kidney disorder, a skin disorder, a blood disorder, a fibrotic disorder, a skeletal disorder, or a muscle order. In some cases, the condition, disease, or disorder is caused by a genetic mutation (*e.g.,* an insertion, deletion, or point mutation). In some cases, the condition, disease, or disorder is hereditary. In some cases, the condition, disease, or disorder is caused by a virus or bacteria or fungus. In some cases, the condition, disease, or disorder is caused by aberrant gene expression. In some cases, the condition, disease, or disorder is a result of age. In some embodiments, the condition, disease, or disorder is chronic.

[0354] The subject in the method of present disclosure can be an animal. In some embodiments, the subject is an animal cell. In some embodiments, the subject is a mammal. In some embodiments, the subject is a human. In some embodiments, the subject is an aquaculture animal (fish, crabs, shrimp, oysters etc.), a mammal. In some embodiments, the animals cell is from, for example, a pet or zoo animal (cats, dogs, lizards, birds (*e.g.*, parrots), lions, tigers and bears etc.), from a farm or working animal (horses, cows (*e.g.*, dairy and beef cattle) pigs, chickens, turkeys, hens or roosters, goats, sheep, etc.), or a human. In some embodiments, the target cell as disclosed herein is in a subject to whom the method of the present disclosure is applicable.

[0355] The methods described herein can be therapeutic or veterinary methods for treating a subject. In some embodiments, the methods described herein are used to treat a disease resulting from a non-functional, poorly functional, or poorly expressed protein or gene product, for instance, resulting from a genetic mutation in one or more cells of the subject. In some embodiments, the methods described herein are used to treat a genetic disease (*e.g.*, a mutation, a substitution, a deletion, an expansion, or a recombination), a monogenic disease, an inherited metabolic disease, a cancer, a neurodegenerative disease, a cardiovascular disease, a pulmonary disease, a renal disease, a liver disease, a genetic disease, a vascular disease, ophthalmic disease, musculoskeletal disease, lymphatic disease, auditory and inner ear disease, a metabolic disease, an inflammatory disease, an autoimmune disease, or an infectious disease. In some cases, provided herein are pharmaceutical compositions and methods for treating a retinal disease, *e.g.*, Leber congenital amaurosis, by administering a pharmaceutical composition formulated for subretinal injection.

KIT

[0356] In aspects, also provided herein are kits comprising the unit doses containing the lipid delivery particles, systems, compositions or pharmaceutical compositions of the present disclosure. In some embodiments, the kit comprises the lipid delivery particles, compositions, or pharmaceutical formulations of the present disclosure; and an informational medium containing instructions for administering the lipid delivery particle, composition, or pharmaceutical formulation to a subject. The kit can include a label indicating the intended use of lipid delivery particle, composition, or pharmaceutical formulation in the kit. Label can include any writing, or recorded material supplied on or with the kit, or which otherwise accompanies the kit.

[0357] A kit of the present disclosure can include, alternatively or additionally, diagnostic agents and/or other therapeutic agents. In some cases, the kit includes cells or pharmaceutical formulations of the present disclosure and a diagnostic agent that can be used in a diagnostic method for diagnosing a condition, disease, or disorder in a subject.

METHODS OF ADMINISTERING

[0358] In some cases, the composition or pharmaceutical formulation described herein is prepared for administration to a subject. In some cases, the pharmaceutical formulation is prepared to induce a therapeutic or prophylactic effect in a subject. Suitable routes of administrating the pharmaceutical formulation described herein include transdermal, intravesical, intravenous, intravascular, intraosseus, topical, subcutaneous, intradermal, intralesional, intraarticular, intraperitoneal, transmucosal, gingival, intradental, intracochlear, transtympanic, intraorgan, epidural, intrathecal, intramuscular, periocular, intratumoral, intracerebral, intravitreal, and intracerebroventricular administration. In some cases, the pharmaceutical formulation described herein is administered locally to a diseased site (*e.g.,* site of infection or tumor site). In some cases, the pharmaceutical composition described herein is delivered in a controlled release system. In some cases, a pump is used. In some cases, polymeric materials is used for controlled release. In some cases, the pharmaceutical composition described herein is administered to a subject by injection, by means of a catheter, by means of a suppository, or by means of an implant, the implant being of a porous, non-porous, or gelatinous material, including a membrane, such as a sialastic membrane, or a fiber. In some cases, the pharmaceutical formulation is formulated in accordance with routine procedures as a formulation adapted for intravenous or subcutaneous administration to a subject. In some cases, pharmaceutical formulations for administration by injection are solutions in sterile isotonic use as solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients can be supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachets indicating the quantity of active agent. In some cases, if the pharmaceutical is to be administered by infusion, it is dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. In some cases, if the pharmaceutical formulation is administered by injection, an ampoule of sterile water for injection or saline is provided so that the ingredients can be mixed prior to administration.

[0359] A pharmaceutical formulation as described herein can be administered or packaged as a unit dose, for example, in reference to a pharmaceutical formulation to physically discrete units suitable as unitary dosage for the subject, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect in association with the required diluent, carrier, or vehicle.

EXAMPLES

[0360] The following examples are provided to further illustrate some embodiments of the present disclosure, but are not intended to limit the scope of the disclosure; it will be understood by their

exemplary nature that other procedures, methodologies, or techniques known to those skilled in the art may alternatively be used.

Example 1: Identification and Selection of Constructs for the Plasma Membrane Recruitment Element Comprising a Mutant Gag Polyprotein

[0361] Initial candidates for the chimeric protein of the lipid delivery particles will be selected based on various plasma membrane recruitment elements and the different arrangements of payload and the plasma membrane recruitment elements. Exemplary contructs for the plasma membrane recruitment elements can be found in **FIGs. 1A, 1B, 2A, 2B, 3A and 3B**.

[0362] The exemplary sequences for the plasma membrane recruitment elements comprising a mutant gag polyprotein with or without a payload (*e.g.,* base editor, ABE8e) that will be used for lipid delivery particles are listed in **Table 10A**. "BE" stands for base editor, ABE8e; "Myr" stands for myristoylation; "PH" stands for a pleckstrin homology domain or a mutant thereof; "MHRCA" standards for a C-terminal fragment of capsid domain that comprises the major homology region domain.

Table 10A. Exemplary sequences for plasma membrane recruitment elements with or without a base editor payload

Description	Amino Acid Sequence	SEQ ID NO
Plasma membrane recruitment elements comprising an HIV mutant gag		
myr-MHRCA-P2-GCN4LZ-RSVP2B	MGARASVYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQ DVKNWMTETLLVQNANPDCKTILRALGQGASIEEMMTACQ GVGGPSHKARVLAEAMSQVTNTNTAIMGRMKQLEDKVEEL LSKNYHLENEVARLKKLVGERGTASAPPPPYVG	194
myr-MHRCA-P2-GCN4LZ-RSVP2B	GARASVYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQD VKNWMTETLLVQNANPDCKTILRALGQGASIEEMMTACQG VGGPSHKARVLAEAMSQVTNTNTAIMGRMKQLEDKVEELL SKNYHLENEVARLKKLVGERGTASAPPPPYVG	195
myr-HERVK YPXnL-MHRCA-P2-P6PTAP-GCN4LZ-RSVP2B	MGARASVGGGGSGGGGSGGGGSAPYPQPPTRRLNYSPVSIL DIKQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTETLLVQ NANPDCKTILRALGQGASIEEMMTACQGVGGPSHKARVLAE AMSQVTNTNTAIMGLQSRPEPTAPPAESGRMKQLEDKVEEL LSKNYHLENEVARLKKLVGERGTASAPPPPYVG	196
myr-HERVK YPXnL-MHRCA-P2-P6PTAP-GCN4LZ-RSVP2B	GARASVGGGGSGGGGSGGGGSAPYPQPPTRRLNYSPVSILDI KQGPKEPFRDYVDRFFKTLRAEQATQDVKNWMTETLLVQN ANPDCKTILRALGQGASIEEMMTACQGVGGPSHKARVLAEA MSQVTNTNTAIMGLQSRPEPTAPPAESGRMKQLEDKVEELLS KNYHLENEVARLKKLVGERGTASAPPPPYVG	197

myr-MHRCA-P2-GCN4LZ-RSVP2B - NES-CS-BE	MGARASVYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQ DVKNWMTETLLVQNANPDCKTILRALGQGASIEEMMTACQ GVGGPSHKARVLAEAMSQVTNTNTAIMGRMKQLEDKVEEL LSKNYHLENEVARLKKLVGERGTASAPPPPYVGSGGSLQLPP LERLTLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLMENSSGD YKDDDDKKRTADGSEFESPKKKRKVSEVEFSHEYWMRHAL TLAKRARDEREVPVGAVLVLNNRVIGEGWNRAIGLHDPTAH AEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSR IGRVVFGVRNSKRGAAGSLMNVLNYPGMNHRVEITEGILAD ECAALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGSSGSETP GTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYK VPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRLKRTA RRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEED KKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLR LIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQ LFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGL FGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLL AQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMI KRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYI DGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTF DNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIP YYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQS FIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTE GMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIE CFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDIL EDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTG WGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDD SLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKV VDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRI EEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVD QELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKS DNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGG LSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKL IREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNA VVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKA TAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWD KGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSD KLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKL	198

	KSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKY SLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHY EKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADA NLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYF DTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDSG GSKRTADGSEFEPKKKRKV	
myr-MHRCA-P2-GCN4LZ-RSVP2B - NES-CS-BE	GARASVYSPVSILDIKQGPKEPFRDYVDRFFKTLRAEQATQD VKNWMTETLLVQNANPDCKTILRALGQGASIEEMMTACQG VGGPSHKARVLAEAMSQVTNTNTAIMGRMKQLEDKVEELL SKNYHLENEVARLKKLVGERGTASAPPPPYVGSGGSLQLPPL ERLTLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLMENSSGD YKDDDDKKRTADGSEFESPKKKRKVSEVEFSHEYWMRHAL TLAKRARDEREVPVGAVLVLNNRVIGEGWNRAIGLHDPTAH AEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSR IGRVVFGVRNSKRGAAGSLMNVLNYPGMNHRVEITEGILAD ECAALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGSSGSETP GTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYK VPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRLKRTA RRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEED KKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLR LIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQ LFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGL FGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLL AQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMI KRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYI DGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTF DNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIP YYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQS FIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTE GMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIE CFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDIL EDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTG WGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDD SLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKV VDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRI EEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVD QELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKS DNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGG	199

	LSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKL IREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNA VVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKA TAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWD KGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSD KLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKL KSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKY SLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHY EKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADA NLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYF DTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDSG GSKRTADGSEFEPKKKRKV	
PH-MHRCA-P2-GCN4LZ-RSVP2B	MSDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKER PQDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTV IERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSYSPVSILDIKQGPKEPFRDYVDRFFKTLRA EQATQDVKNWMTETLLVQNANPDCKTILRALGQGASIEEM MTACQGVGGPSHKARVLAEAMSQVTNTNTAIMGRMKQLED KVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVG	200
PH-MHRCA-P2-GCN4LZ-RSVP2B	SDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERP QDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVI ERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSYSPVSILDIKQGPKEPFRDYVDRFFKTLRA EQATQDVKNWMTETLLVQNANPDCKTILRALGQGASIEEM MTACQGVGGPSHKARVLAEAMSQVTNTNTAIMGRMKQLED KVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVG	201
PH-MHRCA-P2-GCN4LZ-RSVP2B - NES-CS-BE	MSDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKER PQDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTV IERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSYSPVSILDIKQGPKEPFRDYVDRFFKTLRA EQATQDVKNWMTETLLVQNANPDCKTILRALGQGASIEEM MTACQGVGGPSHKARVLAEAMSQVTNTNTAIMGRMKQLED KVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVGSGG SLQLPPLERLTLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLM ENSSGDYKDDDDKKRTADGSEFESPKKKRKVSEVEFSHEYW	202

	MRHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRAIGL HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAG AMIHSRIGRVVFGVRNSKRGAAGSLMNVLNYPGMNHRVEIT EGILADECAALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGS SGSETPGTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAV ITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESF LVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLV QTYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGE KKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDD LDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGY AGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRK QRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGAS AQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKY VTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENE DILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRR YTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLI HDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQT VKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRER MKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNR GKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAE RGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAY LNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKR NSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKS KKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLA SHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVIL ADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGG DSGGSKRTADGSEFEPKKKRKV	

PH-MHRCA-P2-GCN4LZ-RSVP2B - NES-CS-BE	SDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERP QDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVI ERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSYSPVSILDIKQGPKEPFRDYVDRFFKTLRA EQATQDVKNWMTETLLVQNANPDCKTILRALGQGASIEEM MTACQGVGGPSHKARVLAEAMSQVTNTNTAIMGRMKQLED KVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVGSGG SLQLPPLERLTLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLM ENSSGDYKDDDDKKRTADGSEFESPKKKRKVSEVEFSHEYW MRHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRAIGL HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAG AMIHSRIGRVVFGVRNSKRGAAGSLMNVLNYPGMNHRVEIT EGILADECAALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGS SGSETPGTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAV ITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESF LVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLV QTYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGE KKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDD LDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGY AGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRK QRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGAS AQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKY VTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENE DILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRR YTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLI HDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQT VKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRER MKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNR GKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAE RGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAY	203

	LNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKR NSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKS KKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLA SHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVIL ADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGG DSGGSKRTADGSEFEPKKKRKV	
Plasma membrane recruitment elements comprising an MMLV mutant gag		
myr-MHRCA-GCN4LZ-RSVP2B	MGQTVTTPLSLTLGAGRSPTNLAKVKGITQGPNESPSAFLER LKEAYRRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLERLE DLKNKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEERRR TEDEQKEKERDRRRHREMSKLLGRMKQLEDKVEELLSKNY HLENEVARLKKLVGERGTASAPPPPYVG	204
myr-MHRCA-GCN4LZ-RSVP2B	GQTVTTPLSLTLGAGRSPTNLAKVKGITQGPNESPSAFLERLK EAYRRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLERLEDL KNKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEERRRTE DEQKEKERDRRRHREMSKLLGRMKQLEDKVEELLSKNYHL ENEVARLKKLVGERGTASAPPPPYVG	205
myr-PTAP-YPXnL-PPPY-MHRCA-GCN4LZ-RSVP2B	MGQTVTTPLSLTLGGGGSGGGGSGGGGSLPPSAPSLPLEGGG GSGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTE DPPPYRDPRAGRSPTNLAKVKGITQGPNESPSAFLERLKEAY RRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLERLEDLKNK TLGDLVREAEKIFNKRETPEEREERIRRETEEKEERRRTEDEQ KEKERDRRRHREMSKLLGRMKQLEDKVEELLSKNYHLENE VARLKKLVGERGTASAPPPPYVG	206
myr-PTAP-YPXnL-PPPY-MHRCA-GCN4LZ-RSVP2B	GQTVTTPLSLTLGGGGSGGGGSGGGGSLPPSAPSLPLEGGGG SGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTED PPPYRDPRAGRSPTNLAKVKGITQGPNESPSAFLERLKEAYRR YTPYDPEDPGQETNVSMSFIWQSAPDIGRKLERLEDLKNKTL GDLVREAEKIFNKRETPEEREERIRRETEEKEERRRTEDEQKE KERDRRRHREMSKLLGRMKQLEDKVEELLSKNYHLENEVA RLKKLVGERGTASAPPPPYVG	207
myr-PTAP-YPXnL-PPPY-MHRCA-	MGQTVTTPLSLTLGGGGSGGGGSGGGGSLPPSAPSLPLEGGG GSGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTE DPPPYRDPRAGRSPTNLAKVKGITQGPNESPSAFLERLKEAY	208

GCN4LZ-RSVP2B - NES-CS-BE	RRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLERLEDLKNK TLGDLVREAEKIFNKRETPEEREERIRRETEEKEERRRTEDEQ KEKERDRRRHREMSKLLGRMKQLEDKVEELLSKNYHLENE VARLKKLVGERGTASAPPPPYVGSGGSLQLPPLERLTLGSLQ LPPLERLTLGSLQLPPLERLTLTSTLLMENSSGDYKDDDDKK RTADGSEFESPKKKRKVSEVEFSHEYWMRHALTLAKRARDE REVPVGAVLVLNNRVIGEGWNRAIGLHDPTAHAEIMALRQG GLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVFGVR NSKRGAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDF YRMPRQVFNAQKKAQSSINSGGSSGGSSGSETPGTSESATPES SGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVL GNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKN RICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFG NIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMI KFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASG VDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGL TPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADL FLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDL TLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYK FIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLG ELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSR FAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLP NEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQ KKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDR FNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDRE MIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIR DKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQV SGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRH KPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILK EHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYD VDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKR QLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSK LVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYP KLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIM NFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKV LSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDP KKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIM	

	ERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKR MLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNE QKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNK HRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTST KEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRTADGSEFE PKKKRKV	
myr-PTAP- YPXnL-PPPY- MHRCA- GCN4LZ- RSVP2B - NES- CS-BE	GQTVTTPLSLTLGGGGSGGGGSGGGGSLPPSAPSLPLEGGGG SGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTED PPPYRDPRAGRSPTNLAKVKGITQGPNESPSAFLERLKEAYRR YTPYDPEDPGQETNVSMSFIWQSAPDIGRKLERLEDLKNKTL GDLVREAEKIFNKRETPEEREERIRRETEEKEERRRTEDEQKE KERDRRRHREMSKLLGRMKQLEDKVEELLSKNYHLENEVA RLKKLVGERGTASAPPPPYVGSGGSLQLPPLERLTLGSLQLPP LERLTLGSLQLPPLERLTLTSTLLMENSSGDYKDDDDKKRTA DGSEFESPKKKRKVSEVEFSHEYWMRHALTLAKRARDEREV PVGAVLVLNNRVIGEGWNRAIGLHDPTAHAEIMALRQGGLV MQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVFGVRNSK RGAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRM PRQVFNAQKKAQSSINSGGSSGGSSGSETPGTSESATPESSGG SSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLGNT DRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRIC YLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIV DEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFR GHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVD AKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTP NFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFL AAKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTL LKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFI KPILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGEL HAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRF AWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLP NEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQ KKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDR FNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDRE MIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIR DKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQV SGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRH KPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILK	209

	EHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYD VDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKR QLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSK LVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYP KLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIM NFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKV LSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDP KKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIM ERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKR MLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNE QKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNK HRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTST KEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRTADGSEFE PKKKRKV	
myr-PTAP- YPXnL-PPPY- CA-GCN4LZ- RSVP2B	MGQTVTTPLSLTLGGGGSGGGGSGGGGSLPPSAPSLPLEGGG GSGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTE DPPPYRDPRGGSPLRAGGNGQLQYWPFSSSDLYNWKNNNPS FSEDPGKLTALIESVLITHQPTWDDCQQLLGTLLTGEEKQRV LLEARKAVRGDDGRPTQLPNEVDAAFPLERPDWDYTTQAGR NHLVHYRQLLLAGLQNAGRSPTNLAKVKGITQGPNESPSAFL ERLKEAYRRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLER LEDLKNKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEER RRTEDEQKEKERDRRRHREMSKLLGRMKQLEDKVEELLSKN YHLENEVARLKKLVGERGTASAPPPPYVG	210
myr-PTAP- YPXnL-PPPY- CA-GCN4LZ- RSVP2B	GQTVTTPLSLTLGGGGSGGGGSGGGGSLPPSAPSLPLEGGGG SGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTED PPPYRDPRGGSPLRAGGNGQLQYWPFSSSDLYNWKNNNPSF SEDPGKLTALIESVLITHQPTWDDCQQLLGTLLTGEEKQRVL LEARKAVRGDDGRPTQLPNEVDAAFPLERPDWDYTTQAGR NHLVHYRQLLLAGLQNAGRSPTNLAKVKGITQGPNESPSAFL ERLKEAYRRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLER LEDLKNKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEER RRTEDEQKEKERDRRRHREMSKLLGRMKQLEDKVEELLSKN YHLENEVARLKKLVGERGTASAPPPPYVG	211
myr-PTAP- YPXnL-PPPY- CA-GCN4LZ-	MGQTVTTPLSLTLGGGGSGGGGSGGGGSLPPSAPSLPLEGGG GSGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTE DPPPYRDPRGGSPLRAGGNGQLQYWPFSSSDLYNWKNNNPS	212

RSVP2B - NES-CS-BE	FSEDPGKLTALIESVLITHQPTWDDCQQLLGTLLTGEEKQRV LLEARKAVRGDDGRPTQLPNEVDAAFPLERPDWDYTTQAGR NHLVHYRQLLLAGLQNAGRSPTNLAKVKGITQGPNESPSAFL ERLKEAYRRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLER LEDLKNKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEER RRTEDEQKEKERDRRRHREMSKLLGRMKQLEDKVEELLSKN YHLENEVARLKKLVGERGTASAPPPPYVGSGGSLQLPPLERL TLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLMENSSGDYKD DDDKKRTADGSEFESPKKKRKVSEVEFSHEYWMRHALTLA KRARDEREVPVGAVLVLNNRVIGEGWNRAIGLHDPTAHAEI MALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGR VVFGVRNSKRGAAGSLMNVLNYPGMNHRVEITEGILADECA ALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGSSGSETPGTS ESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPS KKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRR YTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKH ERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYL ALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEE NPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNL IALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIG DQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYD EHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGA SQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSI PHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGP LARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERM TNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRK PAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSV EISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLT LTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLS RKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKE DIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELV KVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRIEEGIK ELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDI NRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPS EEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELD KAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVK VITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGT ALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKY	

	FFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRD FATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIA RKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVK ELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFE LENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLK GSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDK VLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTID RKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRT ADGSEFEPKKKRKV	
myr-PTAP- YPXnL-PPPY- CA-GCN4LZ- RSVP2B - NES- CS-BE	GQTVTTPLSLTLGGGGSGGGGSGGGGSLPPSAPSLPLEGGGG SGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTED PPPYRDPRGGSPLRAGGNGQLQYWPFSSSDLYNWKNNNPSF SEDPGKLTALIESVLITHQPTWDDCQQLLGTLLTGEEKQRVL LEARKAVRGDDGRPTQLPNEVDAAFPLERPDWDYTTQAGR NHLVHYRQLLLAGLQNAGRSPTNLAKVKGITQGPNESPSAFL ERLKEAYRRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLER LEDLKNKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEER RRTEDEQKEKERDRRRHREMSKLLGRMKQLEDKVEELLSKN YHLENEVARLKKLVGERGTASAPPPPYVGSGGSLQLPPLERL TLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLMENSSGDYKD DDDKKRTADGSEFESPKKKRKVSEVEFSHEYWMRHALTLA KRARDEREVPVGAVLVLNNRVIGEGWNRAIGLHDPTAHAEI MALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGR VVFGVRNSKRGAAGSLMNVLNYPGMNHRVEITEGILADECA ALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGSSGSETPGTS ESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPS KKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRR YTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKH ERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYL ALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEE NPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNL IALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIG DQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYD EHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGA SQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSI PHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGP LARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERM TNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRK	213

	PAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSV EISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLT LTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLS RKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKE DIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELV KVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRIEEGIK ELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDI NRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPS EEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELD KAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVK VITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGT ALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKY FFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRD FATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIA RKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVK ELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFE LENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLK GSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDK VLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTID RKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRT ADGSEFEPKKKRKV	
PH-PTAP- YPXnL-PPPY- MHRCA- GCN4LZ- RSVP2B	MSDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKER PQDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTV IERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSGGGSGGGGSGGGGSLPPSAPSLPLEGGGG SGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTED PPPYRDPRAGRSPTNLAKVKGITQGPNESPSAFLERLKEAYRR YTPYDPEDPGQETNVSMSFIWQSAPDIGRKLERLEDLKNKTL GDLVREAEKIFNKRETPEEREERIRRETEEKEERRRTEDEQKE KERDRRRHREMSKLLGRMKQLEDKVEELLSKNYHLENEVA RLKKLVGERGTASAPPPPYVG	214
PH-PTAP- YPXnL-PPPY- MHRCA- GCN4LZ- RSVP2B	SDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERP QDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVI ERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSGGGSGGGGSGGGGSLPPSAPSLPLEGGGG SGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTED	215

	PPPYRDPRAGRSPTNLAKVKGITQGPNESPSAFLERLKEAYRR YTPYDPEDPGQETNVSMSFIWQSAPDIGRKLERLEDLKNKTL GDLVREAEKIFNKRETPEEREERIRRETEEKEERRRTEDEQKE KERDRRRHREMSKLLGRMKQLEDKVEELLSKNYHLENEVA RLKKLVGERGTASAPPPPYVG	
PH-PTAP- YPXnL-PPPY- MHRCA- GCN4LZ- RSVP2B - NES- CS-BE	MSDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKER PQDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTV IERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSGGGSGGGGSGGGGSLPPSAPSLPLEGGGG SGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTED PPPYRDPRGGSPLRAGGNGQLQYWPFSSSDLYNWKNNNPSF SEDPGKLTALIESVLITHQPTWDDCQQLLGTLLTGEEKQRVL LEARKAVRGDDGRPTQLPNEVDAAFPLERPDWDYTTQAGR NHLVHYRQLLLAGLQNAGRSPTNLAKVKGITQGPNESPSAFL ERLKEAYRRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLER LEDLKNKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEER RRTEDEQKEKERDRRRHREMSKLLGRMKQLEDKVEELLSKN YHLENEVARLKKLVGERGTASAPPPPYVGSGGSLQLPPLERL TLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLMENSSGDYKD DDDKKRTADGSEFESPKKKRKVSEVEFSHEYWMRHALTLA KRARDEREVPVGAVLVLNNRVIGEGWNRAIGLHDPTAHAEI MALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGR VVFGVRNSKRGAAGSLMNVLNYPGMNHRVEITEGILADECA ALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGSSGSETPGTS ESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPS KKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRR YTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKH ERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYL ALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEE NPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNL IALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIG DQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYD EHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGA SQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSI PHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGP LARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERM TNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRK	216

	PAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSV EISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLT LTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLS RKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKE DIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELV KVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRIEEGIK ELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDI NRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPS EEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELD KAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVK VITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGT ALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKY FFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRD FATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIA RKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVK ELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFE LENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLK GSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDK VLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTID RKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRT ADGSEFEPKKKRKV	
PH-PTAP- YPXnL-PPPY- MHRCA- GCN4LZ- RSVP2B - NES- CS-BE	SDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERP QDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVI ERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSGGGSGGGGSGGGGSLPPSAPSLPLEGGGG SGGGGSGGGGSAPYPQPPTRRLNGGGGSGGGGSGGGGSTED PPPYRDPRGGSPLRAGGNGQLQYWPFSSSDLYNWKNNNPSF SEDPGKLTALIESVLITHQPTWDDCQQLLGTLLTGEEKQRVL LEARKAVRGDDGRPTQLPNEVDAAFPLERPDWDYTTQAGR NHLVHYRQLLLAGLQNAGRSPTNLAKVKGITQGPNESPSAFL ERLKEAYRRYTPYDPEDPGQETNVSMSFIWQSAPDIGRKLER LEDLKNKTLGDLVREAEKIFNKRETPEEREERIRRETEEKEER RRTEDEQKEKERDRRRHREMSKLLGRMKQLEDKVEELLSKN YHLENEVARLKKLVGERGTASAPPPPYVGSGGSLQLPPLERL TLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLMENSSGDYKD DDDKKRTADGSEFESPKKKRKVSEVEFSHEYWMRHALTLA KRARDEREVPVGAVLVLNNRVIGEGWNRAIGLHDPTAHAEI	217

	MALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGR VVFGVRNSKRGAAGSLMNVLNYPGMNHRVEITEGILADECA ALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGSSGSETPGTS ESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPS KKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRR YTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKH ERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYL ALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEE NPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNL IALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIG DQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYD EHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGA SQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSI PHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGP LARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERM TNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRK PAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSV EISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLT LTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLS RKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKE DIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELV KVMGRHKPENIVIEMARENQTTQKGQKNSRERMKRIEEGIK ELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMYVDQELDI NRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPS EEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELD KAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVK VITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGT ALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKY FFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRD FATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIA RKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVK ELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFE LENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLK GSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDK VLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTID RKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRT ADGSEFEPKKKRKV	
Plasma membrane recruitment elements comprising an HERVK-113 gag		

myr-MHRCA-GCN4LZ-RSVP2B	MGQTKSKIKSKYAAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVG	218
myr-MHRCA-GCN4LZ-RSVP2B	GQTKSKIKSKYAAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVG	219
myr-MHRCA-GCN4LZ-RSVP2B-QP12	MGQTKSKIKSKYAAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVGPIQPFVPQGFQGQQPPLSQVFQGISQLPQYNNCPPPQAAVQQ	220
myr-MHRCA-GCN4LZ-RSVP2B-QP12	GQTKSKIKSKYAAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVGPIQPFVPQGFQGQQPPLSQVFQGISQLPQYNNCPPPQAAVQQ	221
myr-YPXnL-PTAP-MHRCA-GCN4LZ-RSVP2B	MGQTKSKIKSKYAAPYPQPPTRRLNPTAPPSAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGERGTASAPPPYVG	222
myr-YPXnL-PTAP-MHRCA-GCN4LZ-RSVP2B	GQTKSKIKSKYAAPYPQPPTRRLNPTAPPSAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGERGTASAPPPYVG	223
myr-YPXnL-PTAP-MHRCA-GCN4LZ-RSVP2B - NES-CS-BE	MGQTKSKIKSKYAAPYPQPPTRRLNPTAPPSAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGERGTASAPPPYVGGSGGSLQLPPLERLTLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLMENSSGDYKDDDDKKRTAD	224

	GSEFESPKKKRKVSEVEFSHEYWMRHALTLAKRARDEREVP VGAVLVLNNRVIGEGWNRAIGLHDPTAHAEIMALRQGGLV MQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVFGVRNSK RGAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRM PRQVFNAQKKAQSSINSGGSSGGSSGSETPGTSESATPESSGG SSGGSDKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLGNT DRHSIKKNLIGALLFDSGETAEATRLKRTARRYTRRKNRIC YLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIV DEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFR GHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVD AKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTP NFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFL AAKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTL LKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFI KPILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGEL HAILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRF AWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLP NEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQ KKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDR FNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDRE MIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIR DKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQV SGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRH KPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILK EHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYD VDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKR QLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSK LVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYP KLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIM NFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKV LSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDP KKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIM ERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKR MLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNE QKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNK HRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTST	

	KEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRTADGSEFE PKKKRKV	
myr-YPXnL-PTAP-MHRCA-GCN4LZ-RSVP2B - NES-CS-BE	GQTKSKIKSKYAAPYPQPPTRRLNPTAPPSAWEKIQDPGSTCP SFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELM AYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAM HKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLK KLVGERGTASAPPPPYVGGSGGSLQLPPLERLTLGSLQLPPLE RLTLGSLQLPPLERLTLTSTLLMENSSGDYKDDDDKKRTADG SEFESPKKKRKVSEVEFSHEYWMRHALTLAKRARDEREVPV GAVLVLNNRVIGEGWNRAIGLHDPTAHAEIMALRQGGLVM QNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVFGVRNSKR GAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRMP RQVFNAQKKAQSSINSGGSSGGSSGSETPGTSESATPESSGGS SGGSDKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLGNTD RHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYL QEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDE VAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRG HFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDA KAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPN FKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLA AKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLL KALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIK PILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELH AILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRFA WMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPN EKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQK KAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRF NASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDRE MIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIR DKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQV SGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRH KPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILK EHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYD VDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKR QLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSK LVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYP KLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIM	225

	NFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKV LSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDP KKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIM ERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKR MLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNE QKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNK HRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTST KEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRTADGSEFE PKKKRKV	
myr-YPXnL- PTAP-CA- GCN4LZ- RSVP2B	MGQTKSKIKSKYAAPYPQPPTRRLNPTAPPSPVTLELMPPGE GAQEGEPPTVEARYKSFSIKMLKDMKEGVKQYGPNSPYMRT LLDSIAHGHRLIPYDWEILAKSSLSPSQFLQFKTWWIDGVQEQ VRRNRAANPPVNIDADQLLGIGQNWSTISQQALMQNEAIEQ VRAICLRAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQD VAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPA GSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLED KVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVG	226
myr-YPXnL- PTAP-CA- GCN4LZ- RSVP2B	GQTKSKIKSKYAAPYPQPPTRRLNPTAPPSPVTLELMPPGEGA QEGEPPTVEARYKSFSIKMLKDMKEGVKQYGPNSPYMRTLL DSIAHGHRLIPYDWEILAKSSLSPSQFLQFKTWWIDGVQEQV RRNRAANPPVNIDADQLLGIGQNWSTISQQALMQNEAIEQVR AICLRAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVA QKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSD VISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVE ELLSKNYHLENEVARLKKLVGERGTASAPPPPYVG	227
myr-YPXnL- PTAP-CA- GCN4LZ- RSVP2B - NES- CS-BE	MGQTKSKIKSKYAAPYPQPPTRRLNPTAPPSPVTLELMPPGE GAQEGEPPTVEARYKSFSIKMLKDMKEGVKQYGPNSPYMRT LLDSIAHGHRLIPYDWEILAKSSLSPSQFLQFKTWWIDGVQEQ VRRNRAANPPVNIDADQLLGIGQNWSTISQQALMQNEAIEQ VRAICLRAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQD VAQKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPA GSDVISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLED KVEELLSKNYHLENEVARLKKLVGERGTASAPPPPYVGGSG GSLQLPPLERLTLGSLQLPPLERLTLGSLQLPPLERLTLTSTLL MENSSGDYKDDDDKKRTADGSEFESPKKKRKVSEVEFSHEY WMRHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRAIG LHDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCA GAMIHSRIGRVVFGVRNSKRGAAGSLMNVLNYPGMNHRVEI	228

	TEGILADECAALLCDFYRMPRQVFNAQKKAQSSINSGGSSGG SSGSETPGTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWA VITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEAT RLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEES FLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDST DKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQL VQTYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPG EKKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDD DLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAP LSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNG YAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLR KQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKIL TFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGA SAQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVK YVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYF KKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEEN EDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRR RYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQL IHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQ TVKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRER MKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNR GKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAE RGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAY LNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKR NSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKS KKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLA SHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVIL ADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGG DSGGSKRTADGSEFEPKKKRKV	
myr-YPXnL- PTAP-CA- GCN4LZ-	GQTKSKIKSKYAAPYPQPPTRRLNPTAPPSPVTLELMPPGEGA QEGEPPTVEARYKSFSIKMLKDMKEGVKQYGPNSPYMRTLL DSIAHGHRLIPYDWEILAKSSLSPSQFLQFKTWWIDGVQEQV	229

RSVP2B - NES-CS-BE	RRNRAANPPVNIDADQLLGIGQNWSTISQQALMQNEAIEQVR AICLRAWEKIQDPGSTCPSFNTVRQGSKEPYPDFVARLQDVA QKSIADEKARKVIVELMAYENANPECQSAIKPLKGKVPAGSD VISEYVKACDGMGGAMHKAMLMAQAITGGRMKQLEDKVE ELLSKNYHLENEVARLKKLVGERGTASAPPPPYVGGSGGSL QLPPLERLTLGSLQLPPLERLTLGSLQLPPLERLTLTSTLLMEN SSGDYKDDDDKKRTADGSEFESPKKKRKVSEVEFSHEYWM RHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRAIGLHD PTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGA MIHSRIGRVVFGVRNSKRGAAGSLMNVLNYPGMNHRVEITE GILADECAALLCDFYRMPRQVFNAQKKAQSSINSGGSSGGSS GSETPGTSESATPESSGGSSGGSDKKYSIGLAIGTNSVGWAVI TDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESF LVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLV QTYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGE KKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDD LDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGY AGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLLRK QRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGAS AQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKY VTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENE DILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRR YTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLI HDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQT VKVVDELVKVMGRHKPENIVIEMARENQTTQKGQKNSRER MKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNR GKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAE RGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAY LNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEI GKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKR	

	NSDKLIARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKS KKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLA SHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVIL ADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGG DSGGSKRTADGSEFEPKKKRKV	
PH-YPXnL- PTAP-MHRCA- GCN4LZ- RSVP2B	MSDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKER PQDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTV IERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSAPYPQPPTRRLNPTAPPSAWEKIQDPGSTC PSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELM AYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAM HKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLK KLVGERGTASAPPPPYVG	230
PH-YPXnL- PTAP-MHRCA- GCN4LZ- RSVP2B	SDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERP QDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVI ERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSAPYPQPPTRRLNPTAPPSAWEKIQDPGSTC PSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELM AYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAM HKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLK KLVGERGTASAPPPPYVG	231
PH-YPXnL- PTAP-MHRCA- GCN4LZ- RSVP2B - NES- CS-BE	MSDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKER PQDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTV IERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSAPYPQPPTRRLNPTAPPSAWEKIQDPGSTC PSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELM AYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAM HKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLK KLVGERGTASAPPPPYVGGSGGSLQLPPLERLTLGSLQLPPLE RLTLGSLQLPPLERLTLTSTLLMENSSGDYKDDDDKKRTADG SEFESPKKKRKVSEVEFSHEYWMRHALTLAKRARDEREVPV GAVLVLNNRVIGEGWNRAIGLHDPTAHAEIMALRQGGLVM QNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVFGVRNSKR	232

	GAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRMP RQVFNAQKKAQSSINSGGSSGGSSGSETPGTSESATPESSGGS SGGSDKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLGNTD RHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYL QEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDE VAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRG HFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDA KAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPN FKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLA AKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLL KALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIK PILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELH AILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRFA WMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPN EKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQK KAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRF NASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDRE MIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIR DKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQV SGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRH KPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILK EHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYD VDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKR QLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSK LVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYP KLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIM NFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKV LSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDP KKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIM ERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKR MLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNE QKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNK HRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTST KEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRTADGSEFE PKKKRKV	
PH-YPXnL- PTAP-MHRCA-	SDVAIVKEGWLHKRGEYIKTWRPRYFLLKNDGTFIGYKERP QDVDQREAPLNNFSVAQCQLMKTERPRPNTFIIRCLQWTTVI	233

GCN4LZ-RSVP2B - NES-CS-BE	ERTFHVETPEEREEWTTAIQTVADGLKKQEEEEMDFRSGSPS DNSGAEEMEVSLAKPKHRVTMNEFEYLKLLGKGTFGKVDPP VVGDGSGSGGVSAPYPQPPTRRLNPTAPPSAWEKIQDPGSTC PSFNTVRQGSKEPYPDFVARLQDVAQKSIADEKARKVIVELM AYENANPECQSAIKPLKGKVPAGSDVISEYVKACDGMGGAM HKAMLMAQAITGGRMKQLEDKVEELLSKNYHLENEVARLK KLVGERGTASAPPPPYVGGSGGSLQLPPLERLTLGSLQLPPLE RLTLGSLQLPPLERLTLTSTLLMENSSGDYKDDDDKKRTADG SEFESPKKKRKVSEVEFSHEYWMRHALTLAKRARDEREVPV GAVLVLNNRVIGEGWNRAIGLHDPTAHAEIMALRQGGLVM QNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVFGVRNSKR GAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRMP RQVFNAQKKAQSSINSGGSSGGSSGSETPGTSESATPESSGGS SGGSDKKYSIGLAIGTNSVGWAVITDEYKVPSKKFKVLGNTD RHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYL QEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDE VAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRG HFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDA KAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPN FKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLA AKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLL KALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIK PILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELH AILRRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRFA WMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPN EKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQK KAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRF NASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDRE MIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIR DKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQV SGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRH KPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILK EHPVENTQLQNEKLYLYYLQNGRDMYVDQELDINRLSDYD VDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKK MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKR QLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSK LVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYP KLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIM	

	NFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKV LSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDP KKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIM ERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKR MLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNE QKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNK HRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTST KEVLDATLIHQSITGLYETRIDLSQLGGDSGGSKRTADGSEFE PKKKRKV	

[0363] Additional exemplary sequences for the plasma membrane recruitment elements comprising a mutant gag polyprotein (*e.g.*, mutant HIV gag, mutant RSV gag, and mutant hGAGKcon) are listed in **Table 10B**.

Table 10B. Exemplary sequences for plasma membrane recruitment elements

Abbreviated Name	Description	Amino Acid Sequence	
RSV ML	Matrix and Late domains of Rous Sarcoma Virus (RSV) Gag	MEAVIKVISSACKTYCGKISPSKKEIGAMLSL LQKEGLLMSPSDLYSPGSWDPITAALSQRAM VLGKSGELKTWGLVLGALKAAREEQVTSEQ AKFWLGLGGGRVSPPGPECIEKPATERRIDKG EEVGETTVQRDAKMAPEEAATPKTVGTSCY HCGTAVGCNCATATASAPPPPYVGSGLYPSL AGVG	234
		EAVIKVISSACKTYCGKISPSKKEIGAMLSLLQ KEGLLMSPSDLYSPGSWDPITAALSQRAMVL GKSGELKTWGLVLGALKAAREEQVTSEQAK FWLGLGGGRVSPPGPECIEKPATERRIDKGEE VGETTVQRDAKMAPEEAATPKTVGTSCYHC GTAVGCNCATATASAPPPPYVGSGLYPSLAG VG	235
RSV MLNC Large	Matrix, Late domains and nucleocapsid of RSV v1	MEAVIKVISSACKTYCGKISPSKKEIGAMLSL LQKEGLLMSPSDLYSPGSWDPITAALSQRAM VLGKSGELKTWGLVLGALKAAREEQVTSEQ AKFWLGLGGGRVSPPGPECIEKPATERRIDKG EEVGETTVQRDAKMAPEEAATPKTVGTSCY HCGTAVGCNCATATASAPPPPYVGSGLYPSL AGVGEGSDLPPSARAPVIIDCFRQKSQPDIQQ LIRAAPSTLTTPGEIIKYVLDRQKIAPLTDQGI	236

		AAAMSSAIQPLVMAVVNRERDGQTGSGGRA RGLCYTCGSPGHYQAQCPKKRKSGNSRERC QLCDGMGHNAKQCRKRDGNQGQRPGRGLS SGPWPGSGG	
		EAVIKVISSACKTYCGKISPSKKEIGAMLSLLQ KEGLLMSPSDLYSPGSWDPITAALSQRAMVL GKSGELKTWGLVLGALKAAREEQVTSEQAK FWLGLGGGRVSPPGPECIEKPATERRIDKGEE VGETTVQRDAKMAPEEAATPKTVGTSCYHC GTAVGCNCATATASAPPPPYVGSGLYPSLAG VGEGSDLPPSARAPVIIDCFRQKSQPDIQQLIR AAPSTLTTPGEIIKYVLDRQKIAPLTDQGIAAA MSSAIQPLVMAVVNRERDGQTGSGGRARGL CYTCGSPGHYQAQCPKKRKSGNSRERCQLC DGMGHNAKQCRKRDGNQGQRPGRGLSSGP WPGSGG	237
RSV MLNC Small	Matrix, Late domains and nucleocapsid of RSV v2	MEAVIKVISSACKTYCGKISPSKKEIGAMLSL LQKEGLLMSPSDLYSPGSWDPITAALSQRAM VLGKSGELKTWGLVLGALKAAREEQVTSEQ AKFWLGLGGGRVSPPGPECIEKPATERRIDKG EEVGETTVQRDAKMAPEEAATPKTVGTSCY HCGTAVGCNCATATASAPPPPYVGSGLYPSL AGVGQPLVMAVVNRERDGQTGSGGRARGL CYTCGSPGHYQAQCPKKRKSGNSRERCQLC DGMGHNAKQCRKRDGNQGQRPGRGLSSGP WPGSGG	238
		EAVIKVISSACKTYCGKISPSKKEIGAMLSLLQ KEGLLMSPSDLYSPGSWDPITAALSQRAMVL GKSGELKTWGLVLGALKAAREEQVTSEQAK FWLGLGGGRVSPPGPECIEKPATERRIDKGEE VGETTVQRDAKMAPEEAATPKTVGTSCYHC GTAVGCNCATATASAPPPPYVGSGLYPSLAG VGQPLVMAVVNRERDGQTGSGGRARGLCYT CGSPGHYQAQCPKKRKSGNSRERCQLCDGM GHNAKQCRKRDGNQGQRPGRGLSSGPWPGS GG	239
Myr RSV LNC Large		MGSSKSKPKDHCGTAVGCNCATATASAPPPP YVGSGLYPSLAGVGEGSDLPPSARAPVIIDCF	240

	Myristoyltion, late domains and nucleocapsid v1	RQKSQPDIQQLIRAAPSTLTTPGEIIKYVLDRQ KIAPLTDQGIAAAMSSAIQPLVMAVVNRERD GQTGSGGRARGLCYTCGSPGHYQAQCPKKR KSGNSRERCQLCDGMGHNAKQCRKRDGNQ GQRPGRGLSSGPWPGSGG	
		GSSKSKPKDHCGTAVGCNCATATASAPPPPY VGSGLYPSLAGVGEGSDLPPSARAPVIIDCFR QKSQPDIQQLIRAAPSTLTTPGEIIKYVLDRQK IAPLTDQGIAAAMSSAIQPLVMAVVNRERDG QTGSGGRARGLCYTCGSPGHYQAQCPKKRK SGNSRERCQLCDGMGHNAKQCRKRDGNQG QRPGRGLSSGPWPGSGG	241
Myr RSV LNC Small	Myristoyltion, late domains and nucleocapsid v2	MGSSKSKPKDHCGTAVGCNCATATASAPPPP YVGSGLYPSLAGVGQPLVMAVVNRERDGQT GSGGRARGLCYTCGSPGHYQAQCPKKRKSG NSRERCQLCDGMGHNAKQCRKRDGNQGQR PGRGLSSGPWPGSGG	242
		GSSKSKPKDHCGTAVGCNCATATASAPPPPY VGSGLYPSLAGVGQPLVMAVVNRERDGQTG SGGRARGLCYTCGSPGHYQAQCPKKRKSGN SRERCQLCDGMGHNAKQCRKRDGNQGQRP GRGLSSGPWPGSGG	243
PH-RSV LNC Large	Pleckstrin homology domain (hPLCδ1) fused to Late domain and nucleocapsid v1	MDSGRDFLTLHGLQDDEDLQALLKGSQLLK VKSSSWRRERFYKLQEDCKTIWQESRKVMR TPESQLFSIEDIQEVRMGHRTEGLEKFARDVP EDRCFSIVFKDQRNTLDLIAPSPADAQHWVL GLHKIIHHSGSMDQRQKLQHWIHSCLRKADK NKDNKMSFKELQNFLKELNIQGDGSGSGGVS HCGTAVGCNCATATASAPPPPYVGSGLYPSL AGVGEGSDLPPSARAPVIIDCFRQKSQPDIQQ LIRAAPSTLTTPGEIIKYVLDRQKIAPLTDQGI AAAMSSAIQPLVMAVVNRERDGQTGSGGRA RGLCYTCGSPGHYQAQCPKKRKSGNSRERC QLCDGMGHNAKQCRKRDGNQGQRPGRGLS SGPWPGSGG	244
		DSGRDFLTLHGLQDDEDLQALLKGSQLLKV KSSSWRRERFYKLQEDCKTIWQESRKVMRTP ESQLFSIEDIQEVRMGHRTEGLEKFARDVPED	245

		RCFSIVFKDQRNTLDLIAPSPADAQHWVLGL HKIIHHSGSMDQRQKLQHWIHSCLRKADKN KDNKMSFKELQNFLKELNIQGDGSGSGGVSH CGTAVGCNCATATASAPPPPYVGSGLYPSLA GVGEGSDLPPSARAPVIIDCFRQKSQPDIQQLI RAAPSTLTTPGEIIKYVLDRQKIAPLTDQGIAA AMSSAIQPLVMAVVNRERDGQTGSGGRARG LCYTCGSPGHYQAQCPKKRKSGNSRERCQLC DGMGHNAKQCRKRDGNQGQRPGRGLSSGP WPGSGG	
PH-RSV LNC Small	Pleckstrin homology domain (hPLCδ1) fused to Late domain and nucleocapsid v2	MDSGRDFLTLHGLQDDEDLQALLKGSQLLK VKSSSWRRERFYKLQEDCKTIWQESRKVMR TPESQLFSIEDIQEVRMGHRTEGLEKFARDVP EDRCFSIVFKDQRNTLDLIAPSPADAQHWVL GLHKIIHHSGSMDQRQKLQHWIHSCLRKADK NKDNKMSFKELQNFLKELNIQGDGSGSGGVS HCGTAVGCNCATATASAPPPPYVGSGLYPSL AGVGQPLVMAVVNRERDGQTGSGGRARGL CYTCGSPGHYQAQCPKKRKSGNSRERCQLC DGMGHNAKQCRKRDGNQGQRPGRGLSSGP WPGSGG	246
PH-RSV LNC Small	Pleckstrin homology domain (hPLCδ1) fused to Late domain and nucleocapsid v2	DSGRDFLTLHGLQDDEDLQALLKGSQLLKV KSSSWRRERFYKLQEDCKTIWQESRKVMRTP ESQLFSIEDIQEVRMGHRTEGLEKFARDVPED RCFSIVFKDQRNTLDLIAPSPADAQHWVLGL HKIIHHSGSMDQRQKLQHWIHSCLRKADKN KDNKMSFKELQNFLKELNIQGDGSGSGGVSH CGTAVGCNCATATASAPPPPYVGSGLYPSLA GVGQPLVMAVVNRERDGQTGSGGRARGLC YTCGSPGHYQAQCPKKRKSGNSRERCQLCD GMGHNAKQCRKRDGNQGQRPGRGLSSGPW PGSGG	247
HIV CAP dDZF1	HIV Gag myristoylation and capsid-dDZF1-RSV late domains	MGARASVSPTSILDIRQGPKEPFRDYVDRFYK TLRAEQASQEVKNWMTETLLVQNANPDCKT ILKALGPGATLEEMMTACQGVGGPGHKARV LAEAMSQVTNPATIMFKCEHCRILFLDHVMF TIHMGCHGFRDPFKCNMCGEKCDGPVGLFV HMARNAHGEKPFYCEHCEITFRDVVMYSLH	248

		KGYHGFRDPFECNICGYHSQDRYEFSSHIVRG EHTASAPPPPYVG	
		GARASVSPTSILDIRQGPKEPFRDYVDRFYKT LRAEQASQEVKNWMTETLLVQNANPDCKTI LKALGPGATLEEMMTACQGVGGPGHKARVL AEAMSQVTNPATIMFKCEHCRILFLDHVMFTI HMGCHGFRDPFKCNMCGEKCDGPVGLFVH MARNAHGEKPFYCEHCEITFRDVVMYSLHK GYHGFRDPFECNICGYHSQDRYEFSSHIVRGE HTASAPPPPYVG	249
HIV CAP dDZF2	HIV Gag myristoylation and capsid-dDZF2-RSV late domains	MGARASVSPTSILDIRQGPKEPFRDYVDRFYK TLRAEQASQEVKNWMTETLLVQNANPDCKT ILKALGPGATLEEMMTACQGVGGPGHKARV LAEAMSQVTNPATIMHHCQHCDMYFADNIL YTIHMGCHSCDDVFKCNMCGEKCDGPVGLF VHMARNAHGEKPTKCVHCGIVFLDEVMYAL HMSCHGFRDPFECNICGYHSQDRYEFSSHIVR GEHTASAPPPPYVG	250
		GARASVSPTSILDIRQGPKEPFRDYVDRFYKT LRAEQASQEVKNWMTETLLVQNANPDCKTI LKALGPGATLEEMMTACQGVGGPGHKARVL AEAMSQVTNPATIMHHCQHCDMYFADNILY TIHMGCHSCDDVFKCNMCGEKCDGPVGLFV HMARNAHGEKPTKCVHCGIVFLDEVMYALH MSCHGFRDPFECNICGYHSQDRYEFSSHIVRG EHTASAPPPPYVG	251
HERV Kcon Large CAP dDZF1	HERV Kcon Gag myristoylation and capsid-dDZF1-RSV late domains v1	MGQTKSKIKSKYASYLSFIKILLKRGGVKVST KNLIKLFQIIEQFCPWFPEQGTLDLKDWKRIG KELKQAGRKGNIIPLTVWNDWAIIKAALEPF QTEEDSVSVSDAPGSCIIDCNENTRKKSQKET EGLHCEYVAEPVMAQSTQNVDYNQLQEVIY PETLKLEGKGPELVGPSESKPRGTSPLPAGQV PVTLQPQKQVKENKTQPPVAYQYWPPAELQ YRPPPESQYGYPGMPPAPQGRAPYPQPPTRR LNPTAPPSRQGSELHEIIDKSRKEGDTEAWQF PVTLEPMPPGEGAQEGEPPTVEARYKSFSIKM LKDMKEGVKQYGPNSPYMRTLLDSIAHGHR LIPYDWEILAKSSLSPSQFLQFKTWWIDGVQE	252

		QVRRNRAANPPVNIDADQLLGIGQNWSTISQ QALMQNEAIEQVRAICLRAWEKIQDPGSTCP SFNTVRQGSKEPYPDFVARLQDVAQKSIADE KARKVIVELMAYENANPECQSAIKPLKGKVP AGSDVISEYVKACDGIGGAMHKAMLMAQAI TGVVLGGQVRFKCEHCRILFLDHVMFTIHMG CHGFRDPFKCNMCGEKCDGPVGLFVHMARN AHGEKPFYCEHCEITFRDVVMYSLHKGYHGF RDPFECNICGYHSQDRYEFSSHIVRGEHTASA PPPPYVG	
HERV Kcon Large CAP dDZF1	HERV Kcon Gag myristoylation and capsid-dDZF1-RSV late domains v1	GQTKSKIKSKYASYLSFIKILLKRGGVKVSTK NLIKLFQIIEQFCPWFPEQGTLDLKDWKRIGK ELKQAGRKGNIIPLTVWNDWAIIKAALEPFQT EEDSVSVSDAPGSCIIDCNENTRKKSQKETEG LHCEYVAEPVMAQSTQNVDYNQLQEVIYPE TLKLEGKGPELVGPSESKPRGTSPLPAGQVPV TLQPQKQVKENKTQPPVAYQYWPPAELQYR PPPESQYGYPGMPPAPQGRAPYPQPPTRRLNP TAPPSRQGSELHEIIDKSRKEGDTEAWQFPVT LEPMPPGEGAQEGEPPTVEARYKSFSIKMLK DMKEGVKQYGPNSPYMRTLLDSIAHGHRLIP YDWEILAKSSLSPSQFLQFKTWWIDGVQEQV RRNRAANPPVNIDADQLLGIGQNWSTISQQA LMQNEAIEQVRAICLRAWEKIQDPGSTCPSFN TVRQGSKEPYPDFVARLQDVAQKSIADEKAR KVIVELMAYENANPECQSAIKPLKGKVPAGS DVISEYVKACDGIGGAMHKAMLMAQAITGV VLGGQVRFKCEHCRILFLDHVMFTIHMGCHG FRDPFKCNMCGEKCDGPVGLFVHMARNAHG EKPFYCEHCEITFRDVVMYSLHKGYHGFRDP FECNICGYHSQDRYEFSSHIVRGEHTASAPPP PYVG	253
hGAGKcon Large CAP dDZF2	hGAGKcon myristoylation and capsid-dDZF2-RSV late domains v1	MGQTKSKIKSKYASYLSFIKILLKRGGVKVST KNLIKLFQIIEQFCPWFPEQGTLDLKDWKRIG KELKQAGRKGNIIPLTVWNDWAIIKAALEPF QTEEDSVSVSDAPGSCIIDCNENTRKKSQKET EGLHCEYVAEPVMAQSTQNVDYNQLQEVIY PETLKLEGKGPELVGPSESKPRGTSPLPAGQV	254

		PVTLQPQKQVKENKTQPPVAYQYWPPAELQ YRPPPESQYGYPGMPPAPQGRAPYPQPPTRR LNPTAPPSRQGSELHEIIDKSRKEGDTEAWQF PVTLEPMPPGEGAQEGEPPTVEARYKSFSIKM LKDMKEGVKQYGPNSPYMRTLLDSIAHGHR LIPYDWEILAKSSLSPSQFLQFKTWWIDGVQE QVRRNRAANPPVNIDADQLLGIGQNWSTISQ QALMQNEAIEQVRAICLRAWEKIQDPGSTCP SFNTVRQGSKEPYPDFVARLQDVAQKSIADE KARKVIVELMAYENANPECQSAIKPLKGKVP AGSDVISEYVKACDGIGGAMHKAMLMAQAI TGVVLGGQVRHHCQHCDMYFADNILYTIHM GCHSCDDVFKCNMCGEKCDGPVGLFVHMA RNAHGEKPTKCVHCGIVFLDEVMYALHMSC HGFRDPFECNICGYHSQDRYEFSSHIVRGEHT ASAPPPPYVG	
hGAGKcon Large CAP dDZF2	hGAGKcon myristoylation and capsid-dDZF2-RSV late domains v1	GQTKSKIKSKYASYLSFIKILLKRGGVKVSTK NLIKLFQIIEQFCPWFPEQGTLDLKDWKRIGK ELKQAGRKGNIIPLTVWNDWAIIKAALEPFQT EEDSVSVSDAPGSCIIDCNENTRKKSQKETEG LHCEYVAEPVMAQSTQNVDYNQLQEVIYPE TLKLEGKGPELVGPSESKPRGTSPLPAGQVPV TLQPQKQVKENKTQPPVAYQYWPPAELQYR PPPESQYGYPGMPPAPQGRAPYPQPPTRRLNP TAPPSRQGSELHEIIDKSRKEGDTEAWQFPVT LEPMPPGEGAQEGEPPTVEARYKSFSIKMLK DMKEGVKQYGPNSPYMRTLLDSIAHGHRLIP YDWEILAKSSLSPSQFLQFKTWWIDGVQEQV RRNRAANPPVNIDADQLLGIGQNWSTISQQA LMQNEAIEQVRAICLRAWEKIQDPGSTCPSFN TVRQGSKEPYPDFVARLQDVAQKSIADEKAR KVIVELMAYENANPECQSAIKPLKGKVPAGS DVISEYVKACDGIGGAMHKAMLMAQAITGV VLGGQVRHHCQHCDMYFADNILYTIHMGCH SCDDVFKCNMCGEKCDGPVGLFVHMARNA HGEKPTKCVHCGIVFLDEVMYALHMSCHGF RDPFECNICGYHSQDRYEFSSHIVRGEHTASA PPPPYVG	255

hGAGKcon Small CAP dDZF1	HIV Gag myristoylation and capsid-dDZF1-RSV late domains v2	MGARASVDPGSTCPSFNTVRQGSKEPYPDFV ARLQDVAQKSIADEKARKVIVELMAYENAN PECQSAIKPLKGKVPAGSDVISEYVKACDGIG GAMHKAMLMAQAITGVVLGGQVRFKCEHC RILFLDHVMFTIHMGCHGFRDPFKCNMCGEK CDGPVGLFVHMARNAHGEKPFYCEHCEITFR DVVMYSLHKGYHGFRDPFECNICGYHSQDR YEFSSHIVRGEHTASAPPPPYVG	256
		GARASVDPGSTCPSFNTVRQGSKEPYPDFVA RLQDVAQKSIADEKARKVIVELMAYENANPE CQSAIKPLKGKVPAGSDVISEYVKACDGIGG AMHKAMLMAQAITGVVLGGQVRFKCEHCRI LFLDHVMFTIHMGCHGFRDPFKCNMCGEKC DGPVGLFVHMARNAHGEKPFYCEHCEITFRD VVMYSLHKGYHGFRDPFECNICGYHSQDRY EFSSHIVRGEHTASAPPPPYVG	257
hGAGKcon Small CAP dDZF2	HIV Gag myristoylation and capsid-dDZF2-RSV late domains v2	MGARASVDPGSTCPSFNTVRQGSKEPYPDFV ARLQDVAQKSIADEKARKVIVELMAYENAN PECQSAIKPLKGKVPAGSDVISEYVKACDGIG GAMHKAMLMAQAITGVVLGGQVRHHCQHC DMYFADNILYTIHMGCHSCDDVFKCNMCGE KCDGPVGLFVHMARNAHGEKPTKCVHCGIV FLDEVMYALHMSCHGFRDPFECNICGYHSQD RYEFSSHIVRGEHTASAPPPPYVG	258
		GARASVDPGSTCPSFNTVRQGSKEPYPDFVA RLQDVAQKSIADEKARKVIVELMAYENANPE CQSAIKPLKGKVPAGSDVISEYVKACDGIGG AMHKAMLMAQAITGVVLGGQVRHHCQHCD MYFADNILYTIHMGCHSCDDVFKCNMCGEK CDGPVGLFVHMARNAHGEKPTKCVHCGIVF LDEVMYALHMSCHGFRDPFECNICGYHSQD RYEFSSHIVRGEHTASAPPPPYVG	259
hGAGKcon Smallv2 CAP dDZF1	hGAGKcon myristoylation and capsid-dDZF1-RSV late domains v3	MGQTKSKDPGSTCPSFNTVRQGSKEPYPDFV ARLQDVAQKSIADEKARKVIVELMAYENAN PECQSAIKPLKGKVPAGSDVISEYVKACDGIG GAMHKAMLMAQAITGVVLGGQVRFKCEHC RILFLDHVMFTIHMGCHGFRDPFKCNMCGEK CDGPVGLFVHMARNAHGEKPFYCEHCEITFR	260

		DVVMYSLHKGYHGFRDPFECNICGYHSQDR YEFSSHIVRGEHTASAPPPPYVG	
		GQTKSKDPGSTCPSFNTVRQGSKEPYPDFVA RLQDVAQKSIADEKARKVIVELMAYENANPE CQSAIKPLKGKVPAGSDVISEYVKACDGIGG AMHKAMLMAQAITGVVLGGQVRFKCEHCRI LFLDHVMFTIHMGCHGFRDPFKCNMCGEKC DGPVGLFVHMARNAHGEKPFYCEHCEITFRD VVMYSLHKGYHGFRDPFECNICGYHSQDRY EFSSHIVRGEHTASAPPPPYVG	261
hGAGKcon Smallv2 CAP dDZF2	hGAGKcon myristoylation and capsid-dDZF2-RSV late domains v3	MGQTKSKDPGSTCPSFNTVRQGSKEPYPDFV ARLQDVAQKSIADEKARKVIVELMAYENAN PECQSAIKPLKGKVPAGSDVISEYVKACDGIG GAMHKAMLMAQAITGVVLGGQVRHHCQHC DMYFADNILYTIHMGCHSCDDVFKCNMCGE KCDGPVGLFVHMARNAHGEKPTKCVHCGIV FLDEVMYALHMSCHGFRDPFECNICGYHSQD RYEFSSHIVRGEHTASAPPPPYVG	262
		GQTKSKDPGSTCPSFNTVRQGSKEPYPDFVA RLQDVAQKSIADEKARKVIVELMAYENANPE CQSAIKPLKGKVPAGSDVISEYVKACDGIGG AMHKAMLMAQAITGVVLGGQVRHHCQHCD MYFADNILYTIHMGCHSCDDVFKCNMCGEK CDGPVGLFVHMARNAHGEKPTKCVHCGIVF LDEVMYALHMSCHGFRDPFECNICGYHSQD RYEFSSHIVRGEHTASAPPPPYVG	263

[0364] Additional constructs for chimeric protein comprising the plasma membrane recruitment element that comprises a mutant gag polyprotein and a payload will be designed with any of arrangements as provided in **Table 11A**.

[0365] Additional constructs for the chimeric protein with a membrane penetrating peptide will be designed with any of the arrangements provided in **Table 11B**.

[0366] The construct for the chimeric protein with a post-translational modification motif will be designed with any of the arrangements provided in **Table 11C**.

[0367] The construct for the lipid delivery particle or the chimeric protein with a particle budding motif and a post-translational modification will be designed with any of the arrangements provided in **Table 12**.

Example 2: Manufacture of Lipid Delivery Particles

[0368] This is a series of steps for the production of lipid delivery particles. Adherent cells will be first transfected to produce lipid delivery particles (*e.g.,* VLPs). A nucleic acid molecule will be generated that encodes a chimeric protein that comprises a PH domain and one, two, or all of: (i) a particle budding motif; (ii) a membrane penetrating peptide; and/or (iii) a post-translational modification motif. In this example, the nucleic acid molecule encodes a chimeric protein comprising a PH domain and a particle budding motif. Another nucleic acid molecule that will be generated encodes an envelope, target specific guide RNA, and a payload protein. The nucleic acid molecules encoding the PH domain, the envelope, the target specific guide RNA, and the payload protein are introduced into HEK293T producer cells to generate the lipid delivery particles comprising protein payload. DNA will be transiently expressed via non-viral methods. The non-viral methods will include chemical-based methods including DEAE-dextran, cationic lipids, or cationic polymers and physical methods including microinjection or electroporation. In this example, cells will be transfected using electroporation.

[0369] The cells will incorporate into the transfection media for approximately 18 hours. Following culturing in the media, the media will be changed out for a new solution or media. This second solution helps promote additional transient production of lipid delivery particles.

[0370] After approximately 30 hours have passed from incorporation in the second media, the lipid delivery particles will be harvested and the harvest will be filtered and collected. Harvesting methods include precipitation, depth filtration, microfiltration, or centrifugation. For this example, cells are harvested using depth filtration. Cell culture supernatant will be passed through a porous material with decreasing pore size to filter. The porous material will be composed of a layer of cellulose, a filter of diatomaceous earth, and a polymeric resin. Depth filtration systems will also be used including Millistak+ Pod from Millipore Sigma, Stax from Pall Corporation, 3M Zeta Plus from Cuno Inc., and Sartoclear P from Sartorius Stedim Biotech.

[0371] The harvested cells will be run through a purification protocol that retains the structural integrity of collected lipid delivery particles. Purification methods include FACS, BACS, MACS, size exclusion chromatography, or anion exchange chromatography.

Example 3: Administration of Lipid Delivery Particles to Patient with a Genetic Disease

[0372] Lipid delivery particles harvested from cell culture will be administered systemically to a subject with a genetic disease or disorder.

[0373] The lipid delivery particles with payload and chimeric protein with different plasma membrane recruitment element and optionally a particle budding motif, a membrane penetrating peptide, or a post-translational modification motif, or combinations thereof, will be provided to a subject with familial hypercholesterolemia (FH) caused by a pathogenic mutation in *PCSK9*. The lipid delivery particle generated and optimized will be provided to the subject intravenously. The gene editing payload protein will be delivered to the target cells, where the guide RNA delivers the gene editing machinery to *PCSK9*, and rectifies the pathogenic mutation. A sample from the subject will be taken after treatment to assess if

the genome alteration is sufficient to restore normal function of the gene or to block pathogenic function of the pathogenic gene. A control sample from the subject will be taken from the subject prior to treatment.

[0374] The treated and control samples will be harvested for genomic DNA using Qiagen Blood & Cell Culture DNA kit. The DNA will be used as a template for PCR, wherein *HEXA* target specific primers flank the insertion locus. PCR will be performed using a high fidelity, proof-reading Taq polymerase (Prime Star, Takara) to isolate the target region of interest. The PCR inserts will be purified and prepared for a next generation sequencing run using a library preparation kit (Nextera XT, Illumina). The library will then be run on the Illumina MiSeq and editing efficiency of each guide RNA and the plasma membrane recruitment element will be determined.

[0375] While preferred embodiments of the present disclosure have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the disclosure. It should be understood that various alternatives to the embodiments of the present disclosure may be employed in practicing the present disclosure. It is intended that the following claims define the scope of the present disclosure and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

What is claimed is:

1. A lipid delivery particle comprising

(a) a lipid membrane;

(b) a plasma membrane recruitment element comprising a mutant gag polyprotein, and

(c) a payload encapsulated by the lipid containing membrane, and

wherein the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein; and

wherein

(1) the plasma membrane recruitment element comprises

(i) a full-length capsid protein;

(ii) a full-length matrix protein;

(iii) a heterologous sequence;

(iv) at least a portion of a nucleocapsid protein;

(v) two or more particle budding motifs;

(vi) at least a portion of a P6 domain; or

(vii) two spacer peptides;

(2) the lipid delivery particle further comprises an envelope protein, wherein the envelope protein comprises an envelope protein from human endogenous retrovirus (HERV) or a mutant thereof; or

(3) the plasma membrane recruitment element is fused to

(i) a cleavable linker;

(ii) a membrane penetrating peptide; or

(iii) a post-translational modification motif.

2. The lipid delivery particle of claim 1, wherein the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a retrovirus; optionally wherein the retrovirus is oncoretroviruses, lentiviruses, or spumaviruses; optionally wherein the retrovirus is Human Immunodeficiency Virus (HIV), Moloney Murine Leukemia Virus (MMLV), or Rous sarcoma virus (RSV).

3. The lipid delivery particle of claim 1, wherein the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a human endogenous retrovirus (HERV) or a gag homology protein (optionally human Arc); optionally wherein the HERV is HERV-K or HERV-W; optionally wherein the HERV-K is HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV-K11p22, or HERV-K12q13; optionally wherein the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a HERV-K113.

4. The lipid delivery particle of claim 1, wherein the mutant gag polyprotein is a mutant of a wild type gag polyprotein of an alpharetrovirus, a betaretrovirus, or a deltaretrovirus, optionally the wild type gag polyprotein comprises the sequence set forth in any one of SEQ ID NOs: 285-298.
5. The lipid delivery particle of any one of claims 1-4, wherein the lipid delivery particle comprises a chimeric protein comprising the plasma membrane recruitment element and the payload.
6. The lipid delivery particle of any one of claims 1-5, wherein the at least a fragment of the matrix protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the matrix protein of a corresponding wild type gag polyprotein.
7. The lipid delivery particle of any one of claims 1-5, wherein the at least a fragment of the matrix protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the matrix protein of a corresponding wild type gag polyprotein.
8. The lipid delivery particle of any one of claims 1-7, wherein the at least a fragment of the RNA-binding phosphoprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein.
9. The lipid delivery particle of any one of claims 1-7, wherein the at least a fragment of the RNA-binding phosphoprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein.
10. The lipid delivery particle of any one of claims 1-9, wherein the at least a fragment of the capsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the capsid protein of a corresponding wild type gag polyprotein.
11. The lipid delivery particle of any one of claims 1-9, wherein the at least a fragment of the capsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the capsid protein of a corresponding wild type gag polyprotein.
12. The lipid delivery particle of any one of claims 1-11, wherein the at least a fragment of the nucleocapsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the nucleocapsid protein of a corresponding wild type gag polyprotein.
13. The lipid delivery particle of any one of claims 1-11, wherein the at least a fragment of the nucleocapsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90,

91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the nucleocapsid protein of a corresponding wild type gag polyprotein.

14. The lipid delivery particle of any one of claims 1-13, wherein the at least a portion of the P6 domain comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the P6 domain of the corresponding wild type gag polyprotein.
15. The lipid delivery particle of any one of claims 1-13, wherein the at least a portion of the P6 domain comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the P6 domain of a corresponding wild type gag polyprotein.
16. The lipid delivery particle of any one of claims 1-15, wherein the plasma membrane recruitment element comprises the full-length capsid protein.
17. The lipid delivery particle of any one of claims 1-15, wherein the plasma membrane recruitment element comprises the full-length matrix protein.
18. The lipid delivery particle of any one of claims 1-17, wherein the plasma membrane recruitment element comprises the heterologous sequence; optionally wherein the heterologous sequence is fused to a fragment of the capsid protein, a matrix protein or a fragment thereof, a nucleocapsid protein or a fragment thereof, a particle budding motif or a fragment thereof; optionally wherein the plasma membrane recruitment element lacks the matrix protein; optionally wherein the fragment of the capsid protein is a C-terminal fragment comprising a major homology region (MHR).
19. The lipid delivery particle of claim 18, wherein the heterologous sequence is fused to the N-terminal of the fragment of the capsid protein or a particle budding motif (optionally a late domain of RSV); optionally wherein the heterologous sequence is a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof.
20. The lipid delivery particle of any one of claims 1-19, wherein the plasma membrane recruitment element comprises at least a portion of the nucleocapsid protein; optionally a N-terminal fragment of the nucleocapsid protein; optionally a C-terminal fragment of the nucleocapsid protein).
21. The lipid delivery particle of any one of claims 1-20, wherein the plasma membrane recruitment element comprises two or more particle budding motifs; optionally wherein (a) at least one of the two or more particle budding motifs is endogenous, (b) at least one of the two or more particle budding motifs is heterologous (optionally RSV P2B or a mutant thereof), (c) at least one of the two or more particle budding motifs comprises a PTAP motif, a PPPY motif, a PPXY motif, a YXXL motif, a YPXnL motif, or any combinations thereof, wherein n is an integer from 1 to 5; or (d) at least one of the two or more particle budding motifs comprises a sequence listed in Table 5.
22. The lipid delivery particle of any one of claims 1-2, or 5-21, wherein the plasma membrane recruitment element comprises at least a portion of the P6 domain; optionally wherein the plasma membrane recruitment element comprises at least a N-terminal fragment of the P6 domain or at least

a C-terminal fragment of the P6 domain; optionally wherein the plasma membrane recruitment element comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV.

23. The lipid delivery particle of any one of claims 1-22, wherein the plasma membrane recruitment element is fused to the post-translational modification motif is selected from the group consisting of: a myristoylation motif, an acetylation motif, an isoprenylation motif, a palmitoylation motif, a farnesylation motif, and any combinations thereof.
24. The lipid delivery particle of any one of claims 1-2, or 5-22, wherein the plasma membrane recruitment element comprises the two spacer peptides; optionally wherein at least one of the two spacer peptides is P2 domain or P1 domain; optionally wherein the two spacer peptides are P2 domain and P1 domain; optionally wherein the plasma membrane recruitment element comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV.
25. The lipid delivery particle of any one of claims 1-24, wherein the lipid delivery particle further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof; optionally wherein the envelope protein comprises hENVH1, hENVH2, hENVH3, hENVK1, hENVK2, hENVK3, hENVK4, hENVK5, hENVK6, hENVT, hENVW, hENVFRD, hENVR, hENVR(b), hENVR(c)2, hENVR(c)1, or hENVKcon, or a mutant thereof.
26. The lipid delivery particle of any one of claims 1-25, wherein the plasma membrane recruitment element is fused to the cleavable linker, and wherein the cleavable linker connects the plasma membrane recruitment element and the payload.
27. The lipid delivery particle of any one of claims 1-26, wherein the plasma membrane recruitment element is fused to the membrane penetrating peptide; optionally wherein (a) the membrane penetrating peptide is linked to the payload or the plasma membrane recruitment element; (b) the membrane penetrating peptide is linked between the payload and the plasma membrane recruitment element; optionally wherein the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in Table 6.
28. The lipid delivery particle of any one of claims 1, 2, or 5-15, wherein the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of HIV, and wherein (1) the plasma membrane recruitment element is fused to the cleavable linker, the membrane penetrating peptide, or the post-translational modification motif; or (2) wherein the lipid delivery particle further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof.
29. The lipid delivery particle of claim 28, wherein the plasma membrane recruitment element comprises (a) at least a fragment of matrix protein of an HIV gag, optionally a N-terminal fragment of the matrix protein of the HIV gag; or (b) a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof.
30. The lipid delivery particle of claim 28 or 29, wherein the plasma membrane recruitment element comprises at least a fragment of capsid protein of the HIV gag; optionally wherein the plasma

membrane recruitment element comprises a full-length capsid protein of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a C-terminal fragment of capsid protein of the HIV gag.

31. The lipid delivery particle of any one of claims 28-30, wherein the plasma membrane recruitment element comprises a spacer peptide of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a P2 domain of the HIV gag, a P1 domain of the HIV gag, or both.
32. The lipid delivery particle of any one of claims 28-31, wherein the plasma membrane recruitment element comprises (a) a heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif, optionally wherein the multimerization motif forms parallel homodimers or parallel heterodimers (optional DZF), optionally wherein the parallel homodimers comprise a coiled-coil, optionally wherein the coiled-coil is a leucine zipper, optionally wherein the plasma membrane recruitment element lacks nucleocapsid protein of the HIV gag; or (b) a full-length nucleocapsid protein of the HIV gag or a fragment thereof.
33. The lipid delivery particle of any one of claims 28-32, wherein the plasma membrane recruitment element comprises a particle budding motif; optionally wherein the plasma membrane recruitment element comprises two or more particle budding motifs; optionally wherein at least one of the particle budding motifs is (a) a particle budding motif of the HIV gag (optionally a N-terminal fragment of the P6 domain of the HIV gag, a PTAP motif, or a full-length P6 domain of the HIV gag); or (b) a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5).
34. The lipid delivery particle of any one of claims 28-33, wherein the plasma membrane recruitment element lacks a matrix protein of the HIV gag, and wherein the plasma membrane recruitment element comprises a N-terminal myristoylation motif, the full-length capsid protein of the HIV gag or a fragment thereof, the multimerization motif (optionally a DZF), and a heterologous particle budding motif (optionally a late domain of RSV) arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
35. The lipid delivery particle of any one of claims 28-33, wherein the plasma membrane recruitment element lacks a matrix protein of the HIV gag, and wherein the plasma membrane recruitment element comprises a heterologous particle budding motif (optionally a late domain of RSV), a N-terminal myristoylation motif, the full-length capsid protein of the HIV gag or a fragment thereof, the multimerization motif (optionally a DZF), arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
36. The lipid delivery particle of any one of claims 28-33,wherein the plasma membrane recruitment element comprises

    (a) the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof;

    (b) the full-length capsid protein of the HIV gag or a fragment thereof;

(c) the multimerization motif (optionally a leucine zipper) or the full-length nucleocapsid protein of the HIV gag or a fragment thereof; and

(d) the particle budding motif;

optionally wherein the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the plasma membrane recruitment element further comprises the P2 domain of the HIV gag located at a position between (b) and (c).

37. The lipid delivery particle of any one of claims 28-33, wherein the plasma membrane recruitment element comprises:

(a) the particle budding motif;

(b) the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof;

(c) the full-length capsid protein of the HIV gag or a fragment thereof; and

(d) the multimerization motif (optionally a leucine zipper) or the full-length nucleocapsid protein of the HIV gag or a fragment thereof; and;

optionally wherein the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the plasma membrane recruitment element further comprises the P2 domain of the HIV gag located at a position between (c) and (d).

38. The lipid delivery particle of claim 36, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the full-length capsid protein of the HIV gag, the P1 domain of the HIV gag, and the P6 domain of the HIV gag or a fragment thereof, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

39. The lipid delivery particle of claim 36, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the leucine zipper, and the P6 domain of the HIV gag or a fragment thereof, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

40. The lipid delivery particle of claim 36, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the leucine zipper, and a particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

41. The lipid delivery particle of claim 36, wherein the plasma membrane recruitment element comprises a particle budding motif, the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, and the leucine

zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

42. The lipid delivery particle of claim 36, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif, a C-terminal fragment of the HIV gag, the P2 domain of the HIV gag, the leucine zipper, and a second particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
43. The lipid delivery particle of claim 36, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, optionally a first particle budding motif, the full-length capsid protein of the HIV gag or a fragment thereof, optionally the P2 domain of the HIV gag, the leucine zipper, and optionally a second particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
44. The lipid delivery particle of claim 43, wherein the plasma membrane recruitment element comprises the first and the second particle budding motif; optionally wherein each of the first and the second particle budding motifs independently (a) is the particle budding motif of the HIV gag; (b) is a heterologous particle budding motif (optionally RSV P2B or a mutant thereof); or (c) comprises a sequence listed in Table 5.
45. The lipid delivery particle of claim 44, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the heterologous particle budding motif, the full-length capsid protein of the HIV gag, the P2 domain, the leucine zipper, and the particle budding motif of the HIV gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof.
46. The lipid delivery particle of claim 45, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the HIV gag, the P2 domain, the full-length nucleocapsid protein of the HIV gag, and the particle budding motif of the HIV gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof.
47. A lipid delivery particle comprising

(a) a lipid membrane;

(b) a plasma membrane recruitment element comprising a mutant gag polyprotein that is not from HIV, and

(c) a payload encapsulated by the lipid containing membrane,

wherein the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein.

48. The lipid delivery particle of claim 47, wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of a retrovirus; optionally wherein the retrovirus is oncoretroviruses, lentiviruses, or spumaviruses; optionally wherein the retrovirus is MMLV.
49. The lipid delivery particle of claim 47, wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of a human endogenous retrovirus (HERV) or a gag homology protein (optionally human Arc or PEG10); optionally wherein the HERV is HERV-K or HERV-W; optionally wherein the HERV-K is HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV-K11p22, or HERV-K12q13; optionally wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of HERV-K113 or a hGAGKcon.
50. The lipid delivery particle of claim 47, wherein the mutant gag polyprotein is a mutant of a wild type gag polyprotein of an alpharetrovirus, a betaretrovirus, or a deltaretrovirus, optionally the wild type gag polyprotein comprises the sequence set forth in any one of SEQ ID NOs: 285-298.
51. The lipid delivery particle of any one of claims 47-49, wherein the lipid delivery particle comprises a chimeric protein comprising the plasma membrane recruitment element and the payload.
52. The lipid delivery particle of any one of claims 47-51, wherein the at least a fragment of the matrix protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the matrix protein of a corresponding wild type gag polyprotein.
53. The lipid delivery particle of any one of claims 47-51, wherein the at least a fragment of the matrix protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the matrix protein of a corresponding wild type gag polyprotein.
54. The lipid delivery particle of any one of claims 47-53, wherein the at least a fragment of the RNA-binding phosphoprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein.
55. The lipid delivery particle of any one of claims 47-53, wherein the at least a fragment of the RNA-binding phosphoprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein.
56. The lipid delivery particle of any one of claims 47-55, wherein the at least a fragment of the capsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%,

70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the capsid protein of a corresponding wild type gag polyprotein.

57. The lipid delivery particle of any one of claims 47-55, wherein the at least a fragment of the capsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the capsid protein of a corresponding wild type gag polyprotein.
58. The lipid delivery particle of any one of claims 47-57, wherein the at least a fragment of the nucleocapsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the nucleocapsid protein of a corresponding wild type gag polyprotein.
59. The lipid delivery particle of any one of claims 47-57, wherein the at least a fragment of the nucleocapsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the nucleocapsid protein of a corresponding wild type gag polyprotein.
60. The lipid delivery particle of any one of claims 1-15, or 47-59, wherein the plasma membrane recruitment element lacks the at least a fragment of a matrix protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the matrix protein.
61. The lipid delivery particle of any one of claims 1, 2, 5-15, 47, 48 or 51-60, wherein the plasma membrane recruitment element lacks the at least a fragment of a RNA-binding phosphoprotein; optionally wherein the plasma membrane recruitment element comprises a mutant of a wild-type gag polyprotein of MMLV.
62. The lipid delivery particle of any one of claims 1-3, 5-15, or 47-61, wherein the plasma membrane recruitment element lacks the at least a fragment of a capsid protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the capsid protein, a C-terminal fragment of the capsid protein, or both.
63. The lipid delivery particle of any one of claims 1-3, 5-15, or 47-62, wherein the plasma membrane recruitment element lacks the gag-endogenous protease cleavage sequence.
64. The lipid delivery particle of any one of claims 1-3, 5-15, or 47-63, wherein the plasma membrane recruitment element lacks the at least a fragment of a nucleocapsid protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the nucleocapsid protein, a C-terminal fragment of the nucleocapsid protein, or both; optionally wherein the plasma membrane recruitment element lacks the nucleocapsid protein.
65. The lipid delivery particle of any one of claims 1-2, 5-21, 23, 25-27, 47-48, or 51-64, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of MMLV.
66. The lipid delivery particle of claim 65, wherein the plasma membrane recruitment element comprises

(a) a matrix protein of the MMLV gag (optionally full-length matrix protein of the MMLV gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the MMLV gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof;

(b) a capsid protein of the MMLV gag or a mutant thereof, optionally wherein the capsid protein of the MMLV gag or a mutant thereof is a full-length capsid protein of the MMLV gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the MMLV gag;

(c) heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif (optionally a leucine zipper); and

(d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the MMLV gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5;

optionally wherein the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element;

optionally wherein the plasma membrane recruitment element further comprises a P12 domain of the MMLV gag or a mutant thereof located between (a) and (b), optionally wherein the P12 domain of the MMLV gag or a mutant thereof is a full-length P12 domain of the MMLV gag, a N-terminal fragment of the full-length P12 domain of the MMLV gag, a C-terminal fragment of the full-length P12 domain of the MMLV gag, or a fragment of the full-length P12 domain of the MMLV gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5).

67. The lipid delivery particle of claim 66, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

68. The lipid delivery particle of claim 66, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and optionally the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

69. The lipid delivery particle of claim 66, wherein the plasma membrane recruitment element comprises the particle budding motif, the pleckstrin homology (PH) domain or a mutant thereof, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper,

arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

70. The lipid delivery particle of claim 66, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
71. The lipid delivery particle of claim 66, wherein the plasma membrane recruitment element comprises the particle budding motif, the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
72. The lipid delivery particle of claim 66, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
73. The lipid delivery particle of claim 66, wherein the plasma membrane recruitment element comprises the particle budding motif, the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
74. The lipid delivery particle of any one of claims 1, 3, 5-21, 23, 25-27, 47, 49, or 51-64, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of hGAGKcon; optionally wherein the plasma membrane recruitment element comprises a N-terminal myristoylation motif of the hGAGKcon gag, a full-length capsid protein of the hGAGKcon gag or a fragment thereof, a multimerization motif (optionally a DZF), and a particle budding motif (optionally a late domain of RSV); optionally wherein the plasma membrane recruitment element comprises a N-terminal myristoylation motif of an HIV gag, a full-length capsid protein of the hGAGKcon gag or a fragment thereof, a multimerization motif (optionally a DZF), and a particle budding motif (optionally a late domain of RSV).
75. The lipid delivery particle of any one of claims 1, 3, 5-21, 23, 25-27, 47, 49, or 51-64, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HERV-K113.
76. The lipid delivery particle of claim 75, wherein the plasma membrane recruitment element comprises: (a) a matrix protein of the HERV-K113 gag (optionally full-length matrix protein of the HERV-K113 gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the HERV-K113 gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof;

(b) a capsid protein of the HERV-K113 gag or a mutant thereof, optionally wherein the capsid protein of the HERV-K113 gag or a mutant thereof is a full-length capsid protein of the HERV-K113 gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the HERV-K113 gag;

(c) heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif (optionally a leucine zipper); and

(d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the HERV-K113 gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5);

(e) an optional QP1 domain of the HERV-K113 gag; and

(f) an optional QP2 domain of the HERV-K113 gag;

optionally wherein (a)-(f) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element;

optionally wherein the plasma membrane recruitment element further comprises a P15 domain of the HERV-K113 gag or a mutant thereof, optionally wherein the P15 domain of the HERV-K113 gag or a mutant thereof is a full-length P15 domain of the HERV-K113 gag, a N-terminal fragment of the full-length P15 domain of the HERV-K113 gag, a C-terminal fragment of the full-length P15 domain of the HERV-K113 gag, or a fragment of the full-length P15 domain of the HERV-K113 gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5).

77. The lipid delivery particle of claim 76, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the HERV-K113 gag, the full-length P15 domain of the HERV-K113 gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

78. The lipid delivery particle of claim 76, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length P15 domain of the HERV-K113 gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, optionally the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

79. The lipid delivery particle of claim 76, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the HERV-K113 gag, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the particle budding

motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

80. The lipid delivery particle of claim 76, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.
81. The lipid delivery particle of any one of claims 76-80, wherein the plasma membrane recruitment element comprises the QP1 domain and the QP2 domain of the HERV-K113 gag.
82. The lipid delivery particle of any one of claims 1-2, 5-21, 23, 25-27, 47, 48, or 51-64, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of RSV; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag and a late domain of the RSV gag; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid protein of the RSV; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of the nucleocapsid protein of the RSV; optionally wherein the plasma membrane recruitment element further comprises a N-terminal myristoylation motif.
83. The lipid delivery particle of any one of claims 28-46 or 65-82, wherein the plasma membrane recruitment element comprises one, two, or three particle budding motif, wherein each of the particle budding motif is selected from a sequence listed in Table 5.
84. The lipid delivery particle of any one of claims 1-83, wherein the plasma membrane recruitment element comprises a major homology region (MHR).
85. The lipid delivery particle of any one of claims 1-17, or 20-84, wherein the plasma membrane recruitment element comprises the heterologous sequence; optionally wherein the heterologous sequence is fused to a fragment of the matrix protein, optionally the N-terminal of the fragment of the matrix protein; optionally wherein the heterologous sequence is a pleckstrin homology (PH) domain or a mutant thereof; optionally wherein the PH domain is a human PH domain; optionally wherein the fragment of the matrix protein lacks a N-terminal myristoylation motif, a N-terminal glycine, a highly basic region (HBR), a N-terminal fragment, or any combination thereof.
86. The lipid delivery particle of any one of claims 5-46, or 51-85, wherein the chimeric protein comprises a cleavable linker; optionally wherein the cleavable linker connects the plasma membrane recruitment element and the payload.
87. The lipid delivery particle of any one of claims 5-46, or 51-86, wherein the chimeric protein comprises a nuclear localization signal (NLS) sequence.

88. The lipid delivery particle of any one of claims 5-46, or 51-87, wherein the chimeric protein comprises a nuclear export signal (NES) sequence.
89. The lipid delivery particle of any one of claims 5-46, or 51-88, wherein the chimeric protein comprises the membrane penetrating peptide, optionally wherein (a) the membrane penetrating peptide is linked to the payload or the plasma membrane recruitment element; or (b) the membrane penetrating peptide connects the payload and the plasma membrane recruitment element; optionally wherein the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in Table 6.
90. The lipid delivery particle of any one of claims 5-46, or 51-89, wherein the chimeric protein comprises the post-translational modification motif that is fused directly to (a) the payload; or (b) the plasma membrane recruitment element; optionally wherein the post-translational modification motif comprises a myristoylation motif, an acetylation motif, an isoprenylation motif, a palmitoylation motif, a farnesylation motif, or combinations thereof.
91. The lipid delivery particle of any one of claims 5-46, or 51-90, wherein the chimeric protein comprises the plasma membrane recruitment element, an optional NLS, the cleavable linker, and the payload arranged in order from N-terminus of the chimeric protein to C-terminus of the chimeric protein.
92. The lipid delivery particle of any one of claims 26-91, wherein the lipid delivery particle comprises the envelope protein; optionally wherein the envelope protein is a retroviral envelope protein or a mutant thereof; optionally wherein the envelope protein is an envelope protein from human endogenous retrovirus (HERV) or a mutant thereof.
93. The lipid delivery particle of any one of claims 1-92, wherein the plasma membrane recruitment element forms part of a basic structure of the lipid delivery particle (optionally a protein core).
94. The lipid delivery particle of any one of claims 1-93, wherein the payload comprises an antibody, a cytokine, a therapeutic protein, a small molecule therapeutics, a therapeutic DNA, and a therapeutic RNA, a ribonucleoprotein, a zinc-finger, a transcription activator-like effector (TALE), or a CRISPR-based genome editor, or any combinations thereof; optionally wherein the payload comprises a NLS, optionally wherein the NLS is an endogenous NLS or a heterologous NLS.
95. The lipid delivery particle of any one of claims 1-94, wherein the lipid delivery particle further comprises a second plasma membrane recruitment element; optionally wherein the second plasma membrane recruitment element is the same as the plasma membrane recruitment element; optionally wherein the second plasma membrane recruitment element is a retroviral gag or a mutant thereof, a HERV gag or a mutant thereof, a pleckstrin homology (PH) domain or a mutant thereof, or a membrane protein or a transmembrane domain thereof or a mutant thereof.
96. The lipid delivery particle of claim 95, wherein the second plasma membrane recruitment element forms part of a basic structure of the lipid delivery particle (optionally a protein core).
97. The lipid delivery particle of claim 1-96, wherein the lipid delivery particle further comprises a protease; optionally wherein the protease is a retroviral protease.

98. The lipid delivery particle of claim 97, wherein the plasma membrane recruitment element is linked to the protease, optionally via a cleavable linker.

99. The lipid delivery particle of claim 97, wherein the second plasma membrane recruitment element is linked to the protease, optionally via a cleavable linker.

100. The lipid delivery particle of any one of claims 1-99, wherein the plasma membrane recruitment element further comprises one or more mutant gag-endogenous protease cleavage sequences relative to a corresponding wildtype gag-endogenous protease cleavage sequence, and wherein the one or more mutant o gag-endogenous protease cleavage sequences have higher cleavage efficiency than that of the corresponding wildtype gag-endogenous protease cleavage sequence.

101. A recombinant protein comprising a plasma membrane recruitment element comprising a mutant gag polyprotein, wherein the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein; and

wherein

(1) the plasma membrane recruitment element comprises

(i) a full-length capsid protein;

(ii) a full-length matrix protein;

(iii) a heterologous sequence;

(iv) at least a portion of a nucleocapsid protein;

(v) two or more particle budding motifs;

(vi) at least a portion of a P6 domain; or

(vii) two spacer peptides;

or

(2) the plasma membrane recruitment element is fused to

(i) a cleavable linker;

(ii) a membrane penetrating peptide; or

(iii) a post-translational modification motif.

102. The recombinant protein of claim 101, wherein the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a retrovirus; optionally wherein the retrovirus is oncoretroviruses, lentiviruses, or spumaviruses; optionally wherein the retrovirus is Human Immunodeficiency Virus (HIV), Moloney Murine Leukemia Virus (MMMLV), or Rous sarcoma virus (RSV).

103. The recombinant protein of claim 101, wherein the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a human endogenous retrovirus (HERV); optionally wherein the HERV is HERV-K or HERV-W; optionally wherein the HERV-K is HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV-K11p22, or HERV-K12q13; optionally wherein the mutant gag polyprotein is a mutant of a wild-type gag polyprotein of a HERV-K113.

104. The recombinant protein of claim 101, wherein the mutant gag polyprotein is a mutant of a wild type gag polyprotein of an alpharetrovirus, a betaretrovirus, or a deltaretrovirus, optionally the wild type gag polyprotein comprises the sequence set forth in any one of SEQ ID NOs: 285-298.

105. The recombinant protein of any one of claims 101-104, wherein the at least a fragment of the matrix protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the matrix protein of a corresponding wild type gag polyprotein.

106. The recombinant protein of any one of claims 101-104, wherein the at least a fragment of the matrix protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the matrix protein of a corresponding wild type gag polyprotein.

107. The recombinant protein of any one of claims 101-106, wherein the at least a fragment of the RNA-binding phosphoprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein.

108. The recombinant protein of any one of claims 101-106, wherein the at least a fragment of the RNA-binding phosphoprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein.

109. The recombinant protein of any one of claims 101-108, wherein the at least a fragment of the capsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the capsid protein of a corresponding wild type gag polyprotein.

110. The recombinant protein of any one of claims 101-108, wherein the at least a fragment of the capsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the capsid protein of a corresponding wild type gag polyprotein.

111. The recombinant protein of any one of claims 101-110, wherein the at least a fragment of the nucleocapsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the nucleocapsid protein of a corresponding wild type gag polyprotein.

112. The recombinant protein of any one of claims 101-110, wherein the at least a fragment of the nucleocapsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the nucleocapsid protein of a corresponding wild type gag polyprotein.

113. The recombinant protein of any one of claims 101-112, wherein the at least a portion of the P6 domain comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the P6 domain of the corresponding wild type gag polyprotein.

114. The recombinant protein of any one of claims 101-112, wherein the at least a portion of the P6 domain comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the P6 domain of a corresponding wild type gag polyprotein.

115. The recombinant protein of any one of claims 101-114, wherein the plasma membrane recruitment element comprises the full-length capsid protein.

116. The recombinant protein of any one of claims 101-114, wherein the plasma membrane recruitment element comprises the full-length matrix protein.

117. The recombinant protein of any one of claims 101-116, wherein the plasma membrane recruitment element comprises the heterologous sequence; optionally wherein the heterologous sequence is fused to a fragment of the capsid protein, a matrix protein or a fragment thereof, a nucleocapsid protein or a fragment thereof, a particle budding motif or a fragment thereof; optionally wherein the plasma membrane recruitment element lacks the matrix protein; optionally wherein the fragment of the capsid protein is a C-terminal fragment.

118. The recombinant protein of claim 117, wherein the heterologous sequence is fused to the N-terminal of the fragment of the capsid protein or a particle budding motif (optionally a late domain of RSV); optionally wherein the heterologous sequence is a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof.

119. The recombinant protein of any one of claims 101-118, wherein the plasma membrane recruitment element comprises at least a portion of a nucleocapsid protein; optionally a N-terminal fragment of the nucleocapsid protein; optionally a C-terminal fragment of the nucleocapsid protein).

120. The recombinant protein or the lipid delivery particle of any one of claims 101-119, wherein the plasma membrane recruitment element comprises two or more particle budding motifs; optionally wherein (a) at least one of the two or more particle budding motifs is endogenous, (b) at least one of the two or more particle budding motifs is heterologous (optionally RSV P2B or a mutant thereof), (c) at least one of the two or more particle budding motifs comprises a PTAP motif, a PPPY motif, a PPXY motif, a YXXL motif, a YPXnL motif, or any combinations thereof, wherein n is an integer from 1 to 5, or (d) at least one of the two or more particle budding motifs comprises a sequence listed in Table 5.

121. The recombinant protein of any one of claims 101, 102, or 105-120, wherein the plasma membrane recruitment element comprises at least a portion of the P6 domain; optionally wherein the plasma membrane recruitment element comprises at least a N-terminal fragment of the P6 domain or at least a C-terminal fragment of the P6 domain; optionally wherein the plasma membrane

recruitment element comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV.

122. The recombinant protein of any one of claims 101-121, wherein the plasma membrane recruitment element is fused to the post-translational modification motif is selected from the group consisting of: a myristoylation motif, an acetylation motif, an isoprenylation motif, a palmitoylation motif, and a farnesylation motif.

123. The recombinant protein of any one of claims 101, 102, or 105-121, wherein the plasma membrane recruitment element comprises the two spacer peptides; optionally wherein at least one of the two spacer peptides is P2 domain or P1 domain; optionally wherein the two spacer peptides are P2 domain and P1 domain; optionally wherein the plasma membrane recruitment element comprises the mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV.

124. The recombinant protein of any one of claims 101-123, wherein the recombinant protein further comprises the envelope protein, and wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof; optionally wherein the envelope protein comprises hENVH1, hENVH2, hENVH3, hENVK1, hENVK2, hENVK3, hENVK4, hENVK5, hENVK6, hENVT, hENVW, hENVFRD, hENVR, hENVR(b), hENVR(c)2, hENVR(c)1, or hENVKcon, or a mutant thereof.

125. The recombinant protein of any one of claims 101-124, wherein the plasma membrane recruitment element is fused to the membrane penetrating peptide; optionally wherein the membrane penetrating peptide is linked to the plasma membrane recruitment element; optionally wherein the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in Table 6.

126. The recombinant protein of claim 101, 122, or 124, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HIV and wherein (1) the plasma membrane recruitment element is fused to the cleavable linker or the membrane penetrating peptide; or (2) wherein the recombinant protein further comprises the envelope protein, wherein the envelope protein comprises the envelope protein from human endogenous retrovirus (HERV) or a mutant thereof.

127. The recombinant protein of claim 126, wherein the plasma membrane recruitment element comprises (a) at least a fragment of matrix protein of an HIV gag, optionally a N-terminal fragment of the matrix protein of the HIV gag; or (b) a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof.

128. The recombinant protein of claim 126 or 127, wherein the plasma membrane recruitment element comprises at least a fragment of capsid protein of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a full-length capsid protein of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a C-terminal fragment of capsid protein of the HIV gag.

129. The recombinant protein of any one of claims 126-128, wherein the plasma membrane recruitment element comprises a spacer peptide of the HIV gag; optionally wherein the plasma membrane recruitment element comprises a P2 domain of the HIV gag, a P1 domain of the HIV gag, or both.

130. The recombinant protein of any one of claims 126-129, wherein the plasma membrane recruitment element comprises (a) a heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif, optionally wherein the multimerization motif forms parallel homodimers or parallel heterodimers (optional DZF), optionally wherein the parallel homodimers comprise a coiled-coil, optionally wherein the coiled-coil is a leucine zipper, optionally wherein the plasma membrane recruitment element lacks nucleocapsid protein of the HIV gag; or (b) a full-length nucleocapsid protein of the HIV gag or a fragment thereof.

131. The recombinant protein of any one of claims 126-130, wherein the plasma membrane recruitment element comprises a particle budding motif; optionally wherein the plasma membrane recruitment element comprises two or more particle budding motifs; optionally wherein at least one of the particle budding motifs is (a) a particle budding motif of the HIV gag (optionally a N-terminal fragment of the P6 domain of the HIV gag, a PTAP motif, or a full-length P6 domain of the HIV gag); or (b) a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5).

132. The recombinant protein of any one of claims 126-131, wherein the plasma membrane recruitment element lacks a matrix protein of the HIV gag and wherein the plasma membrane recruitment element comprises a N-terminal myristoylation motif, the full-length capsid protein of the HIV gag or a fragment thereof, the multimerization motif (optionally a DZF), and a heterologous particle budding motif (optionally a late domain of RSV) arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

133. The recombinant protein of any one of claims 126-131, wherein the plasma membrane recruitment element comprises

(a) the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof;

(b) the full-length capsid protein of the HIV gag or a fragment thereof;

(c) optionally the P2 domain of the HIV gag;

(d) the multimerization motif (optionally a leucine zipper) or the full-length nucleocapsid protein of the HIV gag or a fragment thereof; and

(e) the particle budding motif;

optionally wherein the (a)-(e) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

134. The recombinant protein of claim 133, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the full-length capsid protein of

the HIV gag, the P1 domain of the HIV gag, and the P6 domain of the HIV gag or a fragment thereof, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

135. The recombinant protein of claim 133, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the leucine zipper, and the P6 domain of the HIV gag or a fragment thereof, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

136. The recombinant protein of claim 133, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the full-length capsid protein of the HIV gag or a fragment thereof, the P2 domain of the HIV gag, the leucine zipper, and a particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

137. The recombinant protein of claim 133, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, a first particle budding motif, a C-terminal fragment of the HIV gag, the P2 domain of the HIV gag, the leucine zipper, and a second particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

138. The recombinant protein of claim 133, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, optionally a first particle budding motif, the full-length capsid protein of the HIV gag or a fragment thereof, optionally the P2 domain of the HIV gag, the leucine zipper, and optionally a second particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

139. The recombinant protein of claim 138, wherein the plasma membrane recruitment element comprises the first and the second particle budding motif; optionally wherein each of the first and the second particle budding motifs independently (a) is the particle budding motif of the HIV gag; (b) is a heterologous particle budding motif (optionally RSV P2B or a mutant thereof); or (c) comprises a sequence listed in Table 5.

140. The recombinant protein of claim 139, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag, the heterologous particle budding motif, the full-length capsid protein of the HIV gag, the P2 domain, the leucine zipper, and the particle budding motif of the HIV gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof.

141. The recombinant protein of claim 133, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the matrix protein of the HIV gag or the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the HIV gag, the P2 domain, the

full-length nucleocapsid protein of the HIV gag, and the particle budding motif of the HIV gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof.

142. A recombinant protein comprising a plasma membrane recruitment element comprising a mutant gag polyprotein that is not from HIV, and

wherein the plasma membrane recruitment element lacks at least a fragment of a matrix protein, at least a fragment of a RNA-binding phosphoprotein, at least a fragment of a capsid protein, a gag-endogenous protease cleavage sequence, or at least a fragment of a nucleocapsid protein.

143. The recombinant protein of claim 142, wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of a retrovirus; optionally wherein the retrovirus is oncoretroviruses, lentiviruses, or spumaviruses; optionally wherein the retrovirus is MMLV or RSV.

144. The recombinant protein of claim 142, wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of a human endogenous retrovirus (HERV) or a gag homology protein (optionally human Arc); optionally wherein the HERV is HERV-K or HERV-W; optionally wherein the HERV-K is HERV-K113, HERV-K101, HERV-K102, HERV-K104, HERV-K107, HERV-K108, HERV-K109, HERV-K115, HERV-K11p22, or HERV-K12q13; optionally wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of HERV-K113 or a hGAGKcon.

145. The recombinant protein of claim 142, wherein the mutant gag polyprotein is mutant of a wild-type gag polypeptide of an alpharetrovirus, a betaretrovirus, or a deltaretrovirus, optionally the wild type gag polyprotein comprises the sequence set forth in any one of SEQ ID NOs: 285-298.

146. The recombinant protein of any one of claims 142-145, wherein the at least a fragment of the matrix protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the matrix protein of a corresponding wild type gag polyprotein.

147. The recombinant protein of any one of claims 142-145, wherein the at least a fragment of the matrix protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the matrix protein of a corresponding wild type gag polyprotein.

148. The recombinant protein of any one of claims 142-147, wherein the at least a fragment of the RNA-binding phosphoprotein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein.

149. The recombinant protein of any one of claims 142-147, wherein the at least a fragment of the RNA-binding phosphoprotein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more

contiguous amino acid residues of the RNA-binding phosphoprotein of a corresponding wild type gag polyprotein.

150. The recombinant protein of any one of claims 142-149, wherein the at least a fragment of the capsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the capsid protein of a corresponding wild type gag polyprotein.

151. The recombinant protein of any one of claims 142-149, wherein the at least a fragment of the capsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the capsid protein of a corresponding wild type gag polyprotein.

152. The recombinant protein of any one of claims 142-151, wherein the at least a fragment of the nucleocapsid protein comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the entire amino acid sequence of the nucleocapsid protein of a corresponding wild type gag polyprotein.

153. The recombinant protein of any one of claims 142-151, wherein the at least a fragment of the nucleocapsid protein comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 91, 92, 94, 95, 96, 97, 98, 99, 100, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more contiguous amino acid residues of the nucleocapsid protein of a corresponding wild type gag polyprotein.

154. The recombinant protein of any one of claims 101-114, or 142-153, wherein the plasma membrane recruitment element lacks the at least a fragment of a matrix protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the matrix protein.

155. The recombinant protein of any one of claims 101-114, 142, 143, or 144-154, wherein the plasma membrane recruitment element lacks the at least a fragment of a RNA-binding phosphoprotein; optionally wherein the plasma membrane recruitment element comprises a mutant of a wild-type gag polyprotein of MMLV.

156. The recombinant protein of any one of claims 101-114, or 142-155, wherein the plasma membrane recruitment element lacks the at least a fragment of a capsid protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the capsid protein, a C-terminal fragment of the capsid protein, or both.

157. The recombinant protein of any one of claims 101-114, or 142-156, wherein the plasma membrane recruitment element lacks the gag-endogenous protease cleavage sequence.

158. The recombinant protein of any one of claims 101-114, or 142-157, wherein the plasma membrane recruitment element lacks the at least a fragment of a nucleocapsid protein; optionally wherein the plasma membrane recruitment element lacks a N-terminal fragment of the nucleocapsid protein, a C-terminal fragment of the nucleocapsid protein, or both; optionally wherein the plasma membrane recruitment element lacks the nucleocapsid protein.

159. The recombinant protein of any one of claims 101, 102, 105-114, 115-120, 122, 124-125, 142-143, or 144-158, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of MMLV.

160. The recombinant protein of claim 159, wherein the plasma membrane recruitment element comprises

(a) a matrix protein of the MMLV gag (optionally full-length matrix protein of the MMLV gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the MMLV gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof;

(b) a capsid protein of the MMLV gag or a mutant thereof, optionally wherein the capsid protein of the MMLV gag or a mutant thereof is a full-length capsid protein of the MMLV gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the MMLV gag;

(c) heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif (optionally a leucine zipper); and

(d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the MMLV gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5;

optionally wherein the (a)-(d) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element;

optionally wherein the plasma membrane recruitment element further comprises a P12 domain of the MMLV gag or a mutant thereof located between (a) and (b), optionally wherein the P12 domain of the MMLV gag or a mutant thereof is a full-length P12 domain of the MMLV gag, a N-terminal fragment of the full-length P12 domain of the MMLV gag, a C-terminal fragment of the full-length P12 domain of the MMLV gag, or a fragment of the full-length P12 domain of the MMLV gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5).

161. The recombinant protein of claim 159, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, and the leucine zipper, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

162. The recombinant protein of claim 159, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length P12 domain of the MMLV gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and optionally the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

163. The recombinant protein of claim 159, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the MMLV gag, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

164. The recombinant protein of claim 159, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the MMLV gag or a fragment thereof, the leucine zipper, and the particle budding motif, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

165. The recombinant protein of any one of claims 101, 103-120, 122, 124-125, 142, or 144-158, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of hGAGKcon; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag and a late domain of the RSV gag; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid protein of the RSV gag; optionally wherein the plasma membrane recruitment element comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of the nucleocapsid protein of the RSV; optionally wherein the plasma membrane recruitment element further comprises a N-terminal myristoylation motif of the RSV gag.

166. The recombinant protein of any one of claims 101, 103-120, 122, 124-125, 142, or 144-158, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of HERV-K113.

167. The recombinant protein of claim 166, wherein the plasma membrane recruitment element comprises

(a) a matrix protein of the HERV-K113 gag (optionally full-length matrix protein of the HERV-K113 gag, a N-terminal fragment or a C-terminal fragment of the full-length matrix protein of the HERV-K113 gag), a pleckstrin homology (PH) domain (optionally a human PH domain) or a mutant thereof;

(b) a capsid protein of the HERV-K113 gag or a mutant thereof, optionally wherein the capsid protein of the HERV-K113 gag or a mutant thereof is a full-length capsid protein of the HERV-K113 gag, or a N-terminal fragment of or a C-terminal fragment of the full-length capsid protein of the HERV-K113 gag;

(c) heterologous domain, optionally wherein the heterologous domain comprises a multimerization motif (optionally a leucine zipper); and

(d) an optional particle budding motif, optionally wherein the particle budding motif is particle budding motif of the HERV-K113 gag; optionally wherein the particle budding motif is a heterologous particle budding motif; optionally wherein the heterologous particle budding motif is RSV P2B or a mutant thereof or a sequence listed in Table 5);

(e) an optional QP1 domain of the HERV-K113 gag; and

(f) an optional QP2 domain of the HERV-K113 gag;

optionally wherein (a)-(f) are arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element;

optionally wherein the plasma membrane recruitment element further comprises a P15 domain of the HERV-K113 gag or a mutant thereof, optionally wherein the P15 domain of the HERV-K113 gag or a mutant thereof is a full-length P15 domain of the HERV-K113 gag, a N-terminal fragment of the full-length P15 domain of the HERV-K113 gag, a C-terminal fragment of the full-length P15 domain of the HERV-K113 gag, or a fragment of the full-length P15 domain of the HERV-K113 gag fused to a heterologous particle budding motif (optionally RSV P2B or a mutant thereof or a sequence listed in Table 5).

168. The recombinant protein of claim 167, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the HERV-K113 gag, the full-length P15 domain of the HERV-K113 gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

169. The recombinant protein of claim 167, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length P15 domain of the HERV-K113 gag or a fragment there of that is fused to a heterologous particle budding motif, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, optionally the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

170. The recombinant protein of claim 167, wherein the plasma membrane recruitment element comprises the N-terminal fragment of the full-length matrix protein of the HERV-K113 gag, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

171. The recombinant protein of claim 167, wherein the plasma membrane recruitment element comprises the pleckstrin homology (PH) domain or a mutant thereof, the full-length capsid protein of the HERV-K113 gag or a fragment thereof, the leucine zipper, the particle budding motif, the optional QP1 domain of the HERV-K113 gag, and the optional QP2 domain of the HERV-K113 gag, arranged in order from a N-terminus of the plasma membrane recruitment element to a C-terminus of the plasma membrane recruitment element.

172. The recombinant protein of any one of claims 167-171, wherein the plasma membrane recruitment element comprises the QP1 domain and the QP2 domain of the HERV-K113 gag.

173. The recombinant protein of any one of claims 101-102, 115-120, 122, 124-125, 142-143, or 144-158, wherein the plasma membrane recruitment element comprises a mutant gag polyprotein that is a mutant of a wild-type gag polyprotein of RSV; optionally wherein the mutant gag polyprotein comprises a matrix protein of the RSV gag and a late domain of the RSV gag; optionally wherein the mutant gag polyprotein comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a full-length nucleocapsid protein of the RSV; optionally wherein the mutant gag polyprotein comprises a matrix protein of the RSV gag, a late domain of the RSV gag, and a fragment of the nucleocapsid protein of the RSV; optionally wherein the mutant gag polyprotein comprises a N-terminal myristoylation motif of the RSV gag.

174. The recombinant protein of any one of claims 126-141 or 159-173, wherein the plasma membrane recruitment element comprises one, two, or three particle budding motif, wherein each of the particle budding motif is selected from a sequence listed in Table 5.

175. The recombinant protein of any one of claims 117-174, wherein the plasma membrane recruitment element comprises a MHR.

176. The recombinant protein of any one of claims 101-117, or 120-175, wherein the plasma membrane recruitment element comprises the heterologous sequence; optionally wherein the heterologous sequence is fused to at least a fragment of the matrix protein, optionally the N-terminal of the fragment of the matrix protein; optionally wherein the heterologous sequence is a pleckstrin homology (PH) domain or a mutant thereof; optionally wherein the PH domain is a human PH domain; optionally wherein the fragment of the matrix protein lacks a N-terminal myristoylation motif, a N-terminal glycine, a highly basic region (HBR), a N-terminal fragment, or any combinations thereof.

177. The recombinant protein of any one of claims 101-176, wherein the plasma membrane recruitment element further comprises one or more mutant gag-endogenous protease cleavage sequences relative to a corresponding wildtype gag-endogenous protease cleavage sequence, and wherein the one or more mutant gag-endogenous protease cleavage sequences have higher cleavage efficiency than that of the corresponding wildtype gag-endogenous protease cleavage sequence.

178. A chimeric protein comprising the recombinant protein of any one of 101-177, wherein the chimeric protein comprises a cleavable linker; optionally wherein the cleavable linker connects the plasma membrane recruitment element and a payload.

179. The chimeric protein of claim 178, wherein the chimeric protein comprises a nuclear localization signal (NLS) sequence.

180. The chimeric protein of claim 178 or 179, wherein the chimeric protein comprises a nuclear export signal (NES) sequence.

181. The chimeric protein of any one of claims 178-180, wherein the chimeric protein comprises the membrane penetrating peptide, optionally wherein (a) the membrane penetrating peptide is linked to

the payload or the plasma membrane recruitment element; or (b) the membrane penetrating peptide connects the payload and the plasma membrane recruitment element; optionally wherein the membrane penetrating peptide comprises a sequence having at least about 80% sequence identity to a sequence listed in Table 6.

182. The chimeric protein of any one of claims 178-181, wherein the chimeric protein comprises a post-translational modification motif that is fused directly to (a) the payload; or (b) the plasma membrane recruitment element; optionally wherein the post-translational modification motif comprises a myristoylation motif, an acetylation motif, an isoprenylation motif, a palmitoylation motif, a farnesylation motif, or combinations thereof.

183. The chimeric protein of any one of claims 178-182, wherein the chimeric protein comprises the plasma membrane recruitment element, an optional NLS, the cleavable linker, and the payload arranged in order from N-terminus of the chimeric protein to C-terminus of the chimeric protein.

184. The chimeric protein of any one of claims 178-183, wherein the payload comprises an antibody, a cytokine, a therapeutic protein, a small molecule therapeutics, a therapeutic DNA, and a therapeutic RNA, a ribonucleoprotein, a zinc-finger, a transcription activator-like effector (TALE), or a CRISPR-based genome editor, or any combinations thereof; optionally wherein the payload comprises a NLS, optionally wherein the NLS is an endogenous NLS or a heterologous NLS.

185. A composition comprising a first nucleic acid sequence encoding the recombinant protein of any one of claims 101-177 or the chimeric protein of any one of claims 178-183.

186. The composition of claim 185, wherein the composition comprises a second nucleic acid sequence encoding an envelope protein; optionally wherein the envelope protein is a retroviral envelope protein or a mutant thereof; optionally wherein the envelope protein is an envelope protein from human endogenous retrovirus (HERV) or a mutant thereof.

187. The composition of claim 185 or 186, wherein the composition further comprises a third nucleic acid sequence encoding a second plasma membrane recruitment element; optionally wherein the second plasma membrane recruitment element is the same as the plasma membrane recruitment element; optionally wherein the second plasma membrane recruitment element is a retroviral gag or a mutant thereof, a HERV gag or a mutant thereof, a pleckstrin homology (PH) domain or a mutant thereof, or a membrane protein or a transmembrane domain thereof or a mutant thereof.

188. The composition of any one of claims 185-187, wherein the composition further comprises fourth nucleic acid encoding a protease; optionally wherein the protease is a retroviral protease.

189. The composition of claim 188, wherein the plasma membrane recruitment element is linked to the protease, optionally via a cleavable linker.

190. The composition of claim 188, wherein the second plasma membrane recruitment element is linked to the protease, optionally via a cleavable linker.

191. A system comprising the lipid delivery particle of any one of claims 1-100 or the composition of any one of claims 185-190.

192. The system of claim 191, wherein the system comprises a producer cell, a cell-free extract, or a cell lysate.

193. A pharmaceutical composition comprising (a) the lipid delivery particle of any one of claims 1-100 or the system of claim 191 or 192; and (b) a pharmaceutically acceptable excipient.

194. A kit comprising (a) the lipid delivery particle of any one of claims 1-100, the system of claim 191 or 192, or the pharmaceutical composition of claim 193; and (b) an information material containing instructions for administering a dosage of the lipid delivery particle or the system, or a dosage form of the pharmaceutical composition to a subject.

195. A method of treating a disease or a condition in a subject in need thereof, comprising administering to the subject the lipid delivery particle of any one of claims 1-100, the system of claim 191 or 192, or the pharmaceutical composition of claim 193.

196. A method comprising contacting a cell with the lipid delivery particle of any one of claims 1-100.

197. A method comprising contacting a cell with the system of claim 191 or 192.

198. A method comprising administering the lipid delivery particle of any one of claims 1-100, the system of claim 191 or 192, or the pharmaceutical composition of claim 193 to a subject in need thereof.

199. A method of producing the lipid delivery particle of any one of claims 1-100.

200. The method of claim 199, comprising contacting a producer cell with the composition of any one of claims 185-190.

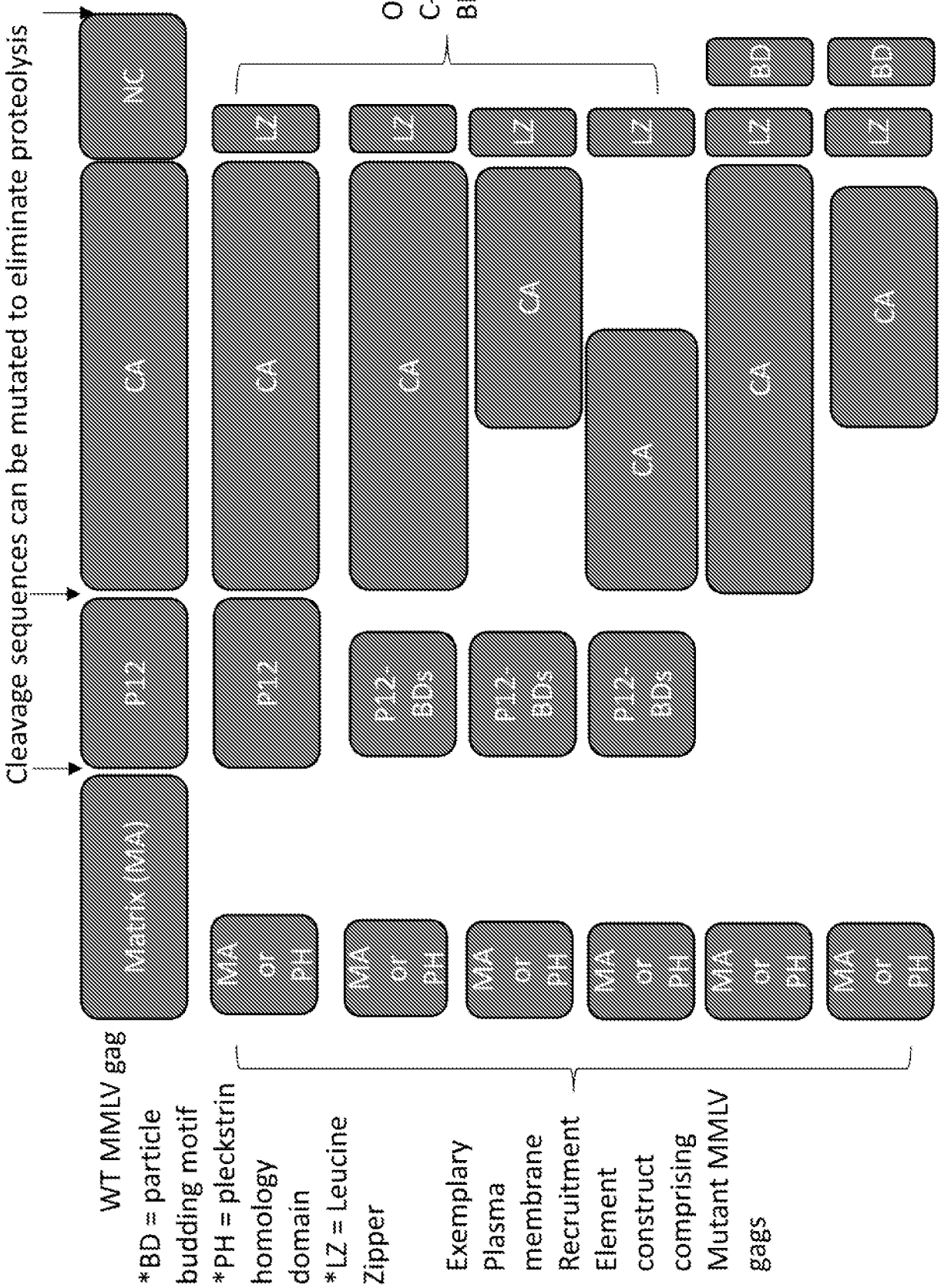

Cleavage sequences can be mutated to eliminate proteolysis
Optional C-terminal BD
WT MMLV gag
*BD = particle budding motif
*PH = pleckstrin homology domain
*LZ = Leucine Zipper
Exemplary Plasma membrane Recruitment Element construct comprising Mutant MMLV gags
Matrix (MA)
p12
CA
NC
MA or PH
p12, BDs
LZ
BD

FIG. 1A

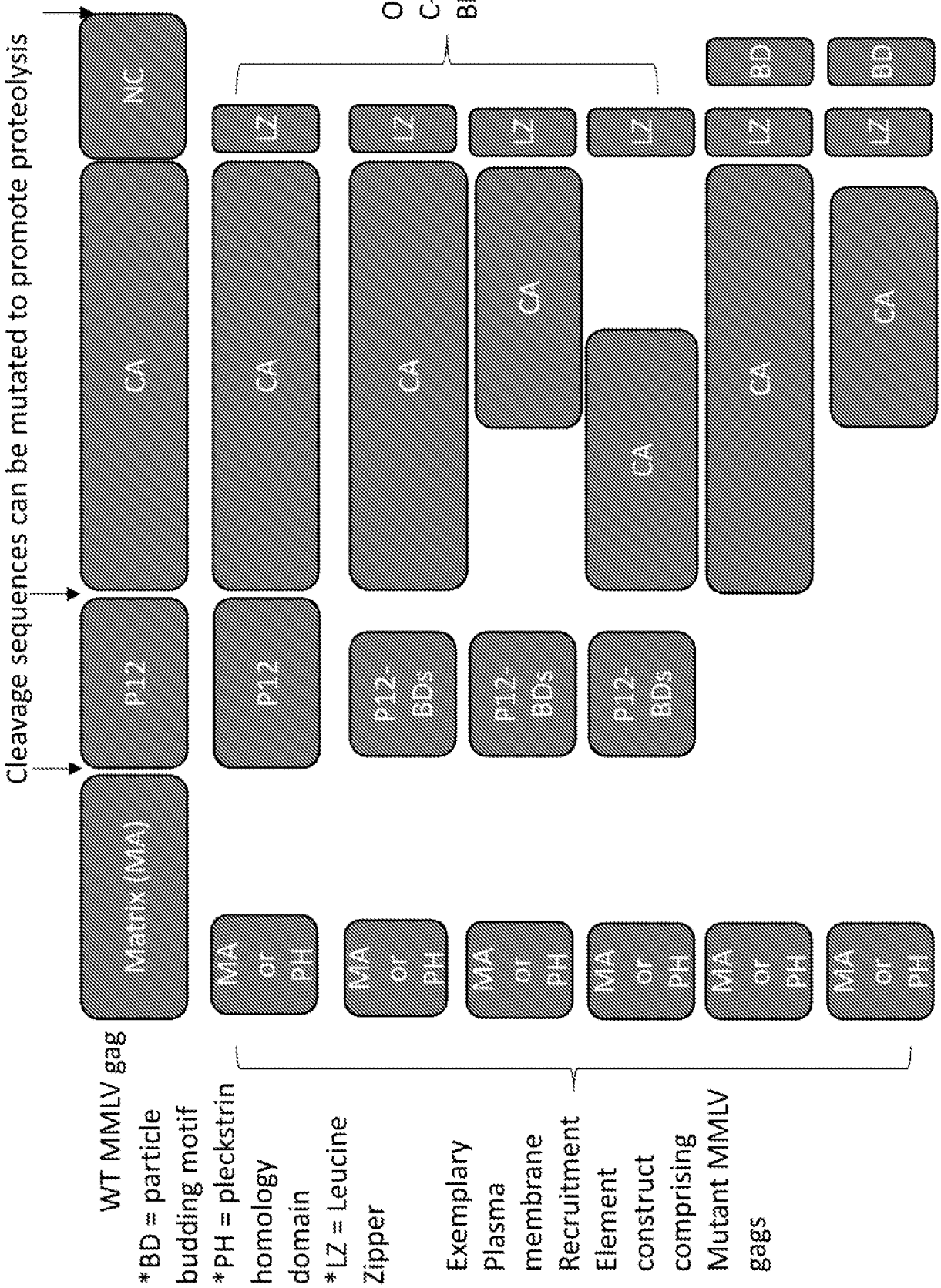

Cleavage sequences can be mutated to promote proteolysis
Optional C-terminal BD
WT MMLV gag
*BD = particle budding motif
*PH = pleckstrin homology domain
*LZ = Leucine Zipper
Exemplary Plasma membrane Recruitment Element construct comprising Mutant MMLV gags
Matrix (MA)
p12
CA
NC
MA or PH
p12, BDs
LZ
BD

FIG. 1B

Cleavage sequences can be mutated to eliminate proteolysis
Matrix (MA)
SP1
P15 domain
Capsid (CA)
Nucleo capsid (NC)
QP1 & QP2
Optional QP1 & QP2
WT HERV-K 113 gag
*BD = particle budding motif
*PH = pleckstrin homology domain
*LZ = Leucine Zipper
Exemplary Plasma membrane Recruitment Element construct comprising Mutant HERV-K 113 gags
MA or PH
P15-BDs
CA
LZ
BD

FIG. 2A

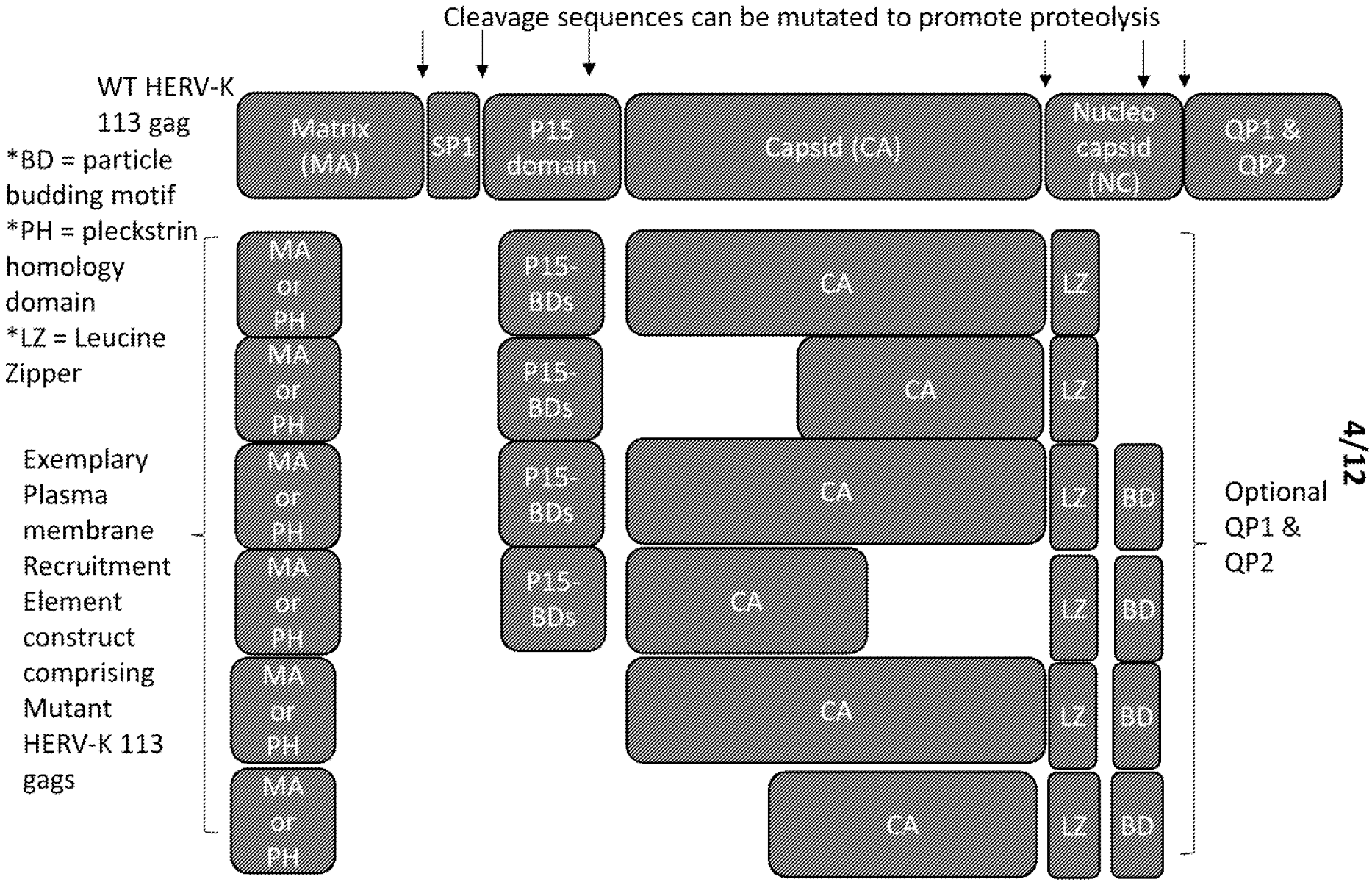

Cleavage sequences can be mutated to promote proteolysis
WT HERV-K 113 gag
*BD = particle budding motif
*PH = pleckstrin homology domain
*LZ = Leucine Zipper
Matrix (MA)
SP1
P15 domain
Capsid (CA)
Nucleo capsid (NC)
QP1 & QP2
Exemplary Plasma membrane Recruitment Element construct comprising Mutant HERV-K 113 gags
MA or PH
P15-BDs
CA
LZ
BD
Optional QP1 & QP2

FIG. 2B

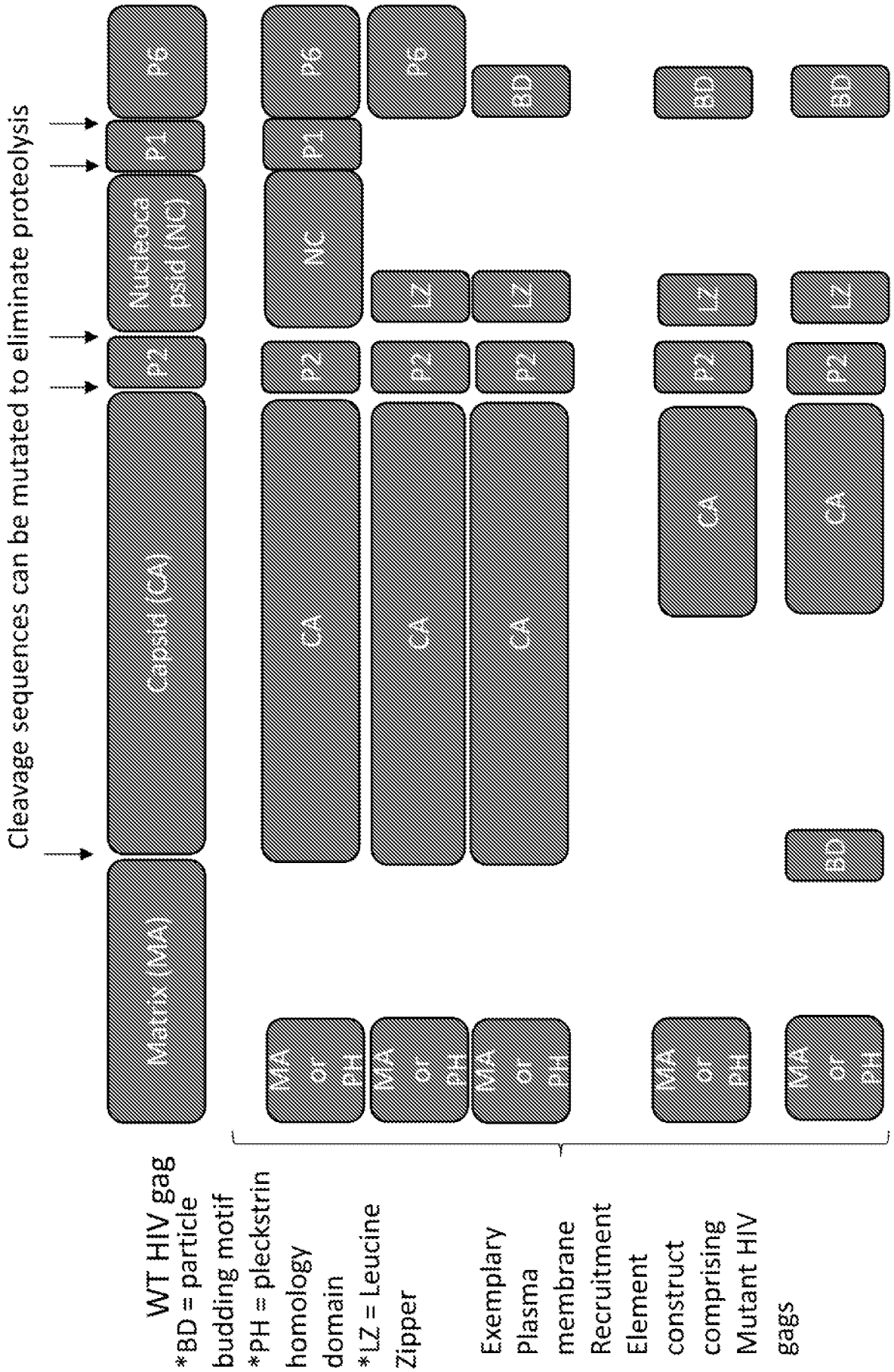

Cleavage sequences can be mutated to eliminate proteolysis
Matrix (MA)
Capsid (CA)
p2
Nucleocapsid (NC)
p1
p6
WT HIV gag
*BD = particle budding motif
*PH = pleckstrin homology domain
*LZ = Leucine Zipper
Exemplary Plasma membrane Recruitment Element construct comprising Mutant HIV gags
MA or PH
CA
p2
NC
p1
p6
LZ
BD

FIG. 3A

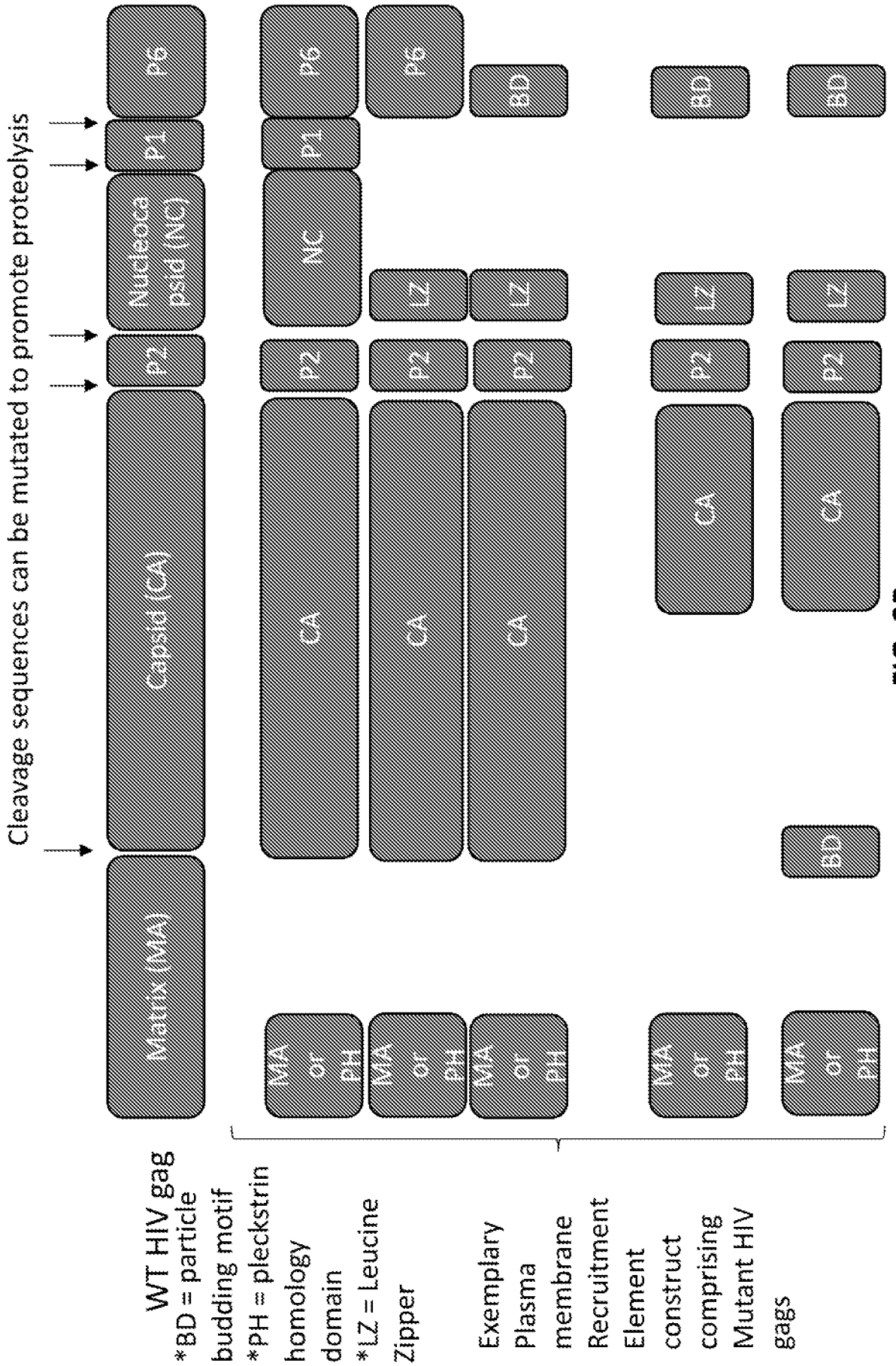

Cleavage sequences can be mutated to promote proteolysis
Matrix (MA)
Capsid (CA)
p2
Nucleocapsid (NC)
p1
p6
WT HIV gag
*BD = particle budding motif
*PH = pleckstrin homology domain
*LZ = Leucine Zipper
Exemplary Plasma membrane Recruitment Element construct comprising Mutant HIV gags
MA or PH
CA
p2
NC
p1
p6
LZ
BD

FIG. 3B

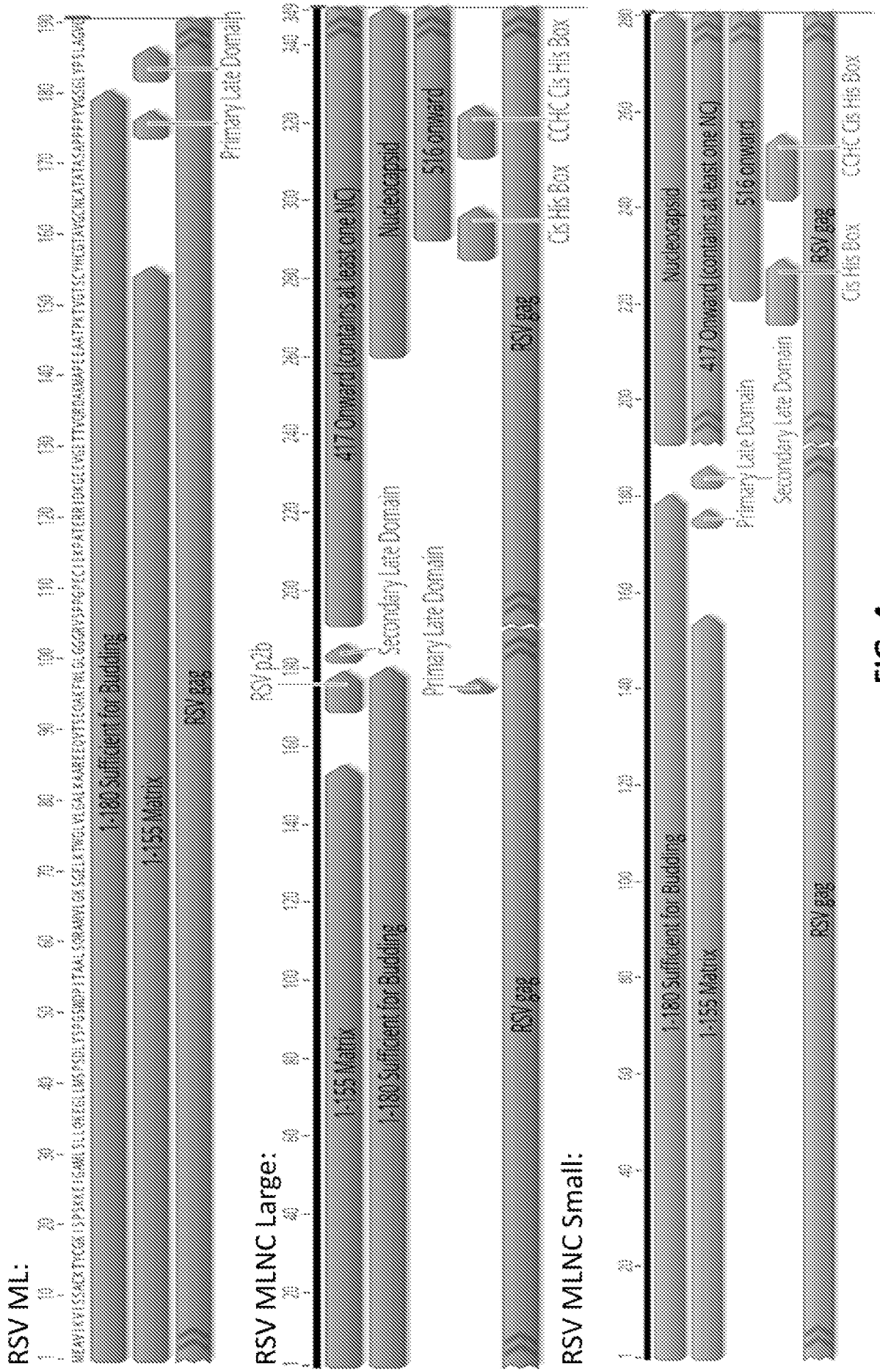

RSV ML:
1-180 Sufficient for Budding
1-155 Matrix
RSV gag
Primary Late Domain
RSV MLNC Large:
RSV p2b
1-155 Matrix
407 Onward contains at least one M2
1-180 Sufficient for Budding
Secondary Late Domain
Nucleocapsid
Shi-onward
Primary Late Domain
RSV gag
CX6C CX5 His Box
CX6C CX5 His Box
RSV MLNC Small:
1-180 Sufficient for Budding
Nucleocapsid
1-155 Matrix
407 Onward contains at least one M2
Primary Late Domain
Secondary Late Domain
Shi-onward
RSV gag
CX6C CX5 His Box
CX6C CX5 His Box

FIG. 4

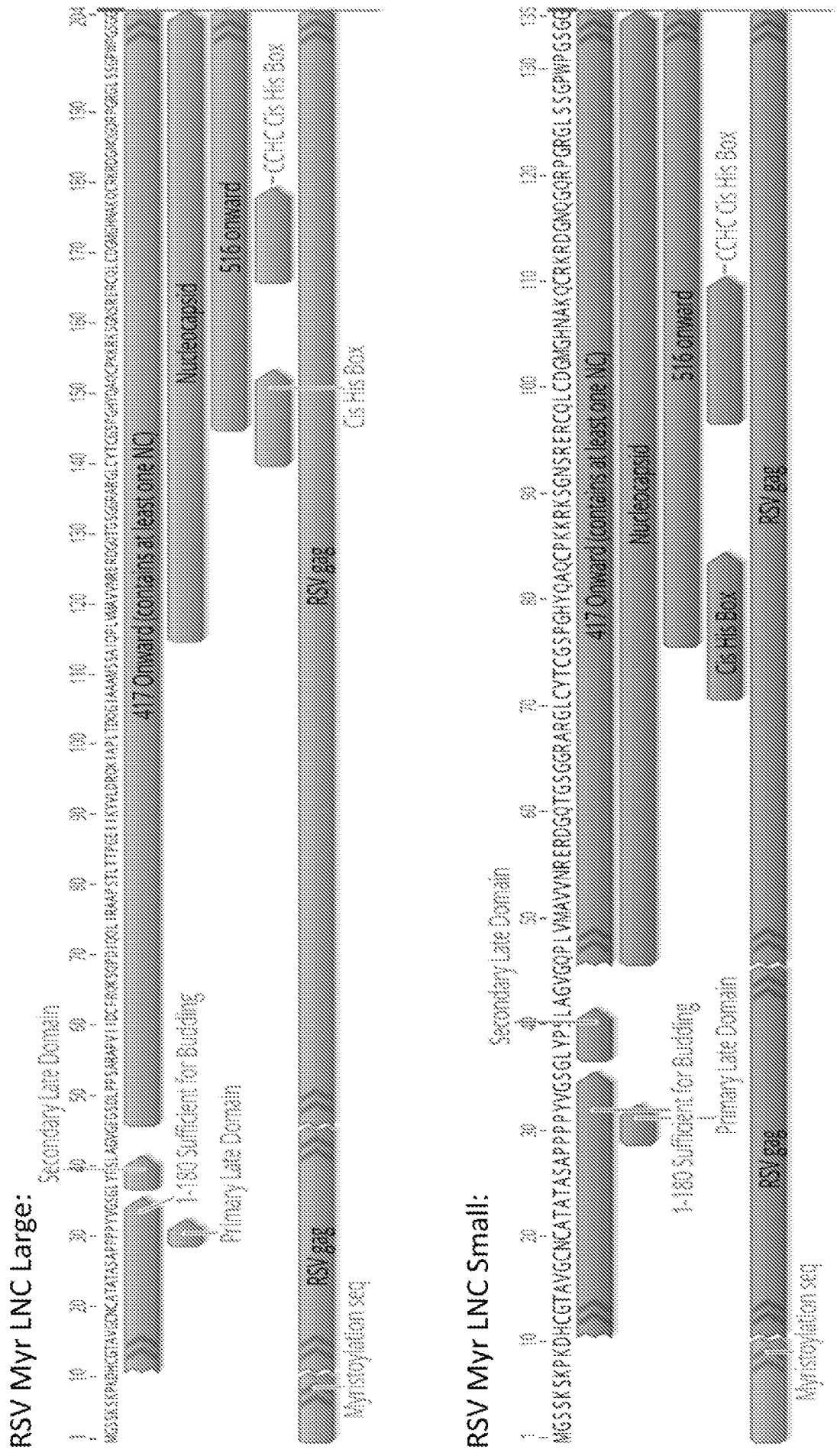

RSV Myr LNC Large:
Secondary Late Domain
1-180 Sufficient for Budding
Primary Late Domain
417Onand (contains at least one M2)
Nucleocapsid
51Gonand
-CCHC Cis His Box
RSV age
Cis His Box
RSV age
Myristoylation seq
RSV Myr LNC Small:
Secondary Late Domain
417Onand (contains at least one M2)
Nucleocapsid
51Gonand
1-180 Sufficient for Budding
Primary Late Domain
Cis His Box
-CCHC Cis His Box
RSV age
RSV age
Myristoylation seq

FIG. 5

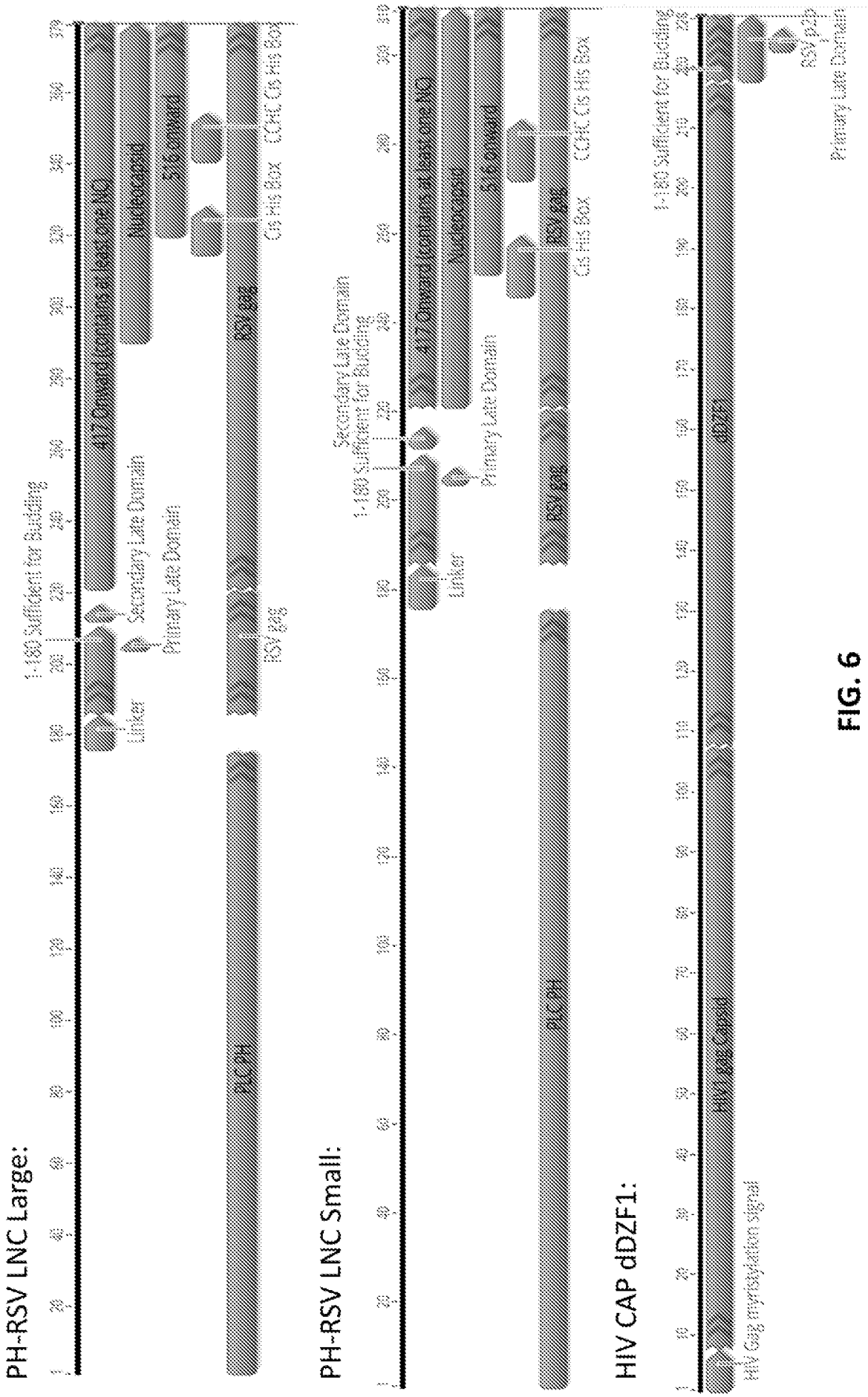

PH-RSV LNC Large:
1-160 Sufficient for Budding
417 Oligomerizes at last one NC
Nucleocapsid
Secondary Late Domain
Linker
Primary Late Domain
SH Domain
PLC PH
RSV gpG
Gs His Box
CCHC Cys His Box
PH-RSV LNC Small:
Secondary Late Domain
1-160 Sufficient for Budding
417 Oligomerizes at last one NC
Nucleocapsid
Linker
Primary Late Domain
SH Domain
PLC PH
RSV gpG
Gs His Box
CCHC Cys His Box
HIV CAP dDZF1:
1-180 Sufficient for Budding
HIV gag Capsid
dDZF1
HIV Gag myristoylation signal
RSV gpG
Primary Late Domain

FIG. 6

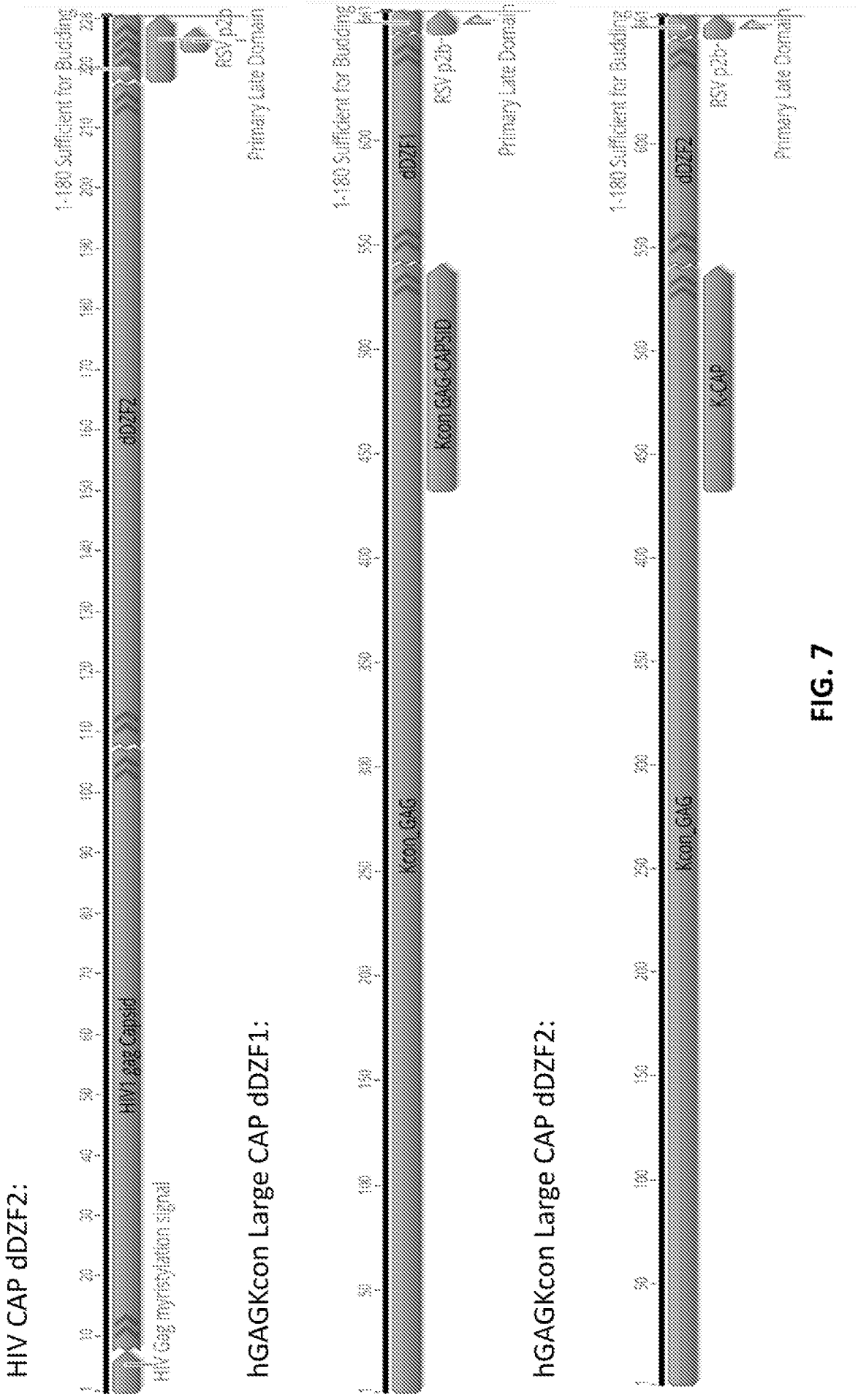

HIV CAP dDZF2:
1-180 Sufficient for Budding
HIV gag Capsid
dDZF2
HIV Gag myristylation signal
RSV p2b
Primary Late Domain
hGAGKcon Large CAP dDZF1:
1-180 Sufficient for Budding
dDZF1
RSV p2b
Primary Late Domain
Kon GAG
Kon GAG CAPSD
hGAGKcon Large CAP dDZF2:
1-180 Sufficient for Budding
dDZF2
RSV p2b
Primary Late Domain
Kon GAG
KCAP

FIG. 7

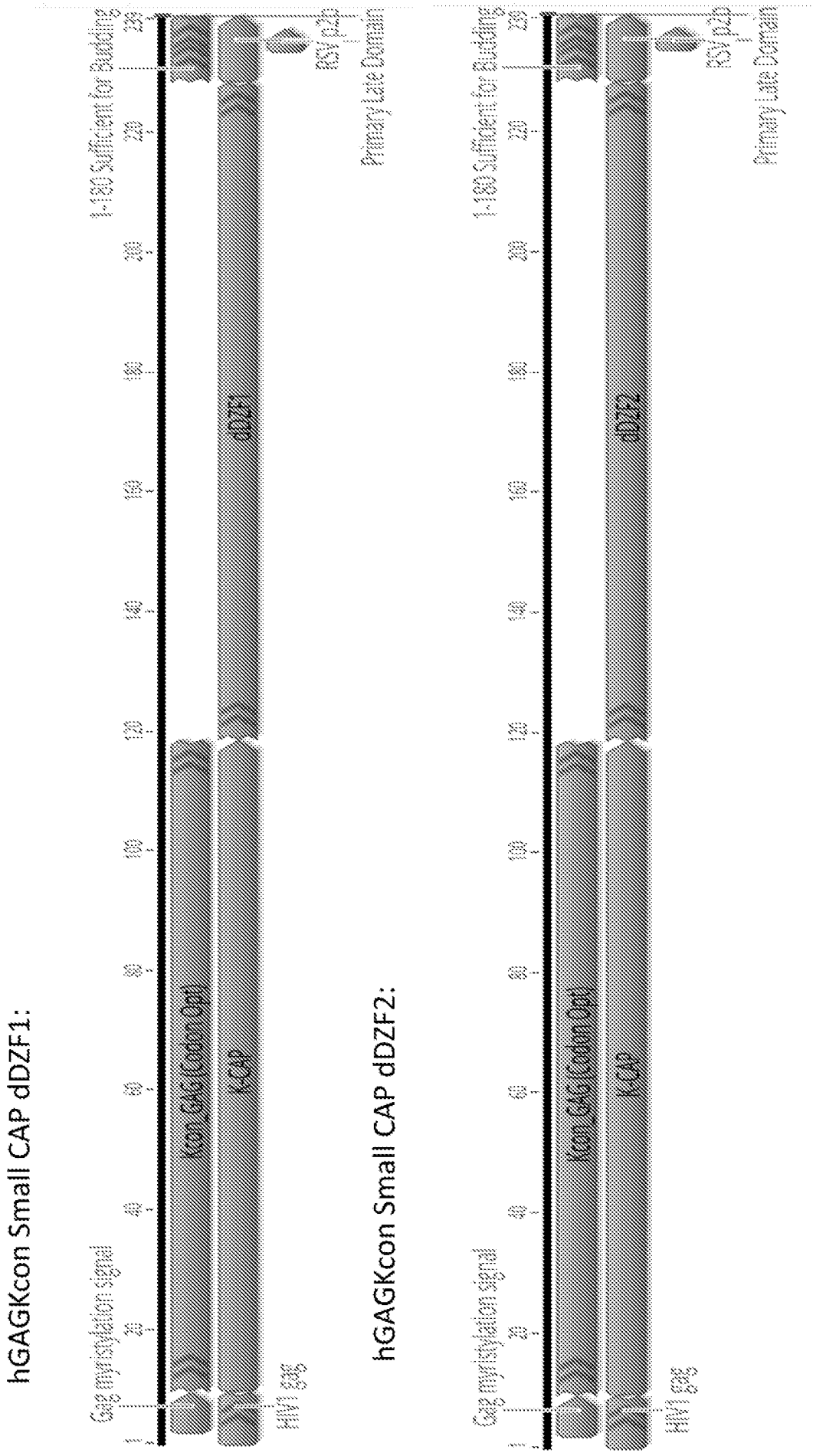

hGAGKcon Small CAP dDZF1:
Gag myristylation signal
1-180 Sufficient for Budding
Primary Late Domain
RSV p2b
HIV1 p6
Kcon GAG Codon Opt
KCAP
dDZF1
hGAGKcon Small CAP dDZF2:
Gag myristylation signal
1-180 Sufficient for Budding
Primary Late Domain
RSV p2b
HIV1 p6
Kcon GAG Codon Opt
KCAP
dDZF2

FIG. 8

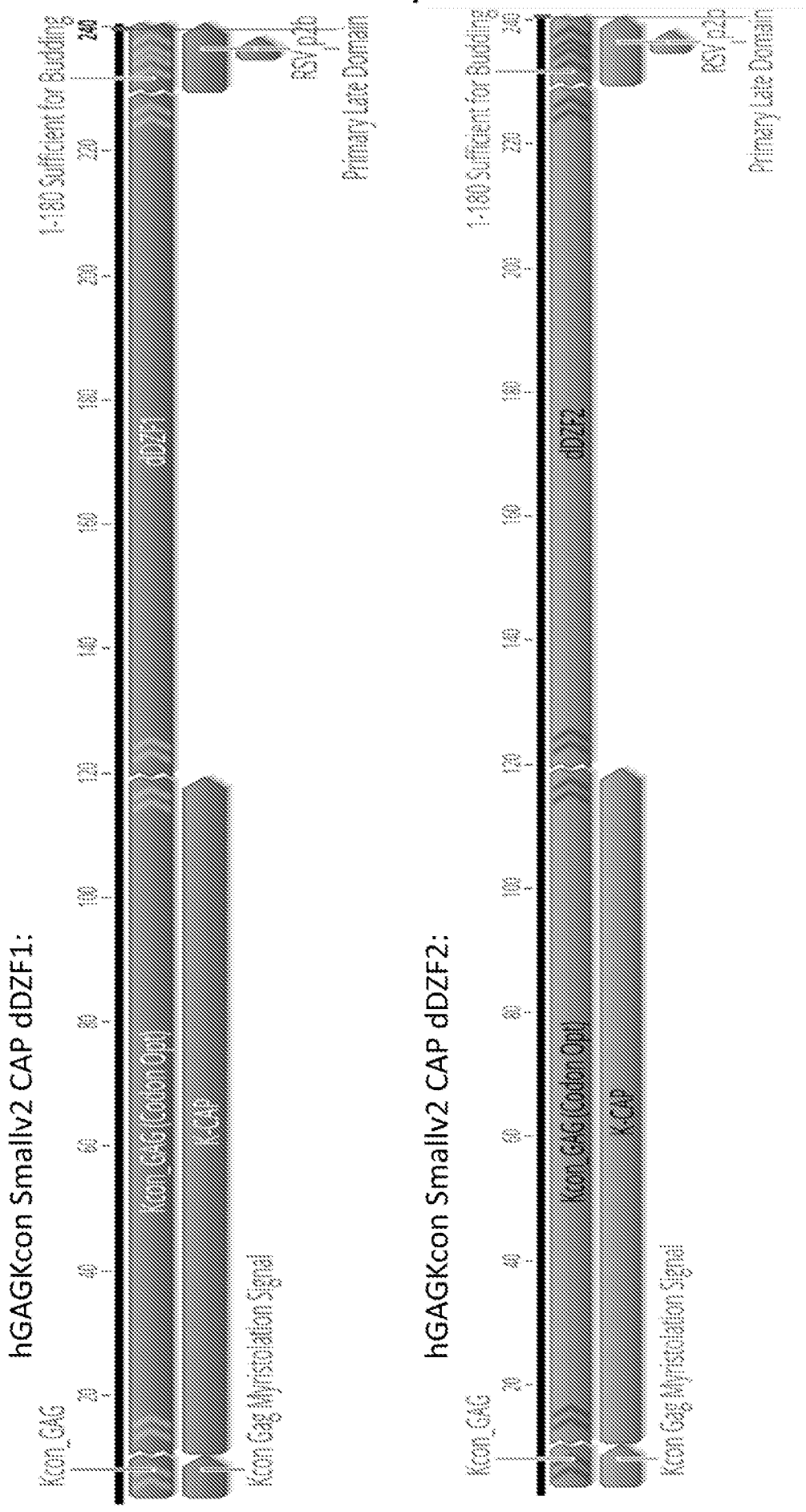

hGAGKcon SmallV2 CAP dDZF1:
Kcon_GAG
Kcon Gag Myristolation Signal
KGP
dDZF1
RSV p2b
Primary Late Domain
1-180 Sufficient for Budding
hGAGKcon SmallV2 CAP dDZF2:
Kcon_GAG
Kcon Gag Myristolation Signal
KGP
dDZF2
RSV p2b
Primary Late Domain
1-180 Sufficient for Budding

FIG. 9