CLAIMS

1. An extracellular vesicle (EV) comprising a biologically active molecule (BAM) covalently linked to the EV via an anchoring moiety (AM), wherein the anchoring moiety comprises:

[AM]-[Linker]n-[BAM] Formula (I)

wherein n is any integer.

2. The extracellular vesicle of claim 1, wherein n is any number between 0 and 10.

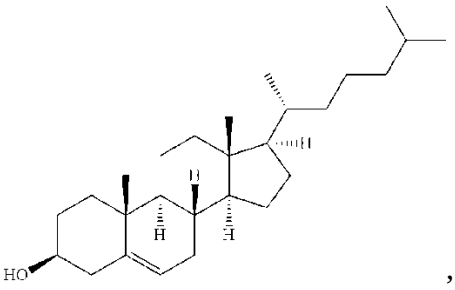
3. The extracellular vesicle of claim 1 or 2, wherein the anchoring moiety comprises a sterol, GM1, a lipid, a vitamin, a small molecule, a peptide, or a combination thereof.

~~4. The extracellular vesicle of any one of claims 1 to 3, wherein the anchoring moiety comprises at least 6 carbon atoms, at least 7 carbon atoms, at least 8 carbon atoms, at least 9 carbon atoms, at least 10 carbon atoms, at least 11 carbon atoms, at least 12 carbon atoms, at least 13 carbon atoms, at least 14 carbon atoms, at least 15 carbon atoms, at least 16 carbon atoms, at least 17 carbon atoms, at least 18 carbon atoms, at least 19 carbon atoms, at least 20 carbon atoms, at least 25 carbon atoms, at least 30 carbon atoms, at least 35 carbon atoms, at least 40 carbon atoms, at least 45 carbon atoms, at least 50 carbon atoms, at least 55 carbon atoms, at least 60 carbon atoms, at least 65 carbon atoms, at least 70 carbon atoms, at least 75 carbon atoms, at least 80 carbon atoms, at least 85 carbon atoms, or at least 90 carbon atoms.~~

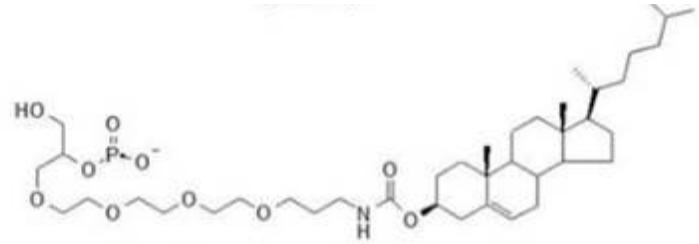
~~5. The extracellular vesicle of any one of claims 1 to 4, wherein the anchoring moiety comprises a sterol, a steroid, a hopanoid, a hydroxysteroid, a secosteroid, an analog thereof, or any combination thereof.~~

~~6. The extracellular vesicle of any one of claims 1 to 4, wherein the anchoring moiety comprises ergosterol, 7-dehydrocholesterol, cholesterol, 24S-hydroxycholesterol, lanosterol, cycloartenol, fucosterol, saringosterol, campesterol, β-sitosterol, sitostanol, coprostanol, avenasterol, stigmasterol, or any combination thereof.~~

~~7.~~4. The extracellular vesicle of claim 3, ~~6,~~ wherein the anchoring moiety is a cholesterol or derivative having a structure selected from the group consisting of ,

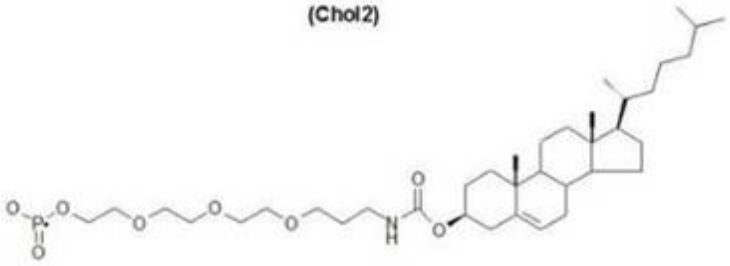


,



, and

(Chol2)



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~~8. The extracellular vesicle of any one of claims 1 to 5, wherein the anchoring moiety comprises a steroid, which is dihydrotestosterone, uvaol, hecigenin, diosgenin, progesterone, cortisol, or any combination thereof.~~

~~9. The extracellular vesicle of any one of claims 1 to 4, wherein the anchoring moiety comprises a lipid.~~

~~10. The extracellular vesicle of claim 9, wherein the anchoring moiety comprises a C2-C60 chain.~~

~~11. The extracellular vesicle of claim 9, wherein the anchoring moiety comprises C4-C40, C2-C38, C2-C36, C2-C34, C2-C32, C2-C30, C4-C30, C2-C28, C4-C28, C2- C26, C4-C26,~~

~~C2-C24, C4-C24, C6-C24, C8-C24, C10-C24, C2-C22, C4-C22, C6-C22, C8-C22, C10-C22, C2-C20, C4-C20, C6-C20, C8-C20, C10-C20, C2-C18, C4-C18, C6-C18, C8-C18, C10-C18, C12-C18, C14-C18, C16-C18, C2-C16, C4-C16, C6-C16, C8-C16, C10-C16, C12-C16, C14-C16, C2-C15, C4-C15, C6-C15, C8-C15, C9-C15, C10-C15, C11-C15, C12-C15, C13-C15, C2-C14, C4-C14, C6-C14, C8-C14, C9-C14, C10-C14, C11-C14, C12-C14, C2-C13, C4-C13, C6-C13, C7-C13, C8-C13, C9-C13, C10-C13, C10-C13, C11-C13, C2-C12, C4-C12, C6-C12, C7-C12, C8-C12, C9-C12, C10-C12, C2-C11, C4-C11, C6-C11, C7-C11, C8-C11, C9-C11, C2-C10, C4-C10, C2-C9, C4-C9, C2-C8, C2-C7, C4-C7, C2-C6, or C4-C6 chain.~~

~~12.~~5. The extracellular vesicle of claim 3, ~~any one of claims 9 to 11,~~ wherein the lipid ~~anchoring moiety~~ comprises a straight chain fatty acid, a branched fatty acid, an unsaturated fatty acid, a monounsaturated fatty acid, a polyunsaturated fatty acid, a hydroxyl fatty acid, a polycarboxylic acid, or any combination thereof.

~~13. The extracellular vesicle of claim 12, wherein the anchoring moiety comprises a straight chain fatty acid, which is butyric acid, caproic acid, caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, arachic acid, behenic acid, lignoceric acid, hexacosanoic acid, octacosanoic acid, triacontanoic acid and n-dotriacontanoic acid, and those having an odd number of carbon atoms, such as propionic acid, n-valeric acid, enanthic acid, pelargonic acid, hendecanoic acid, tridecanoic acid, pentadecanoic acid, heptadecanoic acid, nonadecanoic acid, heneicosanoic acid, tricosanoic acid, pentacosanoic acid, heptacosanoic acid, or any combination thereof.~~

~~14. The extracellular vesicle of claim 12, wherein the anchoring moiety comprises a branched fatty acid, which is isobutyric acid, isocaproic acid, isocaprylic acid, isocapric acid, isolauric acid, 11-methyldodecanoic acid, isomyristic acid, 13-methyl-tetradecanoic acid, isopalmitic acid, 15-methyl-hexadecanoic acid, isostearic acid, 17-methyloctadecanoic acid, isoarachic acid, 19-methyl-eicosanoic acid, α-ethyl-hexanoic acid, α-hexyldecanoic acid, α-heptylundecanoic acid, 2-decyltetradecanoic acid, 2-undecyltetradecanoic acid, 2-decylpentadecanoic acid, 2-undecylpentadecanoic acid, Fine oxocol 1800 acid (product of Nissan Chemical Industries, Ltd.), anteiso fatty acids terminating with an isobutyl group,~~

such as 6-methyl-octanoic acid, 8-methyl-decanoic acid, 10-methyl-dodecanoic acid, 12-methyl-tetradecanoic acid, 14-methyl-hexadecanoic acid, 16-methyl-octadecanoic acid, 18-methyl-eicosanoic acid, 20-methyl-docosanoic acid, 22-methyl-tetracosanoic acid, 24-methyl-hexacosanoic acid, and 26-methyloctacosanoic acid, or any combination thereof.

15. The extracellular vesicle of claim 12, wherein the anchoring moiety comprises an unsaturated fatty acid, which is 4-decenoic acid, caproleic acid, 4-dodecenoic acid, 5-dodecenoic acid, lauroleic acid, 4-tetradecenoic acid, 5-tetradecenoic acid, 9-tetradecenoic acid, palmitoleic acid, 6-octadecenoic acid, oleic acid, 9-octadecenoic acid, 11-octadecenoic acid, 9-eicosenoic acid, cis-11-eicosenoic acid, cetoleic acid, 13-docosenoic acid, 15-tetracosenoic acid, 17-hexacosenoic acid, 6,9,12,15-hexadecatetraenoic acid, linoleic acid, linolenic acid, α-eleostearic acid, β-eleostearic acid, punicic acid, 6,9,12,15-octadecatetraenoic acid, parinaric acid, 5,8,11,14-eicosatetraenoic acid, 5,8,11,14,17-eicosapentaenoic acid, 7,10,13,16,19-docosapentaenoic acid, 4,7,10,13,16,19-docosahexaenoic acid, or any combination thereof.

16. The extracellular vesicle of claim 12, wherein the anchoring moiety comprises a hydroxy fatty acid, which is α-hydroxylauric acid, α-hydroxymyristic acid, α-hydroxypalmitic acid, α-hydroxystearic acid, ω-hydroxylauric acid, α-hydroxyarachic acid, 9-hydroxy-12-octadecenoic acid, ricinoleic acid, α-hydroxybehenic acid, 9-hydroxy-trans-10,12-octadecadienic acid, kamolenic acid, ipurolic acid, 9,10-dihydroxystearic acid, 12-hydroxystearic acid, or any combination thereof.

17. The extracellular vesicle of claim 12, wherein the anchoring moiety comprises a polycarboxylic acid, which is oxalic acid, malonic acid, succinic acid, glutaric acid, adipic acid, pimelic acid, suberic acid, azelaic acid, sebacic acid, D,L-malic acid, or any combination thereof.

18.6. The extracellular vesicle of claim 3, any one of claims 1 to 4, wherein the lipid anchoring moiety comprises a phospholipid.

19. The extracellular vesicle of claim 18, wherein the phospholipid is phosphatidyl choline, phosphatidyl ethanolamine, phosphatidyl glycerol, phosphatidyl serine, phosphatidic acid, 2 lysophosphatidyl choline, sphingomyelin, or any combination thereof.

20. The extracellular vesicle of claim 18, wherein the phospholipid is phosphatidylethanolamines, which is dilauroylphosphatidyl ethanolamine, dimyristoylphosphatidyl ethanolamine, dipalmitoylphosphatidyl ethanolamine, distearoylphosphatidyl ethanolamine, dioleoylphosphatidyl ethanolamine, 1-palmitoyl-2-oleylphosphatidyl ethanolamine, 1-oleyl-2-palmitoylphosphatidyl ethanolamine, dierucoylphosphatidyl ethanolamine, or any combination thereof.

21. The extracellular vesicle of claim 18, wherein the phospholipid is phosphatidyl glycerol, which is dilauroylphosphatidyl glycerol, dimyristoylphosphatidyl glycerol, dipalmitoylphosphatidyl glycerol, distearoylphosphatidyl glycerol, dioleoylphosphatidyl glycerol, 1-palmitoyl-2-oleyl phosphatidyl glycerol, 1-oleyl-2-palmitoyl phosphatidyl glycerol, dierucoylphosphatidyl glycerol, or any combination thereof.

22. The extracellular vesicle of claim 18, wherein the phospholipid is phosphatidyl serine, which is dilauroylphosphatidyl serine, dimyristoylphosphatidyl serine, dipalmitoylphosphatidyl serine, distearoylphosphatidyl serine, dioleoylphosphatidyl serine, 1-palmitoyl-2-oleyl phosphatidyl serine, 1-oleyl-2-palmitoyl phosphatidyl serine, dierucoylphosphatidyl serine, or any combination thereof.

23. The extracellular vesicle of claim 18, wherein the phospholipid is phosphatidic acid, which is dilauroylphosphatidic acid, dimyristoylphosphatidic acid, dipalmitoylphosphatidic acid, distearoylphosphatidic acid, dioleoylphosphatidic acid, 1-palmitoyl-2-oleylphosphatidic acid, 1-oleyl-2-palmitoyl phosphatidic acid, dierucoylphosphatidic acid, or any combination thereof.

24. The extracellular vesicle of claim 18, wherein the phospholipid is phosphatidyl inositol, which is dilauroylphosphatidyl inositol, dimyristoylphosphatidyl inositol, dipalmitoylphosphatidyl inositol, distearoylphosphatidyl inositol, dioleoylphosphatidyl

inositol, 1-palmitoyl-2-oleyl-phosphatidyl inositol, 1-oleyl-2-palmitoyl-phosphatidyl inositol, dierucoylphosphatidyl inositol, or any combination thereof.

25. The extracellular vesicle of claim 18, wherein the phospholipid is a symmetric phospholipid, which is 1,2 dipropionyl sn glycero 3 phosphocholine (03:0 PC); 1,2 dibutyryl sn glycero 3 phosphocholine (04:0 PC); 1,2 dipentanoyl sn glycero 3 phosphocholine (05:0 PC); 1,2 dihexanoyl sn glycero 3 phosphocholine (06:0 PC), 1,2 diheptanoyl sn glycero 3 phosphocholine (07:0 PC); 1,2 dioctanoyl sn glycero 3 phosphocholine (08:0 PC); 1,2 dinonanoyl sn glycero 3 phosphocholine (09:0 PC); 1,2 didecanoyl sn glycero 3 phosphocholine (10:0 PC); 1,2 diundecanoyl sn glycero 3 phosphocholine (11:0 PC, DUPC); 1,2 dilauroyl sn glycero 3 phosphocholine (12:0 PC); 1,2 ditridecanoyl sn glycero 3 phosphocholine (13:0 PC); 1,2 dimyristoyl sn glycero 3 phosphocholine (14:0 PC, DMPC); 1,2 dipentadecanoyl sn glycero 3 phosphocholine (15:0 PC); 1,2 dipalmitoyl sn glycero 3 phosphocholine (16:0 PC, DPPC); 1,2 diphytanoyl sn glycero 3 phosphocholine (4ME 16:0 PC); 1,2 diheptadecanoyl sn glycero 3 phosphocholine (17:0 PC); 1,2 distearoyl sn glycero 3 phosphocholine (18:0 PC, DSPC); 1,2 dinonadecanoyl sn glycero 3 phosphocholine (19:0 PC); 1,2 diarachidoyl sn glycero 3 phosphocholine (20:0 PC); 1,2 dihenarachidoyl sn glycero 3 phosphocholine (21:0 PC); 1,2 dibehenoyl sn glycero 3 phosphocholine (22:0 PC); 1,2 ditricosanoyl sn glycero 3 phosphocholine (23:0 PC); 1,2 dilignoceroyl sn glycero 3 phosphocholine (24:0 PC); 1,2 dimyristoleoyl sn glycero 3 phosphocholine (14:1 (Δ9-Cis) PC); 1,2 dimyristelaidoyl sn glycero 3 phosphocholine (14:1 (Δ9-Trans) PC); 1,2 dipalmitoleoyl sn glycero 3 phosphocholine (16:1 (Δ9-Cis) PC); 1,2 dipalmitelaidoyl sn glycero 3 phosphocholine (16:1 (Δ9-Trans) PC); 1,2 dipetroselenoyl sn glycero 3 phosphocholine (18:1 (Δ6-Cis) PC); 1,2 dioleoyl sn glycero 3 phosphocholine (18:1 (Δ9-Cis) PC, DOPC); 1,2 dielaidoyl sn glycero 3 phosphocholine (18:1 (Δ9-Trans) PC); 1,2 dilinoleoyl sn glycero 3 phosphocholine (18:2 (Cis) PC, DLPC); 1,2 dilinolenoyl sn glycero 3 phosphocholine (18:3 (Cis) PC, DLnPC); 1,2 dieicosenoyl sn glycero 3 phosphocholine (20:1 (Cis) PC); 1,2 diarachidonoyl sn glycero 3 phosphocholine (20:4 (Cis) PC, DAPC); 1,2 dierucoyl sn glycero 3 phosphocholine (22:1 (Cis) PC); 1,2 didocosahexaenoyl sn glycero 3 phosphocholine (22:6 (Cis) PC, DHAPC); 1,2 dinervonoyl sn glycero 3 phosphocholine (24:1 (Cis) PC); 1,2 dihexanoyl sn glycero 3 phosphoethanolamine (06:0 PE); 1,2

~~dioctanoyl sn glycero 3 phosphoethanolamine (08:0 PE); 1,2 didecanoyl sn glycero 3 phosphoethanolamine (10:0 PE); 1,2 dilauroyl sn glycero 3 phosphoethanolamine (12:0 PE), 1,2 dimyristoyl sn glycero 3 phosphoethanolamine (14:0 PE); 1,2 dipentadecanoyl sn glycero 3 phosphoethanolamine (15:0 PE); 1,2 dipalmitoyl sn glycero 3 phosphoethanolamine (16:0 PE); 1,2 diphytanoyl sn glycero 3 phosphoethanolamine (4ME 16:0 PE); 1,2 diheptadecanoyl sn glycero 3 phosphoethanolamine (17:0 PE); 1,2 distearoyl sn glycero 3 phosphoethanolamine (18:0 PE, DSPE); 1,2 dipalmitoleoyl sn glycero 3 phosphoethanolamine (16:1 PE); 1,2 dioleoyl sn glycero 3 phosphoethanolamine (18:1 (Δ9 Cis) PE, DOPE); 1,2 dielaidoyl sn glycero 3 phosphoethanolamine (18:1 (Δ9 Trans) PE); 1,2 dilinoleoyl sn glycero 3 phosphoethanolamine (18:2 PE, DLPE); 1,2 dilinolenoyl sn glycero 3 phosphoethanolamine (18:3 PE, DLnPE); 1,2 diarachidonoyl sn glycero 3 phosphoethanolamine (20:4 PE, DAPE); 1,2 didocosahexaenoyl sn glycero 3 phosphoethanolamine (22:6 PE, DHAPE); 1,2 di O octadecenyl sn glycero 3 phosphocholine (18:0 Diether PC); 1,2 dioleoyl sn glycero 3 phospho rac (1 glycerol) sodium salt (DOPG), or any combination thereof.~~

~~26. The extracellular vesicle of claim 18, wherein the phospholipid is a asymmetric phospholipid, which is 1 myristoyl 2 palmitoyl sn glycero 3 phosphocholine (14:0-16:0 PC, MPPC); 1 myristoyl 2 stearoyl sn glycero 3 phosphocholine (14:0-18:0 PC, MSPC); 1 palmitoyl 2 acetyl sn glycero 3 phosphocholine (16:0-02:0 PC); 1 palmitoyl 2 myristoyl sn glycero 3 phosphocholine (16:0-14:0 PC, PMPC); 1 palmitoyl 2 stearoyl sn glycero 3 phosphocholine (16:0-18:0 PC, PSPC); 1 palmitoyl 2 oleoyl sn glycero 3 phosphocholine (16:0-18:1 PC, POPC); 1 palmitoyl 2 linoleoyl sn glycero 3 phosphocholine (16:0-18:2 PC, PLPC); 1 palmitoyl 2 arachidonoyl sn glycero 3 phosphocholine (16:0-20:4 PC); 1 palmitoyl 2 docosahexaenoyl sn glycero 3 phosphocholine (14:0-22:6 PC); 1 stearoyl 2 myristoyl sn glycero 3 phosphocholine (18:0-14:0 PC, SMPC); 1 stearoyl 2 palmitoyl sn glycero 3 phosphocholine (18:0-16:0 PC, SPPC); 1 stearoyl 2 oleoyl sn glycero 3 phosphocholine (18:0-18:1 PC, SOPC); 1 stearoyl 2 linoleoyl sn glycero 3 phosphocholine (18:0-18:2 PC); 1 stearoyl 2 arachidonoyl sn glycero 3 phosphocholine (18:0-20:4 PC); 1 stearoyl 2 docosahexaenoyl sn glycero 3 phosphocholine (18:0-22:6 PC); 1 oleoyl 2 myristoyl sn glycero 3 phosphocholine (18:1-14:0 PC, OMPC); 1 oleoyl 2 palmitoyl sn glycero 3 phosphocholine (18:1-16:0 PC, OPPC); 1 oleoyl 2 stearoyl sn glycero 3~~

phosphocholine (18:1-18:0 PC, OSPC); 1 palmitoyl 2 oleoyl sn glycero 3 phosphoethanolamine (16:0-18:1 PE, POPE); 1 palmitoyl 2 linoleoyl sn glycero 3 phosphoethanolamine (16:0-18:2 PE); 1 palmitoyl 2 arachidonoyl sn glycero 3 phosphoethanolamine (16:0-20:4 PE); 1 palmitoyl 2 docosahexaenoyl sn glycero 3 phosphoethanolamine (16:0-22:6 PE); 1 stearoyl 2 oleoyl sn glycero 3 phosphoethanolamine (18:0-18:1 PE); 1 stearoyl 2 linoleoyl sn glycero 3 phosphoethanolamine (18:0-18:2 PE); 1 stearoyl 2 arachidonoyl sn glycero 3 phosphoethanolamine (18:0-20:4 PE); 1 stearoyl 2 docosahexaenoyl sn glycero 3 phosphoethanolamine (18:0-22:6 PE); 1 oleoyl 2 cholesterylhemisuccinoyl sn glycero 3 phosphocholine (OChemsPC), or any combination thereof.

27. The extracellular vesicle of claim 8, wherein the phospholipid is a lysolipid.

28. The extracellular vesicle of claim 27, wherein the phospholipid is a lysoglycerophospholipid, a lysoglycosphingoliopid, a lysophosphatidylcholine, a lysophosphatidylethanolamine, a lysophosphatidylinositol, a lysophosphatidylserine, or any combination thereof.

29. The extracellular vesicle of claim 27, wherein the phospholipid is 1 hexanoyl 2 hydroxy sn glycero 3 phosphocholine (06:0 Lyso PC); 1 heptanoyl 2 hydroxy sn glycero 3 phosphocholine (07:0 Lyso PC); 1 octanoyl 2 hydroxy sn glycero 3 phosphocholine (08:0 Lyso PC); 1 nonanoyl 2 hydroxy sn glycero 3 phosphocholine (09:0 Lyso PC); 1 decanoyl 2 hydroxy sn glycero 3 phosphocholine (10:0 Lyso PC); 1 undecanoyl 2 hydroxy sn glycero 3 phosphocholine (11:0 Lyso PC); 1 lauroyl 2 hydroxy sn glycero 3 phosphocholine (12:0 Lyso PC); 1 tridecanoyl 2 hydroxy sn glycero 3 phosphocholine (13:0 Lyso PC); 1 myristoyl 2 hydroxy sn glycero 3 phosphocholine (14:0 Lyso PC); 1 pentadecanoyl 2 hydroxy sn glycero 3 phosphocholine (15:0 Lyso PC); 1 palmitoyl 2 hydroxy sn glycero 3 phosphocholine (16:0 Lyso PC); 1 heptadecanoyl 2 hydroxy sn glycero 3 phosphocholine (17:0 Lyso PC); 1 stearoyl 2 hydroxy sn glycero 3 phosphocholine (18:0 Lyso PC); 1 oleoyl 2 hydroxy sn glycero 3 phosphocholine (18:1 Lyso PC); 1 nonadecanoyl 2 hydroxy sn glycero 3 phosphocholine (19:0 Lyso PC); 1 arachidoyl 2 hydroxy sn glycero 3 phosphocholine (20:0 Lyso PC); 1 behenoyl 2 hydroxy sn glycero 3 phosphocholine (22:0

~~Lyso PC); 1 lignoceroyl 2 hydroxy sn glycero 3 phosphocholine (24:0 Lyso PC); 1 hexacosanoyl 2 hydroxy sn glycero 3 phosphocholine (26:0 Lyso PC); 1 myristoyl 2 hydroxy sn glycero 3 phosphoethanolamine (14:0 Lyso PE); 1 palmitoyl 2 hydroxy sn glycero 3 phosphoethanolamine (16:0 Lyso PE); 1 stearoyl 2 hydroxy sn glycero 3 phosphoethanolamine (18:0 Lyso PE); 1 oleoyl 2 hydroxy sn glycero 3 phosphoethanolamine (18:1 Lyso PE); 1 hexadecyl sn glycero 3 phosphocholine (C16 Lyso PC); or any combination thereof.~~

~~30. The extracellular vesicle of any one of claims 1 to 5, wherein the anchoring moiety comprises a vitamin.~~

~~31.~~7. The extracellular vesicle of claim 3, ~~any one of claims 1 to 5,~~ wherein the vitamin ~~anchoring moiety~~ comprises vitamin D, vitamin K, vitamin E, or any combination thereof.

~~32. The extracellular vesicle of any one of claims 1 to 31, wherein the anchoring moiety further comprises a linker between the biologically active molecule and the anchoring moiety.~~

~~33. The extracellular vesicle of claim 32, wherein the linker comprises a non-cleavable linker.~~

~~34.~~8. The extracellular vesicle of any one of claims 1 to 7, ~~claim 33,~~ wherein the linker comprises a non-cleavable linker comprising ~~comprises~~ polyethylene glycol (PEG), glycerol, alkyl, succinimide, maleimide, or any combination thereof.

~~35.~~9. The extracellular vesicle of claim 8, ~~33,~~ wherein the non-cleavable linker comprises polyethylene glycol (PEG) characterized by a formula R3-(O-CH_2-CH_2)$_n$- or R3-(O-CH_2-CH_2)$_n$-O-, wherein R3 is ~~being~~ hydrogen, methyl or ethyl and n is an integer between 2 and 200.

~~36. The extracellular vesicle of claim 33, wherein the non-cleavable linker comprises diethylene glycol, triethylene glycol, tetraethylene glycol (TEG), hexaethylene glycol (HEG), pentaethylene glycol, or any combination thereof.~~

~~37. The extracellular vesicle of any one of claims 32 to 34, wherein the linker comprises a polyglycerol (PG) having the formula ((R3 O (CH_2 CHOH CH2O)$_n$), wherein R3 is hydrogen, methyl or ethyl, and n is an integer between 3 and 200.~~

~~38.~~10. The extracellular vesicle of claim 8 or 9 ~~any one of claims 32 to 34,~~ wherein the linker comprises a diglycerol, triglycerol, tetraglycerol (TG), pentaglycerol, a hexaglycerol (HG), or any combination thereof.

~~39.~~11. The extracellular vesicle of any one of claims 8 to 10, ~~32 to 34,~~ wherein the linker comprises alkyl.

~~40. The extracellular vesicle of any one of claims 32 to 34, wherein the linker comprises alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, Aryl, heteroaryl, heterocyclyl, cycloalkyl, cycloalkenyl, alkylarylalkyl, alkylarylalkenyl, alkylarylalkynyl, alkenylarylalkyl, alkenyl Reyl alkenyl, alkenyl aryl alkynyl, alkynyl aryl alkyl, alkynyl aryl alkenyl, alkynyl aryl alkynyl, alkyl heteroaryl alkyl, alkyl heteroaryl alkyl, alkyl heteroaryl alkenyl, alkyl heteroaryl alkynyl, alkenyl heteroaryl alkyl, alkenyl heteroaryl alkenyl, alkenyl heteroaryl alkynyl, alkynyl Heteroarylalkyl, alkynylheteroarylalkenyl, alkynylheteroarylalkynyl, alkylheterocyclylalkyl, alkylheterocyclylalkenyl, alkylheterocyclylalkynyl, alkenylheterocyclylalkyl, alkenylheterocyclylalkenyl, alkenylheterocyclylalkynyl, or any combination thereof.~~

~~41. The extracellular vesicle of claim 32, wherein the linker comprises a cleavable linker.~~

~~42.~~12. The extracellular vesicle of any one of claims 1 to 11, ~~claim 41,~~ wherein the linker comprises a cleavable linker that is a redox cleavable linker, a reactive oxygen species cleavable linker, a pH dependent cleavable linker, an enzymatic cleavable linker, a protease cleavable linker, an esterase cleavable linker, a phosphatase cleavable linker, a photoactivated cleavable linker, a self-immolative linker, or any combination thereof.

~~43.~~13. The extracellular vesicle of claim 12, ~~41,~~ wherein the cleavable linker is a self-immolative linker.

~~44.~~14. The extracellular vesicle of claim 12, ~~41,~~ wherein the cleavable linker comprises ~~is~~ a cinnamyl group, a naphthyl group, a biphenyl group, a heterocyclic ring, a homoaromatic group, coumarin, furan, thiophene, thiazole, oxazole, isoxazole, pyrrole, pyrazole, pyridine, imidazone, triazole, or any combination thereof.

~~45.~~15. The extracellular vesicle of any one of claims 12 to 14, ~~41 to 44,~~ wherein the linker has the formula:

$$-A_a-Y_y-$$

wherein each –A- is independently an amino acid unit, a is independently an integer from 1 to 12; -Y- is a spacer unit, and y is 0, 1, or 2.

~~46.~~16. The extracellular vesicle of claim 15, ~~45,~~ wherein -Aa- is a dipeptide, a tripeptide, a tetrapeptide, a pentapeptide, or a hexapeptide.

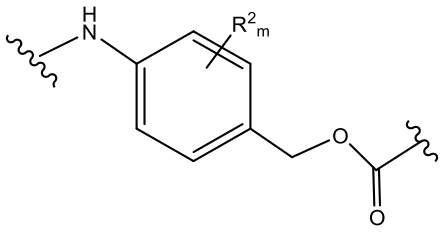
~~47.~~17. The extracellular vesicle of claim 16, ~~46,~~ wherein a is 2 and –Aa- is selected from the group consisting of valine-alanine, valine-citrulline, phenylalanine-lysine, N-methylvaline-citrulline, cyclohexylalanine-lysine, and beta-alanine-lysine.

~~48. The extracellular vesicle of claim 46, wherein said –Aa- is valine-alanine or valine-citrulline.~~

~~49. The extracellular vesicle of any one of claims 45 to 48, wherein y is 1.~~

~~50. The extracellular vesicle of any one of claims 45 to 49, wherein –Y- is a self-immolative spacer.~~

~~51.~~18. The extracellular vesicle of any one of claims 15 to 17, ~~claim 50,~~ wherein $-Y_y-$ has the formula (V):



(V),

wherein each R^2 is independently C_{1-8} alkyl, -O-(C_{1-8} alkyl), halogen, nitro, or cyano; and m is an integer from 0 to 4.

~~52. The extracellular vesicle of claim 51, wherein m is 0, 1, or 2.~~

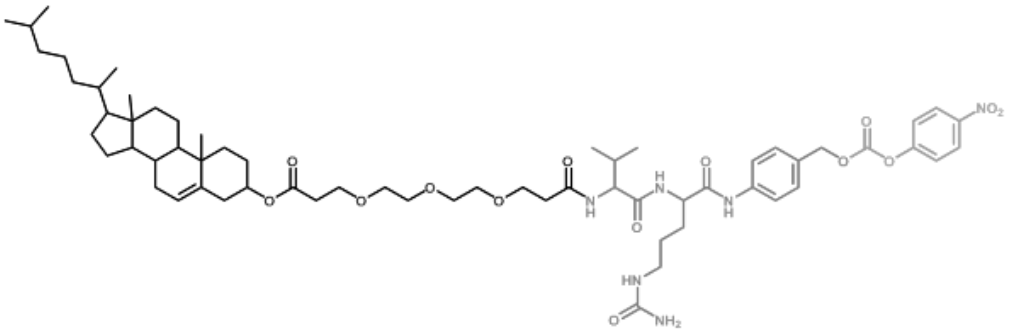
~~53. The extracellular vesicle of claim 51, wherein m is 0.~~

~~54. The extracellular vesicle of any one of claims 45 to 53, wherein the cleavable linker is valine-alanine-p-aminobenzylcarbamate or valine-citrulline-p-aminobenzylcarbamate.~~

~~55. The extracellular vesicle of any one of claims 45 to 49, wherein -Y- is a non self-immolative spacer.~~

~~56. The extracellular vesicle of claim 55, wherein the non self-immolative spacer is -Gly- or -Gly-Gly-.~~

~~57.~~19. The extracellular vesicle of any one of claims 1 to 3, ~~4,~~ wherein the anchoring moiety comprises:



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~~58.~~20. The extracellular vesicle of any one of claims 1 to 3, ~~5,~~ which comprises (i) an anchoring moiety selected from the group consisting of SEQ ID NOS: 301-334 and 401-567, and (ii) a linker selected from the linker combinations of TABLE 1 or TABLE 2.

~~59. The extracellular vesicle of any one of claims 1 to 5, wherein the anchoring moiety comprises a scaffold protein.~~

~~60. The extracellular vesicle of any one of claims 1 to 59, further comprising a scaffold moiety.~~

~~61.~~21. The extracellular vesicle of any one of claims 1 to 20, ~~claim 59 or 60,~~ wherein the extracellular vesicle or the anchoring moiety comprises a ~~and/or the~~ scaffold moiety that is Scaffold ~~scaffold~~ X or Scaffold Y.

~~62.~~22. The extracellular vesicle of claim 21, ~~61,~~ wherein the Scaffold X is selected from the group consisting of prostaglandin F2 receptor negative regulator (the PTGFRN protein); basigin (the BSG protein); immunoglobulin superfamily member 2 (the IGSF2 protein); immunoglobulin superfamily member 3 (the IGSF3 protein); immunoglobulin superfamily member 8 (the IGSF8 protein); integrin beta-1 (the ITGB1 protein); integrin alpha-4 (the ITGA4 protein); 4F2 cell-surface antigen heavy chain (the SLC3A2 protein); a class of ATP transporter proteins (the ATP1A1, ATP1A2, ATP1A3, ATP1A4, ATP1B3, ATP2B1, ATP2B2, ATP2B3, ATP2B4 proteins); a functional fragment thereof; and any combination thereof.

~~63. The extracellular vesicle of claim 61, wherein the Scaffold X is PTGFRN protein or a functional fragment thereof.~~

~~64. The extracellular vesicle of claim 61, wherein the Scaffold X comprises an amino acid sequence as set forth in SEQ ID NO:302.~~

~~65. The extracellular vesicle of claim 61, wherein the Scaffold X comprises an amino acid sequence at least 50%, at least 60%, at least 70%, 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 about 100% identical to SEQ ID NO:302.~~

~~66. The extracellular vesicle of claim 59 or 60, wherein the anchoring moiety and/or the scaffold moiety is scaffold Y.~~

~~67. The extracellular vesicle of claim 66, wherein the Scaffold Y is a scaffold protein that is capable of anchoring the biologically active molecule on the luminal surface of the extracellular vesicle and/or on the exterior surface of the extracellular vesicle.~~

~~68.~~23. The extracellular vesicle of claim 21, ~~66 or 67,~~ wherein the Scaffold Y is selected from the group consisting of myristoylated alanine rich Protein Kinase C substrate (the MARCKS protein), myristoylated alanine rich Protein Kinase C substrate like 1 (the MARCKSL1 protein), brain acid soluble protein 1 (the BASP1 protein), a functional fragment thereof, and any combination thereof.

69. The extracellular vesicle of any one of claims 66 to 68, wherein the Scaffold Y is a BASP1 protein or a functional fragment thereof.

70. The extracellular vesicle of any one of claims 66 to 69, wherein the Scaffold Y comprises an N terminus domain (ND) and an effector domain (ED), wherein the ND and/or the ED are associated with the luminal surface of the EV.

71. The extracellular vesicle of claim 70, wherein the ND is associated with the luminal surface of the exosome via myristoylation.

72. The extracellular vesicle of claim 70 or 71, wherein the ED is associated with the luminal surface of the exosome by an ionic interaction.

73. The extracellular vesicle of any one of claims 70 to 72, wherein the ED comprises (i) a basic amino acid or (ii) two or more basic amino acids in sequence, wherein the basic amino acid is selected from the group consisting of Lys, Arg, His, and any combination thereof.

74. The extracellular vesicle of claim 73, wherein the basic amino acid is (Lys)n, wherein n is an integer between 1 and 10.

75. The extracellular vesicle of any one of claims 70 to 74, wherein the ED comprises Lys (K), KK, KKK, KKKK (SEQ ID NO: 405), KKKKK (SEQ ID NO: 406), Arg (R), RR, RRR, RRRR (SEQ ID NO: 407); RRRRR (SEQ ID NO: 408), KR, RK, KKR, KRK, RKK, KRR, RRK, (K/R)(K/R)(K/R)(K/R) (SEQ ID NO: XX), (K/R)(K/R)(K/R)(K/R)(K/R) (SEQ ID NO: XX), or any combination thereof.

76. The extracellular vesicle of any one of claims 70 to 75, wherein the ND comprises the amino acid sequence as set forth in G:X2:X3:X4:X5:X6, wherein G represents Gly; wherein ":" represents a peptide bond, wherein each of the X2 to the X6 is independently an amino acid, and wherein the X6 comprises a basic amino acid.

77. The extracellular vesicle of claim 76, wherein:

(i) the X2 is selected from the group consisting of Pro, Gly, Ala, and Ser;

(ii) the X4 is selected from the group consisting of Pro, Gly, Ala, Ser, Val, Ile, Leu, Phe, Trp, Tyr, Gln and Met;

(iii) the X5 is selected from the group consisting of Pro, Gly, Ala, and Ser;

(iv) the X6 is selected from the group consisting of Lys, Arg, and His; or

(v) any combination of (i)-(iv).

78. The extracellular vesicle of any one of claims 70 to 77, wherein the ND comprises the amino acid sequence of G:X2:X3:X4:X5:X6, wherein

(i) G represents Gly;

(ii) ":" represents a peptide bond;

(iii) the X2 is an amino acid selected from the group consisting of Pro, Gly, Ala, and Ser;

(iv) the X3 is an amino acid;

(v) the X4 is an amino acid selected from the group consisting of Pro, Gly, Ala, Ser, Val, Ile, Leu, Phe, Trp, Tyr, Gln and Met;

(vi) the X5 is an amino acid selected from the group consisting of Pro, Gly, Ala, and Ser; and

(vii) the X6 is an amino acid selected from the group consisting of Lys, Arg, and His.

79. The extracellular vesicle of any one of claims 76 to 78, wherein the X3 is selected from the group consisting of Asn, Gln, Ser, Thr, Asp, Glu, Lys, His, and Arg.

80. The extracellular vesicle of any one of claims 70 to 79, wherein the ND and the ED are joined by a linker.

81. The extracellular vesicle of claim 80, wherein the linker comprises one or more amino acids.

82. The method of any one of claims 70 to 81, wherein the ND comprises an amino acid sequence selected from the group consisting of (i) GGKLSKK (SEQ ID NO: 411), (ii) GAKLSKK (SEQ ID NO: 412), (iii) GGKQSKK (SEQ ID NO: 413), (iv) GGKLAKK (SEQ ID NO: 414), (v) GGKLSK (SEQ ID NO: 415), or (vi) any combination thereof.

83. The extracellular vesicle of claim 82, wherein the ND comprises an amino acid sequence selected from the group consisting of (i) GGKLSKKK (SEQ ID NO: 438), (ii) GGKLSKKS (SEQ ID NO: 439), (iii) GAKLSKKK (SEQ ID NO: 440), (iv) GAKLSKKS (SEQ ID NO: 441), (v) GGKQSKKK (SEQ ID NO: 442), (vi) GGKQSKKS (SEQ ID NO: 443), (vii) GGKLAKKK (SEQ ID NO: 444), (viii) GGKLAKKS (SEQ ID NO: 445), and (ix) any combination thereof.

84. The extracellular vesicle of any one of claims 70 to 83, wherein the ND comprises the amino acid sequence GGKLSKK (SEQ ID NO: 411).

85. The extracellular vesicle of any one of claims 70 to 84, wherein the Scaffold Y is at least about 8, at least about 9, at least about 10, at least about 11, at least about 12, at least about 13, at least about 14, at least about 15, at least about 16, at least about 17, at least about 18, at least about 19, at least about 20, at least about 21, at least about 22, at least about 23, at least about 24, at least about 25, at least about 30, at least about 35, at least about 40, at least about 45, at least about 50, at least about 55, at least about 60, at least about 65, at least about 70, at least about 75, at least about 80, at least about 85, at least about 90, at least about 95, at least about 100, at least about 105, at least about 110, at least about 120, at least about 130, at least about 140, at least about 150, at least about 160, at least about 170, at least about 180, at least about 190, or at least about 200 amino acids in length.

86. The extracellular vesicle of any one of claims 70 to 85, wherein the Scaffold Y comprises (i) GGKLSKKKKGYNVN (SEQ ID NO: 446), (ii) GAKLSKKKKGYNVN (SEQ ID NO: 447), (iii) GGKQSKKKKGYNVN (SEQ ID NO: 448), (iv) GGKLAKKKKGYNVN (SEQ ID NO: 449), (v) GGKLSKKKKGYSGG (SEQ ID NO: 450), (vi) GGKLSKKKKGSGGS (SEQ ID NO: 451), (vii) GGKLSKKKKSGGSG (SEQ ID NO: 452), (viii) GGKLSKKKSGGSGG (SEQ ID NO: 453), (ix) GGKLSKKSGGSGGS (SEQ ID NO:

~~454), (x) GGKLSKSGGSGGSV (SEQ ID NO: 455), or (xi) GAKKSKKRFSFKKS (SEQ ID NO: 456).~~

~~87. The extracellular vesicle of any one of claims 70 to 85, wherein the Scaffold Y consists of (i) GGKLSKKKKGYNVN (SEQ ID NO: 446), (ii) GAKLSKKKKGYNVN (SEQ ID NO: 447), (iii) GGKQSKKKKGYNVN (SEQ ID NO: 448), (iv) GGKLAKKKKGYNVN (SEQ ID NO: 449), (v) GGKLSKKKKGYSGG (SEQ ID NO: 450), (vi) GGKLSKKKKGSGGS (SEQ ID NO: 451), (vii) GGKLSKKKKSGGSG (SEQ ID NO: 452), (viii) GGKLSKKKSGGSGG (SEQ ID NO: 453), (ix) GGKLSKKSGGSGGS (SEQ ID NO: 454), (x) GGKLSKSGGSGGSV (SEQ ID NO: 455), or (xi) GAKKSKKRFSFKKS (SEQ ID NO: 456).~~

~~88. The extracellular vesicle of any one of claim 70 to 87, wherein the Scaffold Y does not comprise Met at the N terminus.~~

~~89. The extracellular vesicle of any one of claims 70 to 88, wherein the Scaffold Y comprises a myristoylated amino acid residue at the N terminus of the scaffold protein.~~

~~90. The extracellular vesicle of claim 89, wherein the amino acid residue at the N terminus of the Scaffold Y is Gly.~~

~~91.~~24. The extracellular vesicle of any one of claims 1 to 23, ~~90,~~ wherein the biologically active molecule is linked to the anchoring moiety and/or the scaffold moiety on the exterior surface of the EV.

~~92. The extracellular vesicle of any one of claims 1 to 90, wherein the biologically active molecule is linked to the anchoring moiety and/or the scaffold moiety on the luminal surface of the EV.~~

~~93.~~25. The extracellular vesicle of any one of claims 1 to 24, ~~92,~~ wherein the biologically active molecule is a polypeptide, a peptide, a polynucleotide (DNA and/or RNA), a chemical compound, or any combination thereof.

~~94. The extracellular vesicle of claim 93, wherein the biologically active molecule is a chemical compound.~~

~~95. The extracellular vesicle of claim 94, wherein the chemical compound is a small molecule.~~

~~96.~~26. The extracellular vesicle of any one of claims 1 to 25, ~~95,~~ wherein the biologically active molecule comprises an antisense oligonucleotide (ASO), a siRNA, a miRNA, a shRNA, a nucleic acid, or any combination thereof.

~~97. The extracellular vesicle of any one of claims 1 to 96, wherein the biologically active molecule comprises a peptide, a protein, an antibody or an antigen binding fragment thereof, or any combination thereof.~~

~~98. The extracellular vesicle of claim 97, wherein the antigen binding fragment thereof comprises scFv, (scFv)2, Fab, Fab', F(ab')2, F(ab1)2, Fv, dAb, and Fd fragment, diabodys, antibody-related polypeptide, or any fragment thereof.~~

~~99. The extracellular vesicle of claim 96, wherein the biologically active molecule comprises an ASO.~~

~~100. The extracellular vesicle of claim 99, wherein the ASO targets a transcript.~~

~~101. The extracellular vesicle of claim 100, wherein the transcript is a STAT6 transcript, a CEBP/β transcript, a STAT3 transcript, a KRAS transcript, a NRAS transcript, an NLPR3 transcript, a PMP22 transcript, or any combination thereof.~~

~~102. The extracellular vesicle of claim 101, wherein the STAT6 transcript comprises SEQ ID NO: 13.~~

~~103. The extracellular vesicle of claim 102, wherein the ASO comprises a sequence selected from the group consisting of SEQ ID NO: 601 to SEQ ID NO: 703.~~

~~104. The extracellular vesicle of claim 101, wherein the CEBP/β transcript comprises SEQ ID NO: 23.~~

~~105. The extracellular vesicle of claim 104, wherein the ASO comprises a sequence selected from the group consisting of SEQ ID NO: 704 to SEQ ID NO: 806.~~

~~106. The extracellular vesicle of claim 101, wherein the STAT3 transcript comprises SEQ ID NO: 43.~~

~~107. The extracellular vesicle of claim 106, wherein the ASO comprises a sequence selected from the group consisting of SEQ ID NO: 889 to SEQ ID NO: 988.~~

~~108. The extracellular vesicle of claim 101, wherein the NRAS transcript comprises SEQ ID NO: 53.~~

~~109. The extracellular vesicle of claim 108, wherein the ASO comprises a sequence selected from the group consisting of SEQ ID NO: 989 to SEQ ID NO: 1088.~~

~~110. The extracellular vesicle of claim 101, wherein the NLPR3 transcript comprises SEQ ID NO: 3.~~

~~111. The extracellular vesicle of claim 110, wherein the ASO comprises a sequence selected from the group consisting of SEQ ID NO: 101 to SEQ ID NO: 200.~~

~~112. The extracellular vesicle of claim 101, wherein the KRAS transcript is a KRAS mutant transcript.~~

~~113. The extracellular vesicle of claim 101, wherein the KRAS mutant is KRAS G12D.~~

~~114. The extracellular vesicle of claim 112, wherein the KRAS transcript comprises SEQ ID NO: 32.~~

~~115. The extracellular vesicle of claim 114, wherein the ASO comprises a sequence selected from the group consisting of SEQ ID NO: 807 to SEQ ID NO: 888.~~

~~116. The extracellular vesicle of claim 101, wherein the PMP22 transcript comprises SEQ ID NO: 58.~~

~~117. The extracellular vesicle of claim 116, wherein the ASO comprises a sequence selected from the group consisting of SEQ ID NOS: 62-95 and 201-270.~~

~~118. The extracellular vesicle of any one of claims 1 to 117, wherein the EV is an exosome.~~

~~119.~~27. A pharmaceutical composition comprising the extracellular vesicle of any one of claims 1 to 26 ~~118~~ and a pharmaceutically acceptable carrier.

~~120. A method of conjugating a biologically active molecule to an EV, comprising linking an anchoring moiety to the EV.~~

~~121.~~28. A kit comprising the EV of any one of claims ~~claim~~ 1 to 26 ~~118~~ and instructions for use.

~~122. A kit comprising reagents to conjugate a biologically active molecule to an EV, and instructions to conduct the conjugation, thereby making the EV of any one of claims 1 to 118.~~

~~123.~~29. ~~A method of treating or preventing a disease or disorder in a subject in need thereof comprising administering the EV~~ The extracellular vesicle of any one of claims 1 to 26 for use in ~~treating~~the treatment or ~~preventing~~prevention of a disease or disorder. ~~118 to the subject.~~

~~124.~~30. The extracellular vesicle ~~method~~ of claim 29, ~~121,~~ wherein the disease or disorder is a cancer, an inflammatory disorder, a neurodegenerative disorder, a central nervous diseases, or a metabolic disease.

~~125. The method of claim 121 or 122, wherein the EV is administered intravenously, intraperitoneally, nasally, orally, intramuscularly, subcutaneously, parenterally, or intratumorally.~~

31. Use of the extracellular vesicle of any one of claims 1 to 26 in the manufacture of a medicament for the treatment of a cancer, an inflammatory disorder, a neurodegenerative disorder, a central nervous diseases, or a metabolic disease.