WHAT IS CLAIMED IS:

1. A method of loading a payload to an extracellular vesicle (EV) comprising mixing the payload with the ~~extracellular vesicle~~EV in a loading buffer comprising a salt at a concentration lower than about 200 mM, about 190 mM, about 180 mM, about 170 mM, about 160 mM, about 150 mM, about 140 mM, about 130 mM, about 120 mM, or about 110 mM.

~~2. The method of claim 1, wherein the salt concentration is between about 1 mM and about 150 mM, between about 5 mM and about 150 mM, between about 10 mM and about 150 mM, between about 20 mM and about 150 mM, between about 30 mM and about 150 mM, between about 40 mM and about 150 mM, between about 50 mM and about 150 mM, between about 60 mM and about 150 mM, between about 70 mM and about 150 mM, between about 80 mM and about 150 mM, between about 10 mM and about 130 mM, between about 20 mM and about 130 mM, between about 30 mM and about 130 mM, between about 40 mM and about 130 mM, between about 50 mM and about 130 mM, between about 10 mM and about 120 mM, between about 20 mM and about 120 mM, between about 30 mM and about 120 mM, between about 40 mM and about 120 mM, between about 50 mM and about 120 mM, between about 60 mM and about 120 mM, between about 70 mM and about 120 mM, between about 80 mM and about 120 mM, between about 50 mM and about 100 mM, between about 100 mM and about 150 mM, or between about 90 mM and about 110 mM.~~

~~3. The method of claim 1, wherein the salt concentration is about 10 mM, about 20 mM, about 30 mM, about 40 mM, about 50 mM, about 60 mM, about 70 mM, about 80 mM, about 90 mM, about 100 mM, about 110 mM, about 120 mM, about 130 mM, about 140 mM, about 150 mM, about 160 mM, about 170 m, about 180 mM, or about 190 mM.~~

~~4. The method of claim 1, wherein the salt concentration is about 50 mM, about 60 mM, about 70 mM, about 80 mM, about 90 mM, about 100 mM, about 110 mM, about 120 mM, about 130 mM, about 140 mM, or about 150 mM.~~

~~5. A method of loading a payload to an extracellular vesicle comprising mixing the payload with the extracellular vesicle in a loading buffer comprising a salt at a concentration between about 200 mM and about 450 mM.~~

~~6. The method of claim 5, wherein the salt concentration is about 200 mM, about 250 mM, about 300 mM, about 350 mM, about 400 mM, or about 450 mM.~~

~~7.~~2. The method of ~~any one of claims 1 to 6~~claim 1, wherein the salt comprises NaCl (sodium chloride), KCl (potassium chloride), PO_4 (phosphate salt), $CaCl_2$ (calcium chloride), $MgCl_2$ (magnesium chloride), Mg_2SO_4 (magnesium sulfate), $ZnCl_2$ (zinc chloride), $MnCl_2$ (manganese chloride), $MnSO_4$ (manganese sulfate), NaSCN (sodium thiocyanate), KSCN (potassium thiocyanate), LiCl (lithium chloride), K_2HPO_4 (dipotassium phosphate), Na_2SO_4 (sodium sulfate), $NaPO_4$ (sodium phosphate), K_2SO_4 (potassium phosphate), sodium acetate, sodium bromide, sodium iodide, potassium bromide, lithium bromide, sodium fluoride, potassium fluoride, lithium fluoride, lithium iodide, potassium acetate, lithium acetate, potassium iodide, calcium sulfate, sodium sulfate, chromium trichloride, chromium sulfate, sodium citrate, iron (III) chloride, yttrium (III) chloride, potassium sulfate, ferrous chloride, calcium citrate, magnesium phosphate, ferric chloride, arginine-HCl, or any combination thereof, wherein the loading buffer comprising the salt increases the loading of the payload to the EV by at least about 2 fold compared to a corresponding loading buffer without the salt or with a lower concentration of the salt.

~~8. The method of any one of claims 1 to 7, wherein the loading buffer comprising the salt increases the loading of the payload to the EV by at least about 2 fold, at least about 3 fold, at least about 4 fold, at least about 5 fold, at least about 6 fold, at least about 7 fold, at least about 8 fold, at least about 9 fold, at least about 10 fold, at least about 15-fold, at least about 20-fold, at least about 25-fold, at least about 30-fold, at least about 35-fold, at least about 40-fold, at least about 45-fold, or at least about 50-fold or more compared to a corresponding loading buffer without the salt or with a lower concentration of the salt.~~

~~9.~~3. ~~A method of loading a payload to an extracellular vesicle~~The method of claim 1 or 2, further comprising mixing the payload with the ~~extracellular vesicle~~EV at a loading temperature higher than 4 ºC, wherein the loading temperature increases the loading of the payload to the EV by at least about 2 fold, at least about 3 fold, at least about 4 fold, at least about 5 fold, at least about 6 fold, at least about 7 fold, at least about 8 fold, at least about 9 fold, at least about 10 fold, at least about 15-fold, at least about 20-fold, at least about 25-fold, at least about 30-fold, at least

about 35-fold, at least about 40-fold, at least about 45-fold, or at least about 50-fold or more compared to the loading at a reference temperature, which is lower than the loading temperature.

~~10. The method of claim 9, wherein the loading temperature is between about 5 ºC and about 40 ºC, between about 10 ºC and about 40 ºC, between about 15 ºC and about 40 ºC, between about 20 ºC and about 40 ºC, between about 25 ºC and about 40 ºC, between about 30 ºC and about 40 ºC, between about 35 ºC and about 40 ºC, between about 5 ºC and about 38 ºC, between about 10 ºC and about 38 ºC, between about 15 ºC and about 38 ºC, between about 20 ºC and about 38 ºC, between about 25 ºC and about 38 ºC, between about 30 ºC and about 38 ºC, between about 35 ºC and about 38 ºC, between about 5 ºC and about 37 ºC, between about 10 ºC and about 37 ºC, between about 15 ºC and about 37 ºC, between about 20 ºC and about 37 ºC, between about 25 ºC and about 37 ºC, between about 30 ºC and about 37 ºC, or between about 35 ºC and about 37 ºC.~~

~~11. The method of claim 9 or 10, wherein the loading temperature is about 5 ºC, about 10 ºC, about 15 ºC, about 20 ºC, about 25 ºC, about 30 ºC, about 35 ºC, about 37 ºC, about 40 ºC, about 50 ºC, about 55 ºC, about 60 ºC, about 65 ºC, or about 70 ºC.~~

~~12. The method of any one of claims 9 to 11, wherein the loading temperature increases the loading of the payload to the EV by at least about 2 fold, at least about 3 fold, at least about 4 fold, at least about 5 fold, at least about 6 fold, at least about 7 fold, at least about 8 fold, at least about 9 fold, at least about 10 fold, at least about 15-fold, at least about 20-fold, at least about 25-fold, at least about 30-fold, at least about 35-fold, at least about 40-fold, at least about 45-fold, or at least about 50-fold or more compared to the loading at a reference temperature, which is lower than the loading temperature.~~

~~13.~~4. ~~A~~ The method of any one claims 1 to 3, further comprising ~~loading a payload to an extracellular vesicle comprising~~ mixing the payload with the ~~extracellular vesicle~~EV for a loading duration longer than about one hour, wherein the loading duration increases the loading of the payload to the EV by at least about 2 fold, at least about 3 fold, at least about 4 fold, at least about 5 fold, at least about 6 fold, at least about 7 fold, at least about 8 fold, at least about 9 fold, at least about 10 fold, at least about 15-fold, at least about 20-fold, at least about 25-fold, at least about 30-fold, at least about 35-fold, at least about 40-fold, at least about 45-fold, or at least about 50-

fold or more compared to the loading for a reference duration, which is shorter than the loading duration.

~~14. The method of claim 13, wherein the loading duration is between about one hour and about 48 hours, between about one hour and about 42 hours, between about one hour and about 36 hours, between about one hour and about 30 hours, between about one hour and about 24 hours, between about six hours and about 48 hours, between about six hours and about 42 hours, between about six hours and about 36 hours, between about six hours and about 30 hours, between about six hours and about 24 hours, between about 12 hours and about 48 hours, between about 12 hours and about 42 hours, between about 12 hours and about 36 hours, between about 12 hours and about 30 hours, or between about 12 hours and about 24 hours.~~

~~15. The method of claim 13 or 14, wherein the loading duration is about 6 hours, about 12 hours, about 24 hours, about 30 hours, about 36 hours, about 42 hours, about 48 hours, about three days, about four days, about five days, about six days, or about seven days.~~

~~16. The method of any one of claims 13 to 15, wherein the loading duration increases the loading of the payload to the EV by at least about 2 fold, at least about 3 fold, at least about 4 fold, at least about 5 fold, at least about 6 fold, at least about 7 fold, at least about 8 fold, at least about 9 fold, at least about 10 fold, at least about 15 fold, at least about 20 fold, at least about 25 fold, at least about 30 fold, at least about 35 fold, at least about 40 fold, at least about 45 fold, or at least about 50 fold or more compared to the loading for a reference duration, which is shorter than the loading duration.~~

~~17. A method of loading a payload to an extracellular vesicle comprising mixing the payload with the extracellular vesicle in a loading buffer comprising a salt at a concentration lower than 200 mM, at a loading temperature between about 5 ºC and about 50 ºC, and for a loading duration between one hour to about 48 hours.~~

~~18. The method of claim 17, wherein the salt concentration is between about 1 mM and about 150 mM, between about 5 mM and about 150 mM, between about 10 mM and about 150 mM, between about 20 mM and about 150 mM, between about 30 mM and about 150 mM, between about 40 mM and about 150 mM, between about 50 mM and about 150 mM, between about 60~~

mM and about 150 mM, between about 70 mM and about 150 mM, between about 80 mM and about 150 mM, between about 10 mM and about 130 mM, between about 20 mM and about 130 mM, between about 30 mM and about 130 mM, between about 40 mM and about 130 mM, between about 50 mM and about 130 mM, between about 10 mM and about 120 mM, between about 20 mM and about 120 mM, between about 30 mM and about 120 mM, between about 40 mM and about 120 mM, between about 50 mM and about 120 mM, between about 60 mM and about 120 mM, between about 70 mM and about 120 mM, between about 80 mM and about 120 mM, between about 50 mM and about 100 mM, between about 100 mM and about 150 mM, or between about 90 mM and about 110 mM.

19. The method of claim 17 or 18, wherein the salt concentration is about 10 mM, about 20 mM, about 30 mM, about 40 mM, about 50 mM, about 60 mM, about 70 mM, about 80 mM, about 90 mM, about 100 mM, about 110 mM, about 120 mM, about 130 mM, about 140 mM, about 150 mM, about 160 mM, about 170 m, about 180 mM, or about 190 mM.

20. The method of claim 19, wherein the salt concentration is about 50 mM, about 60 mM, about 70 mM, about 80 mM, about 90 mM, about 100 mM, about 110 mM, about 120 mM, about 130 mM, about 140 mM, or about 150 mM.

21. The method of any one of claims 17 to 20, wherein the salt comprises NaCl (sodium chloride), KCl (potassium chloride), PO_4 (phosphate salt), $CaCl_2$ (calcium chloride), $MgCl_2$ (magnesium chloride), Mg_2SO_4 (magnesium sulfate), $ZnCl_2$ (zinc chloride), $MnCl_2$ (manganese chloride), $MnSO_4$ (manganese sulfate), NaSCN (sodium thiocyanate), KSCN (potassium thiocyanate), LiCl (lithium chloride), K_2HPO_4 (dipotassium phosphate), Na_2SO_4 (sodium sulfate), $NaPO_4$ (sodium phosphate), K_2SO_4 (potassium phosphate), sodium acetate, sodium bromide, sodium iodide, potassium bromide, lithium bromide, sodium fluoride, potassium fluoride, lithium fluoride, lithium iodide, potassium acetate, lithium acetate, potassium iodide, calcium sulfate, sodium sulfate, chromium trichloride, chromium sulfate, sodium citrate, iron (III) chloride, yttrium (III) chloride, potassium sulfate, ferrous chloride, calcium citrate, magnesium phosphate, ferric chloride, arginine-HCl, or any combination thereof.

22. The method of any one of claims 17 to 21, wherein the loading temperature is between about 5 ºC and about 40 ºC, between about 10 ºC and about 40 ºC, between about 15 ºC and about

~~40 ºC, between about 20 ºC and about 40 ºC, between about 25 ºC and about 40 ºC, between about 30 ºC and about 40 ºC, between about 35 ºC and about 40 ºC, between about 5 ºC and about 38 ºC, between about 10 ºC and about 38 ºC, between about 15 ºC and about 38 ºC, between about 20 ºC and about 38 ºC, between about 25 ºC and about 38 ºC, between about 30 ºC and about 38 ºC, between about 35 ºC and about 38 ºC, between about 5 ºC and about 37 ºC, between about 10 ºC and about 37 ºC, between about 15 ºC and about 37 ºC, between about 20 ºC and about 37 ºC, between about 25 ºC and about 37 ºC, between about 30 ºC and about 37 ºC, or between about 35 ºC and about 37 ºC.~~

~~23. The method of any one of claims 17 to 22, wherein the loading temperature is about 5 ºC, about 10 ºC, about 15 ºC, about 20 ºC, about 25 ºC, about 30 ºC, about 35 ºC, about 37 ºC, about 40 ºC, or about 50 ºC.~~

~~24. The method of any one of claims 17 to 23, wherein the loading duration is between about one hour and about 48 hours, between about one hour and about 42 hours, between about one hour and about 36 hours, between about one hour and about 30 hours, between about one hour and about 24 hours, between about six hours and about 48 hours, between about six hours and about 42 hours, between about six hours and about 36 hours, between about six hours and about 30 hours, between about six hours and about 24 hours, between about 12 hours and about 48 hours, between about 12 hours and about 42 hours, between about 12 hours and about 36 hours, between about 12 hours and about 30 hours, or between about 12 hours and about 24 hours.~~

~~25. The method of any one of claims 17 to 24, wherein the loading duration is about 6 hours, about 12 hours, about 24 hours, about 30 hours, about 36 hours, about 42 hours, or about 48 hours.~~

~~26. The method of claim 17, wherein the salt concentration is between about 50 mM and about 150 mM, the loading temperature is between about 30 ºC and about 40 ºC, and the loading duration is between about 20 hours and about 30 hours.~~

~~27. The method of claim 17, wherein the salt concentration is between about 50 mM and about 150 mM, the loading temperature is between about 30 ºC and about 40 ºC, and the loading duration is between about 12 hours and about 30 hours.~~

~~28. A method of loading a payload to an extracellular vesicle comprising mixing the payload with the extracellular vesicle in a loading buffer comprising a salt at a concentration of about 100 mM, at a loading temperature of about 37 ºC, and for a loading duration of about 24 hours.~~

~~29.~~5. A method of loading a payload to an extracellular vesicle (EV) comprising mixing the payload with the extracellular vesicle in a loading buffer comprising a salt at a concentration of between about ~~150~~ 1 mM and about 450 mM, at a loading temperature of between about ~~37~~ 5 ºC to about 70 ºC, and for a loading duration between about ~~24 hours~~1 hour and about seven days.

~~30. The method of claim 29, wherein the salt concentration is about 150 mM, about 200 mM, about 250 mM, about 300 mM, about 350 mM, about 400 mM, or about 450 mM.~~

~~31. The method of claim 29 or 30, wherein the salt comprises NaCl (sodium chloride), KCl (potassium chloride), PO_4 (phosphate salt), $CaCl_2$ (calcium chloride), $MgCl_2$ (magnesium chloride), Mg_2SO_4 (magnesium sulfate), $ZnCl_2$ (zinc chloride), $MnCl_2$ (manganese chloride), $MnSO_4$ (manganese sulfate), NaSCN (sodium thiocyanate), KSCN (potassium thiocyanate), LiCl (lithium chloride), K_2HPO_4 (dipotassium phosphate), Na_2SO_4 (sodium sulfate), $NaPO_4$ (sodium phosphate), K_2SO_4 (potassium phosphate), sodium acetate, sodium bromide, sodium iodide, potassium bromide, lithium bromide, sodium fluoride, potassium fluoride, lithium fluoride, lithium iodide, potassium acetate, lithium acetate, potassium iodide, calcium sulfate, sodium sulfate, chromium trichloride, chromium sulfate, sodium citrate, iron (III) chloride, yttrium (III) chloride, potassium sulfate, ferrous chloride, calcium citrate, magnesium phosphate, ferric chloride, arginine-HCl, or any combination thereof.~~

~~32. The method of any one of claims 29 to 32, wherein the loading temperature is about 37 ºC, about 40 ºC, about 45 ºC, about 50 ºC, about 55 ºC, about 60 ºC, about 65 ºC, or about 70 ºC.~~

~~33. The method of any one of claims 29 to 33, wherein the loading duration is about 24 hours, about two days, about three days, about four days, about five days, about six days, or about seven days.~~

~~34. The method of any one of claims 17 to 33, wherein the loading at the salt concentration at the loading temperature for the loading duration increases loading of the payload to the extracellular vesicle by at least about 1-fold, at least about 2-fold, at least about 3-fold, at least~~

~~about 4-fold, at least about 5-fold, at least about 6-fold, at least about 7-fold, at least about 8-fold, at least about 9-fold, at least about 10-fold, at least about 12-fold, at least about 14-fold, at least about 16-fold, at least about 18-fold, at least about 20-fold, at least about 25-fold, at least about 30-fold, at least about 35-fold, at least about 40-fold, at least about 45-fold, or at least about 50-fold or more compared to the loading without the salt, at a temperature of 4 ºC, and/or for a duration of one hour.~~

~~35.~~6. The method of any one of claims 1 to ~~34~~5, further comprising, after the mixing, measuring the amount of payload loaded to the EVs and determining the load density of the EVs, wherein one or more loading parameters are adjusted to further increase the load density of the EVs, and wherein the one or more loading parameters are selected from: a salt concentration of the loading buffer, loading temperature, loading duration, payload feed concentration, EV feed concentration, or a combination thereof.

~~36. The method of claim 35, wherein one or more loading parameters are adjusted to further increase the load density of the EVs, and wherein the one or more loading parameters are selected from: a salt concentration of the loading buffer, loading temperature, loading duration, payload feed concentration, EV feed concentration, or a combination thereof.~~

~~37. The method of claim 35 or 36, wherein the amount of payload loaded to the EVs is measured using particle counters, NTA, ultraviolet adsorption, visible adsorption, fluorescence, near infrared, infrared, static light scattering, dynamic light scattering, obscuration, Raman spectroscopy, turbidity, or a combination thereof.~~

~~38. The method of any one of claims 1 to 37, wherein the mixing occurs in a batch mode, semi-batch mode, semi-continuous mode, or continuous mode.~~

~~39.~~7. A method of decreasing the dissociation of a payload from an extracellular vesicle (EV) after EV loading comprising loading the payload to the EV according to the method of any one of claims 1 to ~~38~~6, wherein the dissociation of the payload from the EV is reduced by at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, or about 100% compared to the corresponding dissociation observed when the payload is not loaded to the EV.

~~40. The method of claim 39, wherein the dissociation of the payload from the EV is reduced by at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, or about 100% compared to the corresponding dissociation observed when the payload is not loaded to the EV according to the method of any one of claims 1 to 38.~~

~~41.~~8. A method of increasing the stability of an extracellular vesicle (EV) loaded with a payload comprising loading the payload to the EV according to the method of any one of claims 1 to ~~38~~6, wherein the stability of the EV loaded with the payload is increased by at least about at least about 1 fold, at least about 2 fold, at least about 3 fold, at least about 4 fold, at least about 5 fold, at least about 6 fold, at least about 7 fold, at least about 8 fold, at least about 9 fold, at least about 10 fold, at least about 12 fold, at least about 14 fold, at least about 16 fold, at least about 18 fold, at least about 20 fold, at least about 25-fold, at least about 30-fold, at least about 35-fold, at least about 40-fold, at least about 45-fold, or at least about 50-fold or more compared to the corresponding stability observed when the payload is not loaded to the EV.

~~42. The method of claim 41, wherein the stability of the EV loaded with the payload is increased by at least about at least about 1 fold, at least about 2 fold, at least about 3 fold, at least about 4 fold, at least about 5 fold, at least about 6 fold, at least about 7 fold, at least about 8 fold, at least about 9 fold, at least about 10 fold, at least about 12 fold, at least about 14 fold, at least about 16 fold, at least about 18 fold, at least about 20 fold, at least about 25-fold, at least about 30-fold, at least about 35-fold, at least about 40-fold, at least about 45-fold, or at least about 50-fold or more compared to the corresponding stability observed when the payload is not loaded to the EV according to the method of any one of claims 1 to 38.~~

~~43.~~9. A method of improving one or more properties of an extracellular vesicle after loading with a payload comprising loading the payload to the EV according to the method of any one of claims 1 to ~~38~~6, wherein the one or more properties comprise: inter-particle interaction, particle rigidity, particle size, or a combination thereof, and wherein the improvement in the one or more properties allow for increased filterability of the EV.

~~44. The method of claim 43, wherein the one or more properties comprise: inter-particle interaction, particle rigidity, particle size, or a combination thereof.~~

~~45. The method of claim 43 or 44, wherein the improvement in the one or more properties allow for increased filterability of the EV.~~

~~46.~~10. The method of any one of claims 1 to ~~45~~9, wherein the loading buffer further comprises one or more of the following components: tris, sucrose, glucose, trehalose, mannose, sorbitol, mannitol, glycerol, histidine, arginine, methionine, tryptophan, tyrosine, sodium phosphate, potassium phosphate, polymers, surfactants (*e.g.*, polysorbates 80 and 20), chelating agents (*e.g.*, EDTA, citrate), inorganic acids, or any combination thereof.

~~47. The method of claim 46, wherein the one or more components comprise tris, sucrose, glucose, trehalose, mannose, sorbitol, mannitol, glycerol, histidine, arginine, methionine, tryptophan, tyrosine, sodium phosphate, potassium phosphate, polymers, surfactants (*e.g.*, polysorbates 80 and 20), chelating agents (*e.g.*, EDTA, citrate), inorganic acids, or any combination thereof.~~

~~48. The method of claim 47, wherein the one or more components is sucrose.~~

~~49. The method of claim 48, wherein the sucrose is at a concentration lower than about 10 % w/v, lower than about 9 % w/v, lower than about 8 % w/v, lower than about 7 % w/v, lower than about 6% w/v, lower than about 5 % w/v, lower than about 4 % w/v, lower than about 3% w/v, or lower than about 2.5 % w/v.~~

~~50. The method of claim 48, wherein the sucrose is at a concentration between about 1 % w/v and about 10 % w/v, between about 2 % w/v and about 10 % w/v, between about 3 % w/v and about 10 % w/v, between about 4 % w/v and about 10 % w/v, between about 5 % w/v and about 10 % w/v, between about 1 % w/v and about 8 % w/v, between about 2 % w/v and about 8 % w/v, between about 3 % w/v and about 8 % w/v, between about 4 % w/v and about 8 % w/v, between about 5 % w/v and about 8 % w/v, between about 1 % w/v and about 5 % w/v, between about 2 % w/v and about 5 % w/v, between about 3 % w/v and about 5 % w/v, between about 4 % w/v and about 5 % w/v, or between about 5 % w/v and about 6 % w/v.~~

~~51. The method of any one of claims 1 to 50, wherein the loading buffer is at an osmolarity between about 100 and about 600 mOsm/kg.~~

~~52. The method of claim 51, wherein the loading buffer is at an osmolarity between about 275 and about 450, between about 280 and about 450, between about 300 and about 450, between about 275 and about 400, between about 280 and about 400, between about 300 and about 400, between about 275 and about 380, between about 280 and about 380, between about 300 and about 380, between about 275 and about 350, between about 280 and about 350, between about 300 and about 350, between about 275 and about 310, between about 280 and about 310, or between about 300 and about 310 mOsm/kg.~~

~~53. The method of claim 51 or 52, wherein the loading buffer is at an osmolarity of about 360, about 370, about 380, about 390, about 395, or about 400 mOsm/kg.~~

~~54. The method of any one of claims 1 to 53, wherein the loading buffer is at a pH between about 6 and about 8.~~

~~55. The method of claim 54, wherein the pH is between about 6 and about 7 or between about 7 and about 8.~~

~~56. The method of claim 54, wherein the pH is about 6, about 7, or about 8.~~

~~57. The method of any one of claims 1 to 53, wherein the loading buffer is at a pH of about 9.~~

~~58.~~11. The method of any one of claims 1 to ~~57~~10, wherein the payload comprises a peptide, a small molecule, an oligonucleotide, an antisense oligonucleotide (ASO), a PMO, an mRNA, an miRNA, an lcRNA, an antagomir, a tRNA, a siRNA, peptide nucleic acid, a cell penetrating peptide, an adjuvant, a protein, a carbohydrate, a sugar, an amino acid, or any combination thereof, and wherein the payload in the loading buffer is at a concentration between about 100 and about 2500 µM.

~~59. The method of any one of claims 1 to 58, wherein the payload comprises a nucleic acid.~~

~~60. The method of claim 59, wherein the nucleic acid comprises a contiguous sequence in length that is less than about 40, less than about 35, less than about 30, less than about 25, less than about 20, less than about 19, less than about 18, less than about 17, less than about 16, or less than about 15 nucleotides.~~

~~61. The method of claim 59 or 60, wherein the nucleic acid comprises a contiguous sequence in length between about 10 and about 30, between about 14 and about 30, between about 15 and about 30, between about 16 and about 30, between about 17 and about 30, between about 18 and about 30, between about 19 and about 30, between about 20 and about 30, between about 10 and about 25, between about 14 and about 25, between about 15 and about 25, between about 16 and about 25, between about 17 and about 25, between about 18 and about 25, between about 19 and about 25, between about 20 and about 25, between about 10 and about 22, between about 14 and about 22, between about 15 and about 22, between about 16 and about 22, between about 17 and about 22, between about 18 and about 22, between about 19 and about 22, or between about 20 and about 22.~~

~~62. The method of any one of claims 59 to 61, wherein the nucleic acid comprises an antisense oligonucleotide.~~

~~63. The method of claim 62, wherein the antisense oligonucleotide specifically binds to one or more genes and reduces an expression of the protein encoded by the one or more genes.~~

~~64. The method of claim 63, wherein the one or more genes comprise *STAT6*, *Kras*, *Nras*, *PMP22*, *C/EBPβ*, *STAT3*, *NLRP3*, or any combination thereof.~~

~~65. The method of any one of claims 1 to 64, wherein the payload in the loading buffer is at a concentration between about 100 and about 1000 μM.~~

~~66. The method of claim 65, wherein the payload in the loading buffer is at a concentration between about 100 μM and about 200 μM, between about 200 μM and about 300 μM, between about 300 μM and about 400 μM, between about 400 μM and about 500 μM, between about 500 μM and about 600 μM, between about 600 μM and about 700 μM, between about 700 μM and about 800 μM, between about 800 μM and about 900 μM, or between about 900 μM and 1000 μM.~~

~~67. The method of claim 65, wherein the payload in the loading buffer is at a concentration of about 100 μM, about 200 μM, about 300 μM, about 400 μM, about 500 μM, about 600 μM, about 700 μM, about 800 μM, about 900 μM, or about 1000 μM.~~

~~68. The method of any one of claims 1 to 64, wherein the payload in the loading buffer is at a concentration between about 1000 µM and about 2500 µM.~~

~~69. The method of claim 65, wherein the payload comprises the nucleotide sequence set forth in any one of SEQ ID NOs: 41 to 112, and the concentration of the payload is about 600 µM.~~

~~70.~~12. The method of any one of claims ~~69~~1 to 11, wherein the payload is conjugated to an anchoring moiety, wherein the anchoring moiety comprises a sterol, GM1, a lipid, a phospholipid, a vitamin, a small molecule, a peptide, or a combination thereof.

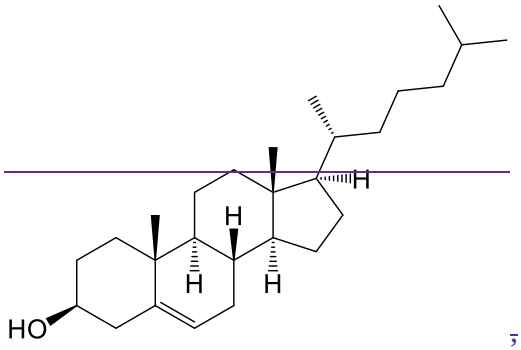
~~71. The method of claim 70, wherein the anchoring moiety comprises a sterol, GM1, a lipid, a phospholipid, a vitamin, a small molecule, a peptide, or a combination thereof.~~

~~72. The method of claim 70 or 71, 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.~~

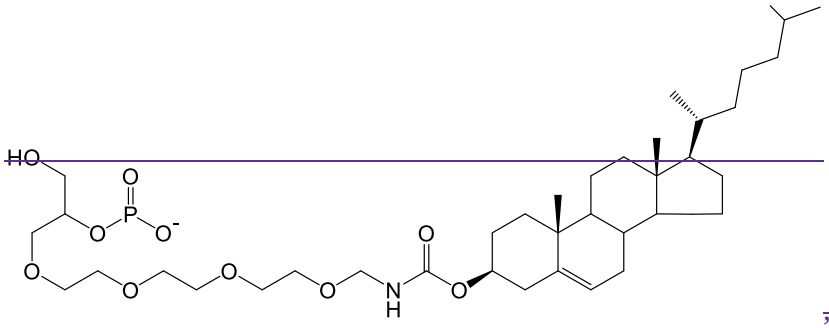
~~73. The method of claim 71 or 72, wherein the anchoring moiety comprises a sterol, a steroid, a hopanoid, a hydroxysteroid, a secosteroid, an analog thereof, or any combination thereof.~~

~~74. The method of any one of claims 71 to 73, 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.~~

~~75. The method of claim 74, wherein the anchoring moiety is a cholesterol or derivative having a structure selected from the group consisting of~~

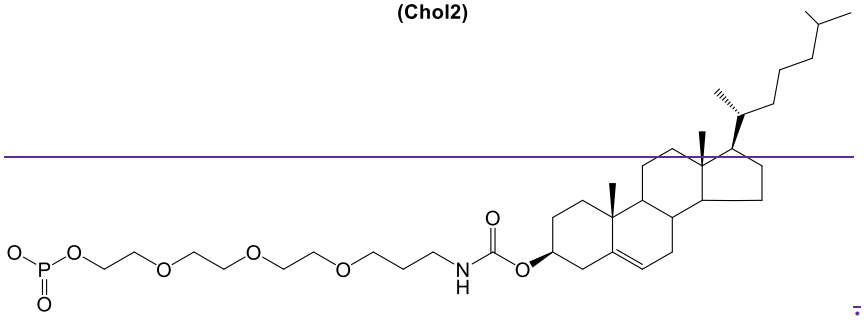


;



, and

(Chol2)



.

76. The method of any one of claims 71 to 75, wherein the anchoring moiety comprises a steroid, which is dihydrotestosterone, uvaol, hecigenin, diosgenin, progesterone, cortisol, or any combination thereof.

77. The method of claim 71, wherein the anchoring moiety comprises a lipid.

78. The method of any one of claims 71 to 77, wherein the anchoring moiety comprises a C_2-C_{60} chain.

79. The method of claim 78, wherein the anchoring moiety comprises C_4-C_{40}, C_2-C_{38}, C_2-C_{36}, C_2-C_{34}, C_2-C_{32}, C_2-C_{30}, C_4-C_{30}, C_2-C_{28}, C_4-C_{28}, C_2-C_{26}, C_4-C_{26}, C_2-C_{24}, C_4-C_{24}, C_6-C_{24}, C_8-C_{24}, C_{10}-C_{24}, C_2-C_{22}, C_4-C_{22}, C_6-C_{22}, C_8-C_{22}, C_{10}-C_{22}, C_2-C_{20}, C_4-C_{20}, C_6-C_{20}, C_8-C_{20}, C_{10}-C_{20}, C_2-C_{18},

~~C_4-C_{18}, C_6-C_{18}, C_8-C_{18}, C_{10}-C_{18}, C_{12}-C_{18}, C_{14}-C_{18}, C_{16}-C_{18}, C_2-C_{16}, C_4-C_{16}, C_6-C_{16}, C_8-C_{16}, C_{10}-C_{16}, C_{12}-C_{16}, C_{14}-C_{16}, C_2-C_{15}, C_4-C_{15}, C_6-C_{15}, C_8-C_{15}, C_9-C_{15}, C_{10}-C_{15}, C_{11}-C_{15}, C_{12}-C_{15}, C_{13}-C_{15}, C_2-C_{14}, C_4-C_{14}, C_6-C_{14}, C_8-C_{14}, C_9-C_{14}, C_{10}-C_{14}, C_{11}-C_{14}, C_{12}-C_{14}, C_2-C_{13}, C_4-C_{13}, C_6-C_{13}, C_7-C_{13}, C_8-C_{13}, C_9-C_{13}, C_{10}-C_{13}, C_{10}-C_{13}, C_{11}-C_{13}, C_2-C_{12}, C_4-C_{12}, C_6-C_{12}, C_7-C_{12}, C_8-C_{12}, C_9-C_{12}, C_{10}-C_{12}, C_2-C_{11}, C_4-C_{11}, C_6-C_{11}, C_7-C_{11}, C_8-C_{11}, C_9-C_{11}, C_2-C_{10}, C_4-C_{10}, C_2-C_9, C_4-C_9, C_2-C_8, C_2-C_7, C_4-C_7, C_2-C_6, or C_4-C_6 chain.~~

~~80. The method of any one of claims 71 to 79, wherein the 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.~~

~~81. The method of claim 80, 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.~~

~~82. The method of any one of claims 71 to 81, wherein the anchoring moiety comprises a branched fatty acid, 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, 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.~~

~~83. The method of any one of claims 71 to 82, 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.~~

~~84. The method of any one of claims 71 to 83, 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.~~

~~85. The method of any one of claims 71 to 84, 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.~~

~~86. The method of claim 71, wherein the anchoring moiety comprises a phospholipid.~~

~~87. The method of claim 86, wherein the phospholipid is phosphatidyl choline, phosphatidyl ethanolamine, phosphatidyl glycerol, phosphatidyl serine, phosphatidic acid, 2-lysophosphatidyl choline, sphingomyelin, or any combination thereof.~~

~~88. The method of claim 71, wherein the anchoring moiety comprises a vitamin.~~

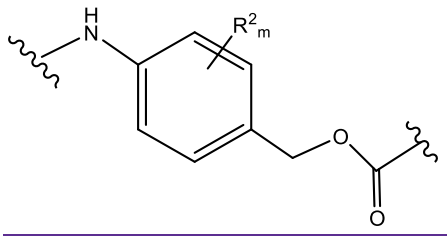
~~89. The method of claim 88, wherein the anchoring moiety comprises vitamin D, vitamin K, niacin, pyridoxone, vitamin E, or any combination thereof.~~

13. The method of ~~any one of claims 70 to 89~~claim 12, wherein the anchoring moiety further comprises a linker between the payload and the anchoring moiety, 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,

wherein $–Y_y-$ has the formula (V):



(V),

~~90.~~ 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.

~~91. The method of claim 90, wherein the linker comprises a non-cleavable linker.~~

~~92. The method of claim 91, wherein the non-cleavable linker comprises polyethylene glycol (PEG), glycerol, alkyl, phosphorothioate, succinimide, maleimide, or any combination thereof.~~

~~93. The method of claim 91, wherein the non-cleavable linker comprises polyethylene glycol (PEG) characterized by a formula R3-(O-CH_2-CH_2)$_n$- or R3-(0-CH_2-CH_2)$_n$-O-, wherein R3 being hydrogen, methyl or ethyl and n is an integer between 2 and 200.~~

~~94. The method of claim 91, wherein the non-cleavable linker comprises diethylene glycol, triethylene glycol, tetraethylene glycol (TEG), hexaethylene glycol (HEG), pentaethylene glycol, or any combination thereof.~~

~~95. The method of claim 90 or 91, wherein the linker comprises a polyglycerol (PG) having the formula ((R3 O (CH_2 CHOH CH_2O)$_n$), wherein R3 is hydrogen, methyl or ethyl, and n is an integer between 3 and 200.~~

96. The method of claim 90 or 91, wherein the linker comprises a diglycerol, triglycerol, tetraglycerol (TG), pentaglycerol, a hexaglycerol (HG), or any combination thereof.

97. The method of claim 90 or 91, wherein the linker comprises alkyl.

98. The method of claim 90, wherein the linker comprises a cleavable linker.

99. The method of claim 98, wherein the cleavable linker 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, an oxidoreductate cleavable linker, a phospholipase cleavable linker, a phosphatase cleavable linker, a photoactivated cleavable linker, a self-immolative linker, or any combination thereof.

100. The method of claim 99, wherein the cleavable linker is a self-immolative linker.

101. The method of claim 99, wherein the cleavable linker 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.

102. The method of any one of claims 99 to 101, 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.

103. The method of claim 102, wherein $-A_a-$ is a dipeptide, a tripeptide, a tetrapeptide, a pentapeptide, or a hexapeptide.

104. The method of claim 102, wherein a is 2 and $-A_a-$ is selected from the group consisting of valine-alanine, valine-citrulline, gluatmic acid-valine-citrulline, phenylalanine-lysine, N-methylvaline-citrulline, glycine-histidine-leucine-glycine, cyclohexylalanine-lysine, and beta-alanine-lysine.

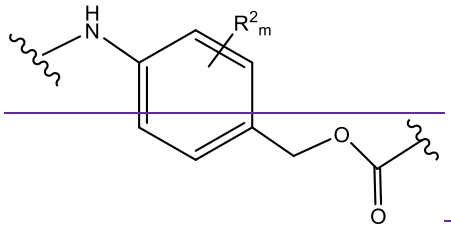
~~105. The method of claim 102, wherein A_a is valine-alanine or valine-citrulline or glutamic acid-valine-citrulline.~~

~~106. The method of claim 102, wherein A_a is arginine, lysine, or both.~~

~~107. The method of any one of claims 102 to 106, wherein y is 1.~~

~~108. The method of any one of claims 102 to 107, wherein Y is a self-immolative spacer.~~

~~109. The method of claim 108, wherein Y_y has the formula (V):~~



~~(V),~~

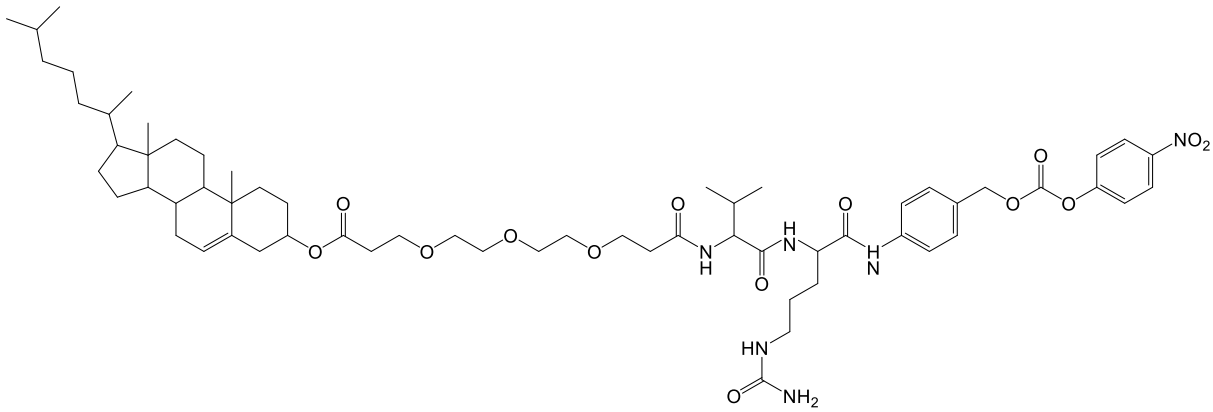
~~wherein each R^2 is independently C_{1-8} alkyl, O (C_{1-8} alkyl), halogen, nitro, or cyano; and m is an integer from 0 to 4.~~

~~110. The method of claim 109, wherein m is 0, 1, or 2.~~

~~111. The method of claim 110, wherein m is 0.~~

~~112. The method of claim 110, wherein the cleavable linker is valine-alanine p-aminobenzylcarbamate or valine-citrulline p-aminobenzylcarbamate.~~

~~113.~~14. The method of claim ~~70~~12, wherein the anchoring moiety comprises:



~~114.~~15. The method of claim ~~70~~13, which comprises (i) a payload comprising the nucleotide sequence set forth in any one of SEQ ID NOs: 41 to 112, and (ii) a linker selected from the linker combinations of TABLE 1 or TABLE 2, wherein the payload is conjugated to a cholesterol.

~~115. The method of claim 114, wherein the payload is conjugated to a cholesterol.~~

~~116.~~16. The method of claim ~~115~~15, wherein the payload comprises 5'GbsCbsAbsdAsdGsdAsdTs(5MdC)s(5MdC)s(5MdC)sdGsdGsdAsdTsdTs(5MdC)sdGsGbsTbs Cb3', wherein Nb is an LNA, dN is a DNA, (5MdC) is 5-Methyl-dC, s is phosphorothioate, TEG is triethylene glycol, and HEG is hexaethylene glycol.

~~117. The method of claim 114 or 115, wherein the payload is linked to the cholesterol by TEG-HEG.~~

~~118. The method of any one of claims 1 to 117, wherein the extracellular vesicle is at a concentration of at least about $1x10^{11}$, at least about $2x10^{11}$, at least about $3x10^{11}$, at least about $4x10^{11}$, at least about $5x10^{11}$, at least about $6x10^{11}$, at least about $7x10^{11}$, at least about $8x10^{11}$, at least about $9x10^{11}$, at least about $1x10^{12}$, at least about $2x10^{12}$, at least about $3x10^{12}$, at least about $4x10^{12}$, at least about $5x10^{12}$, at least about $6x10^{12}$, at least about $7x10^{12}$, at least about $8x10^{12}$, at least about $9x10^{12}$, at least about $1x10^{13}$, at least about $2x10^{13}$, at least about $3.0x10^{13}$ p/mL, at least about $4x10^{13}$ p/mL, at least about $5x10^{13}$ p/mL, at least about $6x10^{13}$ p/mL, at least about $7x10^{13}$ p/mL, at least about $8x10^{13}$ p/mL, at least about $9x10^{13}$ p/mL, or at least about $1x10^{14}$ particles/mL.~~

~~119. The method of any one of claims 1 to 118, wherein the extracellular vesicle is at a concentration between about $1x10^{12}$ and about $5x10^{13}$ particles/mL, about $1x10^{12}$ and about $4x10^{13}$ particles/mL, about $1x10^{12}$ and about $3x10^{13}$ particles/mL, about $1x10^{12}$ and about $2x10^{13}$ particles/mL, about $2x10^{12}$ and about $5x10^{13}$ particles/mL, about $2x10^{12}$ and about $4x10^{13}$ particles/mL, about $2x10^{12}$ and about $3x10^{13}$ particles/mL, about $2x10^{12}$ and about $2x10^{13}$ particles/mL, about $3x10^{12}$ and about $5x10^{13}$ particles/mL, about $3x10^{12}$ and about $4x10^{13}$ particles/mL, about $3x10^{12}$ and about $3x10^{13}$ particles/mL, about $3x10^{12}$ and about $2x10^{13}$ particles/mL, about $4x10^{12}$ and about $5x10^{13}$ particles/mL, about $4x10^{12}$ and about $4x10^{13}$~~

~~particles/mL, about $4x10^{12}$ and about $3x10^{13}$ particles/mL, about $4x10^{12}$ and about $2x10^{13}$ particles/mL, about $5x10^{12}$ and about $5x10^{13}$ particles/mL, about $5x10^{12}$ and about $4x10^{13}$ particles/mL, about $5x10^{12}$ and about $3x10^{13}$ particles/mL, or about $5x10^{12}$ and about $2x10^{13}$ particles/mL.~~

~~120. The method of any one of claims 1 to 119, wherein the extracellular vesicle is at a concentration between about $5x10^{12}$ and about $2x10^{13}$ particles/mL.~~

~~121. The method of any one of claims 1 to 120, wherein the extracellular vesicle is at a concentration of about $1x10^{13}$ particles/mL.~~

~~122.~~17. The method of any one of claims 1 to ~~121~~16, wherein the ~~extracellular vesicle~~EV further comprises a protein in the membrane of the ~~extracellular vesicle~~EV, wherein the protein comprises 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.

~~123. The method of claim 122, wherein the protein comprises 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.~~

~~124. The method of claim 123, wherein the protein comprises a PTGFRN protein or a functional fragment thereof.~~

~~125.~~18. An extracellular vesicle (EV) prepared by the method of any one of claims 1 to ~~124~~17.

~~126. An extracellular vesicle comprising payloads on the external surface of the extracellular vesicle, wherein the number of payloads on the surface of the extracellular vesicle is at least about 1,000, at least about 2,000, at least about 3,000, at least about 4000, at least about 5000, at least about 6000, at least about 7000, at least about 8000, at least about 9000, at least about 10,000, at least about 11,000, at least about 12000, at least about 13,000, at least about 14,000, at least about 15,000, at least about 16,000, at least about 17,000, at least about 18,000, at least about 20,000, at least about 25,000, or at least about 30,000.~~

~~127. The extracellular vesicle of claim 126, wherein the number of payloads on the surface of the extracellular vesicle is between about 5,000 and about 20,000, about 6,000 and about 20,000, about 7,000 and about 20,000, about 8,000 and about 20,000, about 9,000 and about 20,000, about 10,000 and about 20,000, about 5,000 and about 18,000, about 6,000 and about 18,000, about 7,000 and about 18,000, about 8,000 and about 18,000, about 9,000 and about 18,000, about 10,000 and about 18,000, about 5,000 and about 15,000, about 6,000 and about 15,000, about 7,000 and about 15,000, about 8,000 and about 15,000, about 9,000 and about 15,000, or about 10,000 and about 15,000.~~

~~128. The extracellular vesicle of claim 126, wherein the number of payloads on the surface of the extracellular vesicle is between about 10,000 and about 15,000.~~

~~129. The extracellular vesicle of any one of claims 126 to 128, wherein the payload comprises the nucleotide sequence set forth in any one of SEQ ID NOs: 41 to 112.~~

~~130. The method of claim 129, wherein the payload is conjugated to a sterol, GM1, a lipid, a phospholipid, a vitamin, a small molecule, a peptide, or a combination thereof.~~

~~131. The extracellular vesicle of claim 130, wherein the payload is conjugated to a cholesterol.~~

~~132. The extracellular vesicle of any one of claims 126 to 131, wherein the payload comprises 5'GbsCbsAbsdAsdGsdAsdTs(5MdC)s(5MdC)s(5MdC)sdGsdGsdAsdTsdTs(5MdC)sdGsGbsTbs~~

~~Cb3' (SEQ ID NO: 48), wherein Nb is an LNA, dN is a DNA, (5MdC) is 5-Methyl-dC, and s is phosphorothioate.~~

~~133. The extracellular vesicle of claim 132, wherein the payload is linked to the cholesterol by TEG-HEG.~~

~~134. A population of extracellular vesicles comprising the extracellular vesicle of any one of claims 125 to 133.~~

~~135. The population of extracellular vesicles of claim 134, wherein at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99% or about 100% of the extracellular vesicles are the extracellular vesicle of any one of claims 126 to 133.~~

~~136. A composition comprising the extracellular vesicle of any one of claims 125 to 133 or the population of extracellular vesicles of any one of claims 134 or 135.~~

~~137.~~19. A pharmaceutical composition comprising the ~~extracellular vesicle~~EV of claim 18 ~~any one of claims 125 to 133 or the population of extracellular vesicles of any one of claims 134 or 135~~.

~~138.~~20. ~~A method of treating~~Use of the EV of claim 18 or pharmaceutical composition of claim 19 in the manufacture of a medicament for the treatment of a disease or condition in a subject in need thereof ~~comprising administering the extracellular vesicle of any one of claims 125 to 133 or the population of extracellular vesicles of any one of claims 134 or 135 to the subject in need thereof~~.