CLAIMS

1. A multilamellar lipid vesicle having covalent crosslinks between lipid bilayers.

2. The multilamellar lipid vesicle of claim 1, wherein the vesicle comprises a functionalized lipid.

3. The multilamellar lipid vesicle of claim 1 or 2, wherein the vesicle comprises phosphocholine.

4. The multilamellar lipid vesicle of claim 1, 2 or 3, wherein the vesicle comprises phosphoglycerol.

5. The multilamellar lipid vesicle of claim 2, 3 or 4, wherein the functionalized lipid is a maleimide functionalized lipid.

6. The multilamellar lipid vesicle of any one of the foregoing claims, wherein the vesicle comprises an agent.

7. The multilamellar lipid vesicle of claim 6, wherein the agent is a prophylactic agent, a therapeutic agent, or a diagnostic agent.

8. The multilamellar lipid vesicle of claim 6, wherein the agent is an antigen.

9. The multilamellar lipid vesicle of claim 6, wherein the agent is an adjuvant.

10. The multilamellar lipid vesicle of claim 6, wherein the agent is a protein.

11. The multilamellar lipid vesicle of claim 6, wherein the agent is encapsulated within the vesicle.

12. The multilamellar lipid vesicle of claim 6 or 11, wherein the agent is encapsulated between the lipid bilayers.

13. The multilamellar lipid vesicles of any one of claims 1-12, wherein the vesicles are conjugated to polyethylene glycol (PEG).

14. The multilamellar lipid vesicles of the any one of claims 1-13, wherein the vesicles comprise DOPC, DOPG and a maleimide functionalized lipid.

15. The multilamellar lipid vesicles of claim 14, wherein the maleimide functionalized lipid is a maleimide functionalized phosphoethanolamine.

16. A composition comprising the multilamellar lipid vesicle of any one of claims 1-15 and a pharmaceutically acceptable carrier.

17. A composition comprising the multilamellar lipid vesicle of any one of claims 1-15 and an excipient suitable for lyophilization.

18. A composition comprising the multilamellar lipid vesicle of claim 17, wherein the excipient suitable for lyophilization comprises sucrose.

19. A method comprising

contacting liposomes comprising a functionalized lipid with a divalent cation to form fused liposomes, and

contacting the fused liposomes with a crosslinker to form multilamellar lipid vesicles having covalent crosslinks between lipid bilayers.

20. The method of claim 19, wherein the functionalized lipid is a maleimide-functionalized lipid.

21. The method of claim 19 or 20, wherein the liposomes comprise phosphocholine.

22. The method of claim 19, 20 or 21, wherein the liposomes comprise phosphoglycerol.

23. The method of claim 19, wherein the liposomes comprise a maleimide-functionalized lipid, phosphocholine and phosphoglycerol.

24. The method of any one of claims 19-23, wherein the functionalized lipid is a functionalized phosphoethanolamine.

25. The method of claim 23, wherein the maleimide-functionalized lipid is maleimide-functionalized phosphoethanolamine.

26. The method of any one of claims 19-25, wherein the crosslinker is a dithiol crosslinker.

27. The method of any one of claims 19-25, wherein the crosslinker is dithiolthrietol (DTT).

28. The method of any one of claims 19-27, further comprising conjugated polyethylene glycol (PEG) to the surface of the multilamellar lipid vesicles having covalent crosslinks between lipid bilayers.

29. The method of any one of claims 19-28, wherein the divalent cations are $Ca^{2+}$.

30. The method of any one of claims 19-29, wherein the divalent cations are $Mg^{2+}$.

31. The method of any one of claims 19-30, wherein the contacting occurs in an aqueous buffer.

32. The method of any one of claims 19-31, wherein the liposomes comprise an agent.

33. The method of claim 32, wherein the agent is a prophylactic agent, a therapeutic agent, or a diagnostic agent.

34. The method of any one of claims 1-15, wherein the liposomes are prepared using DOPC, DOPG and a maleimide functionalized lipid at a molar ratio of 40:10:50.

34. The method of any one of claims 8, wherein dithiol crosslinker to maleimide functionalized lipid molar ratio is 1:2.

36. A method comprising

contacting a multilamellar lipid vesicle comprising a functionalized lipid with a crosslinker to form multilamellar lipid vesicles having covalent crosslinks between lipid bilayers.

37. A method comprising

administering to a subject a multilamellar lipid vesicle having covalent crosslinked lipid bilayers and that comprises an agent, in an effective amount.

38. The method of claim 37, wherein the multilamellar lipid vesicle comprises a biodegradable lipid.

39. The method of claim 37 or 38, wherein the multilamellar lipid vesicle comprises a phospholipid.

40. The method of claim 37, 38 or 39, wherein the multilamellar lipid vesicle comprises phosphocholine, phosphoglycerol, and/or phosphoethanolamine.

41. The method of any one of claims 37-40, wherein the multilamellar lipid vesicle comprises a functionalized lipid.

42. The method of claim 41 wherein the functionalized lipid is a maleimide functionalized lipid.

43. The method of claim 42, wherein the maleimide functionalized lipid is a maleimide functionalized phosphoethanolamine.

44. The method of any one of claims 37-43, wherein the agent is a prophylactic agent.

45. The method of any one of claims 37-43, wherein the agent is a therapeutic agent.

46. The method of any one of claims 37-45, wherein the agent is an antigen.

47. The method of any one of claims 37-45, wherein the agent is an adjuvant.

48. The method of any one of claims 37-45, wherein the multilamellar lipid vesicle comprises more than one agent.

49. The method of any one of claims 37-45, wherein the multilamellar lipid vesicle comprises two agents.

50. The method of claim 49, wherein the multilamellar lipid vesicle comprises an antigen and an adjuvant.

51. The method of any one of claims 37-50, wherein the multilamellar lipid vesicle is conjugated to PEG on its external surface.

52. A method comprising

contacting a multilamellar lipid vesicle having covalent crosslinked lipid bilayers and that comprises an agent, with a cell in vitro.

# CLAIMS

1. A multilamellar lipid vesicle having covalent crosslinks between lipid bilayers.

2. The multilamellar lipid vesicle of claim 1, wherein the vesicle comprises a functionalized lipid.

3. The multilamellar lipid vesicle of claim 1, wherein the vesicle comprises a phosphocholine.

4. The multilamellar lipid vesicle of claim 1, wherein the vesicle comprises a phosphoglycerol.

5. The multilamellar lipid vesicle of any one of claims 1-4, wherein the vesicle comprises an agent.

6. The multilamellar lipid vesicle of claim 5, wherein the agent is a prophylactic agent.

7. The multilamellar lipid vesicle of claim 5, wherein the agent is a therapeutic agent.

8. The multilamellar lipid vesicle of claim 5, wherein the agent is a diagnostic agent.

9. The multilamellar lipid vesicle of claim 5, wherein the agent is an antigen.

10. The multilamellar lipid vesicle of claim 5, wherein the agent is an adjuvant.

11. The multilamellar lipid vesicle of claim 5, wherein the agent is a protein.

12. The multilamellar lipid vesicle of any one of claims 5-11, wherein the agent is (a) encapsulated within the vesicle or (b) encapsulated between the lipid bilayers.

13. The multilamellar lipid vesicle of any one of claims 1-12, wherein the vesicle is (a) conjugated to polyethylene glycol (PEG) and/or (b) comprises DOPC, DOPG and a maleimide-functionalized lipid.

14. A composition comprising the multilamellar lipid vesicle of any one of claims 1-13 and a pharmaceutically acceptable carrier.

15. A composition comprising the multilamellar lipid vesicle of any one of claims 1-13 and an excipient suitable for lyophilization.

16. A method comprising

contacting liposomes comprising a functionalized lipid with a divalent cation to form fused liposomes, and

contacting the fused liposomes with a crosslinker to form multilamellar lipid vesicles having covalent crosslinks between lipid bilayers.

17. The method of claim 16, wherein the functionalized lipid is a maleimide-functionalized lipid.

18. The method of claim 16 or 17, wherein the liposomes comprise phosphocholine and/or phosphoglycerol.

19. The method of claim 16, wherein the liposomes comprise a maleimide-functionalized lipid, phosphocholine and phosphoglycerol.

20. The method of any one of claims 16-19, wherein the functionalized lipid is a functionalized phosphoethanolamine.

21. The method of any one of claims 16-20, wherein the crosslinker is a dithiol crosslinker or dithiolthrietol (DTT).

22. The method of any one of claims 16-21, further comprising conjugating polyethylene glycol (PEG) to the surface of the multilamellar lipid vesicles having covalent crosslinks between lipid bilayers.

23. The method of any one of claims 16-22, wherein the divalent cations are $Ca^{2+}$ and/or $Mg^{2+}$.

24. The method of any one of claims 16-23, wherein the liposomes comprise an agent.

25. The method of any one of claims 16-24, wherein the liposomes are prepared using DOPC, DOPG and a maleimide-functionalized lipid at a molar ratio of 40:10:50.

26. The method of any one of claims 21-25, wherein dithiol crosslinker to maleimide-functionalized lipid molar ratio is 1:2.

27. A method comprising

contacting a multilamellar lipid vesicle comprising a functionalized lipid with a crosslinker to form multilamellar lipid vesicles having covalent crosslinks between lipid bilayers.

28. A pharmaceutical composition comprising

a multilamellar lipid vesicle having covalently crosslinked lipid bilayers and comprising an agent in an effective amount.

29. The pharmaceutical composition of claim 28, wherein the multilamellar lipid vesicle comprises a biodegradable lipid.

30. The pharmaceutical composition of claim 28, wherein the multilamellar lipid vesicle comprises a phospholipid.

31. The pharmaceutical composition of claim 28, wherein the multilamellar lipid vesicle comprises phosphocholine.

32. The pharmaceutical composition of claim 28, wherein the multilamellar lipid vesicle comprises phosphoglycerol.

33. The pharmaceutical composition of claim 28, wherein the multilamellar lipid vesicle comprises phosphoethanolamine.

34. The pharmaceutical composition of claim 28, wherein the multilamellar lipid vesicle comprises a functionalized lipid.

35. The pharmaceutical composition of any one of claims 28-34, wherein the agent is a prophylactic agent.

36. The pharmaceutical composition of any one of claims 28-34, wherein the agent is a therapeutic agent.

37. The pharmaceutical composition of any one of claims 28-34, wherein the agent is an antigen.

38. The pharmaceutical composition of any one of claims 28-34, wherein the agent is an adjuvant.

39. The pharmaceutical composition of any one of claims 28-38, wherein the multilamellar lipid vesicle comprises more than one agent.

40. The pharmaceutical composition of any one of claims 28-39, wherein the multilamellar lipid vesicle is conjugated to PEG on its external surface.

41. A method comprising

contacting a multilamellar lipid vesicle having covalently crosslinked lipid bilayers and that comprises an agent, with a cell in vitro.

42. The multilamellar lipid vesicle of any one of claims 2-13, wherein the functionalized lipid is a maleimide-functionalized lipid.

43. The multilamellar lipid vesicle of claim 13, wherein the maleimide-functionalized lipid is a maleimide-functionalized phosphoethanolamine.

44. The composition of claim 15, wherein the excipient suitable for lyophilization comprises sucrose.

45. The method of claim 19, wherein the maleimide-functionalized lipid is maleimide-functionalized phosphoethanolamine.

46. The method of claim 23, wherein the contacting occurs in an aqueous buffer.

47. The method of claim 24, wherein the agent is a prophylactic agent, a therapeutic agent, or a diagnostic agent.

48. The pharmaceutical composition of claim 34, wherein the functionalized lipid is a maleimide-functionalized lipid.

49. The pharmaceutical composition of claim 48, wherein the maleimide-functionalized lipid is a maleimide-functionalized phosphoethanolamine.

50. The pharmaceutical composition of claim 39, wherein the multilamellar lipid vesicle comprises two agents.

51. The pharmaceutical composition of claim 50, wherein the multilamellar lipid vesicle comprises antigen and an adjuvant.

52. The multilamellar lipid vesicle of claim 5, wherein the agent is an antibody, an antibody fragment, a fusion protein, an enzyme, a co-factor, a receptor, a ligand, an antigen, a cytokine or a chemokine.

53. The multilamellar lipid vesicle of claim 52, wherein the agent is an antibody or an antibody fragment.

54. The multilamellar lipid vesicle of claim 53, wherein the antibody or the antibody fragment is respectively an immunostimulatory antibody or an immunostimulatory antibody fragment.

55. The multilamellar lipid vesicle of claim 53, wherein the antibody or the antibody fragment binds to a cancer antigen.

56. The multilamellar lipid vesicle of claim 55, wherein the cancer antigen is expressed on the surface of a cancer cell.

57. The multilamellar lipid vesicle of claim 9 further comprising an adjuvant.

58. The multilamellar lipid vesicle of claim 9, wherein the antigen is human papillomavirus (HPV) protein.

59. The multilamellar lipid vesicle of claim 58 further comprising an adjuvant.

60. A composition comprising:

a multilamellar lipid vesicle having at least two lipid bilayers covalently crosslinked to each other through headgroups that react with covalent crosslinkers to form covalent crosslinks between the at least two lipid bilayers; and

an agent.

61. The composition of claim 60, wherein the multilamellar lipid vesicle comprises the agent.

62. The composition of claim 61, wherein the agent is an antibody, an antibody fragment, a fusion protein, an enzyme, a co-factor, a receptor, a ligand, an antigen, a cytokine or a chemokine.

63. The composition of claim 62, wherein the agent is an antibody or an antibody fragment that binds to a cancer antigen.

64. The composition of claim 62, wherein the agent is an antigen, and the composition further comprising comprises an adjuvant.

65. The composition of claim 64, wherein the multilamellar lipid vesicle comprises the adjuvant.

66. The composition of claim 61, wherein the agent is an antigen that is human papillomavirus (HPV) protein.