CLAIMS

1. An anti-ENDO180 antibody or antigen-binding fragment thereof selected from

a. the monoclonal antibody produced by the hybridoma cell line E3-8D8 (BCCM Accession Number LMBP 7203CB);

b. an antibody or fragment thereof that binds to the same epitope as the antibody of (a);

c. a humanized antibody of (a) or (b); and

d. a recombinant polypeptide comprising amino acid sequences set forth in SEQ ID NO: 6;

wherein upon contact with a cell expressing ENDO180 the antibody or antigen binding fragment thereof is internalized into the cell.

2. A composition comprising the anti-ENDO180 antibody or antigen binding fragment thereof of claim 1, and a pharmaceutically acceptable carrier.

3. The composition of claim 2 further comprising a moiety selected from a detectable label, a cytotoxic agent and a therapeutic agent.

4. The composition of claim 2 or 3 wherein the carrier comprises a lipid particle, a polysaccharide particle or a combination thereof

5. The composition of claim 4, wherein the particle comprises a lipidated polysaccharide particle.

6. The composition of claim 5 wherein the carrier comprises a lipidated glycosaminoglycan.

7. The composition of any one of claims 2-6 wherein the anti-ENDO180 antibody or antigen-binding fragment thereof is immobilized on the particle.

8. The composition of claim 3, wherein the moiety is a therapeutic agent.

9. The composition of claim 8 wherein therapeutic agent is an inhibitory oligonucleotide.

10. The composition of claim 9 wherein the inhibitory oligonucleotide is selected from an antisense compound, a chemically modified siRNA compound, an unmodified siRNA compound, a chemically modified shRNA compound, an unmodified shRNA compound, a chemically modified miRNA compound, and an unmodified miRNA compound.

11. The composition of claim 10 wherein the inhibitory oligonucleotide is a chemically modified siRNA compound.

12. The composition of claim 11 wherein the chemically modified siRNA compound inhibits expression of a human target gene set forth in Table A.

13. The composition of claim 3 wherein the moiety is attached to the antibody or antigen-binding fragment.

14. The composition of claim 3 wherein the moiety is encapsulated within the lipid particle.

15. Use of a composition of any one of claims 3 or 8-14 for the manufacture of a medicament for delivering a moiety to an ENDO180 expressing cell in a subject.

16. Use of a composition of any one of claims 8-14, for the manufacture of a medicament for treating a subject afflicted with cancer, fibrosis or macrophage associated disease.

17. Use of a composition of any one of claims 2-14, for the manufacture of a medicament for inhibiting growth of a cancer cell.

18. The use of claim 15 or 16, wherein the composition is for systemic or local administration.

19. The use of claim 18, wherein the composition is for intravenous administration.

20. The hybridoma cell line E3-8D8, deposited with the BCCM with Accession Number LMBP 7203CB.

21. An isolated anti-ENDO180 antibody or antigen-binding fragment thereof secreted by the hybridoma cell line of claim 20.

22. An antibody or antibody or antigen-binding fragment thereof that binds to the same epitope as the antibody of claim 21

23. An antibody or antigen-binding fragment thereof of claim 21 or 22 which is humanized.

24. An antibody or antibody or antigen-binding fragment thereof of claim 21 or 22 which is chimeric.

25. A conjugate comprising

a) the antibody or antibody or antigen-binding fragment of any one of claims 21-24;

b) a moiety selected from a detectable label, a cytotoxic agent and a therapeutic agent; and

c) optionally a linker which links a) to b).

26. The conjugate of claim 25, comprising a linker

27. The conjugate of claim 26, wherein the linker attaches the 3' terminus of the antibody or antigen-binding fragment to the moiety.

28. The conjugate of claim 26, wherein the linker is selected from a polypeptide linker, peptide linker, lipid linker or nucleic acid linker.

29. The conjugate of claim 28, wherein the linker is selected from protamine, a fragment of protamine, (Arg)9, biotin-avidin, and antennapedia peptide.

30. The conjugate of claim 28, wherein the linker is a nucleic acid linker.

31. The conjugate of claim 25 wherein the moiety is a therapeutic agent.

32. The conjugate of claim 26 wherein therapeutic agent is an inhibitory oligonucleotide.

33. The conjugate of claim 32 wherein the inhibitory oligonucleotide is selected from an antisense compound, a chemically modified siRNA compound, an unmodified siRNA compound, a chemically modified shRNA compound, an unmodified shRNA compound, a chemically modified miRNA compound, and an unmodified miRNA compound.

34. The conjugate of claim 33 wherein the inhibitory oligonucleotide is a chemically modified siRNA compound.

35. The conjugate of claim 34 wherein the chemically modified siRNA compound inhibits expression of a human target gene set forth in Table A.

36. A composition comprising the conjugate of any one of claims 25-35; and a carrier.

37. The composition of claim 36 wherein the carrier comprises a lipid particle, a polysaccharide particle or a combination thereof.

38. The composition of claim 37, wherein the lipid particle is a lipidated polysaccharide particle.

39. The composition of claim 38 wherein the carrier comprises a lipidated glycosaminoglycan.

40. Use of a conjugate of claim 25 or composition of any one of claims 36-39 for the manufacture of a medicament for delivering a moiety to an ENDO180 expressing cell in a subject.

41. Use of the composition of any one of claims 36-39, for the manufacture of a medicament for treating a subject afflicted with cancer, fibrosis or macrophage associated disease.

42. An anti-ENDO180 antibody or antigen-binding fragment comprising a polypeptide sequence set forth in SEQ ID NO:6.

43. The antibody or antigen-binding fragment of claim 42 wherein the antibody or antigen-binding fragment is selected from the group consisting of a full IgG, a Fab fragment, a Fab' fragment, an F(ab')2 fragment, the variable portion of the heavy and/or light chains thereof, a Fab miniantibody, and a scFv.

44. An isolated polynucleotide having SEQ ID NO:5 which encodes the polypeptide of claim 42.

45. An antibody or antibody or antigen-binding fragment thereof of claim 43 which is humanized.

46. An antibody or antibody or antigen-binding fragment thereof of claim 43 which is chimeric.

47. A conjugate comprising

a) the antibody or antibody or antigen-binding fragment of any one of claims 42-46;

b) a moiety selected from a detectable label, a cytotoxic agent and a therapeutic agent; and

c) optionally a linker which links a) to b).

48. The conjugate of claim 47, comprising a linker

49. The conjugate of claim 48, wherein the linker attaches the 3' terminus of the antibody or antigen-binding fragment to the moiety.

50. The conjugate of claim 49, wherein the linker is selected from a polypeptide linker, peptide linker, lipid linker or nucleic acid linker.

51. The conjugate of claim 50, wherein the linker is selected from protamine, a fragment of protamine, (Arg)9, biotin-avidin, and antennapedia peptide.

52. The conjugate of claim 50, wherein the linker is a nucleic acid linker.

53. The conjugate of claim 47 wherein the moiety is a therapeutic agent.

54. The conjugate of claim 53 wherein therapeutic agent is an inhibitory oligonucleotide.

55. The conjugate of claim 54 wherein the inhibitory oligonucleotide is selected from an antisense compound, a chemically modified siRNA compound, an unmodified siRNA compound, a chemically modified shRNA compound, an unmodified shRNA compound, a chemically modified miRNA compound, and an unmodified miRNA compound.

56. The conjugate of claim 55 wherein the inhibitory oligonucleotide is a chemically modified siRNA compound.

57. The conjugate of claim 56 wherein the chemically modified siRNA compound inhibits expression of a human target gene set forth in Table A.

58. A composition comprising the conjugate of any one of claims 47-57; and a carrier.

59. The composition of claim 58 wherein the carrier comprises a lipid particle, a polysaccharide particle or a combination thereof.

60. The composition of claim 59, wherein the lipid particle is a lipidated polysaccharide particle.

61. The composition of claim 60 wherein the carrier comprises a lipidated glycosaminoglycan.

62. Use of a conjugate of claim 47 or a composition of any one of claims 63-66 for the manufacture of a medicament for delivering a moiety to an ENDO180 expressing cell in a subject.

63. The composition of any one of claims 58-61, for the manufacture of a medicament for treating a subject afflicted with cancer, fibrosis or macrophage associated disease.

64. Use of a composition comprising

a) an anti-ENDO180 antibody or antigen binding fragment thereof;

b) a therapeutic moiety;

c) a carrier; and

d) optionally a linker that links a) to b);

in the manufacture of a medicament for delivering a therapeutic moiety to an ENDO180 expressing cell in a subject.

65. Use of a composition comprising:

a) an anti-ENDO180 antibody or antigen binding fragment thereof;

b) a therapeutic moiety;

c) a carrier; and

d) optionally a linker that links a) to b);

in the manufacture of a medicament for treating a proliferative disease selected from cancer, fibrosis and a macrophage associated disease.

66. The use of claim 65 wherein the proliferative disease selected is cancer.

67. The use of claim 65 wherein the proliferative disease selected is fibrosis.

68. The use of any one of claims 62-67 wherein the carrier comprises a lipid particle, a polysaccharide particle or a combination thereof.

69. The use of claim 68, wherein the lipid particle is a lipidated polysaccharide particle.

70. The use of claim 69 wherein the carrier comprises a lipidated glycosaminoglycan.

71. The use of claim 64 wherein therapeutic agent is an inhibitory oligonucleotide.

72. The use of claim 71 wherein the inhibitory oligonucleotide is selected from an antisense compound, a chemically modified siRNA compound, an unmodified siRNA compound, a chemically modified shRNA compound, an unmodified shRNA compound, a chemically modified miRNA compound, and an unmodified miRNA compound.

73. The use of claim 72 wherein the inhibitory oligonucleotide is a chemically modified siRNA compound.

74. The use of claim 73 wherein the chemically modified siRNA compound inhibits expression of a human target gene set forth in Table A.

CLAIMS

1. An anti-ENDO180 antibody or antigen-binding fragment thereof selected from

a. the monoclonal antibody produced by the hybridoma cell line E3-8D8 (BCCM Accession Number LMBP 7203CB);

b. an antibody or fragment thereof that binds to the same epitope as the antibody of (a);

c. a humanized antibody of (a) or (b);

d. a recombinant polypeptide comprising amino acid sequences set forth in SEQ ID NO: 6 or a variant thereof; and

e. a recombinant polypeptide comprising CDR3 having amino acid sequences set forth in SEQ ID NO:7 and 8, or variants thereof;

wherein upon contact with a cell expressing ENDO180 the antibody or antigen binding fragment thereof is internalized into the cell.

2. A composition comprising anti-ENDO180 antibody or antigen binding fragment thereof of claim, and a pharmaceutically acceptable carrier.

3. The composition of claim 2 further comprising a moiety selected from a detectable label, a cytotoxic agent and a therapeutic agent.

4. The composition of claim 2 or 3 wherein the carrier comprises a lipid particle, a polysaccharide particle or a combination thereof

5. The composition of claim 4, wherein the particle comprises a lipidated polysaccharide particle.

6. The composition of claim 5 wherein the carrier comprises a lipidated glycosaminoglycan.

7. The composition of any one of claims 2-6 wherein the anti-ENDO180 antibody or antigen-binding fragment thereof is immobilized on the particle.

8. The composition of any one of claims 3-7 wherein the moiety is a therapeutic agent.

9. The composition of claim 8 wherein therapeutic agent is an inhibitory oligonucleotide.

~~10. The composition of claim 9 wherein the inhibitory oligonucleotide is selected from an~~ antisense compound, a chemically modified siRNA compound, an unmodified siRNA compound, a chemically modified shRNA compound, an unmodified shRNA compound, a chemically modified miRNA compound, and an unmodified miRNA compound.

11. The composition of claim 10 wherein the inhibitory oligonucleotide is a chemically modified siRNA compound.

12. The composition of claim 11 wherein the chemically modified siRNA compound inhibits expression of a target gene associated with cancer, fibrosis or macrophage associated disease.

13. The composition of claim 12 wherein the chemically modified siRNA compound inhibits expression of a human target gene set forth in Table A.

14. The composition of claim 2 wherein the moiety is attached to the antibody or antigen-binding fragment.

15. The composition of claim 4 wherein the moiety is encapsulated within the lipid particle.

16. A method of delivering a moiety to an ENDO180 expressing cell in a subject comprising administering to the subject a composition of any one of claims 2-15 such that the therapeutic agent is delivered to the cell.

17. Use of a composition of any one of claims 8-15 method for treating a subject afflicted with cancer, fibrosis or macrophage associated disease.

18. A method of inhibiting the growth of a cancer cell expressing ENDO180 comprising contacting the cell with a composition of any one of claims 2-15 thereby inhibiting growth of the cancer cell.

19. The method of claim 16 or 17, wherein the composition is administered systemically or locally.

20. The method of claim 19, wherein the composition is administered intravenously.

21. The hybridoma cell line E3-8D8, deposited with the BCCM with Accession Number LMBP 7203CB.

22. An isolated anti-ENDO180 antibody or antigen-binding fragment thereof secreted by the hybridoma cell line of claim 21.

23. An antibody or antibody or antigen-binding fragment thereof that binds to the same epitope as the antibody of claim 22.

24. An antibody or antigen-binding fragment thereof of claim 22 or 23 which is humanized.

25. An antibody or antibody or antigen-binding fragment thereof of claim 22 or 23 which is chimeric.

26. A conjugate comprising

a) the antibody or antibody or antigen-binding fragment of any one of claims 22-25;

b) a moiety selected from a detectable label, a cytotoxic agent and a therapeutic agent; and

c) optionally a linker which links a) to b).

27. The conjugate of claim 26, comprising a linker

28. The conjugate of claim 27, wherein the linker attaches the 3' terminus of the antibody or antigen-binding fragment to the moiety.

29. The conjugate of claim 27, wherein the linker is selected from a polypeptide linker, peptide linker, lipid linker or nucleic acid linker.

30. The conjugate of claim 29, wherein the linker is selected from protamine, a fragment of protamine, (Arg)9, biotin-avidin, and antennapedia peptide.

31. The conjugate of claim 29, wherein the linker is a nucleic acid linker.

32. The conjugate of claim 26 wherein the moiety is a therapeutic agent.

33. The conjugate of claim 27 wherein therapeutic agent is an inhibitory oligonucleotide.

34. The conjugate of claim 33 wherein the inhibitory oligonucleotide is selected from an antisense compound, a chemically modified siRNA compound, an unmodified siRNA compound, a chemically modified shRNA compound, an unmodified shRNA compound, a chemically modified miRNA compound, and an unmodified miRNA compound.

35. The conjugate of claim 34 wherein the inhibitory oligonucleotide is a chemically modified siRNA compound.

36. The conjugate of claim 35 wherein the chemically modified siRNA compound inhibits expression of a target gene associated with cancer, fibrosis or macrophage associated disease.

37. The conjugate of claim 36 wherein the chemically modified siRNA compound inhibits expression of a human target gene set forth in Table A.

38. A composition comprising the conjugate of any one of claims 26-37; and a carrier.

39. The composition of claim 38 wherein the carrier comprises a lipid particle, a polysaccharide particle or a combination thereof.

40. The composition of claim 39, wherein the lipid particle is a lipidated polysaccharide particle.

41. The composition of claim 40 wherein the carrier comprises a lipidated glycosaminoglycan.

42. A method of delivering a moiety to an ENDO180 expressing cell in a subject comprising administering to the subject a conjugate of claim 26 or composition of any one of claims 38-41 such that the moiety is delivered to the cell.

43. A method of treating a subject afflicted with cancer, fibrosis or macrophage associated disease, comprising administering to the subject a composition of any one of claims 38-41 in an amount effective to treat the subject.

44. An anti-ENDO180 antibody or antigen-binding fragment comprising heavy chain CDR3 fragment having an amino acid sequence set forth in SEQ ID NO:7.

45. The anti-ENDO180 antibody or antigen-binding fragment of claim 44 further comprising light chain CDR3 fragment having an amino acid sequence set forth in SEQ ID NO:8.

46. The antibody or antigen-binding fragment of claim 44 or 45 wherein the antibody or antigen-binding fragment is selected from the group consisting of a full IgG, a Fab fragment, a Fab' fragment, an F(ab')2 fragment, the variable portion of the heavy and/or light chains thereof, a Fab miniantibody, and a scFv.

47. The antibody or antigen-binding fragment of claim 46 wherein the antibody comprises a polypeptide sequence set forth in SEQ ID NO:5.

48. An isolated polynucleotide having SEQ ID NO:6 which encodes the polypeptide of claim 47.

49. An antibody or antibody or antigen-binding fragment thereof of claim 46 which is humanized.

50. An antibody or antibody or antigen-binding fragment thereof of claim 46 which is chimeric.

51. A conjugate comprising

a) the antibody or antibody or antigen-binding fragment of any one of claims 44-50;

b) a moiety selected from a detectable label, a cytotoxic agent and a therapeutic agent; and

c) optionally a linker which links a) to b).

52. The conjugate of claim 51, comprising a linker

53. The conjugate of claim 52, wherein the linker attaches the 3' terminus of the antibody or antigen-binding fragment to the moiety.

54. The conjugate of claim 53, wherein the linker is selected from a polypeptide linker, peptide linker, lipid linker or nucleic acid linker.

55. The conjugate of claim 54, wherein the linker is selected from protamine, a fragment of protamine, (Arg)9, biotin-avidin, and antennapedia peptide.

56. The conjugate of claim 54, wherein the linker is a nucleic acid linker.

57. The conjugate of claim 51 wherein the moiety is a therapeutic agent.

58. The conjugate of claim 57 wherein therapeutic agent is an inhibitory oligonucleotide.

59. The conjugate of claim 58 wherein the inhibitory oligonucleotide is selected from an antisense compound, a chemically modified siRNA compound, an unmodified siRNA compound, a chemically modified shRNA compound, an unmodified shRNA compound, a chemically modified miRNA compound, and an unmodified miRNA compound.

60. The conjugate of claim 59 wherein the inhibitory oligonucleotide is a chemically modified siRNA compound.

61. The conjugate of claim 60 wherein the chemically modified siRNA compound inhibits expression of a target gene associated with cancer, fibrosis or macrophage associated disease.

62. The conjugate of claim 61 wherein the chemically modified siRNA compound inhibits expression of a human target gene set forth in Table A.

63. A composition comprising the conjugate of any one of claims 51-62; and a carrier.

64. The composition of claim 63 wherein the carrier comprises a lipid particle, a polysaccharide particle or a combination thereof.

65. The composition of claim 64, wherein the lipid particle is a lipidated polysaccharide particle.

66. The composition of claim 65 wherein the carrier comprises a lipidated glycosaminoglycan.

67. A method of delivering a moiety to an ENDO180 expressing cell in a subject comprising administering to the subject a conjugate of claim 51 or a composition of any one of claims 63-66 such that the moiety is delivered to the cell.

68. A method of treating a subject afflicted with cancer, fibrosis or macrophage associated disease, comprising administering to the subject a composition of any one of claims 63-66 in an amount effective to treat the subject.

69. A method of delivering a therapeutic moiety to an ENDO180 expressing cell in a subject comprising administering to the subject a composition comprising

a) an anti-ENDO180 antibody or antigen binding fragment thereof;

b) a therapeutic moiety;

c) a carrier; and

d) optionally a linker that links a) to b);

such that the moiety is delivered to the cell.

70. The method of claim 69 wherein the subject is afflicted with a proliferative disease selected from cancer, fibrosis and a macrophage associated disease.

71. The method of claim 70 wherein the proliferative disease selected is cancer.

72. The method of claim 70 wherein the proliferative disease selected is fibrosis.

~~73. The method of any one of claims 67-72 wherein the carrier comprises a lipid particle, a~~ polysaccharide particle or a combination thereof.

74. The method of claim 73, wherein the lipid particle is a lipidated polysaccharide particle.

75. The method of claim 74 wherein the carrier comprises a lipidated glycosaminoglycan.

76. The method of claim 69 wherein therapeutic agent is an inhibitory oligonucleotide.

77. The method of claim 76 wherein the inhibitory oligonucleotide is selected from an antisense compound, a chemically modified siRNA compound, an unmodified siRNA compound, a chemically modified shRNA compound, an unmodified shRNA compound, a chemically modified miRNA compound, and an unmodified miRNA compound.

78. The method of claim 77 wherein the inhibitory oligonucleotide is a chemically modified siRNA compound.

79. The method of claim 78 wherein the chemically modified siRNA compound inhibits expression of a target gene associated with cancer, fibrosis or macrophage associated disease.

80. The method of claim 79 wherein the chemically modified siRNA compound inhibits expression of a human target gene set forth in Table A.