CLAIMS

What is claimed is:

1. A humanized antibody that specifically binds an EC1 domain of a mammalian Cadherin-11 protein and antagonizes said mammalian Cadherin-11 protein, comprising an antibody variable heavy chain region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67 and SEQ ID NO:69.

2. The humanized antibody of Claim 1, wherein the antibody inhibits one or more Cadherin-11-mediated activities selected from the group consisting of binding of the mammalian Cadherin-11 protein to one or more other Cadherin-11 proteins, aggregation of cells that express the mammalian Cadherin-11 protein, induction of enzyme expression, induction of cytokine expression, induction of growth factor expression, migration of cells expressing the mammalian Cadherin-11 protein and destruction of cartilage.

3. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:69.

4. The humanized antibody of Claim 1, wherein the antibody comprises an antibody variable light chain region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:71, SEQ ID NO:73, and SEQ ID NO:75.

5. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:61 and the antibody variable light chain region comprises SEQ ID NO:71.

6. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:61 and the antibody variable light chain region comprises SEQ ID NO:73.

7. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:61 and the antibody variable light chain region comprises SEQ ID NO:75.

8. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:63 and the antibody variable light chain region comprises SEQ ID NO:71.

9. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:63 and antibody variable light chain region comprises SEQ ID NO:73.

10. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:63 and the antibody variable light chain region comprises SEQ ID NO:75.

11. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:65 and the antibody variable light chain region comprises SEQ ID NO:71.

12. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:65 and the antibody variable light chain region comprises SEQ ID NO:73.

13. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:65 and the antibody variable light chain region comprises SEQ ID NO:75.

14. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:67 and the antibody variable light chain region comprises SEQ ID NO:71.

15. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:67 and the antibody variable light chain region comprises SEQ ID NO:73.

16. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:67 and the antibody variable light chain region comprises SEQ ID NO:75.

17. The humanized antibody of Claim 4, wherein the antibody variable light chain region comprises SEQ ID NO:71.

18. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:69 and the antibody variable light chain region comprises SEQ ID NO:73.

19. The humanized antibody of Claim 4, wherein the antibody variable heavy chain region comprises SEQ ID NO:69 and the antibody variable light chain region comprises SEQ ID NO:75.

20. The humanized antibody of Claim 1, wherein the antibody binds an epitope that is present in SEQ ID NO:3.

21. The humanized antibody of Claim 1, wherein the antibody binds an epitope that is present in SEQ ID NO:10.

22. The humanized antibody of Claim 1, wherein the antibody binds an epitope that comprises SEQ ID NO:11.

23. The humanized antibody of Claim 1, wherein the antibody is a whole antibody.

24. The humanized antibody of Claim 1, wherein the antibody is an antibody fragment.

25. The humanized antibody of Claim 24, wherein the antibody fragment is selected from the group consisting of an Fab, an Fab', an $F(ab')_2$ and an scFv.

26. A humanized antibody that specifically binds an EC1 domain of a mammalian Cadherin-11 protein and antagonizes said mammalian Cadherin-

11 protein, comprising an antibody variable heavy chain region comprising SEQ ID NO:69 and an antibody variable light chain region comprising SEQ ID NO:71.

27. The humanized antibody of Claim 26, wherein the antibody inhibits one or more Cadherin-11-mediated activities selected from the group consisting of binding of the mammalian Cadherin-11 protein to one or more other Cadherin-11 proteins, aggregation of cells that express the mammalian Cadherin-11 protein, induction of enzyme expression, induction of cytokine expression, induction of growth factor expression, migration of cells expressing the mammalian Cadherin-11 protein and destruction of cartilage.

28. The humanized antibody of Claim 26, wherein the antibody is a whole antibody.

29. The humanized antibody of Claim 26, wherein the antibody is an antibody fragment.

30. The humanized antibody of Claim 29, wherein the antibody fragment is selected from the group consisting of an Fab, an Fab', an $F(ab')_2$ and an scFv.

31. A pharmaceutical composition comprising a humanized antibody that specifically binds an EC1 domain of a mammalian Cadherin-11 protein and antagonizes said mammalian Cadherin-11 protein, and a pharmaceutically-acceptable carrier, wherein the antibody comprises an antibody variable heavy chain region comprising SEQ ID NO:69 and antagonizes said mammalian Cadherin-11 protein.

32. The pharmaceutical composition of Claim 31, wherein the antibody comprises an antibody variable light chain region comprising SEQ ID NO:71.

33. The pharmaceutical composition of Claim 31, wherein the antibody inhibits aggregation of cells that express said mammalian Cadherin-11.

34. The pharmaceutical composition of Claim 31 , wherein the antibody is a whole antibody.

35. The pharmaceutical composition of Claim 31, wherein the antibody is an antibody fragment.

36. The pharmaceutical composition of Claim 31 , further comprising a disease-modifying anti-rheumatic drug.

37. The pharmaceutical composition of Claim 36, wherein the disease-modifying anti-rheumatic drug is methotrexate.

38. The pharmaceutical composition of Claim 31, further comprising an anti-inflammatory agent.

39. The pharmaceutical composition of Claim 38, wherein the anti-inflammatory agent is an NSA1D or a steroid.

40. An isolated nucleic acid encoding the humanized antibody of Claim 1.

41. The isolated nucleic acid of Claim 40, wherein said nucleic acid is present in a vector.

42. An isolated cell expressing the humanized antibody of Claim 1.

43. A humanized antibody that specifically binds an EC 1 domain of a mammalian Cadherin- 1 1 protein for use in the treatment of a Cadherin-1 1 -mediated disorder in a mammalian subject, wherein the antibody comprises an antibody variable heavy chain region comprising SEQ ID NO:69 and antagonizes said mammalian Cadherin-1 1 protein.

44. The antibody of claim 43, wherein aggregation of cells that express said mammalian Cadherin-1 1 protein is inhibited in one or more joints of said subject.

45. The antibody of claim 43, wherein the antibody comprises an antibody variable light chain region comprising SEQ ID NO:71.

46. The antibody of claim 43, wherein the antibody is a whole antibody.

47. The antibody of claim 43, wherein the antibody is an antibody fragment.

48. The antibody of claim 43, wherein the Cadherin-1 1 -mediated disorder is selected from the group consisting of an inflammatory disorder, a fibrosis, and a cancer.

49. The antibody of claim 43, wherein the Cadherin-1 1 -mediated disorder is an inflammatory joint disorder selected from the group consisting of rheumatoid arthritis, psoriatic arthritis, Reiter's syndrome, ankylosing spondylitis, juvenile chronic arthritis, chronic Lyme disease and joint arthritis associated with systemic lupus erythrematosus.

50. The antibody of Claim 43, for use in the treatment of a Caherin-11-mediated disorder in a human.

51. The antibody of Claim 43, for use in the treatment of a Caherin-11-mediated disorder in a mammalian subject, wherein the antibody is administered systemically to said subject.

52. The antibody of Claim 43, for use in the treatment of a Caherin-11-mediated disorder in a mammalian subject, wherein the antibody is administered intravenously to said subject.

53. The antibody of Claim 43, for use in the treatment of a Caherin-11-mediated disorder in a mammalian subject, wherein the antibody is administered by direct injection into a joint of said subject.

54. The antibody of claim 43, wherein the antibody inhibits migration, adhesion, invasion into cartilage, or intercellular signaling of cells that express said mammalian Cadherin-11 protein in one or more joints of said subject.

55. The antibody of claim 43, wherein the antibody inhibits induction of expression or activity of an enzyme selected from the group consisting of a collagenase, a serine protease, and a matrix metalloproteinase in cells that express said mammalian Cadherin-1 1 protein in one or more joints of said subject.

56. The antibody of claim 43, wherein the antibody inhibits induction of expression or activity of a cytokine or growth factor selected from the group consisting of a IL-6, IL-8, RANKL and TRANCE in cells that express said mammalian Cadherin-1 1 protein in one or more joints of said subject.

57. The antibody of Claim 43, for use in the treatment of a Caherin-11-mediated disorder in a mammalian subject, wherein the antibody is administered to said subject in combination with at least one agent selected from the group consisting of a disease-modifying anti-rheumatic drug and an anti-inflammatory agent.

58. Use of a humanized antibody for the treatment of a Cadherin-1 1 -mediated disorder in a mammalian subject in need thereof, wherein the antibody specifically binds an ECI domain of a mammalian Cadherin-1 1 protein and comprises an antibody variable heavy chain region comprising SEQ ID NO:69.

59. The use of Claim 58, wherein the Cadherin-1 1-mediated disorder is an inflammatory disorder.

60. The use of Claim 59, wherein the inflammatory disorder is an inflammatory joint disorder.

61 . The use of Claim 60, wherein the inflammatory joint disorder is rheumatoid arthritis.

62. The use of Claim 58, wherein the Cadherin-11-mediated disorder is fibrosis.

63. The use of Claim 58, wherein the Cadherin-1 1-mediated disorder is cancer.

64. Use of a humanized antibody in the manufacture of a medicament for the treatment of a Cadherin-1 1 -mediated disorder in a mammalian subject, wherein the antibody specifically binds an EC 1 domain of a mammalian Cadherin- 1 1 protein, comprises an antibody variable heavy chain region comprising SEQ ID NO:69 and antagonizes said mammalian Cadherin-1 1 protein.

65. The use of claim 64, wherein aggregation of cells that express said mammalian Cadherin-1 1 protein is inhibited in one or more joints of said subject.

66. The use of claim 64, wherein the antibody comprises an antibody variable light chain region comprising SEQ ID NO:71.

67. The use of claim 64, wherein the antibody is a whole antibody.

68. The use of claim 64, wherein the antibody is an antibody fragment.

69. The use of claim 64, wherein the Cadherin-1 1 -mediated disorder is selected from the group consisting of an inflammatory disorder, a fibrosis, and a cancer.

70. The use of claim 64, wherein the Cadherin-1 1 -mediated disorder is an inflammatory joint disorder selected from the group consisting of rheumatoid arthritis, psoriatic arthritis, Reiter's syndrome, ankylosing spondylitis, juvenile chronic arthritis, chronic Lyme disease and joint arthritis associated with systemic lupus erythrematosus.

71. The use of claim 64, wherein the antibody inhibits migration, adhesion, invasion into cartilage, or intercellular signaling of cells that express said mammalian Cadherin-11 protein in one or more joints of said subject.

72. The use of claim 64, wherein the antibody inhibits induction of expression or activity of an enzyme selected from the group consisting of a collagenase, a serine protease, and a matrix metalloproteinase in cells that express said mammalian Cadherin-1 1 protein in one or more joints of said subject.

73. The use of claim 64, wherein the antibody inhibits induction of expression or activity of a cytokine or growth factor selected from the group consisting of a IL-6, IL-8, RANKL and TRANCE in cells that express said mammalian Cadherin-1 1 protein in one or more joints of said subject.

CLAIMS

What is claimed is:

1. A humanized antibody that specifically binds an EC1 domain of a mammalian Cadherin-11 protein and antagonizes said mammalian Cadherin-11 protein, comprising an antibody variable heavy chain region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:65, SEQ ID NO:67 and SEQ ID NO:69, and an antibody variable light chain region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:71, SEQ ID NO:73, and SEQ ID NO:75.

2. The humanized antibody of Claim 1, wherein the antibody inhibits one or more Cadherin-11-mediated activities selected from the group consisting of binding of the mammalian Cadherin-11 protein to one or more other Cadherin-11 proteins, aggregation of cells that express the mammalian Cadherin-11 protein, induction of enzyme expression, induction of cytokine expression, induction of growth factor expression, migration of cells expressing the mammalian Cadherin-11 protein and destruction of cartilage.

3. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:69.

4. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:61 and the antibody variable light chain region comprises SEQ ID NO:71.

5. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:61 and the antibody variable light chain region comprises SEQ ID NO:73.

6. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:61 and the antibody variable light chain region comprises SEQ ID NO:75.

7. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:63 and the antibody variable light chain region comprises SEQ ID NO:71.

8. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:63 and antibody variable light chain region comprises SEQ ID NO:73.

9. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:63 and the antibody variable light chain region comprises SEQ ID NO:75.

10. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:65 and the antibody variable light chain region comprises SEQ ID NO:71.

11. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:65 and the antibody variable light chain region comprises SEQ ID NO:73.

12. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:65 and the antibody variable light chain region comprises SEQ ID NO:75.

13. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:67 and the antibody variable light chain region comprises SEQ ID NO:71.

14. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:67 and the antibody variable light chain region comprises SEQ ID NO:73.

15. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:67 and the antibody variable light chain region comprises SEQ ID NO:75.

16. The humanized antibody of Claim 1, wherein the antibody variable light chain region comprises SEQ ID NO:71.

17. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:69 and the antibody variable light chain region comprises SEQ ID NO:73.

18. The humanized antibody of Claim 1, wherein the antibody variable heavy chain region comprises SEQ ID NO:69 and the antibody variable light chain region comprises SEQ ID NO:75.

19. The humanized antibody of Claim 1, wherein the antibody binds an epitope that is present in SEQ ID NO:3.

20. The humanized antibody of Claim 1, wherein the antibody binds an epitope that is present in SEQ ID NO:10.

21. The humanized antibody of Claim 1, wherein the antibody binds an epitope that is present in SEQ ID NO:11.

22. The humanized antibody of Claim 1, wherein the antibody is a whole antibody.

23. The humanized antibody of Claim 1, wherein the antibody is an antibody fragment.

24. The humanized antibody of Claim 23, wherein the antibody fragment is selected from the group consisting of an Fab, an Fab', an $F(ab')_2$ and an scFv.

25. A humanized antibody that specifically binds an EC1 domain of a mammalian Cadherin-11 protein and antagonizes said mammalian Cadherin-11 protein, comprising an antibody variable heavy chain region comprising SEQ ID NO:69 and an antibody variable light chain region comprising SEQ ID NO:71.

26. The humanized antibody of Claim 25, wherein the antibody inhibits one or more Cadherin-11-mediated activities selected from the group consisting of binding of the mammalian Cadherin-11 protein to one or more other Cadherin-11 proteins, aggregation of cells that express the mammalian Cadherin-11 protein, induction of enzyme expression, induction of cytokine expression, induction of growth factor expression, migration of cells expressing the mammalian Cadherin-11 protein and destruction of cartilage

27. The humanized antibody of Claim 25, wherein the antibody is a whole antibody.

28. The humanized antibody of Claim 25, wherein the antibody is an antibody fragment.

29. The humanized antibody of Claim 28, wherein the antibody fragment is selected from the group consisting of an Fab, an Fab', an $F(ab')_2$ and an scFv.

30. A pharmaceutical composition comprising a humanized antibody that specifically binds an EC1 domain of a mammalian Cadherin-11 protein and antagonizes said mammalian Cadherin-11 protein, and a pharmaceutically-acceptable carrier, wherein the antibody comprises an antibody variable heavy chain region comprising SEQ ID NO:69 and an antibody variable light chain region comprising SEQ ID NO:71, and antagonizes said mammalian Cadherin-11 protein.

31. The pharmaceutical composition of Claim 30, wherein the antibody inhibits aggregation of cells that express said mammalian Cadherin-11.

32. The pharmaceutical composition of Claim 30, wherein the antibody is a whole antibody.

33. The pharmaceutical composition of Claim 30, wherein the antibody is an antibody fragment.

34. The pharmaceutical composition of Claim 30, further comprising a disease-modifying anti-rheumatic drug.

35. The pharmaceutical composition of Claim 34, wherein the disease-modifying anti-rheumatic drug is methotrexate.

36. The pharmaceutical composition of Claim 30, further comprising an anti-inflammatory agent.

37. The pharmaceutical composition of Claim 36, wherein the anti-inflammatory agent is an NSAID or a steroid.

38. An isolated nucleic acid encoding the humanized antibody of Claim 1.

39. The isolated nucleic acid of Claim 38, wherein said nucleic acid is present in a vector.

40. An isolated cell expressing the humanized antibody of Claim 1.

41. A humanized antibody that specifically binds an EC1 domain of a mammalian Cadherin-11 protein for use in the treatment of a Cadherin-11-mediated disorder in a mammalian subject, wherein the antibody comprises an antibody variable heavy chain region comprising SEQ ID

NO:69 and an antibody variable light chain region comprising SEQ ID NO:71, and antagonizes said mammalian Cadherin-11 protein.

42. The antibody of Claim 41, wherein aggregation of cells that express said mammalian Cadherin-11 protein is inhibited in one or more joints of said subject.

43. The antibody of claim 41, wherein the antibody is a whole antibody.

44. The antibody of claim 41, wherein the antibody is an antibody fragment.

45. The antibody of claim 41, wherein the Cadherin-1 1 -mediated disorder is selected from the group consisting of an inflammatory disorder, a fibrosis, and a cancer.

46. The antibody of claim 41, wherein the Cadherin-1 1 -mediated disorder is an inflammatory joint disorder selected from the group consisting of rheumatoid arthritis, psoriatic arthritis, Reiter's syndrome, ankylosing spondylitis, juvenile chronic arthritis, chronic Lyme disease and joint arthritis associated with systemic lupus erythrematosus.

47. The antibody of Claim 41, for use in the treatment of a Caherin-11- mediated disorder in a human.

48. The antibody of Claim 41, for use in the treatment of a Caherin-11- mediated disorder in a mammalian subject, wherein the antibody is administered systematically to said subject.

49. The antibody of Claim 41, for use in the treatment of a Caherin-11-mediated disorder in a mammalian subject, wherein the antibody is administered intravenously to said subject.

50. The antibody of Claim 41, for use in the treatment of a Caherin-11-mediated disorder in a mammalian subject, wherein the antibody is administered by direct injection into a joint of said subject.

51. The antibody of claim 41, wherein the antibody inhibits migration, adhesion, invasion into cartilage, or intercellular signaling of cells that express said mammalian Cadherin-11 protein in one or more joints of said subject.

52. The antibody of claim 41, wherein the antibody inhibits induction of expression or activity of an enzyme selected from the group consisting of a collagenase, a serine protease, and a matrix

metalloproteinase in cells that express said mammalian Cadherin-1 1 protein in one or more joints of said subject.

53. The antibody of claim 41, wherein the antibody inhibits induction of expression or activity of a cytokine or growth factor selected from the group consisting of a IL-6, IL-8, RANKL and TRANCE in cells that express said mammalian Cadherin-1 1 protein in one or more joints of said subject.

54. The antibody of Claim 41, for use in the treatment of a Caherin-11-mediated disorder in a mammalian subject, wherein the antibody is administered to said subject in combination with at least one agent selected from the group consisting of a disease-modifying anti-rheumatic drug and an anti-inflammatory agent.

55. Use of a humanized antibody for the treatment of a Cadherin-11-mediated disorder in a mammalian subject in need thereof, wherein the antibody specifically binds an EC1 domain of a mammalian Cadherin-11 protein and comprises an antibody variable heavy chain region comprising SEQ ID NO:69 and an antibody variable light chain region comprising SEQ ID NO:71.64

56. The use of Claim 55, wherein the Cadherin-1 1-mediated disorder is an inflammatory disorder.

57. The use of Claim 56, wherein the inflammatory disorder is an inflammatory joint disorder.

58. The use of Claim 57, wherein the inflammatory joint disorder is rheumatoid arthritis.

59. The use of Claim 55, wherein the Cadherin-11-mediated disorder is fibrosis.

60. The use of Claim 55, wherein the Cadherin-1 1-mediated disorder is cancer.

61. Use of a humanized antibody in the manufacture of a medicament for the treatment of a Cadherin-11-mediated disorder in a mammalian subject, wherein the antibody specifically binds an EC 1 domain of a mammalian Cadherin-11 protein, comprises an antibody variable heavy chain region comprising SEQ ID NO:69 and an antibody variable light chain region comprising SEQ ID NO:71, and antagonizes said mammalian Cadherin-11 protein.

62. The use of claim 61, wherein aggregation of cells that express said mammalian Cadherin-1 1 protein is inhibited in one or more joints of said subject.

63. The use of claim 61, wherein the antibody is a whole antibody.

64. The use of claim 61, wherein the antibody is an antibody fragment.

65. The use of claim 61, wherein the Cadherin-1 1 -mediated disorder is selected from the group consisting of an inflammatory disorder, a fibrosis, and a cancer.

66. The use of claim 61, wherein the Cadherin-1 1 -mediated disorder is an inflammatory joint disorder selected from the group consisting of rheumatoid arthritis, psoriatic arthritis, Reiter's syndrome, ankylosing spondylitis, juvenile chronic arthritis, chronic Lyme disease and joint arthritis associated with systemic lupus erythrematosus.

67. The use of claim 61, wherein the antibody inhibits migration, adhesion, invasion into cartilage, or intercellular signaling of cells that express said mammalian Cadherin-11 protein in one or more joints of said subject.

68. The use of claim 61, wherein the antibody inhibits induction of expression or activity of an enzyme selected from the group consisting of a collagenase, a serine protease, and a matrix metalloproteinase in cells that express said mammalian Cadherin-1 1 protein in one or more joints of said subject.

69. The use of claim 61, wherein the antibody inhibits induction of expression or activity of a cytokine or growth factor selected from the group consisting of a IL-6, IL-8, RANKL and TRANCE in cells that express said mammalian Cadherin-1 1 protein in one or more joints of said subject.