

CLAIMS

What is claimed is:

1. A method of inhibiting T cell-mediated pulmonary inflammation in a subject that has asthma comprising, administering to a subject an anti-CD6 antibody, or an antigen binding fragment thereof, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises heavy and light chain variable regions comprising amino acid sequences as set forth in SEQ ID NOs: 1 and 2.
2. A method of inhibiting T cell-mediated pulmonary inflammation in a subject that has asthma comprising, administering to a subject an anti-CD6 antibody, or an antigen binding fragment thereof.
3. A method of preventing or attenuating the migration of a T cell into and through a pulmonary tissue in response to an asthma-inducing antigen comprising, administering to a subject an anti-CD6 antibody, or an antigen binding fragment thereof.
4. A method of modulating or attenuating a symptom or the severity of asthma comprising, administering to a subject an anti-CD6 antibody, or an antigen binding fragment thereof.
5. A method of modulating or attenuating a symptom or the severity of asthma comprising, contacting a T-cell with an anti-CD6 antibody, or an antigen binding fragment thereof.
6. The method of any one of the preceding claims, wherein the asthma is severe asthma.
7. The method of any one of the preceding claims, wherein the asthma is characterized by low or no blood eosinophils.

8. The method of any one of the preceding claims, wherein the asthma is refractory to steroid treatment.
9. The method of any one of the preceding claims, wherein the asthma is a neutrophilic asthma.
10. The method of any one of claims 1-8, wherein the asthma is a mixed inflammation asthma.
11. The method of any one of claims 1-8, wherein the asthma is paucigranulocytic.
12. The method of any one of the preceding claims, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, binds to a CD6 protein on the surface of a T cell.
13. The method of claim 12, wherein the T cell is a Th1, Th17, or a Th1 and Th17 T cell.
14. The method of any one of the preceding claims, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, is EQ001, or an antigen binding fragment of EQ001.
15. The method of any one of claims 2-13, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, binds to domain 1 or 3 on CD6.
16. The method of any one of claims 1-13, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, binds to domain 3 on CD6.
17. The method of any one of the preceding claims, wherein the binding of the anti-CD6 antibody, or the antigen binding fragment thereof, to the CD6 protein on the surface of a T cell modulates the activity and/or migration of the T cell.

18. The method of any one of the preceding claims, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, is a humanized antibody.
19. The method of any one of claims 2-13, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, is selected from the group consisting of: UMCD6 mAb, Itolizumab (EQ001), an anti-CD6 antibody described on Table 2, and an anti-CD6 antibody disclosed herein.
20. The method of any one of claims 2-13, wherein the anti-CD6 monoclonal antibody is an antibody produced by secreting hybridoma IOR-T1A deposited with the ECACC as deposit No. ECACC 96112640; an antibody having the same sequence as said antibody produced by said secreting hybridoma; or an antibody having the same CDR sequences of said antibody produced by said secreting hybridoma.
21. The method of any one of claims 2-20, comprising administering an antigen binding fragment of the anti-CD6 monoclonal antibody EQ001.
22. The method of claim 21, wherein the antigen binding fragment is selected from an Fv, Fab, CDR1, CDR2, CDR3, combination of CDRs, variable region, heavy chain(s), and light chain(s).
23. The method of any one of claims 2-13, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises one or more CDR sequence selected from SEQ ID NOS: 5-10.
24. The method of any one of claims 2-13, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises heavy and light chain variable regions comprising amino acid sequences as set forth in SEQ ID NOS: 1 and 2.

25. The method of claim 1 or 24, wherein SEQ ID NOs: 1 and 2 are encoded by SEQ ID NOs: 3 and 4 respectively.
26. The method of any one of claims 2-13, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises a VH sequence that is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 1.
27. The method of any one of claims 2-13, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises a VK sequence that is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 2.
28. The method of any one of claims 2-13, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises a VH sequence that is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 1 and a VK sequence that is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 2.
29. The method of any one of the preceding claims, wherein the method further comprises administering one or more additional agent capable of treating, preventing, or attenuating one or more asthma related symptom.
30. The method of claim 29, wherein the additional agent comprises an agent that is capable of modulating the immune system.
31. The method of any one of claims 29-30, wherein the additional agent comprises an agent that is immunosuppressant.
32. The method of any one of claims 29-30, wherein the additional agent comprises a long-acting beta agonist, a short-acting beta agonist, or a combination thereof.

33. The method of any one of claims 29-32, wherein the additional agent comprises albuterol.
34. The method of claim 33, wherein the albuterol is administered in a dosage form selected from: an aerosol powder; a solution; a capsule; and a powder suspension.
35. The method of any one of claims 29-34, wherein the additional agent comprises a corticosteroid.
36. The method of claim 35, wherein the corticosteroid is administered as an inhaled formulation.
37. The method of claim 36, wherein the corticosteroid is administered in a dosage form selected from a tablet, a delayed release capsule; an extended release tablet; an extended release capsule; a syrup; a solution; an elixir; a suspension; a delayed release tablet; a liquid; and a disintegrating tablet.
38. The method of any one of claims 29-37, wherein the additional agent comprises Ipratropium.
39. The method of claim 38, wherein the Ipratropium is administered in a spray dosage form.
40. The method of any one of the preceding claims, wherein the method further comprises administration of intubation, mechanical ventilation, and/or oxygen therapy.
41. The method of any one of the preceding claims, wherein the anti-CD6 antibody, or antigen binding fragment thereof, is administered as a pharmaceutical composition comprising one or more pharmaceutically acceptable salts, excipients or vehicles.

42. The method of claim 41, wherein the composition comprises one or more agent selected from the group consisting of carriers, excipients, diluents, antioxidants, preservatives, coloring, flavoring and diluting agents, emulsifying agents, suspending agents, solvents, fillers, bulking agents, buffers, delivery vehicles, tonicity agents, cosolvents, wetting agents, complexing agents, buffering agents, antimicrobials, and /or surfactants.
43. A method of inhibiting T cell-mediated pulmonary inflammation in a subject that has asthma comprising, administering to a subject an anti-CD6 antibody, or an antigen binding fragment thereof, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises heavy and light chain variable regions comprising amino acid sequences as set forth in SEQ ID NOs: 1 and 2, and wherein the asthma is characterized by low or no blood eosinophils.
44. The method of claim 43, wherein the asthma is resistant or refractory to steroid treatment.
45. The method of claim 43 or 44, wherein the asthma is a neutrophilic asthma.
46. The method of claim 43 or 44, wherein the asthma is a mixed inflammation asthma.
47. The method of claim 43 or 44, wherein the asthma is paucigranulocytic.
48. The method of any one of claims 43-47, wherein the T cell is selected from (i) a Th1 T cell, (ii) a Th17 T cell, or (iii) a Th1 and Th17 T cell.
49. The method of any one of claims 43-48, wherein the subject has blood eosinophils counts ≤ 300 cells/ μ l.
50. The method of any one of claims 43-49, wherein the subject has a non-allergic asthma.

51. The method of any one of claims 43-50, wherein the anti-CD6 antibody is EQ001.
52. A method of inhibiting T cell-mediated pulmonary inflammation in a subject that has asthma comprising, administering to a subject an anti-CD6 antibody, or an antigen binding fragment thereof, wherein the asthma is characterized by low or no blood eosinophils.
53. A method of preventing or attenuating the migration of a T cell into and through a pulmonary tissue in response to an asthma-inducing antigen, wherein the asthma is characterized by low or no blood eosinophils, comprising administering to a subject an anti-CD6 antibody, or an antigen binding fragment thereof.
54. A method of modulating or attenuating a symptom or the severity of asthma comprising, administering to a subject an anti-CD6 antibody, or an antigen binding fragment thereof when the asthma is characterized by low or no blood eosinophils.
55. A method of modulating or attenuating a symptom or the severity of asthma, comprising contacting a T-cell with an anti-CD6 antibody, or an antigen binding fragment thereof, wherein the asthma is characterized by low or no blood eosinophils.
56. The method of any one of claims 52-55, wherein the asthma is resistant or refractory to steroid treatment.
57. The method of any one of claims 52-56, wherein the asthma is a neutrophilic asthma.
58. The method of any one of claims 52-55, wherein the asthma is a mixed inflammation asthma.
59. The method of any one of claims 52-55, wherein the asthma is paucigranulocytic.

60. The method of any one of claims 52-59, wherein the T cell is selected from (i) a Th1 T cell, (ii) a Th17 T cell, or (iii) a Th1 and Th17 T cell.
61. The method of any one of claims 52-60, wherein the subject has blood eosinophils counts ≤ 300 cells/ μ l.
62. The method of any one of claims 52-61, wherein the subject has a non-allergic asthma.
63. The method of any one of claims 52-62, wherein the asthma is severe asthma.
64. The method of any one of claims 52-63, wherein the asthma is severe asthma.
65. The method of any one of claims 52-63, wherein the anti-CD6 antibody or an antigen binding fragment thereof is EQ001 or an antigen binding fragment thereof.
66. The method of any one of claims 52-63, wherein the anti-CD6 antibody is EQ001.
67. The method of any one of claims 52-63, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, binds to domain 1 or 3 on CD6.
68. The method of any one of claims 52-63, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, binds to domain 3 on CD6.
69. The method of any one of claims 52-63, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, is selected from the group consisting of: UMCD6 mAb, Itolizumab (EQ001), an anti-CD6 antibody described on Table 2, and an anti-CD6 antibody disclosed herein.

70. The method of any one of claims 52-63, wherein the anti-CD6 monoclonal antibody is an antibody produced by secreting hybridoma IOR-T1A deposited with the ECACC as deposit No. ECACC 96112640; an antibody having the same sequence as said antibody produced by said secreting hybridoma; or an antibody having the same CDR sequences of said antibody produced by said secreting hybridoma.

71. The method of any one of claims 52-63, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises one or more CDR sequence selected from SEQ ID NOS: 5-10.

72. The method of any one of claims 52-63, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises heavy and light chain variable regions comprising amino acid sequences as set forth in SEQ ID NOS: 1 and 2.

73. The method of claims 72, wherein SEQ ID NOS: 1 and 2 are encoded by SEQ ID NOS: 3 and 4 respectively.

74. The method of any one of claims 52-63, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises a VH sequence that is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 1.

75. The method of any one of claims 52-63, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises a VK sequence that is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 2.

76. The method of any one of claims 52-63, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, comprises a VH sequence that is at least 80% identical to the amino

acid sequence as set forth in SEQ ID NO: 1 and a VK sequence that is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 2.

77. The method of any one of claims 52-76, wherein the antigen binding fragment is selected from an Fv, Fab, CDR1, CDR2, CDR3, combination of CDRs, variable region, heavy chain(s), and light chain(s).

78. The method of any one of claims 52-77, wherein the anti-CD6 antibody, or the antigen binding fragment thereof, binds to a CD6 protein on the surface of a T cell.

79. The method of any one of claims 52-78, wherein the binding of the anti-CD6 antibody, or the antigen binding fragment thereof, to the CD6 protein on the surface of a T cell modulates the activity and/or migration of the T cell.

80. The method of any one of claims 52-79, wherein the method further comprises administering one or more additional agent capable of treating, preventing, or attenuating one or more asthma related symptom.

81. The method of claim 80, wherein the additional agent comprises an agent that is capable of modulating the immune system.

82. The method of claim 80 or 81, wherein the additional agent comprises an agent that is immunosuppressant.

83. The method of any one of claims 80-82, wherein the additional agent comprises a long-acting beta agonist, a short-acting beta agonist, or a combination thereof.

84. The method of any one of claims 80-83, wherein the additional agent comprises albuterol.
85. The method of claim 84, wherein the albuterol is administered in a dosage form selected from: an aerosol powder; a solution; a capsule; and a powder suspension.
86. The method of any one of claims 80-82, wherein the additional agent comprises a corticosteroid.
87. The method of claim 86, wherein the corticosteroid is administered as an inhaled formulation.
88. The method of claim 80, wherein the additional agent comprises Ipratropium.
89. The method of claim 88, wherein the Ipratropium is administered in a spray dosage form.
90. The method of any one of claims 80-89, wherein the method further comprises administration of intubation, mechanical ventilation, and/or oxygen therapy.
91. The method of any one of claims 80-90, wherein the anti-CD6 antibody, or antigen binding fragment thereof, is administered as a pharmaceutical composition comprising one or more pharmaceutically acceptable salts, excipients or vehicles.
92. The method of claim 91, wherein the composition comprises one or more agent selected from the group consisting of carriers, excipients, diluents, antioxidants, preservatives, coloring, flavoring and diluting agents, emulsifying agents, suspending agents, solvents, fillers, bulking agents, buffers, delivery vehicles, tonicity agents, cosolvents, wetting agents, complexing agents, buffering agents, antimicrobials, and /or surfactants.