

WHAT IS CLAIMED:

1. ~~An isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising a heavy chain variable region (VH) complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:22, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:23, a VH CDR3 comprising the amino acid sequence of SEQ ID NO:24, a light chain variable region (VL) CDR1 comprising the amino acid sequence of SEQ ID NO:25, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:26, 27, or 28, and a VL CDR3 sequence comprising the amino acid sequence of SEQ ID NO:29.~~
2. ~~The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising the amino acid sequence of SEQ ID NO:6, 7, or 8.~~
3. ~~The antibody or antigen-binding fragment thereof of claim 1 or claim 2, wherein the antibody or antigen-binding fragment thereof comprises a VL comprising the amino acid sequence of SEQ ID NO:9, 10, or 11.~~
4. ~~An isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:6, 7, or 8.~~
5. ~~An isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises the amino acid sequence of SEQ ID NO:9, 10, or 11.~~

6. ~~An isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, comprising a heavy chain variable region and a light chain variable region comprising the amino acid sequences of:~~
- ~~(a) — SEQ ID NOs:6 and 9, respectively;~~
 - ~~(b) — SEQ ID NOs:6 and 10, respectively;~~
 - ~~(c) — SEQ ID NOs:6 and 11, respectively;~~
 - ~~(d) — SEQ ID NOs:7 and 9, respectively;~~
 - ~~(e) — SEQ ID NOs:7 and 10, respectively;~~
 - ~~(f) — SEQ ID NOs:7 and 11, respectively;~~
 - ~~(g) — SEQ ID NOs:8 and 9, respectively;~~
 - ~~(h) — SEQ ID NOs:8 and 10, respectively; or~~
 - ~~(i) — SEQ ID NOs:8 and 11, respectively.~~
7. ~~The antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the antibody or antigen-binding fragment further comprises a heavy chain constant region.~~
8. ~~The antibody or antigen-binding fragment thereof of claim 7, wherein the heavy chain constant region is a murine IgG₁- or IgG_{2a}-heavy chain constant region.~~
9. ~~The antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein the antibody or antigen-binding fragment further comprises a light chain constant region.~~
10. ~~The antibody or antigen-binding fragment thereof of claim 9, wherein the light chain constant region is a murine IgGκ light chain constant region.~~
11. ~~The antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:16, 17, 18, 89, 90, or 91.~~
12. ~~The antibody or antigen-binding fragment thereof of any one of claims 1-6 or 11, wherein the antibody or antigen-binding fragment thereof comprises a light chain comprising the amino acid sequence of SEQ ID NO:19, 30, or 31.~~

13. ~~The antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the antibody or antigen-binding fragment comprises a heavy chain and a light chain comprising the amino acid sequences of:~~
- ~~(a) — SEQ ID NOs:16 and 19, respectively;~~
 - ~~(b) — SEQ ID NOs:16 and 30, respectively;~~
 - ~~(c) — SEQ ID NOs:16 and 31, respectively;~~
 - ~~(d) — SEQ ID NOs:17 and 19, respectively;~~
 - ~~(e) — SEQ ID NOs:17 and 30, respectively;~~
 - ~~(f) — SEQ ID NOs:17 and 31, respectively;~~
 - ~~(g) — SEQ ID NOs:18 and 19, respectively;~~
 - ~~(h) — SEQ ID NOs:18 and 30, respectively;~~
 - ~~(i) — SEQ ID NOs:18 and 31, respectively;~~
 - ~~(j) — SEQ ID NOs: 89 and 19, respectively;~~
 - ~~(k) — SEQ ID NOs: 90 and 19, respectively; or~~
 - ~~(l) — SEQ ID NOs: 91 and 19, respectively.~~
14. ~~An isolated antibody or antigen-binding fragment thereof that specifically binds to human B7-H4, wherein the antibody or antigen-binding fragment thereof comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of an antibody selected from the group consisting of J512, J513, J514, J515, J516, J517, J518, J519, J520, J521, and J522.~~
15. ~~The antibody or antigen-binding fragment thereof of claim 14, wherein the CDRs are the Kabat-defined CDRs, the Chothia-defined CDRs, or the AbM-defined CDRs.~~
16. ~~An isolated antibody or antigen-binding fragment thereof that specifically binds to the same epitope of human B7-H4 as the antibody or antigen-binding fragment thereof of any one of claims 1-15.~~
17. ~~An isolated antibody or antigen-binding fragment thereof that competitively inhibits binding of the antibody or antigen-binding fragment thereof of any one of claims 1-15 to human B7-H4.~~

18. ~~The antibody or antigen binding fragment thereof of any one of claims 1-17, wherein the antibody or antigen binding fragment thereof is a murine antibody or antigen binding fragment thereof.~~
19. ~~The antibody or antigen binding fragment thereof of any one of claims 1-18, which is a full length antibody.~~
20. ~~The antibody or antigen binding fragment thereof of any one of claims 1-18, which is an antigen binding fragment.~~
21. ~~The antigen binding fragment of claim 20, wherein the antigen binding fragment comprises a Fab, Fab', F(ab')₂, single chain Fv (scFv), disulfide linked Fv, minibody, F(ab')₃, diabody, (scFv)₂, or scFv-Fc.~~
22. ~~The antibody or antigen binding fragment thereof of any one of claims 1-21, further comprising a detectable label.~~
23. ~~An isolated polynucleotide comprising a nucleic acid molecule encoding the heavy chain variable region or heavy chain of the antibody or antigen binding fragment thereof of any one of claims 1-22.~~
24. ~~The isolated polynucleotide of claim 23, wherein the nucleic acid molecule encodes the VH of SEQ ID NO:6, 7, or 8 or the heavy chain of SEQ ID NO:16, 17, or 18.~~
25. ~~The isolated polynucleotide of claim 24, wherein the nucleic acid molecule comprises the sequence of SEQ ID NO:12, 13, 14, 93, 94, or 95.~~
26. ~~An isolated polynucleotide comprising a nucleic acid molecule encoding the light chain variable region or light chain of the antibody or antigen binding fragment thereof of any one of claims 1-22.~~

- ~~27. The isolated polynucleotide of claim 26, wherein the nucleic acid molecule encodes the VL of SEQ ID NO:9, 10, or 11 or the light chain of SEQ ID NO:19, 30, or 31.~~
- ~~28. The isolated polynucleotide of claim 27, wherein the nucleic acid molecule comprises the sequence of SEQ ID NO:15, 96, or 97.~~
- ~~29. An isolated polynucleotide comprising a nucleic acid molecule encoding the heavy chain variable region or heavy chain of the antibody or antigen binding fragment thereof of any one of claims 1-22 and the light chain variable region or light chain of the antibody or antigen binding fragment thereof of any one of claims 1-22.~~
- ~~30. An isolated vector comprising the polynucleotide of any one of claims 23-29.~~
- ~~31. A host cell comprising the polynucleotide of any one of claims 23-29, the vector of claim 30, or a first vector comprising the polynucleotide of any one of claims 23-25 and a second vector comprising the polynucleotide of any one of claims 26-28.~~
- ~~32. The host cell of claim 31, which is a CHO or HEK cell.~~
- ~~33. A method of producing an antibody or antigen binding fragment thereof that specifically binds to human B7-H4 comprising culturing the host cell of claim 31 or 32 so that the nucleic acid molecule is expressed and the antibody or antigen binding fragment thereof is produced.~~
- ~~34. An isolated antibody or antigen binding fragment thereof that specifically binds to human B7-H4 and is encoded by the polynucleotide of any one of claims 23-29.~~
- ~~35. A method for detecting B7-H4 in a sample comprising contacting the sample with the antibody or antigen binding fragment thereof of any one of claims 1-22 or 34, optionally wherein the method further comprises detecting binding of the antibody or antigen binding fragment thereof to B7-H4.~~

36. ~~The method of claim 35, wherein the sample is obtained from a cancer in a subject.~~
37. ~~The method of claim 36, further comprising administering a therapeutic anti B7-H4 antibody or antigen-binding fragment thereof to the subject after B7-H4 has been detected.~~
38. ~~A method of treating a B7-H4 expressing cancer in a subject, the method comprising administering to the subject a therapeutic anti B7-H4 antibody or antigen-binding fragment thereof, wherein B7-H4 expression was detected in a sample obtained from the subject using the antibody or antigen-binding fragment thereof of any one of claims 1-21 or 33.~~
39. ~~The method of claim 38, further comprising detecting the B7-H4 in the sample obtained from the cancer.~~
40. ~~The method of any one of claims 35-39, wherein the detected B7-H4 is cell membrane B7-H4.~~
41. ~~The method of any one of claims 35-39, wherein the detected B7-H4 is cytoplasmic B7-H4.~~
42. ~~The method of any one of claims 35-39, wherein B7-H4 is detected in whole cells.~~
43. ~~The method of any one of claims 35-42, wherein the B7-H4 is detected on circulating tumor cells.~~
44. ~~The method of any one of claims 35-43, wherein the sample is solid tissue, biopsy, ascites, blood plasma, serum, lymph fluid, or a tumor from a subject.~~
45. ~~The method of any one of claims 36-44, wherein the cancer is selected from the group consisting of breast cancer, ductal carcinoma, endometrial carcinoma, ovarian cancer,~~

non-small cell lung cancer, pancreatic cancer, thyroid cancer, kidney cancer and bladder cancer.

46. — The method of claim 45, wherein the breast cancer is triple negative breast cancer or wherein the non-small cell lung cancer is squamous cell carcinoma.
47. — The method of any one of claims 35-46, wherein the method of detection uses an enzyme linked immunosorbent assay (ELISA), a fluorescence activated cell sorter (FACS) assay, or immunohistochemistry (IHC).
48. — The method of claim 47, wherein the method of detection uses IHC and the concentration of the antibody or antigen binding fragment thereof of any one of claims 1-21 or 34 is about 1 to about 50 µg/ml.
49. — The method of claim 48, wherein the concentration of the antibody or antigen binding fragment thereof is about 1 to about 20 µg/ml.
50. — The method of claim 49, wherein the concentration of the antibody or antigen binding fragment thereof is about 10 µg/mL.
51. — The method of any one of claims 47-50, wherein the method of detection uses IHC and 3,3'-diaminobenzidine (DAB) is used for detection
52. — The method of any one of claims 36-51, wherein the subject is human.
53. — A kit comprising the antibody or antigen binding fragment thereof of any one of claims 1-21 or 34 and a) a detection reagent, b) a B7-H4 antigen, c) a therapeutic anti-B7-H4 antibody, or d) a combination of any of (a) through (c).

54. ~~The method or kit of any one of claims 37-53, wherein the therapeutic antibody or antigen-binding fragment comprises the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 of 20502 or 22213.~~
55. ~~The method or kit of claim 54, wherein the CDRs are the Kabat-defined CDRs, the Chothia-defined CDRs, or the AbM-defined CDR.~~
56. ~~The method or kit of claim 55, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequences of SEQ ID NOs:32-37, respectively or the amino acid sequences of SEQ ID NOs:58-63, respectively.~~
57. ~~The method or kit of any one of claims 37-56, wherein the therapeutic antibody or antigen-binding fragment comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:54 or SEQ ID NO:64.~~
58. ~~The method or kit of any one of claims 37-56, wherein the therapeutic antibody or antigen-binding fragment comprises a heavy chain variable region and a light chain variable region, wherein the light chain variable region comprises the amino acid sequence of SEQ ID NO:55 or SEQ ID NO:65.~~
59. ~~The method or kit of any one of claims 37-56, wherein the therapeutic antibody or antigen-binding fragment comprises (i) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:54 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:55 or (ii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:64 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:65.~~
60. ~~The method or kit of any one of claims 37-56, wherein the therapeutic antibody or antigen-binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:56 or SEQ ID NO:74.~~

61. ~~The method or kit of any one of claims 37-56, wherein the therapeutic antibody or antigen-binding fragment thereof comprises a light chain comprising the amino acid sequence of SEQ ID NO:57 or SEQ ID NO:75.~~
62. ~~The method or kit of any one of claims 37-56, wherein the therapeutic antibody or antigen-binding fragment thereof comprises (i) a heavy chain comprising the amino acid sequence of SEQ ID NO:56 and a light chain comprising the amino acid sequence of SEQ ID NO:57 or (ii) a heavy chain comprising the amino acid sequence of SEQ ID NO:74 and a light chain comprising the amino acid sequence of SEQ ID NO:75.~~

Claims

1. An invention not claimed in any divisional application.