[0004i] In one aspect, provided herein is a chimeric antigen receptor (CAR) comprising the antibody fragment as described herein.

[0004j] In one aspect, provided herein is a modified immune cell, comprising a chimeric antigen receptor (CAR), wherein said CAR comprises the CAR as described herein.

[0004k] In one aspect, provided herein is a plurality of modified immune cells as described herein.

[0004l] In one aspect, provided herein is a use of the isolated monoclonal antibody as described herein, the modified immune cell(s) as described herein, or the ADC as described herein in the manufacture of a medicament for inhibiting the growth of a cell that displays a GPC3 epitope that is specifically recognized by the antibody as described herein.

[0004m] In one aspect, provided herein is a composition comprising a therapeutically effective amount of the isolated monoclonal antibody as described herein, the modified immune cell(s) as described herein, or the ADC as described herein, and a pharmaceutically acceptable carrier.

[0004n] In one aspect, provided herein is a use of the composition as described herein in the manufacture of a medicament for treating a selected subject having a cancer that expresses GPC3.

[0004o] In one aspect, provided herein is a use of the antibody as described herein in the preparation of a medicament for the treatment of cancer.

[0004p] In one aspect, provided herein is a use of the modified immune cell(s) as described herein in the preparation of a medicament for the treatment of cancer.

[0004q] In one aspect, provided herein is a use of the ADC as described herein in the preparation of a medicament for the treatment of cancer.

[0004r] In one aspect, provided herein is a use of the CAR as described herein in the preparation of a medicament for the treatment of cancer.

[0004s] In one aspect, provided herein is a composition as described herein, the antibody as described herein, the modified immune cell(s) as described herein, the ADC as described herein, or the CAR as described herein for use in therapy.

[0005] In one embodiment, anti-GPC3 antibodies of the invention bind to a GPC3 epitope that is positioned in a C-terminal beta chain of GPC3. In one embodiment, the anti-GPC3 antibody comprises a heavy chain variable region comprising SEQ ID NO: 2 and a light chain variable region comprising SEQ ID NO: 4.

[0006] In one embodiment, the heavy chain of an anti-GPC3 antibody of the present invention comprises a complementary determining region (CDR) 1 set forth as SEQ ID NO: 6, a CDR2 set forth as SEQ ID NO: 8, and a CDR3 set forth as SEQ ID NO: 10.

[0007] In one embodiment, the light chain of an anti-GPC3 antibody of the present invention comprises a CDR1 set forth as SEQ ID NO: 13, a CDR2 set forth as SEQ ID NO: 15, and a CDR3 set forth as SEQ ID NO: 17.

[0008] In one embodiment, the heavy chain of an anti-GPC3 antibody of the present invention comprises a complementary determining region (CDR) 1 set forth as SEQ ID NO: 6, a CDR2 set forth as SEQ ID NO: 8, and a CDR3 set forth as SEQ ID NO: 10, and the light chain of the an anti-GPC3 antibody of the present invention comprises a CDR1 set forth as SEQ ID NO: 13, a CDR2 set forth as SEQ ID NO: 15, and a CDR3 set forth as SEQ ID NO: 17.

[0009] In one embodiment, the heavy chain of an anti-GPC3 antibody comprises a CDR1, a CDR2, and a CDR3, respectively set forth as amino acid residues 31-35, 50-66, and 99-105 of SEQ ID NO: 2, and the light chain of the antibody comprises a CDR1, a CDR2, and a CDR3 respectively set forth as amino acid residues 24-34, 50-56, and 89-97 of SEQ ID NO: 4.

[0010] In one embodiment, the invention provides an anti-GPC3 antibody that competes with an antibody comprising a heavy chain variable region comprising SEQ ID NO:2 and a light chain variable region comprising SEQ ID NO: 4 for binding to GPC3.

[0011] Anti-GPC3 antibodies of the invention include, for example, monoclonal antibodies, antibody fragments, including Fab, Fab', F(ab')2, and Fv fragments, diabodies, single domain antibodies, chimeric antibodies, humanized antibodies, single-chain antibodies and antibodies that competitively inhibit the binding of an antibody comprising a heavy chain variable region comprising SEQ ID NO:2 and a light chain variable region comprising SEQ ID NO:4 to the GPC3.

What is claimed is:

1. An isolated monoclonal antibody that binds glypican-3 (GPC3), wherein:

the heavy chain of the anti-GPC3 antibody comprises a complementary determining region (CDR) 1 set forth as SEQ ID NO: 6, a CDR2 set forth as SEQ ID NO: 8, and a CDR3 set forth as SEQ ID NO: 10, and the light chain of the antibody comprises a CDR1 set forth as SEQ ID NO: 13, a CDR2 set forth as SEQ ID NO: 15, and a CDR3 set forth as SEQ ID NO: 17.

2. The isolated monoclonal antibody of claim 1, wherein:

The heavy chain of the antibody comprises a CDR1, a CDR2, and a CDR3, respectively set forth as amino acid residues 31-35, 50-66, and 99-105 of SEQ ID NO: 2, and the light chain of the antibody comprises a CDR1, a CDR2, and a CDR3 respectively set forth as amino acid residues 24-34, 50-56, and 89-97 of SEQ ID NO: 4.

3. The isolated monoclonal antibody of claim 1, wherein the heavy chain of the antibody comprises SEQ ID NO: 2, and the light chain of the antibody comprises SEQ ID NO: 4.

4. The isolated monoclonal antibody of claim 1, wherein the antibody comprises:

(i) a variable heavy (VH) domain comprising the amino acid sequence of SEQ ID NO: 2; and

(ii) a variable light (VL) domain comprising the amino acid sequence of SEQ ID NO: 4.

5. The isolated monoclonal antibody of any one of claims 1-4, wherein the antibody is a chimeric or humanized antibody.

6. The isolated monoclonal antibody of any one of claims 1-5, wherein the antibody is a bispecific antibody.

7. The isolated monoclonal antibody of any one of claims 1-5, wherein the antibody is an antibody fragment.

8. The isolated monoclonal antibody of claim 7, wherein the antibody is a Fab fragment, a Fab' fragment, a $F(ab)'_2$ fragment, a single chain variable fragment (scFv), or a disulfide stabilized variable fragment (dsFv).

9. A method of detecting GPC3 in a tissue preparation, the method comprising:

contacting the tissue preparation with the isolated monoclonal antibody of claim 1 under conditions sufficient for formation of a complex of the isolated monoclonal antibody of claim 1 with GPC3 present on the cell membrane of cells of the tissue preparation; and

detecting binding of the antibody to the tissue preparation.

10. The method of claim 9, wherein the tissue preparation comprises a hepatocellular carcinoma (HCC), melanoma, squamous cell carcinoma of the lung, Merkel cell carcinoma, or ovarian clear cell carcinoma tumor biopsy.

11. The method of claim 9, wherein the monoclonal antibody is directly labeled.

12. The method of claim 9, further comprising:

contacting a second antibody that specifically binds the monoclonal antibody with the tissue preparation; and

detecting the binding of the second antibody.

13. The method of any one of claims 9-12, wherein detecting the binding of the antibody to the tissue sample further comprises scoring an amount of the complex detected.

14. The method of claim 13, wherein said scoring is done by a pathologist.

15. The method of claim 13, wherein said detecting the presence of the complex is done via digitization; and

wherein said scoring is automated based on the digitization of the detected complex.

16. The method of any one of claims 13-15, wherein said scoring further comprises determining a staining intensity of the complex detected via immunohistochemistry using an integer scale from 0 (negative) to 3+, recording the percentage of positively stained cells at each intensity level, and calculating a membrane-associated H-score based on the percentage of positively stained cells at each intensity level.

17. A method for predicting a therapeutic effect of an anti-GPC3 immunotherapy on a cancer, the cancer characterized in that cells of the cancer express GPC3, the method comprising:

detecting the presence of said cells in a subject via the method of any one of claims 9-16, wherein when the complex of the anti-GPC3 antibody with GPC3 expressed on the membrane of the cancer cells is detected, the anti-GPC3 immunotherapy is predicted to have a therapeutic effect on the cancer in the subject.

18. The method of claim 17, wherein the method of predicting the therapeutic effect is conducted prior to the subject having received any anti-GPC3 immunotherapy.

19. The method of claim 17, wherein the method of predicting the therapeutic effect is conducted while the subject is already in the process of receiving the anti-GPC3 immunotherapy.

20. The method of claim 17, wherein the anti-GPC3 immunotherapy comprises a chimeric antigen receptor (CAR) T cell therapy, or CAR NK cell therapy, wherein the CAR is designed to specifically recognize membrane-bound GPC3.

21. The method of claim 17, wherein the anti-GPC3 immunotherapy comprises an anti-GPC3 antibody.

22. An isolated nucleic acid molecule encoding the monoclonal antibody of claim 1.

23. The isolated nucleic acid molecule of claim 22, wherein:

a nucleotide sequence encoding the heavy chain of the monoclonal antibody comprises SEQ ID NO: 1 and a nucleotide sequence encoding the light chain of the antibody comprises SEQ ID NO: 3.

24. An expression vector comprising the isolated nucleic acid molecule of claim 22 or claim 23.

25. An isolated host cell transformed with the expression vector of claim 24.

26. A bispecific antibody, comprising the monoclonal antibody of claim 1.

27. An antibody-drug conjugate (ADC), comprising the isolated monoclonal antibody of claim 1.

28. A chimeric antigen receptor (CAR) comprising the antibody fragment of claim 7 or claim 8.

29. A modified immune cell, comprising a chimeric antigen receptor (CAR), wherein said CAR comprises the CAR of claim 28.

30. The modified immune cell of claim 29, wherein the modified immune cell is a modified T cell.

31. The modified immune cell of claim 30, wherein the modified immune cell is an αβ T cell.

32. The modified immune cell of claim 30, wherein the modified immune cell is a γδ T cell.

33. The modified immune cell of claim 29, wherein the modified immune cell is a modified NK cell.

34. A plurality of modified immune cells according to any one of claims 29-33.

35. Use of the isolated monoclonal antibody of claim 1, the modified immune cell(s) of any one of claims 29-34, or the ADC according to claim 27 in the manufacture of a medicament for inhibiting the growth of a cell that displays a GPC3 epitope that is specifically recognized by the antibody of claim 1.

36. A composition comprising a therapeutically effective amount of the isolated monoclonal antibody of any one of claims 1-6, the modified immune cell(s) of any one of claims 29-34, or the ADC of claim 27, and a pharmaceutically acceptable carrier.

37. Use of the composition according to claim 36 in the manufacture of a medicament for treating a selected subject having a cancer that expresses GPC3.

38. The use of claim 37, wherein the cancer is liver cancer, ovarian cancer, gastric cancer, Merkel cell carcinoma, or lung cancer.

39. Use of the antibody according to any one of claims 1-8 in the preparation of a medicament for the treatment of cancer.

40. Use of the modified immune cell(s) according to any one of claims 29-33 in the preparation of a medicament for the treatment of cancer.

41. Use of the ADC of claim 27 in the preparation of a medicament for the treatment of cancer.

42. Use of the CAR of claim 28 in the preparation of a medicament for the treatment of cancer.

43. The composition according to claim 36, the antibody according to any one of claims 1-8, the modified immune cell(s) according to any one of claims 29-33, the ADC of claim 27, or the CAR of claim 28 for use in therapy.