the antibody to the sample relative to a control sample detects cancer in the subject. In some embodiments, the methods further comprise contacting a second antibody that specifically recognizes the GPC3-specific antibody with the sample, and detecting binding of the second antibody.

Further provided is a method of treating a subject with cancer, for example HCC, melanoma, squamous cell carcinoma of the lung or ovarian clear cell carcinoma, by selecting a subject with a cancer that expresses GPC3 and administering to the subject a therapeutically effective amount of a monoclonal antibody specific for GPC3, or an immunoconjugate comprising the antibody.

Also provided is a method for inhibiting tumor growth in a subject by selecting a subject with a cancer that expresses GPC3 and administering to the subject a therapeutically effective amount of an antibody, immunoconjugate or composition disclosed herein.

Further provided is the use of a therapeutically effective amount of the composition as disclosed herein in the manufacture of a medicament for treating cancer in a subject with a cancer that expresses GPC3.

Further provided is the use of a therapeutically effective amount of the composition as disclosed herein in the manufacture of a medicament for inhibiting tumor growth or metastasis in a subject with a cancer that expresses GPC3 .

The foregoing and other objects, features, and advantages of the invention will become more apparent from the following detailed description, which proceeds with reference to the accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGS. 1A-1E: Discovery of new monoclonal antibodies to GPC3. (FIG. 1A) Schematic structure of GPC3. The human *GPC3* gene encodes a 70 kDa precursor protein of 580 amino acids. In the mature form at the cell membrane, a GPI anchor replaces the C-terminal signal (predicted cleavage site: S560). The core protein is held together by cysteine residues forming disulfide bridges. Heparan sulfate (HS) chains are attached to the polypeptide core. The immunization peptide corresponding to the C-terminal end of mature GPC3 is indicated. (FIG. 1B) High-throughput flow cytometry screening. Representative histograms obtained with positive (top panel) and negative supernatant (bottom panel). Each hybridoma was tested for GPC3-specific

mAb production by a simultaneous binding assay incorporating a 1:1 mixture of antigen-positive A431/G1 cells and antigen-negative A431 cells in a flow cytometry analysis. (FIG. 1C) Flow cytometry analysis of five selected mouse hybridoma clones (YP6, YP7, YP8, YP9 and YP9.1) (solid lines) and 1G12, a control anti-GPC3 mAb (dotted lines, in the middle) using A431/G1 and Hep3B. Filled peak: isotype control. (FIG. 1D) ELISA analysis of five hybridoma clones on recombinant GPC3 proteins. GPC3: recombinant GPC3-human Fc; GPC3ΔHS: recombinant GPC3 without HS; control: BSA; 1G12: a commercial anti-GPC3 mAb. (FIG. 1E) Western blot analysis

16. The isolated immunoconjugate of claim 15, wherein the toxin is PE38 comprising the amino acid sequence of SEQ ID NO: 1.

17. The isolated immunoconjugate of any one of claims 13-16, comprising the amino acid sequence of residues 2-597 of SEQ ID NO: 35, residues 2-597 of SEQ ID NO: 28, residues 2-597 of SEQ ID NO: 31, or residues 2-597 of SEQ ID NO: 33.

18. The isolated immunoconjugate of claim 13, wherein the effector molecule is a detectable label.

19. A composition comprising a therapeutically effective amount of the isolated immunoconjugate of any one of claims 13-18 in a pharmaceutically acceptable carrier.

20. ~~A method of treating a subject with cancer, comprising selecting a subject with a cancer that expresses GPC3 and administering to the subject~~ Use of a therapeutically effective amount of the composition of claim 12 or claim 19 in the manufacture of a medicament for~~, thereby~~ treating ~~the~~ cancer in ~~the~~ a subject with a cancer that expresses GPC3.

21. ~~A method of inhibiting tumor growth or metastasis, comprising selecting a subject with a cancer that expresses GPC3 and administering to the subject~~ Use of a therapeutically effective amount of the composition of claim 12 or claim 19 in the manufacture of a medicament~~, thereby~~for inhibiting tumor growth or metastasis in a subject with a cancer that expresses GPC3 .

22. A method of determining if a subject has cancer, or a method of confirming the diagnosis of cancer in a subject, comprising:

contacting a sample from the subject with the monoclonal antibody of any of claims 1-11; and

detecting binding of the antibody to the sample,

wherein an increase in binding of the antibody to the sample as compared to binding of the antibody to a control sample identifies the subject as having cancer, or confirms the diagnosis of cancer in the subject.

23. The method of claim 22, wherein the monoclonal antibody is directly labeled.