

CLAIMS:

1. An isolated monoclonal antibody or antigen-binding fragment thereof which binds to the MUC1 SEA domain, wherein said antibody comprises:
 - a. a heavy chain complementarity determining region (CDRH) 1 denoted by SEQ ID NO. 25, CDRH2 denoted by SEQ ID NO. 26, CDRH3 denoted by SEQ ID NO. 27, and a light chain complementarity determining region (CDRL) 1 denoted by SEQ ID NO. 28, a CDRL2 denoted by SEQ ID NO. 29, and a CDRL3 denoted by SEQ ID NO. 30; or
 - b. a heavy chain complementarity determining region (CDRH) 1 denoted by SEQ ID NO. 31, CDRH2 denoted by SEQ ID NO. 32, CDRH3 denoted by SEQ ID NO. 33, and the light chain complementarity determining region (CDRL) 1 denoted by SEQ ID NO. 34, a CDRL2 denoted by SEQ ID NO. 35, and a CDRL3 denoted by SEQ ID NO. 36; or
 - c. a heavy chain complementarity determining region (CDRH) 1 denoted by SEQ ID NO. 37, CDRH2 denoted by SEQ ID NO. 38, CDRH3 denoted by SEQ ID NO. 39, and the light chain complementarity determining region (CDRL) 1 denoted by SEQ ID NO. 40, a CDRL2 denoted by SEQ ID NO. 41, and a CDRL3 denoted by SEQ ID NO. 42; or
 - d. a heavy chain complementarity determining region (CDRH) 1 denoted by SEQ ID NO. 43, CDRH2 denoted by SEQ ID NO. 44, CDRH3 denoted by SEQ ID NO. 45, and the light chain complementarity determining region (CDRL) 1 denoted by SEQ ID NO. 46, a CDRL2 denoted by SEQ ID NO. 47, and a CDRL3 denoted by SEQ ID NO. 48; or
 - e. a heavy chain complementarity determining region (CDRH) 1 denoted by SEQ ID NO. 49, CDRH2 denoted by SEQ ID NO. 50, CDRH3 denoted by SEQ ID NO. 51, and the light chain complementarity determining region (CDRL) 1 denoted by SEQ ID NO. 52, a CDRL2 denoted by SEQ ID NO. 53, and a CDRL3 denoted by SEQ ID NO. 54; or
 - f. a heavy chain complementarity determining region (CDRH) 1 denoted by SEQ ID NO. 55, CDRH2 denoted by SEQ ID NO. 56, CDRH3 denoted by SEQ ID NO. 57, and the light chain complementarity determining region (CDRL) 1 denoted by SEQ ID NO. 58, a CDRL2 denoted by SEQ ID NO. 59, and a CDRL3 denoted by SEQ ID NO. 60.

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2. The isolated monoclonal antibody according to claim 1, wherein said antibody comprises a heavy chain variable region and a light chain variable region, wherein:
- a. said heavy chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to the nucleic acid sequence denoted by SEQ ID NO. 1 and wherein said light chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to SEQ ID NO. 2;
or
 - b. said heavy chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to the nucleic acid sequence denoted by SEQ ID NO. 3 and wherein said light chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to SEQ ID NO. 4;
or
 - c. said heavy chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to the nucleic acid sequence denoted by SEQ ID NO. 5 and wherein said light chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to SEQ ID NO. 6;
or
 - d. said heavy chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to the nucleic acid sequence denoted by SEQ ID NO. 7 and wherein said light chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to SEQ ID NO. 8;
or
 - e. said heavy chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to the nucleic acid sequence denoted by SEQ ID NO. 9 and wherein said light chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to SEQ ID NO. 10;
or
 - f. said heavy chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to the nucleic acid sequence denoted by SEQ ID NO. 11 and wherein said light chain variable region is encoded by a nucleic acid sequence which is at least 70% identical to SEQ ID NO. 12.

3. The isolated monoclonal antibody according to claim 1 or claim 2, wherein said antibody comprises:
 - a. a heavy chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 13 or a variant thereof and a light chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 14, or a variant thereof; or
 - b. a heavy chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 15 or a variant thereof and a light chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 16, or a variant thereof; or
 - c. a heavy chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 17 or a variant thereof and a light chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 18, or a variant thereof; or
 - d. a heavy chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 19 or a variant thereof and a light chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 20, or a variant thereof; or
 - e. a heavy chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 21 or a variant thereof and a light chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 22, or a variant thereof; or
 - f. a heavy chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 23 or a variant thereof and a light chain variable region comprising the amino acid sequence denoted by SEQ ID NO. 24, or a variant thereof.
4. The isolated monoclonal antibody or antigen-binding fragment thereof according to any one of the preceding claims, wherein said antibody is a mouse antibody, a chimeric antibody, a humanized antibody, or a human antibody.
5. The isolated monoclonal antibody or antigen-binding fragment thereof according to any one of the preceding claims, wherein said antigen-binding

fragment thereof is Fv, single chain Fv (scFv), single chain Fv-Fc (scFv-Fc), Fab', Fab, F(ab')₂ or F(ab)₂.

6. The isolated monoclonal antibody or antigen-binding fragment thereof according to any one of the preceding claims, wherein said antibody or antigen-binding fragment thereof identify MUC1 SEA in immunohistochemistry performed on formaldehyde fixed sections from Fresh Frozen (FF) tissues, and/or on Paraffin Embedded and Formaldehyde Fixed (PEFF) tissues, and/or by fluorescence-activated cell sorting (FACS) analysis of MUC1-expressing human cells.
7. An isolated nucleic acid molecule comprising a nucleotide sequence encoding an antibody or any antigen-binding fragment thereof according to any one of claims 1-6.
8. An expression vector comprising the isolated nucleic acid molecule according to claim 7.
9. A host cell transfected with the expression vector according to claim 8.
10. An immunoconjugate comprising the antibody or antigen-binding fragment thereof according to any one of claims 1-6 and an additional cytotoxic or therapeutic agent.
11. The immunoconjugate according to claim 10 wherein said cytotoxic agent is selected from a group consisting of alkylating drugs, anthracyclines, pyrimidine derivatives, vinca alkaloids, photodynamic drugs, platinum-containing compounds, taxanes, topoisomerase inhibitors, ribosome inactivating agents, agents that induce DNA damage, tubulin inhibitors, anti-mitotic agents, radioisotopes, cytotoxic antibodies and bacterial toxins.
12. The immunoconjugate according to claim 10 wherein said cytotoxic agent is pseudomonas exotoxin.
13. The immunoconjugate according to any one of claims 10 to 12, wherein said immunoconjugate reduces tumor volume upon administration to a subject with cancer.
14. A bispecific antibody comprising the antibody or antigen-binding fragment thereof according to any one of claims 1-6 and a second antibody binding a different antigen target.

15. A pharmaceutical composition comprising as an active ingredient the isolated monoclonal antibody or antigen-binding fragment thereof according to any one of claims 1-6, or immunoconjugate according to any one of claims 10 to 13, the bispecific antibody of claim 14 and a pharmaceutically acceptable carrier, excipient, or diluent.
16. The pharmaceutical composition according to claim 15, wherein said pharmaceutical composition further comprises an additional therapeutic agent.
17. A method of treatment or amelioration of a disease or disorder comprising administering to a subject in need thereof a therapeutically effective amount of at least one isolated monoclonal antibody or antigen-binding fragment thereof according to any one of claims 1-6, or the immunoconjugate according to any one of claims 10 to 13, the bispecific antibody of claim 14, or the pharmaceutical composition according to claim 15 or 16.
18. The method according to claim 17, wherein said disease or disorder is cancer.
19. The method according to claim 18, wherein said cancer is a MUC1 expressing cancer.
20. The method according to claim 18, wherein said cancer is selected from the group consisting of, lung carcinoma, prostate carcinoma, breast carcinoma, ovarian carcinoma, colon carcinoma, pancreatic carcinoma, multiple myeloma, and acute myelogenous leukemia.
21. The method according to claim 17, wherein said disease or disorder is an autoimmune or an inflammatory disease.
22. The method according to claim 21, wherein said autoimmune or inflammatory disease is selected from a group consisting of rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, amyloidosis, and autoimmune pancreatitis.
23. The method according to claim 17, wherein said disease or disorder is a non-malignant clinically significant abnormal growth condition, e.g., cysts, for example renal cysts, thyroid cysts and thyroid masses, or hepatic cysts.
24. The method according to any one of claims 17-23, wherein said method further comprises administering to a subject in need thereof an additional therapeutic agent.

25. The isolated monoclonal antibody or antigen-binding fragment thereof according to any one of claims 1-6, the immunoconjugate according to any one of claims 10 to 13, the bispecific antibody of claim 14, or the pharmaceutical composition according to claim 15 or 16 for use in a method of treatment or amelioration of a disease or disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of said isolated monoclonal antibody or antigen-binding fragment thereof, said immunoconjugate or said pharmaceutical composition.
26. The isolated monoclonal antibody or antigen-binding fragment thereof, or immunoconjugate, or bispecific antibody, or pharmaceutical composition for use according to claim 25, wherein said disease or disorder is cancer.
27. The isolated monoclonal antibody or antigen-binding fragment thereof, or immunoconjugate, or bispecific antibody, or pharmaceutical composition for use according to claim 25, wherein said disease or disorder is an autoimmune or an inflammatory disease, or wherein said disease or disorder is a non-malignant abnormal growth condition, e.g., cysts, for example renal cysts, thyroid cysts and thyroid masses, or hepatic cysts.
28. The isolated monoclonal antibody or antigen-binding fragment thereof, or immunoconjugate, or bispecific antibody or pharmaceutical composition for use according to any one of claims 25-27, wherein said method further comprises administering to a subject in need thereof an additional therapeutic agent.
29. A method of diagnosing a disease or disorder in a subject, wherein said disease or disorder is associated with MUC-1 expression, said method comprising:
 - a. contacting a biopsy obtained from said patient with at least one isolated monoclonal antibody or antigen-binding fragment thereof according to any one of claims 1-6; and
 - b. detecting said isolated monoclonal antibody or any antigen-binding fragment thereof;wherein detection of cells over-expressing MUC1 SEA in the biopsy indicates that the subject is diagnosed with said disease or disorder.
30. The method according to claim 29, wherein said disease or disorder is cancer.

31. The method according to claim 29, wherein said disease or disorder is an autoimmune or an inflammatory disease, or wherein said disease or disorder is a non-malignant abnormal growth condition, e.g., cysts, for example renal cysts, thyroid cysts and thyroid masses, or hepatic cysts.
32. The method of any one of claims 29-31 wherein said isolated monoclonal antibody or antigen-binding fragment thereof is detectably labelled.
33. A method of imaging of a disease or disorder, said method comprising:
 - a. introducing at least one isolated monoclonal antibody or antigen-binding fragment thereof according to any one of claims 1-6 into a subject, wherein said antibody or antigen-binding fragment thereof are detectably labelled with a radioisotope or a visualizable agent; and
 - b. visualizing said detectably-labelled isolated monoclonal antibody or any antigen-binding fragment thereof;wherein detection of cells and/or tissues labelled with said isotope or visualizable agent indicates the presence and/or the location and/or extent and/or the presence of metastases of said disease or disorder in said subject.
34. The method according to claim 33, wherein said disease or disorder is cancer.
35. The method according to claim 33, wherein said disease or disorder is an autoimmune or inflammatory disease, or wherein said disease or disorder is a non-malignant abnormal growth condition, e.g., cysts, for example renal cysts, thyroid cysts and thyroid masses, or hepatic cysts.