Claims

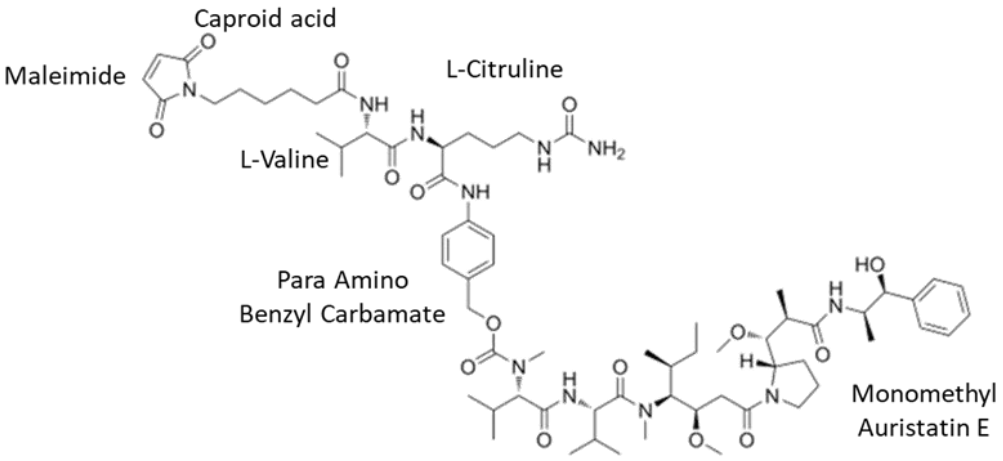
1. A humanized monoclonal antibody which binds to the MUC1 SEA domain, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO 11; and

a light chain variable region comprising the amino acid sequence of SEQ ID NO 15.

2. The humanized antibody of claim 1 , wherein the constant domain of the heavy chain comprises the amino acid sequence of SEQ ID NO: 39 and the constant domain of the light chain comprises the amino acid sequence of SEQ ID NO: 40.

3. A humanized monoclonal antibody which binds to the MUC1 SEA domain, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 37 and a light chain comprising the amino acid sequence of SEQ ID NO: 38, and optionally

, wherein the moiety



is conjugated through its maleimide terminus to the light chain of the humanized antibody.

4. The humanized monoclonal antibody of claim 3, wherein the heavy chain has the amino acid sequence of SEQ ID NO: 37 and a light chain has the amino acid sequence of SEQ ID NO: 38.

5. The humanized monoclonal antibody of any one of the preceding claims, wherein the 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. A humanized antibody that binds to an epitope in the MUC1 SEA domain, preferably with a binding affinity K_D less than 100 pM.

7. The humanized antibody of claim 6, wherein the humanized antibody comprises a means for binding an epitope in the SEA domain of MUC1 (SEQ ID NO: 41) formed from arginine at position 1108, glutamic acid at position 1109, asparagine at position 1113 and glutamic acid at position 1118 of MUC1, and/or wherein the humanized antibody binds to the same epitope as a chimeric antibody comprising a heavy chain variable region and a light chain variable region comprising the amino acid sequences of SEQ ID NOs: 1 and 2, respectively, and/or wherein the antibody is a humanized form of any one of chimeric antibodies DMB4F4 (4F4), DMB7F3 (7F3), or DMB10F10 (10F10).

8. A humanized antibody that binds to an epitope in the SEA domain of MUC1 (SEQ ID NO: 41) formed from arginine at position 1108, glutamic acid at position 1109, asparagine at position 1113 and glutamic acid at position 1118 of MUC1.

9. A humanized antibody that binds to the same epitope as a chimeric antibody comprising a heavy chain variable region and a light chain variable region comprising the amino acid sequences of SEQ ID NOs: 1 and 2, respectively.

10. An isolated nucleic acid molecule comprising a nucleotide sequence encoding an antibody of any one of the preceding claims.

11. An expression vector comprising the isolated nucleic acid molecule of claim 10.

12. A host cell transfected with the expression vector according to claim 11.

13. An immunoconjugate comprising the antibody of any one of claims 1-9 and an additional cytotoxic or therapeutic agent, and optionally, 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, or wherein said cytotoxic agent is pseudomonas exotoxin, or wherein said cytotoxic agent is monomethyl auristatin E (MMAE), and optionally wherein the antibody is conjugated to maleimidocaproyl-Val-Cit-PABC-MMAE.

14. An immunoconjugate comprising a humanized monoclonal antibody conjugated to maleimidocaproyl-Val-Cit-PABC-MMAE, where the antibody (i) binds to the MUC1 SEA domain and (ii) comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 37 and a light chain comprising the amino acid sequence of SEQ ID NO: 38.

15. The immunoconjugate according to any one of claims 13-14, wherein said immunoconjugate reduces tumor volume upon administration to a subject with cancer.

16. A pharmaceutical composition comprising (a) the humanized monoclonal antibody of any one of claim 1-9, the immunoconjugate of any one of claims 13-15, and (b) a pharmaceutically acceptable carrier, excipient, or diluent, optionally comprising an additional therapeutic agent.

17. Use of a therapeutically effective amount of at least one humanized monoclonal antibody of any one of claims 1-9, or the immunoconjugate of any one of claims 13-15, or the pharmaceutical composition of claim 16 in the manufacture of a medicament in the treatment and amelioration of a disease or disorder.

18. The use according to claim 17, wherein the disease or disorder is cancer, for example MUC1 expressing cancer, or wherein the cancer is selected from lung carcinoma, prostate carcinoma, breast carcinoma, ovarian carcinoma, colon carcinoma, pancreatic carcinoma, multiple myeloma, and acute myelogenous leukemia.

19. The use according to claim 17, wherein the disease or disorder is an autoimmune or an inflammatory disease, and optionally, wherein the autoimmune or inflammatory disease is selected from rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, amyloidosis, and autoimmune pancreatitis, or, wherein the disease or disorder is a non-malignant clinically significant abnormal growth condition.

20. The use according to any one of claims 17-19, wherein said medicament is adapted to be provided in combination with an additional therapeutic agent.

21. A method of diagnosing a disease or disorder in a subject, wherein the disease or disorder is associated with MUC-1 expression, the method comprising

(a) contacting a biopsy obtained from the patient with at least one monoclonal antibody of to any one of claims 1-9; and

(b) detecting the monoclonal antibody,

wherein detection of cells over-expressing MUC1 SEA in the biopsy indicates that the subject is diagnosed with the disease or disorder, and optionally wherein the disease or disorder is cancer or wherein the 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, and optionally wherein the monoclonal antibody is detectably labelled.

22. Use of at least one monoclonal antibody of any one of claims 1-9 in the manufacture of an imaging agent to image a disease or disorder, wherein the antibody is detectably labelled with a radioisotope or a visualizable agent in order to be visualized; and wherein the detection of cells and/or tissues labelled with the isotope or visualizable agent indicates the presence and/or the location and/or extent and/or the presence of metastases of the disease or disorder in the subject, and optionally wherein the disease or disorder is cancer or wherein the disease or disorder is an autoimmune or inflammatory disease, or wherein the 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.