CLAIMS

1. A humanized antibody or a fragment or derivative thereof which is capable of binding to a mucin protein and which comprises at least a portion of the heavy chain variable region which comprises a proline residue at amino acid position 28 according to the Kabat numbering; wherein

(i) the antibody or fragment or derivative thereof

(a) specifically binds the glycosylated MUC1 tumor epitope, and

(b) comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 16 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 28;

or wherein

(ii) the fragment or derivative of the antibody is a functional fragment or derivative of the antibody of (i) having the characteristics (a) and (b), said functional fragment or derivative

(a) showing cross-specificity with an antibody comprising the amino acid sequence of SEQ ID NO: 16 and SEQ ID NO: 28, and

(b) comprising an amino acid sequence which is at least 80% identical to the amino acid sequence of SEQ ID NO: 16, and an amino acid sequence which is at least 80% identical to the amino sequence of SEQ ID NO: 28; and

(c) being capable of binding to the glycosylated MUC1 tumor epitope with a lower dissociation constant than a fragment or derivative of an antibody which is identical to the functional fragment or derivative except that it does not comprise a proline residue at position 28, according to the Kabat numbering, of the heavy chain variable region.

2. The antibody or fragment or derivative thereof according to claim 1, having one or more of the following characteristics:

(a) the specific binding to its epitope is dependent on the conformation and/or the glycosylation pattern of the epitope;

(b) it is capable of specifically binding a peptide comprising the amino acid sequence PDTR;

(c) it is capable of specifically binding a peptide comprising the amino acid sequence PDTR, which is glycosylated at the threonine residue with N-acetyl galactosamine (Tn) or galactose ß1-3 N-acetyl galactosamine (TF);

(d) it is capable of specifically binding a peptide comprising the amino acid sequence PDTRP, wherein the binding is increased if the epitope is glycosylated at the threonine residue with N-acetyl galactosamine (Tn) or galactose β1-3N-acetyl galactosamine (TF);

(e) it specifically binds the glycosylated MUC1 tumor epitope such that the strength of the bond is increased at least by a factor 20 in comparison with the bond to the non-glycosylated peptide of identical length and identical peptide sequence.

3. The antibody or fragment or derivative thereof according to claim 1 or 2, wherein the functional fragment or derivative has one or more of the following characteristics:

(a) it comprises the complementarity determining regions,

(i) CDR1 having the amino acid sequence of SEQ ID NO: 1,

(ii) CDR2 having the amino acid sequence of SEQ ID NO: 3, and

(iii) CDR3 having the amino acid sequence of SEQ ID NO: 5;

(b) it comprises the antibody framework regions selected from the following:

(i) FRH1, FRH2, FRH3 and FRH4 for the variable heavy chain VH have the following amino acid sequences, the amino acid position corresponding to the numeration according to Kabat:

for FRH1 (SEQ ID NO: 7)

Pos.	Amino acid
1	E
2	V
3	Q or K
4	L
5	V
6	E
7	S
8	G
9	G
10	G
11	L
12	V
13	Q
14	P
15	G
16	G

17	S
18	L or M
19	R
20	L
21	S
22	C
23	A or V
24	A
25	S
26	G
27	F
28	P
29	F
30	S

for FRH2 (SEQ ID NO: 9)

Pos.	Amino acid
36	W
37	V
38	R
39	Q
40	A or S
41	P
42	G or E
43	K
44	G
45	L
46	E
47	W
48	V
49	G or A

for FRH3 (SEQ ID NO: 11)

Pos.	Amino acid
66	R
67	F

68	T
69	I
70	S
71	R
72	D
73	D
74	S
75	K
76	N or S
77	S
78	L or V
79	Y
80	L
81	Q
82	M
82a	N
82b	S
82c	L
83	K
84	T
85	E
86	D
87	T
88	A
89	V
90	Y
91	Y
92	C
93	T or A
94	R

for FRH4 (SEQ ID NO: 13)

Pos.	Amino acid
103	W
104	G
105	Q

106	G
107	T
108	L
109	V or L
110	T
111	V
112	S
113	S

(ii) and optionally FRL1, FRL2, FRL3 and FRL4 for the light chain variable region VL have the following amino acid sequences, the amino acid position corresponding to the numeration according to Kabat:

for FRL1 (SEQ ID NO: 23)

Pos.	Amino acid
1	D
2	I
3	V
4	M
5	T
6	Q
7	S
8	P
9	L
10	S
11	L or N
12	P
13	V
14	T
15	P
16	G
17	E or D
18	P
19	A
20	S
21	I
22	S

23	C

for FRL2 (SEQ ID NO: 24)

Pos.	Amino acid
35	W
36	Y
37	L
38	Q
39	K
40	P
41	G
42	Q
43	S
44	P
45	Q
46	L
47	L
48	I
49	Y

for FRL3 (SEQ ID NO: 25)

Pos.	Amino acid
57	G
58	V
59	P
60	D
61	R
62	F
63	S
64	G
65	S
66	G
67	S
68	G
69	T
70	D

71	F
72	T
73	L
74	K or R
75	I
76	S
77	R
78	V
79	E
80	A
81	E
82	D
83	V
84	G
85	V
86	Y
87	Y
88	C

for FRL4 (SEQ ID NO: 26)

Pos.	Amino acid
98	F
99	G
100	Q or G
101	G
102	T
103	K
104	V
105	E
106	I
107	K
108	R

(c) it comprises a framework region 1 comprising the amino acid sequence of SEQ ID NO: 7 or 8;

(d) it comprises a heavy chain variable region of an antibody comprising the amino acid sequence of SEQ ID NO: 15 or 16;

(e) it comprises a light chain variable region of an antibody comprising the amino acid sequence of SEQ ID NO: 27 or 28;

(f) it shows cross-specificity with the antibody Pankomab comprising the amino acid sequences of SEQ ID NO: 29 as heavy chain variable region and SEQ ID NO: 30 as light chain variable region.

4. The antibody or fragment or derivative thereof according to any one of claims 1 to 3, wherein said functional fragment or derivative comprises an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO: 16, and an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO: 28.

5. The antibody or fragment or derivative thereof according to claim 4, wherein said functional fragment or derivative comprises an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO: 16, and an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO: 28.

6. The antibody or fragment or derivative thereof according to claim 4 or 5, wherein the functional fragment or derivative comprises a heavy chain variable region comprising the following set of complementarity determining regions

(i) CDR1 having the amino acid sequence of SEQ ID NO: 1,

(ii) CDR2 having the amino acid sequence of SEQ ID NO: 3, and

(iii) CDR3 having the amino acid sequence of SEQ ID NO: 5.

7. The antibody or fragment or derivative thereof according to any one of claim 1 to 6, wherein the fragment or derivative of the antibody is selected from the group consisting of

(i) Fab fragments, monovalent fragments consisting of the variable region and the first constant domain of each the heavy and the light chain;

(ii) $F(ab)_2$ fragments, bivalent fragments comprising two Fab fragments linked by a disulfide bridge at the hinge region;

(iii) Fv fragments consisting of the heavy chain and light chain variable region of a single arm of an antibody;

(iv) scFv fragments, Fv fragments consisting of a single polypeptide chain;

(v) $(Fv)_2$ fragments consisting of two Fv fragments covalently linked together; and

(vi) multibodies consisting of a heavy chain variable region and a light chain variable region covalently linked together in such a manner that association of the heavy

chain and light chain variable regions can only occur intermolecular but not intramolecular.

8. The antibody or fragment or derivative thereof according to any one of claims 1 to 7, comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 16 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 28.

9. The antibody or fragment or derivative thereof according to any one of claim 1 to 8, having a glycosylation pattern which has one or more of the following characteristics:

(a) it is a human glycosylation pattern;

(b) it enhances the binding affinity of the antibody to its specific epitope, the binding affinity of the antibody to one or more of its downstream receptors, the complement dependent cytotoxicity (CDC) of the antibody, and/or the antibody-dependent cell-mediated cytotoxicity (ADCC) of the antibody; and/or

(c) it is a glycosylation pattern as obtained when expressing the antibody or fragment or derivative thereof in a cell line selected from the group consisting of K562, KG1, MUTZ-3, NM-F9 [DSM ACC2606], NM-D4 [DSM ACC2605], NM-H9D8 [DSM ACC 2806], NM-H9D8-E6 [DSM ACC 2807], NM H9D8-E6Q12 [DSM ACC 2856], and GT-2X [DSM ACC 2858].

10. The antibody or fragment or derivative thereof according to any one of claim 1 to 9, having an isotype selected from the group consisting of IgG, IgM, IgA, IgE and IgD.

11. A conjugate consisting of the antibody or fragment or derivative thereof according to any one of claims 1 to 10 coupled to a further agent.

12. The conjugate according to claim 11, wherein the further agent is selected from the group consisting of antibodies or fragments of antibodies, enzymes, interaction domains, stabilizing domains, signaling sequences, detectable labels, fluorescent dyes, toxins, catalytic antibodies, cytolytic components, immunomodulators, immunoeffectors, MHC class I or class II antigens, chelators for radioactive labeling, radioisotopes, liposomes, transmembrane domains, viruses, cells, agents capable of killing cancer cells, cytotoxic agents, radionuclides and cytotoxin.

13. An isolated nucleic acid encoding the antibody or fragment or derivative thereof according to any one of claims 1 to 10.

14. An expression cassette or vector comprising the nucleic acid according to claim 13 and a promoter operatively connected with said nucleic acid.

15. A host cell comprising the nucleic acid according to claim 13 or the expression cassette or vector according to claim 14.

16. A composition comprising the antibody or fragment or derivative thereof according to any one of claims 1 to 10, the conjugate according to claim 11 or 12, the nucleic acid according to claim 13, the expression cassette or vector according to claim 14, or the host cell according to claim 15.

17. The composition according to claim 16 being a pharmaceutical composition which further comprises one or more components selected from the group consisting of solvents, diluents, and excipients.

18. The antibody or fragment or derivative thereof according to any one of claims 1 to 10, the conjugate according to claim 11 or 12, or the composition according to claim 16 or 17 for use in medicine.

19. The antibody or fragment or derivative thereof according to any one of claims 1 to 10, the conjugate according to claim 11 or 12, or the composition according to claim 16 or 17 for use in the treatment, prognosis, diagnosis and/or monitoring of cancer.

20. The antibody or fragment or derivative thereof, conjugate or composition according to claim 19, wherein the cancer is selected from the group consisting of leukemias, seminomas, melanomas, teratomas, lymphomas, neuroblastomas, gliomas, rectal cancer, endometrial cancer, kidney cancer, adrenal cancer, thyroid cancer, blood cancer, skin cancer, cancer of the brain, cervical cancer, intestinal cancer, liver cancer, colon cancer, stomach cancer, intestine cancer, head and neck cancer, gastrointestinal cancer, lymph node cancer, esophagus cancer, colorectal cancer, pancreas cancer, ear, nose and throat (ENT) cancer, breast cancer, prostate cancer, cancer of the uterus, ovarian cancer and lung cancer.

21. A method for improving the antigen binding and/or recognition of an antibody or a fragment or derivative thereof which is capable of binding to a mucin protein and which comprises at least a portion of the heavy chain variable region, wherein the antibody or fragment or derivative thereof

(a) is capable of specifically binding a glycosylated MUC1 tumor epitope; and

(b) comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 28 or is a functional fragment or derivative thereof comprising an amino acid sequence which is at least 80% identical to the amino acid sequence of SEQ ID NO: 38, and an amino acid sequence which is at least 80% identical to the amino acid sequence of SEQ ID NO: 28;

comprising the step of providing a proline residue at position 28 of the heavy chain variable region, according to the Kabat numbering.

22. The method according to claim 19, having at least one or more of the following characteristics:

(a) the amino acid residue in position 28 is obtained by introducing a mutation into the nucleic acid coding for the antibody or fragment or derivative thereof, wherein the mutation is introduced in the codon coding for said amino acid residue;

(b) improving the antigen binding and/or antigen recognition includes enhancing the affinity of the antibody or fragment or derivative thereof to its antigen and/or increasing the specificity of the antibody or fragment or derivative thereof towards its antigen.

23. A method for preparing a nucleic acid according to claim 13, comprising the steps of

(a) providing a nucleic acid comprising the nucleic acid sequence coding for an antibody or a fragment or derivative thereof which is capable of binding to MUC1 and which comprises a heavy chain variable region, wherein the heavy chain variable region does not comprise a proline residue at amino acid position 28 according to the Kabat numbering;

(b) introducing a mutation into the codon coding for amino acid number 28, according to the Kabat numbering, of the heavy chain variable region so that said codon codes for a proline residue.

24. Use of the antibody or fragment or derivative thereof according to any one of claims 1 to 10, the conjugate according to claim 11 or 12, or the composition according to claim 16 or 17 in the manufacture of a medicament for the treatment prognosis, diagnosis and/or monitoring of cancer.

25. The use according to claim 24, wherein the cancer is selected from the group consisting of leukemias, seminomas, melanomas, teratomas, lymphomas, neuroblastomas, gliomas, rectal cancer, endometrial cancer, kidney cancer, adrenal cancer, thyroid cancer, blood cancer, skin cancer, cancer of the brain, cervical cancer, intestinal cancer, liver cancer, colon cancer, stomach cancer, intestine cancer, head and neck cancer, gastrointestinal cancer, lymph node cancer, esophagus cancer, colorectal cancer, pancreas cancer, ear, nose and throat (ENT) cancer, breast cancer, prostate cancer, cancer of the uterus, ovarian cancer and lung cancer.