

Claims

1. An antibody that binds to human MUC17 as depicted in SEQ ID NO: 1, wherein said antibody binds cell surface-associated MUC17 protein.
2. The antibody according to claim 1, wherein said antibody comprises a variable heavy chain comprising a CDR3 region depicted in SEQ ID NO: 4.
3. The antibody according to claim 1 or 2, wherein said antibody further comprises the heavy chain CDR1 and CDR2 regions as depicted in SEQ ID Nos: 2 and 3 and/or the light chain CDR1, CDR2 and/or CDR3 regions depicted in SEQ ID Nos: 6, 7, and 8.
4. The antibody according to any one of the preceding claims, wherein the antibody comprises a VH region and/or a VL region as comprised in SEQ ID Nos: 5 and/or 9.
5. The antibody according to any one of the preceding claims, wherein the antibody is a monoclonal antibody.
6. The antibody according to any one of the preceding claims, wherein the antibody specifically binds to human and cynomolgus monkey MUC17 when used in vitro in immunohistochemistry assays, to MUC17 expressing cells in fluorescence activated cell sorting assays, and to MUC17 expressing fixed and permeabilized cells, optionally wherein the antibody does not bind to the secreted form of huMUC17.
7. The antibody according to any one of the preceding claims, which is an IgG, IgD, IgE, IgM or IgA antibody, preferably an IgG antibody, such as an IgG1, IgG2, IgG3 or IgG4 antibody.
8. A polynucleotide encoding an antibody as defined in any one of the preceding claims.
9. A vector comprising the polynucleotide as defined in claim 8.
10. A host cell transformed or transfected with the polynucleotide as defined in claim 8 or with the vector as defined in claim 9.
11. A process for producing an antibody as defined in any one of claims 1 to 7, said process comprising the steps of culturing a host cell as defined in claim 10 under conditions allowing the expression of said antibody and recovering the produced antibody from the culture.
12. A hybridoma producing the antibody according to any one of the preceding claims.
13. A composition comprising an antibody as defined in any one of claims 1 to 7, or as produced according to the process of claim 11.

14. A detection system comprising the antibody as defined in any one of claims 1 to 7, or as produced according to the process of claim 11, or a composition according to claim 13.
15. Use of an antibody as defined in any one of claims 1-7 or as produced according to the process of claim 11 or of the detection system of claim 14 in a diagnostic method.
16. An antibody as defined in any one of claims 1-7 or as produced according to the process of claim 11, the composition of claim 13, or of the detection system of claim 14 for use in a method of detecting neoplastic growth.
17. The antibody or detection system for use according to claim 16 in a method of detecting neoplastic growth comprising determining the quantity of expression of MUC17 in a sample from a patient suspected to suffer from a cancer and, optionally, in a negative control sample and, further optionally, in a positive control sample.
18. The antibody or detection system for use according to any one of claims 16 and 17 in a method of detecting neoplastic growth comprising determining the quantity of expression of MUC17 in a sample from a patient suspected to suffer from a cancer and in a negative control sample, further comprising comparing the expression quantities of MUC17 between the samples, optionally wherein the expression quantities in the negative control and/or the positive control may be derived from stored data in at least one negative control sample and/or at least one positive control sample obtained in a method of detecting neoplastic growth comprising determining the quantity of expression of MUC17, further optionally, wherein the expression quantities in the negative control sample and/or the positive control sample may be derived from stored data comprising averaged expression quantities of more than one negative control sample and/or more than one positive control sample obtained in a method of detecting neoplastic growth comprising determining the quantity of expression of MUC17.
19. The antibody or detection system for use according to any one of claims 17 and 18 in a method of detecting neoplastic growth comprising determining the quantity of expression of MUC17 in a sample, wherein the sample is either a solid tissue sample or a liquid tissue sample.
20. A method for detecting and/or quantifying MUC17 expression in a sample, comprising the steps of:
 - (a) using an antibody as defined in or produced according to any one of the preceding claims, or using a detection system of claim 14, for determining the expression quantity of MUC17 in a sample; and
 - (b) comparing the expression quantity of MUC17 determined in step (a) to
 - (i) a pre-defined value for the MUC17 expression quantity,

- (ii) the expression quantity of MUC17 determined in a control sample, or
- (iii) the expression quantity of MUC17 determined in a sample obtained from the same source or subject at a previous time point.

21. A method for diagnosing a neoplastic disease associated with expression quantity of MUC17 or increased expression quantity of MUC17, comprising the steps of:

- (a) using an antibody or a composition as defined in or produced according to the preceding claims, or using a detection system of claim 14, for determining the expression quantity of MUC17 in a sample; and
- (b) comparing the expression quantity of MUC17 determined in step (a) to
 - (i) a pre-defined cut-off value for the expression quantity of MUC17, indicating absence of such disease, or
 - (ii) the expression quantity of MUC17 determined in a negative control sample representing absence of such neoplastic disease,

wherein a higher expression quantity of MUC17 determined in step (a) as compared to the pre-defined cut-off value of (i) or the expression quantity of MUC17 determined in the negative control sample of (ii) indicates the presence of a disease associated with expression of MUC17 or increased expression quantity of MUC17.

22. A method for monitoring the progression of a disease associated with expression of MUC17 or with increased expression quantity of MUC17 or for monitoring the response to treatment of a disease associated with expression of MUC17 or with increased expression quantity of MUC17, comprising the steps of:

- (a) using an antibody as defined in any one of the preceding claims, or using a detection system of claim 14, for determining the expression quantity of MUC17 at a first time point in a sample obtained from a subject diagnosed with such disease;
- (b) using an antibody as defined in any one of the preceding claims, or using a detection system of claim 14, for determining the expression quantity of MUC17 at a second time point or after treatment in a sample obtained from the subject; and
- (c) comparing the expression quantity of MUC17 determined in step (a) to the expression quantity of MUC17 determined in step (b);

wherein a higher expression quantity of MUC17 determined in step (a) as compared to the expression quantity of MUC17 determined in step (b) indicates that the disease is progressing, and/or wherein a lower expression quantity of MUC17 determined in step (a) as compared to the expression quantity of

MUC17 determined in step (b) indicates that said disease is entering remission or that said disease is responding to the treatment.

23. The use or the product for use of any one of claims 15 to 19 or the method of any one of claims 20 to 22, wherein the sample is a biological sample, preferably a human biological sample, such as a tissue sample, or a sample comprising cultured cells.

24. The use or the product for use of any one of claims 15 to 19 or the method of any one of claims 20 to 23, wherein the sample is obtained from a human subject, preferably a human subject suspected of having or having a disease associated with expression of MUC17 or increased expression quantity of MUC17, or a subject having received treatment for a disease associated with expression of MUC17 or increased expression quantity of MUC17.

25. The use or the product for use of any one of claims 15 to 19 or the method of any one of claims 20 to 24, wherein the disease is selected from the group comprising esophageal cancer, gastric cancer, gastrointestinal cancer, gastroesophageal cancer, including gastroesophageal junction cancer, and pancreas cancer.

26. A method of treatment of a patient, preferably a human patient, having at least one cancer selected from the group comprising esophageal cancer, gastric cancer, gastrointestinal cancer, gastroesophageal cancer, including gastroesophageal junction cancer, and/or pancreas cancer, wherein said patient has an increased expression of MUC17 on a cancer cell, particularly a cell of a colorectal carcinoma, a gastric carcinoma, a pancreatic carcinoma, colon adenocarcinoma, esophageal carcinoma, pancreatic adenocarcinoma, rectum adenocarcinoma, and stomach adenocarcinoma.

27. The method of treatment according to claim 26, wherein said increased expression was determined in a method according to any one of claims 20 to 22, or wherein the use or the product for use of any one of claims 15 to 19, 23, and/or 24 is comprised.

28. The method of treatment according to claim 26 and 27 comprising the administration of a drug to said patient, wherein the drug is selected from the group comprising small molecules, peptidic drugs, antibodies and derivatives thereof, toxins, radiation therapy, and surgery.

29. The method of treatment according to any one of claims 26 to 28, wherein the drug is an antibody construct comprising at least two domains, wherein one domain binds selectively to MUC17.

30. The method of treatment according to any one of claims 26 to 29, wherein the drug is an antibody construct comprising at least two domains, wherein another domain binds selectively to CD3, to human CD3, particularly to the human CD3 Epsilon chain.

31. The method of treatment according to any one of claims 26 to 30, wherein the drug is an antibody construct further comprising a third domain which comprises two polypeptide monomers, each comprising a hinge, a CH2 domain and a CH3 domain, wherein said two polypeptide monomers are fused to each other via a peptide linker.

32. The method of treatment according to any one of claims 26 to 31, wherein the drug is a single chain antibody construct.

33. The method of treatment according to any one of claims 26 to 32, wherein the drug is an antibody construct, wherein said third domain comprises in an amino to carboxyl order:

hinge-CH2-CH3-linker-hinge-CH2-CH3.

34. The method of treatment according to any one of claims 26 to 33, wherein the drug is an antibody construct, wherein each of said polypeptide monomers in the third domain has an amino acid sequence that is at least 90% identical to a sequence selected from the group from the group consisting of: SEQ ID NO: 22-29.

35. The method of treatment according to any one of claims 26 to 34, wherein the drug is an antibody construct, wherein each of said polypeptide monomers has an amino acid sequence selected from SEQ ID NO: 22-29.

36. The method of treatment according to any one of claims 26 to 35, wherein the drug is an antibody construct, wherein the CH2 domain comprises an intra domain cysteine disulfide bridge.

37. The method of treatment according to any one of claims 26 to 36, wherein the drug is an antibody construct, wherein

- (i) the first domain comprises two antibody variable domains and the second domain comprises two antibody variable domains;
- (ii) the first domain comprises one antibody variable domain and the second domain comprises two antibody variable domains;
- (iii) the first domain comprises two antibody variable domains and the second domain comprises one antibody variable domain; or
- (iv) the first domain comprises one antibody variable domain and the second domain comprises one antibody variable domain.

38. The method of treatment according to any one of claims 26 to 37, wherein the drug is an antibody construct, wherein the first and second domain are fused to the third domain via a peptide linker.

39. The method of treatment according to any one of claims 26 to 38, wherein the drug is an antibody construct, wherein the antibody construct comprises in an amino to carboxyl order:
- (a) the first domain;
 - (b) a peptide linker preferably having an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-12;
 - (c) the second domain.
40. The method of treatment according to any one of claims 26 to 39, wherein the drug is an antibody construct, wherein the antibody construct further comprises in an amino to carboxyl order:
- (d) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 10, 11, 12, 17, 18, 19 and 20.
 - (e) the first polypeptide monomer of the third domain;
 - (f) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 13, 14, 15 and 16; and
 - (g) the second polypeptide monomer of the third domain.
41. The method of treatment according to any one of claims 26 to 40, wherein the drug is an antibody construct, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 526 (aa 4171 to 4296 according to uniprot Q685J3 numbering).
42. The method of treatment according to any one of claims 26 to 41, wherein the drug is an antibody construct, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 527 (aa 4184 to 4291 according to uniprot Q685J3 numbering).
43. The method of treatment according to any one of claims 26 to 42, wherein the drug is an antibody construct, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 528 (aa 4131 to 4243 according to uniprot Q685J3 numbering).
44. The method of treatment according to any one of claims 26 to 43, wherein the drug is an antibody construct, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 529 (aa 4244 to 4389 according to uniprot Q685J3 numbering).
45. The method of treatment according to any one of claims 26 to 44, wherein the drug is an antibody construct, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 528 (aa 4131 to 4243 according to uniprot Q685J3 numbering).

but not to an epitope within MUC17 which corresponds to SEQ ID NO. 529 (aa 4244 to 4389 according to uniprot Q685J3 numbering).

46. The method of treatment according to any one of claims 26 to 45, wherein the drug is an antibody construct, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 530 (aa 4171 to 4390 according to uniprot Q685J3 numbering) or SEQ ID NO. 531 (aa 4184 to 4390 according to uniprot Q685J3 numbering) but not to an epitope within MUC17 which corresponds to SEQ ID NO. 532 (aa 4291 to 4390 according to uniprot Q685J3 numbering) or to an epitope within MUC17 which corresponds to SEQ ID NO. 533 (aa 4341 to 4390 according to uniprot Q685J3 numbering).
47. The method of treatment according to any one of claims 26 to 46, wherein the drug is an antibody construct, wherein the ratio between cytotoxicity and binding affinity (EC_{50}/K_D)*1000 is below 250, wherein the cytotoxicity is determined in NUGC-4 cells as target cells and huPBMC as effector cells, and wherein the binding affinity is determined by a surface plasmon resonance-based assay.
48. The method of treatment according to any one of claims 26 to 47, wherein the drug is an antibody construct, wherein the ratio between cytotoxicity and binding affinity (EC_{50}/K_D)*1000 is below 125, wherein the cytotoxicity is determined in NUGC-4 cells as target cells and huPBMC as effector cells, and wherein the binding affinity is determined by a surface plasmon resonance-based assay.
49. The method of treatment according to any one of claims 26 to 48, wherein the drug is an antibody construct, wherein the ratio between cytotoxicity and binding affinity (EC_{50}/K_D)*1000 is below 21, wherein the cytotoxicity is determined in NUGC-4 cells as target cells and huPBMC as effector cells, and wherein the binding affinity is determined by a surface plasmon resonance-based assay.
50. The method of treatment according to any one of claims 26 to 49, wherein the drug is an antibody construct, wherein the first binding domain comprises a VH region comprising CDR-H 1, CDR-H2 and CDR-H3 selected from:
 - (a) CDR-H1 as depicted in SEQ ID NO. 31, CDR-H2 as depicted in SEQ ID NO. 32 and CDR-H3 as depicted in SEQ ID NO. 33;
 - (b) CDR-H1 as depicted in SEQ ID NO. 42, CDR-H2 as depicted in SEQ ID NO. 43 and CDR-H3 as depicted in SEQ ID NO. 44;

- (c) CDR-H1 as depicted in SEQ ID NO. 53, CDR-H2 as depicted in SEQ ID NO. 54 and CDR-H3 as depicted in SEQ ID NO. 55;
- (d) CDR-H1 as depicted in SEQ ID NO. 64, CDR-H2 as depicted in SEQ ID NO. 65 and CDR-H3 as depicted in SEQ ID NO. 66;
- (e) CDR-H1 as depicted in SEQ ID NO. 75, CDR-H2 as depicted in SEQ ID NO. 76 and CDR-H3 as depicted in SEQ ID NO. 77;
- (f) CDR-H1 as depicted in SEQ ID NO. 86, CDR-H2 as depicted in SEQ ID NO. 87 and CDR-H3 as depicted in SEQ ID NO. 88;
- (g) CDR-H1 as depicted in SEQ ID NO. 97, CDR-H2 as depicted in SEQ ID NO. 98 and CDR-H3 as depicted in SEQ ID NO. 99;
- (h) CDR-H1 as depicted in SEQ ID NO. 108, CDR-H2 as depicted in SEQ ID NO. 109 and CDR-H3 as depicted in SEQ ID NO. 110;
- (i) CDR-H1 as depicted in SEQ ID NO. 119, CDR-H2 as depicted in SEQ ID NO. 120 and CDR-H3 as depicted in SEQ ID NO. 121;
- (j) CDR-H1 as depicted in SEQ ID NO. 130, CDR-H2 as depicted in SEQ ID NO. 131 and CDR-H3 as depicted in SEQ ID NO. 132;
- (k) CDR-H1 as depicted in SEQ ID NO. 141, CDR-H2 as depicted in SEQ ID NO. 142 and CDR-H3 as depicted in SEQ ID NO. 143;
- (l) CDR-H1 as depicted in SEQ ID NO. 152, CDR-H2 as depicted in SEQ ID NO. 153 and CDR-H3 as depicted in SEQ ID NO. 154;
- (m) CDR-H1 as depicted in SEQ ID NO. 163, CDR-H2 as depicted in SEQ ID NO. 164 and CDR-H3 as depicted in SEQ ID NO. 165;
- (n) CDR-H1 as depicted in SEQ ID NO. 174, CDR-H2 as depicted in SEQ ID NO. 175 and CDR-H3 as depicted in SEQ ID NO. 176;
- (o) CDR-H1 as depicted in SEQ ID NO. 185, CDR-H2 as depicted in SEQ ID NO. 186 and CDR-H3 as depicted in SEQ ID NO. 187;
- (p) CDR-H1 as depicted in SEQ ID NO. 196, CDR-H2 as depicted in SEQ ID NO. 197 and CDR-H3 as depicted in SEQ ID NO. 198;

- (q) CDR-H1 as depicted in SEQ ID NO. 207, CDR-H2 as depicted in SEQ ID NO. 208 and CDR-H3 as depicted in SEQ ID NO. 209;
- (r) CDR-H1 as depicted in SEQ ID NO. 218, CDR-H2 as depicted in SEQ ID NO. 219 and CDR-H3 as depicted in SEQ ID NO. 220;
- (s) CDR-H1 as depicted in SEQ ID NO. 229, CDR-H2 as depicted in SEQ ID NO. 230 and CDR-H3 as depicted in SEQ ID NO. 231;
- (t) CDR-H1 as depicted in SEQ ID NO. 240, CDR-H2 as depicted in SEQ ID NO. 241 and CDR-H3 as depicted in SEQ ID NO. 242;
- (u) CDR-H1 as depicted in SEQ ID NO. 251, CDR-H2 as depicted in SEQ ID NO. 252 and CDR-H3 as depicted in SEQ ID NO. 253;
- (v) CDR-H1 as depicted in SEQ ID NO. 262, CDR-H2 as depicted in SEQ ID NO. 263 and CDR-H3 as depicted in SEQ ID NO. 264;
- (w) CDR-H1 as depicted in SEQ ID NO. 273, CDR-H2 as depicted in SEQ ID NO. 274 and CDR-H3 as depicted in SEQ ID NO. 275;
- (x) CDR-H1 as depicted in SEQ ID NO. 284, CDR-H2 as depicted in SEQ ID NO. 285 and CDR-H3 as depicted in SEQ ID NO. 286;
- (y) CDR-H1 as depicted in SEQ ID NO. 295, CDR-H2 as depicted in SEQ ID NO. 296 and CDR-H3 as depicted in SEQ ID NO. 297;
- (z) CDR-H1 as depicted in SEQ ID NO. 306, CDR-H2 as depicted in SEQ ID NO. 307 and CDR-H3 as depicted in SEQ ID NO. 308;
- (aa) CDR-H1 as depicted in SEQ ID NO. 317, CDR-H2 as depicted in SEQ ID NO. 318 and CDR-H3 as depicted in SEQ ID NO. 319;
- (ab) CDR-H1 as depicted in SEQ ID NO. 328, CDR-H2 as depicted in SEQ ID NO. 329 and CDR-H3 as depicted in SEQ ID NO. 330;
- (ac) CDR-H1 as depicted in SEQ ID NO. 339, CDR-H2 as depicted in SEQ ID NO. 340 and CDR-H3 as depicted in SEQ ID NO. 341;
- (ad) CDR-H1 as depicted in SEQ ID NO. 350, CDR-H2 as depicted in SEQ ID NO. 351 and CDR-H3 as depicted in SEQ ID NO. 352;

- (ae) CDR-H1 as depicted in SEQ ID NO. 361, CDR-H2 as depicted in SEQ ID NO. 362 and CDR-H3 as depicted in SEQ ID NO. 363;
- (af) CDR-H1 as depicted in SEQ ID NO. 372, CDR-H2 as depicted in SEQ ID NO. 373 and CDR-H3 as depicted in SEQ ID NO. 374;
- (ag) CDR-H1 as depicted in SEQ ID NO. 383, CDR-H2 as depicted in SEQ ID NO. 384 and CDR-H3 as depicted in SEQ ID NO. 385;
- (ah) CDR-H1 as depicted in SEQ ID NO. 394, CDR-H2 as depicted in SEQ ID NO. 395 and CDR-H3 as depicted in SEQ ID NO. 396;
- (ai) CDR-H1 as depicted in SEQ ID NO. 405, CDR-H2 as depicted in SEQ ID NO. 406 and CDR-H3 as depicted in SEQ ID NO. 407;
- (aj) CDR-H1 as depicted in SEQ ID NO. 416, CDR-H2 as depicted in SEQ ID NO. 417 and CDR-H3 as depicted in SEQ ID NO. 418;
- (ak) CDR-H1 as depicted in SEQ ID NO. 427, CDR-H2 as depicted in SEQ ID NO. 428 and CDR-H3 as depicted in SEQ ID NO. 429;
- (al) CDR-H1 as depicted in SEQ ID NO. 438, CDR-H2 as depicted in SEQ ID NO. 439 and CDR-H3 as depicted in SEQ ID NO. 440;
- (am) CDR-H1 as depicted in SEQ ID NO. 449, CDR-H2 as depicted in SEQ ID NO. 450 and CDR-H3 as depicted in SEQ ID NO. 451;
- (an) CDR-H1 as depicted in SEQ ID NO. 460, CDR-H2 as depicted in SEQ ID NO. 461 and CDR-H3 as depicted in SEQ ID NO. 462;
- (ao) CDR-H1 as depicted in SEQ ID NO. 471, CDR-H2 as depicted in SEQ ID NO. 472 and CDR-H3 as depicted in SEQ ID NO. 473;
- (ap) CDR-H1 as depicted in SEQ ID NO. 482, CDR-H2 as depicted in SEQ ID NO. 483 and CDR-H3 as depicted in SEQ ID NO. 484;
- (aq) CDR-H1 as depicted in SEQ ID NO. 493, CDR-H2 as depicted in SEQ ID NO. 494 and CDR-H3 as depicted in SEQ ID NO. 495;
- (ar) CDR-H1 as depicted in SEQ ID NO. 504, CDR-H2 as depicted in SEQ ID NO. 505 and CDR-H3 as depicted in SEQ ID NO. 506; and

- (as) CDR-H1 as depicted in SEQ ID NO. 515, CDR-H2 as depicted in SEQ ID NO. 516 and CDR-H3 as depicted in SEQ ID NO. 517; wherein preferred are
 - (c) CDR-H1 as depicted in SEQ ID NO. 53, CDR-H2 as depicted in SEQ ID NO. 54 and CDR-H3 as depicted in SEQ ID NO. 55;
 - (n) CDR-H1 as depicted in SEQ ID NO. 174, CDR-H2 as depicted in SEQ ID NO. 175 and CDR-H3 as depicted in SEQ ID NO. 176;
 - (ac) CDR-H1 as depicted in SEQ ID NO. 339, CDR-H2 as depicted in SEQ ID NO. 340 and CDR-H3 as depicted in SEQ ID NO. 341; and
 - (aj) CDR-H1 as depicted in SEQ ID NO. 416, CDR-H2 as depicted in SEQ ID NO. 417 and CDR-H3 as depicted in SEQ ID NO. 418.
51. The method of treatment according to any one of claims 26 to 50, wherein the drug is an antibody construct, wherein the first binding domain comprises a VL region comprising CDR-H1, CDR-L2 and CDR-L3 selected from:
- (a) CDR-L1 as depicted in SEQ ID NO. 34, CDR-L2 as depicted in SEQ ID NO. 35 and CDR-L3 as depicted in SEQ ID NO. 36;
 - (b) CDR-L1 as depicted in SEQ ID NO. 45, CDR-L2 as depicted in SEQ ID NO. 46 and CDR-L3 as depicted in SEQ ID NO. 47;
 - (c) CDR-L1 as depicted in SEQ ID NO. 56, CDR-L2 as depicted in SEQ ID NO. 57 and CDR-L3 as depicted in SEQ ID NO. 58;
 - (d) CDR-L1 as depicted in SEQ ID NO. 67, CDR-L2 as depicted in SEQ ID NO. 68 and CDR-L3 as depicted in SEQ ID NO. 69;
 - (e) CDR-L1 as depicted in SEQ ID NO. 78, CDR-L2 as depicted in SEQ ID NO. 79 and CDR-L3 as depicted in SEQ ID NO. 80;
 - (f) CDR-L1 as depicted in SEQ ID NO. 89, CDR-L2 as depicted in SEQ ID NO. 90 and CDR-L3 as depicted in SEQ ID NO. 91;
 - (g) CDR-L1 as depicted in SEQ ID NO. 100, CDR-L2 as depicted in SEQ ID NO. 101 and CDR-L3 as depicted in SEQ ID NO. 102;
 - (h) CDR-L1 as depicted in SEQ ID NO. 111, CDR-L2 as depicted in SEQ ID NO. 112 and CDR-L3 as depicted in SEQ ID NO. 113;

- (i) CDR-L1 as depicted in SEQ ID NO. 122, CDR-L2 as depicted in SEQ ID NO. 123 and CDR-L3 as depicted in SEQ ID NO. 124;
- (j) CDR-L1 as depicted in SEQ ID NO. 133, CDR-L2 as depicted in SEQ ID NO. 134 and CDR-L3 as depicted in SEQ ID NO. 135;
- (k) CDR-L1 as depicted in SEQ ID NO. 144, CDR-L2 as depicted in SEQ ID NO. 145 and CDR-L3 as depicted in SEQ ID NO. 146;
- (l) CDR-L1 as depicted in SEQ ID NO. 155, CDR-L2 as depicted in SEQ ID NO. 156 and CDR-L3 as depicted in SEQ ID NO. 157;
- (m) CDR-L1 as depicted in SEQ ID NO. 166, CDR-L2 as depicted in SEQ ID NO. 167 and CDR-L3 as depicted in SEQ ID NO. 168;
- (n) CDR-L1 as depicted in SEQ ID NO. 177, CDR-L2 as depicted in SEQ ID NO. 178 and CDR-L3 as depicted in SEQ ID NO. 179;
- (o) CDR-L1 as depicted in SEQ ID NO. 188, CDR-L2 as depicted in SEQ ID NO. 189 and CDR-L3 as depicted in SEQ ID NO. 190;
- (p) CDR-L1 as depicted in SEQ ID NO. 199, CDR-L2 as depicted in SEQ ID NO. 200 and CDR-L3 as depicted in SEQ ID NO. 201;
- (q) CDR-L1 as depicted in SEQ ID NO. 210, CDR-L2 as depicted in SEQ ID NO. 211 and CDR-L3 as depicted in SEQ ID NO. 212;
- (r) CDR-L1 as depicted in SEQ ID NO. 221, CDR-L2 as depicted in SEQ ID NO. 222 and CDR-L3 as depicted in SEQ ID NO. 223;
- (s) CDR-L1 as depicted in SEQ ID NO. 232, CDR-L2 as depicted in SEQ ID NO. 233 and CDR-L3 as depicted in SEQ ID NO. 234;
- (t) CDR-L1 as depicted in SEQ ID NO. 243, CDR-L2 as depicted in SEQ ID NO. 244 and CDR-L3 as depicted in SEQ ID NO. 245;
- (u) CDR-L1 as depicted in SEQ ID NO. 254, CDR-L2 as depicted in SEQ ID NO. 255 and CDR-L3 as depicted in SEQ ID NO. 256;
- (v) CDR-L1 as depicted in SEQ ID NO. 265, CDR-L2 as depicted in SEQ ID NO. 266 and CDR-L3 as depicted in SEQ ID NO. 267;

- (w) CDR-L1 as depicted in SEQ ID NO. 276, CDR-L2 as depicted in SEQ ID NO. 277 and CDR-L3 as depicted in SEQ ID NO. 278;
- (x) CDR-L1 as depicted in SEQ ID NO. 287, CDR-L2 as depicted in SEQ ID NO. 288 and CDR-L3 as depicted in SEQ ID NO. 289;
- (y) CDR-L1 as depicted in SEQ ID NO. 298, CDR-L2 as depicted in SEQ ID NO. 299 and CDR-L3 as depicted in SEQ ID NO. 300;
- (z) CDR-L1 as depicted in SEQ ID NO. 309, CDR-L2 as depicted in SEQ ID NO. 310 and CDR-L3 as depicted in SEQ ID NO. 311;
- (aa) CDR-L1 as depicted in SEQ ID NO. 320, CDR-L2 as depicted in SEQ ID NO. 321 and CDR-L3 as depicted in SEQ ID NO. 322;
- (ab) CDR-L1 as depicted in SEQ ID NO. 331, CDR-L2 as depicted in SEQ ID NO. 332 and CDR-L3 as depicted in SEQ ID NO. 333;
- (ac) CDR-L1 as depicted in SEQ ID NO. 342, CDR-L2 as depicted in SEQ ID NO. 343 and CDR-L3 as depicted in SEQ ID NO. 344;
- (ad) CDR-L1 as depicted in SEQ ID NO. 353, CDR-L2 as depicted in SEQ ID NO. 354 and CDR-L3 as depicted in SEQ ID NO. 355;
- (ae) CDR-L1 as depicted in SEQ ID NO. 364, CDR-L2 as depicted in SEQ ID NO. 365 and CDR-L3 as depicted in SEQ ID NO. 366;
- (af) CDR-L1 as depicted in SEQ ID NO. 375, CDR-L2 as depicted in SEQ ID NO. 376 and CDR-L3 as depicted in SEQ ID NO. 377;
- (ag) CDR-L1 as depicted in SEQ ID NO. 386, CDR-L2 as depicted in SEQ ID NO. 387 and CDR-L3 as depicted in SEQ ID NO. 388;
- (ah) CDR-L1 as depicted in SEQ ID NO. 397, CDR-L2 as depicted in SEQ ID NO. 398 and CDR-L3 as depicted in SEQ ID NO. 399;
- (ai) CDR-L1 as depicted in SEQ ID NO. 408, CDR-L2 as depicted in SEQ ID NO. 409 and CDR-L3 as depicted in SEQ ID NO. 410;
- (aj) CDR-L1 as depicted in SEQ ID NO. 419, CDR-L2 as depicted in SEQ ID NO. 420 and CDR-L3 as depicted in SEQ ID NO. 421;

- (ak) CDR-L1 as depicted in SEQ ID NO. 430, CDR-L2 as depicted in SEQ ID NO. 431 and CDR-L3 as depicted in SEQ ID NO. 432;
 - (al) CDR-L1 as depicted in SEQ ID NO. 441, CDR-L2 as depicted in SEQ ID NO. 442 and CDR-L3 as depicted in SEQ ID NO. 443;
 - (am) CDR-L1 as depicted in SEQ ID NO. 452, CDR-L2 as depicted in SEQ ID NO. 453 and CDR-L3 as depicted in SEQ ID NO. 454;
 - (an) CDR-L1 as depicted in SEQ ID NO. 463, CDR-L2 as depicted in SEQ ID NO. 464 and CDR-L3 as depicted in SEQ ID NO. 465;
 - (ao) CDR-L1 as depicted in SEQ ID NO. 474, CDR-L2 as depicted in SEQ ID NO. 475 and CDR-L3 as depicted in SEQ ID NO. 476;
 - (ap) CDR-L1 as depicted in SEQ ID NO. 485, CDR-L2 as depicted in SEQ ID NO. 486 and CDR-L3 as depicted in SEQ ID NO. 487;
 - (aq) CDR-L1 as depicted in SEQ ID NO. 496, CDR-L2 as depicted in SEQ ID NO. 497 and CDR-L3 as depicted in SEQ ID NO. 498;
 - (ar) CDR-L1 as depicted in SEQ ID NO. 507, CDR-L2 as depicted in SEQ ID NO. 508 and CDR-L3 as depicted in SEQ ID NO. 509; and
 - (as) CDR-L1 as depicted in SEQ ID NO. 518, CDR-L2 as depicted in SEQ ID NO. 519 and CDR-L3 as depicted in SEQ ID NO. 520; wherein preferred are
 - (c) CDR-L1 as depicted in SEQ ID NO. 56, CDR-L2 as depicted in SEQ ID NO. 57 and CDR-L3 as depicted in SEQ ID NO. 58;
 - (n) CDR-L1 as depicted in SEQ ID NO. 177, CDR-L2 as depicted in SEQ ID NO. 178 and CDR-L3 as depicted in SEQ ID NO. 179;
 - (ac) CDR-L1 as depicted in SEQ ID NO. 342, CDR-L2 as depicted in SEQ ID NO. 343 and CDR-L3 as depicted in SEQ ID NO. 344; and
 - (aj) CDR-L1 as depicted in SEQ ID NO. 419, CDR-L2 as depicted in SEQ ID NO. 420 and CDR-L3 as depicted in SEQ ID NO. 421.
52. The method of treatment according to any one of claims 26 to 51, wherein the drug is an antibody construct, wherein the first binding domain comprises a VL region and a VH region selected from the group consisting of:

- (a) a VL region as depicted in SEQ ID NO. 38 and a VH region as depicted in SEQ ID NO. 37;
- (b) a VL region as depicted in SEQ ID NO. 49 and a VH region as depicted in SEQ ID NO. 48;
- (c) a VL region as depicted in SEQ ID NO. 60 and a VH region as depicted in SEQ ID NO. 59;
- (d) a VL region as depicted in SEQ ID NO. 71 and a VH region as depicted in SEQ ID NO. 70;
- (e) a VL region as depicted in SEQ ID NO. 82 and a VH region as depicted in SEQ ID NO. 81;
- (f) a VL region as depicted in SEQ ID NO. 93 and a VH region as depicted in SEQ ID NO. 92;
- (g) a VL region as depicted in SEQ ID NO. 104 and a VH region as depicted in SEQ ID NO. 103;
- (h) a VL region as depicted in SEQ ID NO. 115 and a VH region as depicted in SEQ ID NO. 114;
- (i) a VL region as depicted in SEQ ID NO. 126 and a VH region as depicted in SEQ ID NO. 125;
- (j) a VL region as depicted in SEQ ID NO. 137 and a VH region as depicted in SEQ ID NO. 136;
- (k) a VL region as depicted in SEQ ID NO. 148 and a VH region as depicted in SEQ ID NO. 147;
- (l) a VL region as depicted in SEQ ID NO. 159 and a VH region as depicted in SEQ ID NO. 158;
- (m) a VL region as depicted in SEQ ID NO. 170 and a VH region as depicted in SEQ ID NO. 169;
- (n) a VL region as depicted in SEQ ID NO. 181 and a VH region as depicted in SEQ ID NO. 180;
- (o) a VL region as depicted in SEQ ID NO. 192 and a VH region as depicted in SEQ ID NO. 191;
- (p) a VL region as depicted in SEQ ID NO. 203 and a VH region as depicted in SEQ ID NO. 202;
- (q) a VL region as depicted in SEQ ID NO. 214 and a VH region as depicted in SEQ ID NO. 213;
- (r) a VL region as depicted in SEQ ID NO. 226 and a VH region as depicted in SEQ ID NO. 225;
- (s) a VL region as depicted in SEQ ID NO. 236 and a VH region as depicted in SEQ ID NO. 235;
- (t) a VL region as depicted in SEQ ID NO. 247 and a VH region as depicted in SEQ ID NO. 246;
- (u) a VL region as depicted in SEQ ID NO. 258 and a VH region as depicted in SEQ ID NO. 257;
- (v) a VL region as depicted in SEQ ID NO. 269 and a VH region as depicted in SEQ ID NO. 268;
- (w) a VL region as depicted in SEQ ID NO. 280 and a VH region as depicted in SEQ ID NO. 279;

- (x) a VL region as depicted in SEQ ID NO. 292 and a VH region as depicted in SEQ ID NO. 290;
- (y) a VL region as depicted in SEQ ID NO. 302 and a VH region as depicted in SEQ ID NO. 301;
- (z) a VL region as depicted in SEQ ID NO. 313 and a VH region as depicted in SEQ ID NO. 312;
- (aa) a VL region as depicted in SEQ ID NO. 324 and a VH region as depicted in SEQ ID NO. 323;
- (ab) a VL region as depicted in SEQ ID NO. 335 and a VH region as depicted in SEQ ID NO. 334;
- (ac) a VL region as depicted in SEQ ID NO. 346 and a VH region as depicted in SEQ ID NO. 345;
- (ad) a VL region as depicted in SEQ ID NO. 357 and a VH region as depicted in SEQ ID NO. 356;
- (ae) a VL region as depicted in SEQ ID NO. 368 and a VH region as depicted in SEQ ID NO. 367;
- (af) a VL region as depicted in SEQ ID NO. 379 and a VH region as depicted in SEQ ID NO. 378;
- (ag) a VL region as depicted in SEQ ID NO. 390 and a VH region as depicted in SEQ ID NO. 389;
- (ah) a VL region as depicted in SEQ ID NO. 401 and a VH region as depicted in SEQ ID NO. 400;
- (ai) a VL region as depicted in SEQ ID NO. 412 and a VH region as depicted in SEQ ID NO. 411;
- (aj) a VL region as depicted in SEQ ID NO. 423 and a VH region as depicted in SEQ ID NO. 422;
- (ak) a VL region as depicted in SEQ ID NO. 434 and a VH region as depicted in SEQ ID NO. 433;
- (al) a VL region as depicted in SEQ ID NO. 445 and a VH region as depicted in SEQ ID NO. 444;
- (am) a VL region as depicted in SEQ ID NO. 456 and a VH region as depicted in SEQ ID NO. 455;
- (an) a VL region as depicted in SEQ ID NO. 467 and a VH region as depicted in SEQ ID NO. 466;
- (ao) a VL region as depicted in SEQ ID NO. 478 and a VH region as depicted in SEQ ID NO. 477;
- (ap) a VL region as depicted in SEQ ID NO. 489 and a VH region as depicted in SEQ ID NO. 488;
- (aq) a VL region as depicted in SEQ ID NO. 500 and a VH region as depicted in SEQ ID NO. 499;
- (ar) a VL region as depicted in SEQ ID NO. 511 and a VH region as depicted in SEQ ID NO. 510;
and
- (as) a VL region as depicted in SEQ ID NO. 522 and a VH region as depicted in SEQ ID NO. 521;

53. The method of treatment according to any one of claims 26 to 52, wherein the drug is an antibody construct, wherein the antibody construct comprises a sequence selected from an amino acid sequence as depicted in any of SEQ ID NOs: 39, 50, 61, 72, 83, 94, 105, 116, 127, 138, 149, 160, 171, 182, 193, 204, 215, 226, 237, 248, 259, 270, 281, 292, 303, 314, 325, 336, 347, 358, 369, 380, 391, 402, 413, 424, 435, 446, 457, 468, 479, 490, 501, 512, and 523.
54. The method of treatment according to any one of claims 26 to 53, wherein the drug is an antibody construct, wherein the antibody construct comprises in an amino to carboxyl order:
- (a) the first domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 39, 50, 61, 72, 83, 94, 105, 116, 127, 138, 149, 160, 171, 182, 193, 204, 215, 226, 237, 248, 259, 270, 281, 292, 303, 314, 325, 336, 347, 358, 369, 380, 391, 402, 413, 424, 435, 446, 457, 468, 479, 490, 501, 512, and 523;
 - (b) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-12;
 - (c) the second domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 23, 25, 41, 43, 59, 61, 77, 79, 95, 97, 113, 115, 131, 133, 149, 151, 167, 169, 185 or 187 of WO 2008/119567 or as depicted in SEQ ID NO: 13.
55. The method of treatment according to any one of claims 26 to 54, wherein the drug is an antibody construct claim 25, wherein the antibody construct further comprises in an amino to carboxyl order:
- (d) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 10, 11, 12, 17, 18, 19 and 20.
 - (e) the first polypeptide monomer of the third domain having a polypeptide sequence selected from the group consisting of SEQ ID NOs: 22-29;
 - (f) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 13, 14, 15 and 16; and
 - (g) the second polypeptide monomer of the third domain having a polypeptide sequence selected from the group consisting of SEQ ID NOs: 22-29.
56. The method of treatment according to any one of claims 26 to 55, wherein the drug is an antibody construct having an amino acid sequence selected from the group consisting of:

- SEQ ID NOs: 40, 41, 51, 52, 62, 63, 73, 74, 84, 85, 95, 96, 106, 107, 117, 118, 128, 129, 139, 140, 150, 151, 161, 162, 172, 173, 183, 184, 194, 195, 205, 206, 216, 217, 227, 228, 238, 239, 249, 250, 260, 261, 271, 272, 282, 283, 293, 294, 304, 305, 315, 316, 326, 327, 337, 338, 348, 349, 359, 360, 370, 371, 381, 382, 392, 393, 403, 404, 414, 415, 424, 426, 436, 437, 447, 448, 458, 459, 469, 470, 480, 481, 491, 492, 502, 503, 513, 514, 524 and 525, or having an amino acid having at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identity to said sequences.
57. A diagnostic kit comprising the antibody or the composition and/or detection system according to any one of claims 1-7, 13, 14, 17, 18, and 19.