

a sea urchin sperm protein, enterokinase and agrin (SEA) domain, and a second EGF domain. The SEA domain contains a putative cleavage site that is conserved in other mucins (Moniaux et al., J. Biol. Chem. 2006). MUC17 is a single-pass transmembrane protein with an 80-amino acid cytoplasmic tail that is intracellular (Moniaux et al., J. Biol. Chem. 2006). The expression of MUC17 in healthy adults is restricted to the apical surface of enterocytes, or mature absorptive epithelial cells, that line the intestine (Moniaux et al., J. Biol. Chem. 2006; Johanasson and Hansson, Nat. Rev. Immunology 2016). MUC17 is also expressed by the stomach and pancreas (Moniaux et al., J. Biol. Chem. 2006; Moehle et al., J. Mol. Med. 2006). The biological function of MUC17 is considered to be the maintenance of mucosal barrier integrity in the intestinal tract, such as by mucosal restitution (Luu et al., Int. J. Biochem. Cell Biol. 2010; Resta-Lenert et al., Am. J. Physiology 2011; Johanasson and Hansson, Nat. Rev. Immunology 2016).

[9] MUC17 is aberrantly expressed in some cancers. MUC17 mRNA was shown to be expressed in one pancreatic cancer cell line and three colon cancer cell lines (Gum et al. 2002). Immunohistochemistry studies confirmed expression of the MUC17 protein in pancreatic cancer ((Moniaux et al. 2006). In colon cancer, however, MUC17 protein expression was shown to be decreased (Senapati et al., J. Clin. Pathol. 2010). Nevertheless, the expression patterns of MUC17 make it a potential target for the treatment of different forms of malignancy.

SUMMARY

[10] In view of the conflicting implications in the literature with regard to MUC17 as a potential target for which pathological condition, it is the object of the present disclosure to clearly identify specific conditions associated with MUC17 upregulation and to provide bispecific antibody constructs, such as T cell engaging molecules, which are specifically suitable to bind MUC17 in a MUC17-associated condition, preferably for use in the treatment of said specific conditions. Accordingly, the present disclosure provides an antibody construct characterized by comprising a first domain binding to MUC17, a second domain binding to an extracellular epitope of the human and non-human, e.g. *Macaca* CD3 ϵ chain, and preferably a third domain, which is a specific Fc modality. Moreover, the disclosure provides a polynucleotide encoding the antibody construct, a vector comprising this polynucleotide, and host cells expressing the construct and a pharmaceutical composition comprising the same.

[11] In one example, it is envisaged in the context of the present disclosure to provide an antibody construct comprising:

- a first domain which binds to MUC17 and
- a second domain which binds to an extracellular epitope of the human and the *Macaca* CD3 ϵ chain.

[11a] In one aspect, the present disclosure refers to a bispecific antibody construct comprising:

- a first domain which binds to MUC17, and
- a second domain which binds to an extracellular epitope of the human and the *Macaca* CD3 ϵ chain.

[12] Within said example, it is further envisaged in the context of the present disclosure that the antibody construct comprises 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.

[13] Within said example, it is further envisaged in the context of the present disclosure to provide an antibody construct which is a single chain antibody construct.

5 **[14]** Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct wherein said third domain comprises in an amino to carboxyl order: hinge-CH2-CH3-linker-hinge-CH2-CH3.

10 **[15]** Within said example, it is further envisaged in the context of the present disclosure to provide an antibody construct wherein each of said polypeptide monomers 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: 17-24.

[16] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein each of said polypeptide monomers has an amino acid sequence selected from SEQ ID NO: 17-24.

15 **[17]** Within said example, it is further envisaged in the context of the present disclosure to provide an antibody construct, wherein the CH2 domain comprises an intra domain cysteine disulfide bridge.

[18] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein

20 (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

25 (iv) the first domain comprises one antibody variable domain and the second domain comprises one antibody variable domain.

[19] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein the first and second domain are fused to the third domain via a peptide linker.

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[20] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein the antibody construct comprises in an amino to carboxyl order:

- (a) the first domain;
- (b) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-3;
- (c) the second domain.

[21] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein the antibody construct in addition to (a) to (c) 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: 1, 2, 3, 9, 10, 11 and 12;
- (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: 5, 6, 7 and 8; and
- (g) the second polypeptide monomer of the third domain.

[22] Within said example, it is further envisaged in the context of the present disclosure to provide 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 4171 to 4296 according to uniprot Q685J3 numbering).

[23] Within said example, it is also envisaged in the context of the present disclosure to provide 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 4184 to 4291 according to uniprot Q685J3 numbering).

[24] Within said example, it is further envisaged in the context of the present disclosure to provide 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 4131 to 4243 according to uniprot Q685J3 numbering).

[25] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 531 (aa 4244 to 4389 according to uniprot Q685J3 numbering).

5 **[26]** Within said example, it is further envisaged in the context of the present disclosure to provide 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 4131 to 4243 according to uniprot Q685J3 numbering) but not to an epitope within MUC17 which corresponds to SEQ ID NO. 531 (aa 4244 to 4389 according to uniprot Q685J3 numbering).

10 **[27]** Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 532 (aa 4171 to 4390 according to uniprot Q685J3 numbering) or SEQ ID NO. 533 (aa 4184 to 4390 according to uniprot Q685J3 numbering) but not to an epitope within MUC17 which corresponds to SEQ ID NO. 534 (aa 4291 to 4390 according to uniprot Q685J3 numbering) or to an epitope within MUC17 which corresponds to SEQ ID NO. 535 (aa 4341 to 4390 according to uniprot Q685J3 numbering).

15 **[28]** Within said example, it is further envisaged in the context of the present disclosure to provide an antibody construct, wherein the VH VL arrangement is characterized as 4 lambda 3. The nomenclature is known in the art.

20 **[29]** Within said example, it is further envisaged in the context of the present disclosure to provide an antibody construct, wherein the ratio between cytotoxicity and binding affinity (EC_{50}/K_D)*1000 is below 250, wherein the cytotoxicity is indicated in pM and determined in NUGC-4 cells as target cells and huPBMC as effector cells, and wherein the binding affinity is indicated in nM and determined by a surface plasmon resonance (SPR) assay, such as a Biacore assay. The factor 1000 has been introduced for better readability considering the different dimension between typical EC_{50} and K_D values.

25 **[30]** Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein the ratio between cytotoxicity and binding affinity (EC_{50}/K_D)*1000 is below 125, wherein the cytotoxicity is indicated in pM and determined, e.g., in NUGC-4 cells as target cells and huPBMC as effector cells, and wherein the binding affinity is indicated in nM and determined, e.g., by a surface plasmon resonance-based assay.

30 **[31]** Within said example, it is further envisaged in the context of the present disclosure to provide an antibody construct, wherein the ratio between cytotoxicity and binding affinity (EC_{50}/K_D)*1000 is below 21, wherein the cytotoxicity is indicated in pM and determined, e.g., in NUGC-4 cells as target cells and huPBMC as effector cells, and wherein the binding affinity is indicated in nM and determined by a surface plasmon resonance-based assay. Preferably, cytotoxicity (EC_{50}) is <100 pM and the binding affinity (K_D) is <25 nM.

[32] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein the first binding domain comprises a VH region comprising CDR-H 1, CDR-H2 and CDR-H3 selected from:

- 5 (a) CDR-H1 as depicted in SEQ ID NO. 33, CDR-H2 as depicted in SEQ ID NO. 34 and CDR-H3 as depicted in SEQ ID NO. 35;
- (b) CDR-H1 as depicted in SEQ ID NO. 44, CDR-H2 as depicted in SEQ ID NO. 45 and CDR-H3 as depicted in SEQ ID NO. 46;
- (c) CDR-H1 as depicted in SEQ ID NO. 55, CDR-H2 as depicted in SEQ ID NO. 56 and CDR-H3 as depicted in SEQ ID NO. 57;
- 10 (d) CDR-H1 as depicted in SEQ ID NO. 66, CDR-H2 as depicted in SEQ ID NO. 67 and CDR-H3 as depicted in SEQ ID NO. 68;
- (e) CDR-H1 as depicted in SEQ ID NO. 77, CDR-H2 as depicted in SEQ ID NO. 78 and CDR-H3 as depicted in SEQ ID NO. 79;
- (f) CDR-H1 as depicted in SEQ ID NO. 88, CDR-H2 as depicted in SEQ ID NO. 89 and CDR-H3 as depicted in SEQ ID NO. 90;
- 15 (g) CDR-H1 as depicted in SEQ ID NO. 99, CDR-H2 as depicted in SEQ ID NO. 100 and CDR-H3 as depicted in SEQ ID NO. 101;
- (h) CDR-H1 as depicted in SEQ ID NO. 110, CDR-H2 as depicted in SEQ ID NO. 111 and CDR-H3 as depicted in SEQ ID NO. 112;
- 20 (i) CDR-H1 as depicted in SEQ ID NO. 121, CDR-H2 as depicted in SEQ ID NO. 122 and CDR-H3 as depicted in SEQ ID NO. 123;
- (j) CDR-H1 as depicted in SEQ ID NO. 132, CDR-H2 as depicted in SEQ ID NO. 133 and CDR-H3 as depicted in SEQ ID NO. 134;
- (k) CDR-H1 as depicted in SEQ ID NO. 143, CDR-H2 as depicted in SEQ ID NO. 144 and CDR-H3 as depicted in SEQ ID NO. 145;
- 25 (l) CDR-H1 as depicted in SEQ ID NO. 154, CDR-H2 as depicted in SEQ ID NO. 155 and CDR-H3 as depicted in SEQ ID NO. 156;
- (m) CDR-H1 as depicted in SEQ ID NO. 165, CDR-H2 as depicted in SEQ ID NO. 166 and CDR-H3 as depicted in SEQ ID NO. 167;
- 30 (n) CDR-H1 as depicted in SEQ ID NO. 176, CDR-H2 as depicted in SEQ ID NO. 177 and CDR-H3 as depicted in SEQ ID NO. 178;
- (o) CDR-H1 as depicted in SEQ ID NO. 187, CDR-H2 as depicted in SEQ ID NO. 188 and CDR-H3 as depicted in SEQ ID NO. 189;
- (p) CDR-H1 as depicted in SEQ ID NO. 198, CDR-H2 as depicted in SEQ ID NO. 199 and CDR-H3 as depicted in SEQ ID NO. 200;
- 35 (q) CDR-H1 as depicted in SEQ ID NO. 209, CDR-H2 as depicted in SEQ ID NO. 210 and CDR-H3 as depicted in SEQ ID NO. 211.

- (aj) CDR-H1 as depicted in SEQ ID NO. 418, CDR-H2 as depicted in SEQ ID NO. 419 and CDR-H3 as depicted in SEQ ID NO. 420;
- (ak) CDR-H1 as depicted in SEQ ID NO. 429, CDR-H2 as depicted in SEQ ID NO. 430 and CDR-H3 as depicted in SEQ ID NO. 431;
- 5 (al) CDR-H1 as depicted in SEQ ID NO. 440, CDR-H2 as depicted in SEQ ID NO. 441 and CDR-H3 as depicted in SEQ ID NO. 442;
- (am) CDR-H1 as depicted in SEQ ID NO. 451, CDR-H2 as depicted in SEQ ID NO. 452 and CDR-H3 as depicted in SEQ ID NO. 453;
- (an) CDR-H1 as depicted in SEQ ID NO. 462, CDR-H2 as depicted in SEQ ID NO. 463 and CDR-
- 10 H3 as depicted in SEQ ID NO. 464;
- (ao) CDR-H1 as depicted in SEQ ID NO. 473, CDR-H2 as depicted in SEQ ID NO. 474 and CDR-H3 as depicted in SEQ ID NO. 475;
- (ap) CDR-H1 as depicted in SEQ ID NO. 484, CDR-H2 as depicted in SEQ ID NO. 485 and CDR-H3 as depicted in SEQ ID NO. 486;
- 15 (aq) CDR-H1 as depicted in SEQ ID NO. 495, CDR-H2 as depicted in SEQ ID NO. 496 and CDR-H3 as depicted in SEQ ID NO. 497;
- (ar) CDR-H1 as depicted in SEQ ID NO. 506, CDR-H2 as depicted in SEQ ID NO. 507 and CDR-H3 as depicted in SEQ ID NO. 508; and
- (as) CDR-H1 as depicted in SEQ ID NO. 517, CDR-H2 as depicted in SEQ ID NO. 518 and CDR-
- 20 H3 as depicted in SEQ ID NO. 519; wherein preferred are
- (c) CDR-H1 as depicted in SEQ ID NO. 55, CDR-H2 as depicted in SEQ ID NO. 56 and CDR-H3 as depicted in SEQ ID NO. 57;
- (n) CDR-H1 as depicted in SEQ ID NO. 176, CDR-H2 as depicted in SEQ ID NO. 177 and CDR-H3 as depicted in SEQ ID NO. 178;
- 25 (ac) CDR-H1 as depicted in SEQ ID NO. 341, CDR-H2 as depicted in SEQ ID NO. 342 and CDR-H3 as depicted in SEQ ID NO. 343; and
- (aj) CDR-H1 as depicted in SEQ ID NO. 418, CDR-H2 as depicted in SEQ ID NO. 419 and CDR-H3 as depicted in SEQ ID NO. 420.
- 30 **[33]** Within said example, it is also envisaged in the context of the present disclosure to provide 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. 36, CDR-L2 as depicted in SEQ ID NO. 37 and CDR-L3 as depicted in SEQ ID NO. 38;
- 35 (b) CDR-L1 as depicted in SEQ ID NO. 47, CDR-L2 as depicted in SEQ ID NO. 48 and CDR-L3 as depicted in SEQ ID NO. 49;

- (am) CDR-L1 as depicted in SEQ ID NO. 454, CDR-L2 as depicted in SEQ ID NO. 455 and CDR-L3 as depicted in SEQ ID NO. 456;
- (an) CDR-L1 as depicted in SEQ ID NO. 465, CDR-L2 as depicted in SEQ ID NO. 466 and CDR-L3 as depicted in SEQ ID NO. 467;
- 5 (ao) CDR-L1 as depicted in SEQ ID NO. 476, CDR-L2 as depicted in SEQ ID NO. 477 and CDR-L3 as depicted in SEQ ID NO. 478;
- (ap) CDR-L1 as depicted in SEQ ID NO. 487, CDR-L2 as depicted in SEQ ID NO. 488 and CDR-L3 as depicted in SEQ ID NO. 489;
- (aq) CDR-L1 as depicted in SEQ ID NO. 498, CDR-L2 as depicted in SEQ ID NO. 499 and CDR-L3 as depicted in SEQ ID NO. 500;
- 10 (ar) CDR-L1 as depicted in SEQ ID NO. 509, CDR-L2 as depicted in SEQ ID NO. 510 and CDR-L3 as depicted in SEQ ID NO. 511; and
- (as) CDR-L1 as depicted in SEQ ID NO. 520, CDR-L2 as depicted in SEQ ID NO. 521 and CDR-L3 as depicted in SEQ ID NO. 522; wherein preferred are
- 15 (c) CDR-L1 as depicted in SEQ ID NO. 58, CDR-L2 as depicted in SEQ ID NO. 59 and CDR-L3 as depicted in SEQ ID NO. 60;
- (n) CDR-L1 as depicted in SEQ ID NO. 179, CDR-L2 as depicted in SEQ ID NO. 180 and CDR-L3 as depicted in SEQ ID NO. 181;
- (ac) CDR-L1 as depicted in SEQ ID NO. 344, CDR-L2 as depicted in SEQ ID NO. 345 and CDR-L3 as depicted in SEQ ID NO. 346; and
- 20 (aj) CDR-L1 as depicted in SEQ ID NO. 421, CDR-L2 as depicted in SEQ ID NO. 422 and CDR-L3 as depicted in SEQ ID NO. 423.

[34] Within said example, it is also envisaged in the context of the present disclosure to provide 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. 40 and a VH region as depicted in SEQ ID NO. 39;
- (b) a VL region as depicted in SEQ ID NO. 51 and a VH region as depicted in SEQ ID NO. 50;
- (c) a VL region as depicted in SEQ ID NO. 62 and a VH region as depicted in SEQ ID NO. 61;
- 30 (d) a VL region as depicted in SEQ ID NO. 73 and a VH region as depicted in SEQ ID NO. 72;
- (e) a VL region as depicted in SEQ ID NO. 84 and a VH region as depicted in SEQ ID NO. 83;
- (f) a VL region as depicted in SEQ ID NO. 95 and a VH region as depicted in SEQ ID NO. 94;
- (g) a VL region as depicted in SEQ ID NO. 106 and a VH region as depicted in SEQ ID NO. 105;
- (h) a VL region as depicted in SEQ ID NO. 117 and a VH region as depicted in SEQ ID NO. 116;
- 35 (i) a VL region as depicted in SEQ ID NO. 128 and a VH region as depicted in SEQ ID NO. 127;
- (j) a VL region as depicted in SEQ ID NO. 139 and a VH region as depicted in SEQ ID NO. 138;
- (k) a VL region as depicted in SEQ ID NO. 150 and a VH region as depicted in SEQ ID NO. 149;

[35] Within said example, it is further envisaged in the context of the present disclosure to provide an antibody construct, wherein the antibody construct comprises a sequence selected from an amino acid sequence as depicted in any of SEQ ID NOs: 41, 52, 63, 74, 85, 96, 107, 118, 129, 140, 151, 162, 173, 184, 195, 206, 217, 228, 239, 250, 261, 272, 283, 294, 305, 316, 327, 338, 349, 360, 371, 382, 393, 404, 415, 426, 437, 448, 459, 470, 481, 492, 503, 514, and 525.

[36] Within said example, it is also envisaged in the context of the present disclosure to provide 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: 41, 52, 63, 74, 85, 96, 107, 118, 129, 140, 151, 162, 173, 184, 195, 206, 217, 228, 239, 250, 261, 272, 283, 294, 305, 316, 327, 338, 349, 360, 371, 382, 393, 404, 415, 426, 437, 448, 459, 470, 481, 492, 503, 514, and 525;

(b) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-3;

(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: 15; and

(d) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 9, 10, 11 and 12;

[37] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, wherein the antibody construct further comprises in addition to (a) to (d) an amino to carboxyl order:

(e) the first polypeptide monomer of the third domain having a polypeptide sequence selected from the group consisting of SEQ ID NOs: 17-24;

(f) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 6, 7 and 8; and

(g) the second polypeptide monomer of the third domain having a polypeptide sequence selected from the group consisting of SEQ ID NOs: 17-24.

[38] Within said example, it is also envisaged in the context of the present disclosure to provide an antibody construct, having an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 43, 53, 54, 64, 65, 75, 76, 86, 87, 97, 98, 108, 109, 119, 120, 130, 131, 141, 142, 152, 153, 163, 164, 174, 175, 185, 186, 196, 197, 207, 208, 218, 219, 229, 230, 240, 241, 251, 252, 262, 263, 273, 274, 284, 285, 295, 296, 306, 307, 317, 318, 328, 329, 339, 340, 350, 351, 361, 362, 372, 373, 383, 384, 394, 395,

405, 406, 416, 417, 427, 428, 438, 439, 449, 450, 460, 461, 471, 472, 482, 483, 493, 494, 504, 505, 515, 516, 526 and 527.

[39] In another aspect, it is further envisaged in the context of the present disclosure to provide a polynucleotide encoding an antibody construct of the present disclosure.

5 **[40]** In another aspect, it is also envisaged in the context of the present disclosure to provide a vector comprising a polynucleotide of the present disclosure.

[41] In another aspect, it is further envisaged in the context of the present disclosure to provide a host cell transformed or transfected with the polynucleotide or with the vector of the present disclosure.

10 **[42]** In another aspect, it is also envisaged in the context of the present disclosure to provide a process for the production of an antibody construct of the present disclosure, said process comprising culturing a host cell of the present disclosure under conditions allowing the expression of the antibody construct and recovering the produced antibody construct from the culture.

15 **[43]** In another aspect, it is further envisaged in the context of the present invention to provide a pharmaceutical composition comprising an antibody construct of the present invention, or produced according to the process of the present invention.

[44] Within said aspect, is also envisaged in the context of the present disclosure that the pharmaceutical composition is stable for at least four weeks at about -20°C.

20 **[44a]** In another aspect, it is further envisaged in the context of the present invention to provide the bispecific antibody construct for use in therapy.

[45] It is further envisaged in the context of the present disclosure to provide the antibody construct of the present disclosure, or produced according to the process of the present disclosure, for use in the prevention, treatment or amelioration of a disease selected from a proliferative disease, a tumorous disease, cancer or an immunological disorder.

25 **[46]** Within said example, it is also envisaged in the context of the present disclosure that the disease is a gastrointestinal cancer (e.g. gastric cancer, esophageal cancer, gastroesophageal cancer or colorectal cancer) or pancreatic cancer.

[47] Within said example, it is also envisaged in the context of the present disclosure that the disease is a gastric cancer.

30 **[47a]** In another aspect, it is further envisaged in the context of the present invention to provide use of the bispecific antibody construct in the manufacture of a medicament for the treatment of a proliferative disease, a tumorous disease, cancer, or an immunological disorder, wherein the disease preferably is gastrointestinal cancer or pancreatic cancer, most preferably gastric cancer.

35 **[48]** In another example, it is further envisaged in the context of the present disclosure to provide a method for the treatment or amelioration of a proliferative disease, a tumorous disease, cancer, or an immunological disorder, comprising the step of administering to a subject in need thereof the antibody construct of the present invention, or produced according to the process of the present invention, wherein the disease preferably is gastrointestinal cancer or pancreatic cancer, most preferably gastric cancer.

[49] In another aspect, it is also envisaged in the context of the present disclosure to provide a kit comprising an antibody construct of the present invention, or produced according to the process of the present invention, a polynucleotide of the present invention, a vector of the present invention, and/or a host cell of the present invention.

[49a] In another aspect, it is further envisaged in the context of the present disclosure to provide use of the bispecific antibody construct directed against MUC17 and CD3 in the manufacture of a medicament for the treatment or amelioration of gastrointestinal cancer.

[50] In another example, it is further envisaged in the context of the present disclosure to provide a method for the treatment or amelioration of gastrointestinal cancer, comprising the step of administering to a subject in need thereof a bispecific antibody construct directed against MUC17 and CD3.

[50a] In yet another aspect, it is further envisaged in the context of the present disclosure to provide a bispecific antibody construct directed against MUC17 and CD3 for use in therapy.

[51] In another example, it is further envisaged in the context of the present disclosure to provide a bispecific antibody construct directed against MUC17 and CD3 for use in the treatment or amelioration of gastrointestinal cancer.

DESCRIPTION OF THE FIGURES

[52] Figure 1: FIG. 1 shows an epitope clustering of MUC17. Epitopes E1, E2, E3, E4, E5A and 5B as well as truncated versions of E2 (TR2, TR3, TR4 and TR5, respectively) are marked. Experiments on constructs wherein human MUC17 (brown/grey) was replaced by non-functional mouse MUC3 revealed the respective epitopes. 45 MUC17-scFc bispecific antibody constructs were identified which cover the epitope space E2, comprising the SEA domain.

[53] Figure 2: MUC17 epitope mapping by on-cell binding of the MUC17-scFc bispecific antibody constructs against cells expressing human/mouse chimeric constructs. On-cell binding was assessed by fluorescence-activated cell sorting (FACS), where loss of binding to a chimeric construct indicates the respective (mutated) domain is essential for MUC17-scFc bispecific antibody constructs binding. For example, E2 shows loss of binding upon mutation. Hence, E2 is essential for binding for all four examined bispecific antibody constructs.

[54] Figure 3: MUC17 is expressed in gastric, pancreatic and colorectal cancer cell lines. MUC17 cell surface protein expression was determined by flow cytometry of live cells and are depicted as FACS readouts (A). MUC17 mRNA levels in cancer cell lines were determined by quantitative polymerase chain reaction (qPCR). Values are normalized to those of a constitutively expressed gene (B).

[55] Figure 4: Cytotoxicity assay on three different MUC17 bearing cell lines with different MUC17 expression (A: GSU, B: NUGC-4 and C: Ls174T). Tested constructs are 1 = 32-G6; 2 = 1-B6; 3 = 2-C2 and 4 = 8-B7. Construct 8-B7 is slightly favorable in terms of cytotoxicity.

[56] Figure 5: Soluble MUC17 protein (sMUC17, aa 4131-4243 Uniprot) was added into TDCC assays at 0-1000 ng/ml and activity of the MUC17-scFc bispecific antibody constructs was assessed after 48 h incubation (target cells GSU (A) or NUGC-4 (B), 10:1 human T cells to target cells, readout

Claims

1. A bispecific antibody construct comprising:
 - a first domain which binds to MUC17, and
 - a second domain which binds to an extracellular epitope of the human and the *Macaca* CD3ε chain.
2. The bispecific antibody construct of claim 1 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.
3. The bispecific antibody construct of claim 1 or 2, wherein the antibody construct is a single chain antibody construct.
4. The bispecific antibody construct of claim 2 or 3, wherein said third domain comprises in an amino to carboxyl order:

hinge-CH2-CH3-linker-hinge-CH2-CH3.
5. The bispecific antibody construct of any one of the preceding claims, 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 consisting of: SEQ ID NO: 17-24.
6. The bispecific antibody construct of any one of the preceding claims, wherein each of said polypeptide monomers has an amino acid sequence selected from SEQ ID NO: 17-24.
7. The bispecific antibody construct of any one of the preceding claims, wherein the CH2 domain comprises an intra domain cysteine disulfide bridge.
8. The bispecific antibody construct of any one of the preceding claims, 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.
9. The bispecific antibody construct of any one of the preceding claims, wherein the first and second domain are fused to the third domain via a peptide linker.
10. The bispecific antibody construct according to any one of the preceding claims, 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: 1-3;
 - (c) the second domain.
11. The bispecific antibody construct according to claim 10, 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: 1, 2, 3, 9, 10, 11 and 12.
 - (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: 5, 6, 7 and 8; and
 - (g) the second polypeptide monomer of the third domain.

12. The bispecific antibody construct according to any one of the preceding claims, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 528 (aa 4171 to 4296 according to uniprot Q685J3 numbering).
13. The bispecific antibody construct according to any one of the preceding claims, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 529 (aa 4184 to 4291 according to uniprot Q685J3 numbering).
14. The bispecific antibody construct according to any one of the preceding claims, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 530 (aa 4131 to 4243 according to uniprot Q685J3 numbering).
15. The bispecific antibody construct according to any one of the preceding claims, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 531 (aa 4244 to 4389 according to uniprot Q685J3 numbering).
16. The bispecific antibody construct according to any one of the preceding claims, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 530 (aa 4131 to 4243 according to uniprot Q685J3 numbering) but not to an epitope within MUC17 which corresponds to SEQ ID NO. 531 (aa 4244 to 4389 according to uniprot Q685J3 numbering).
17. The bispecific antibody construct according to any one of the preceding claims, wherein the first domain of the antibody construct binds to an epitope within MUC17 which corresponds to SEQ ID NO. 532 (aa 4171 to 4390 according to uniprot Q685J3 numbering) or SEQ ID NO. 533 (aa 4184 to 4390 according to uniprot Q685J3 numbering) but not to an epitope within MUC17 which corresponds to SEQ ID NO. 534 (aa 4291 to 4390 according to uniprot Q685J3 numbering) or to an epitope within MUC17 which corresponds to SEQ ID NO. 535 (aa 4341 to 4390 according to uniprot Q685J3 numbering).

18. The bispecific antibody construct according to any one of the preceding claims, 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.
19. The bispecific antibody construct according to any one of the preceding claims, 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.
20. The bispecific antibody construct according to any one of the preceding claims, 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.
21. The bispecific antibody construct according to according to any one of the preceding claims, 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. 33, CDR-H2 as depicted in SEQ ID NO. 34 and CDR-H3 as depicted in SEQ ID NO. 35;
 - (b) CDR-H1 as depicted in SEQ ID NO. 44, CDR-H2 as depicted in SEQ ID NO. 45 and CDR-H3 as depicted in SEQ ID NO. 46;
 - (c) CDR-H1 as depicted in SEQ ID NO. 55, CDR-H2 as depicted in SEQ ID NO. 56 and CDR-H3 as depicted in SEQ ID NO. 57;
 - (d) CDR-H1 as depicted in SEQ ID NO. 66, CDR-H2 as depicted in SEQ ID NO. 67 and CDR-H3 as depicted in SEQ ID NO. 68;
 - (e) CDR-H1 as depicted in SEQ ID NO. 77, CDR-H2 as depicted in SEQ ID NO. 78 and CDR-H3 as depicted in SEQ ID NO. 79;
 - (f) CDR-H1 as depicted in SEQ ID NO. 88, CDR-H2 as depicted in SEQ ID NO. 89 and CDR-H3 as depicted in SEQ ID NO. 90;

- (g) CDR-H1 as depicted in SEQ ID NO. 99, CDR-H2 as depicted in SEQ ID NO. 100 and CDR-H3 as depicted in SEQ ID NO. 101;
- (h) CDR-H1 as depicted in SEQ ID NO. 110, CDR-H2 as depicted in SEQ ID NO. 111 and CDR-H3 as depicted in SEQ ID NO. 112;
- (i) CDR-H1 as depicted in SEQ ID NO. 121, CDR-H2 as depicted in SEQ ID NO. 122 and CDR-H3 as depicted in SEQ ID NO. 123;
- (j) CDR-H1 as depicted in SEQ ID NO. 132, CDR-H2 as depicted in SEQ ID NO. 133 and CDR-H3 as depicted in SEQ ID NO. 134;
- (k) CDR-H1 as depicted in SEQ ID NO. 143, CDR-H2 as depicted in SEQ ID NO. 144 and CDR-H3 as depicted in SEQ ID NO. 145;
- (l) CDR-H1 as depicted in SEQ ID NO. 154, CDR-H2 as depicted in SEQ ID NO. 155 and CDR-H3 as depicted in SEQ ID NO. 156;
- (m) CDR-H1 as depicted in SEQ ID NO. 165, CDR-H2 as depicted in SEQ ID NO. 166 and CDR-H3 as depicted in SEQ ID NO. 167;
- (n) CDR-H1 as depicted in SEQ ID NO. 176, CDR-H2 as depicted in SEQ ID NO. 177 and CDR-H3 as depicted in SEQ ID NO. 178;
- (o) CDR-H1 as depicted in SEQ ID NO. 187, CDR-H2 as depicted in SEQ ID NO. 188 and CDR-H3 as depicted in SEQ ID NO. 189;
- (p) CDR-H1 as depicted in SEQ ID NO. 198, CDR-H2 as depicted in SEQ ID NO. 199 and CDR-H3 as depicted in SEQ ID NO. 200;
- (q) CDR-H1 as depicted in SEQ ID NO. 209, CDR-H2 as depicted in SEQ ID NO. 210 and CDR-H3 as depicted in SEQ ID NO. 211;
- (r) CDR-H1 as depicted in SEQ ID NO. 220, CDR-H2 as depicted in SEQ ID NO. 221 and CDR-H3 as depicted in SEQ ID NO. 222;
- (s) CDR-H1 as depicted in SEQ ID NO. 231, CDR-H2 as depicted in SEQ ID NO. 232 and CDR-H3 as depicted in SEQ ID NO. 233;
- (t) CDR-H1 as depicted in SEQ ID NO. 242, CDR-H2 as depicted in SEQ ID NO. 243 and CDR-H3 as depicted in SEQ ID NO. 244;
- (u) CDR-H1 as depicted in SEQ ID NO. 253, CDR-H2 as depicted in SEQ ID NO. 254 and CDR-H3 as depicted in SEQ ID NO. 255;

- (v) CDR-H1 as depicted in SEQ ID NO. 264, CDR-H2 as depicted in SEQ ID NO. 265 and CDR-H3 as depicted in SEQ ID NO. 266;
- (w) CDR-H1 as depicted in SEQ ID NO. 275, CDR-H2 as depicted in SEQ ID NO. 276 and CDR-H3 as depicted in SEQ ID NO. 276;
- (x) CDR-H1 as depicted in SEQ ID NO. 286, CDR-H2 as depicted in SEQ ID NO. 287 and CDR-H3 as depicted in SEQ ID NO. 288;
- (y) CDR-H1 as depicted in SEQ ID NO. 297, CDR-H2 as depicted in SEQ ID NO. 298 and CDR-H3 as depicted in SEQ ID NO. 299;
- (z) CDR-H1 as depicted in SEQ ID NO. 308, CDR-H2 as depicted in SEQ ID NO. 309 and CDR-H3 as depicted in SEQ ID NO. 310;
- (aa) CDR-H1 as depicted in SEQ ID NO. 319, CDR-H2 as depicted in SEQ ID NO. 320 and CDR-H3 as depicted in SEQ ID NO. 321;
- (ab) CDR-H1 as depicted in SEQ ID NO. 330, CDR-H2 as depicted in SEQ ID NO. 331 and CDR-H3 as depicted in SEQ ID NO. 332;
- (ac) CDR-H1 as depicted in SEQ ID NO. 341, CDR-H2 as depicted in SEQ ID NO. 342 and CDR-H3 as depicted in SEQ ID NO. 343;
- (ad) CDR-H1 as depicted in SEQ ID NO. 352, CDR-H2 as depicted in SEQ ID NO. 353 and CDR-H3 as depicted in SEQ ID NO. 354;
- (ae) CDR-H1 as depicted in SEQ ID NO. 363, CDR-H2 as depicted in SEQ ID NO. 364 and CDR-H3 as depicted in SEQ ID NO. 365;
- (af) CDR-H1 as depicted in SEQ ID NO. 374, CDR-H2 as depicted in SEQ ID NO. 375 and CDR-H3 as depicted in SEQ ID NO. 376;
- (ag) CDR-H1 as depicted in SEQ ID NO. 385, CDR-H2 as depicted in SEQ ID NO. 386 and CDR-H3 as depicted in SEQ ID NO. 386;
- (ah) CDR-H1 as depicted in SEQ ID NO. 396, CDR-H2 as depicted in SEQ ID NO. 397 and CDR-H3 as depicted in SEQ ID NO. 398;
- (ai) CDR-H1 as depicted in SEQ ID NO. 407, CDR-H2 as depicted in SEQ ID NO. 408 and CDR-H3 as depicted in SEQ ID NO. 409;
- (aj) CDR-H1 as depicted in SEQ ID NO. 418, CDR-H2 as depicted in SEQ ID NO. 419 and CDR-H3 as depicted in SEQ ID NO. 420;

- (ak) CDR-H1 as depicted in SEQ ID NO. 429, CDR-H2 as depicted in SEQ ID NO. 430 and CDR-H3 as depicted in SEQ ID NO. 431;
 - (al) CDR-H1 as depicted in SEQ ID NO. 440, CDR-H2 as depicted in SEQ ID NO. 441 and CDR-H3 as depicted in SEQ ID NO. 442;
 - (am) CDR-H1 as depicted in SEQ ID NO. 451, CDR-H2 as depicted in SEQ ID NO. 452 and CDR-H3 as depicted in SEQ ID NO. 453;
 - (an) CDR-H1 as depicted in SEQ ID NO. 462, CDR-H2 as depicted in SEQ ID NO. 463 and CDR-H3 as depicted in SEQ ID NO. 464;
 - (ao) CDR-H1 as depicted in SEQ ID NO. 473, CDR-H2 as depicted in SEQ ID NO. 474 and CDR-H3 as depicted in SEQ ID NO. 475;
 - (ap) CDR-H1 as depicted in SEQ ID NO. 484, CDR-H2 as depicted in SEQ ID NO. 485 and CDR-H3 as depicted in SEQ ID NO. 486;
 - (aq) CDR-H1 as depicted in SEQ ID NO. 495, CDR-H2 as depicted in SEQ ID NO. 496 and CDR-H3 as depicted in SEQ ID NO. 497;
 - (ar) CDR-H1 as depicted in SEQ ID NO. 506, CDR-H2 as depicted in SEQ ID NO. 507 and CDR-H3 as depicted in SEQ ID NO. 508; and
 - (as) CDR-H1 as depicted in SEQ ID NO. 517, CDR-H2 as depicted in SEQ ID NO. 518 and CDR-H3 as depicted in SEQ ID NO. 519; wherein preferred are
 - (c) CDR-H1 as depicted in SEQ ID NO. 55, CDR-H2 as depicted in SEQ ID NO. 56 and CDR-H3 as depicted in SEQ ID NO. 57;
 - (n) CDR-H1 as depicted in SEQ ID NO. 176, CDR-H2 as depicted in SEQ ID NO. 177 and CDR-H3 as depicted in SEQ ID NO. 178;
 - (ac) CDR-H1 as depicted in SEQ ID NO. 341, CDR-H2 as depicted in SEQ ID NO. 342 and CDR-H3 as depicted in SEQ ID NO. 343; and
 - (aj) CDR-H1 as depicted in SEQ ID NO. 418, CDR-H2 as depicted in SEQ ID NO. 419 and CDR-H3 as depicted in SEQ ID NO. 420.
22. The bispecific antibody construct according to any one of the preceding claims, 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. 36, CDR-L2 as depicted in SEQ ID NO. 37 and CDR-L3 as depicted in SEQ ID NO. 38;
- (b) CDR-L1 as depicted in SEQ ID NO. 47, CDR-L2 as depicted in SEQ ID NO. 48 and CDR-L3 as depicted in SEQ ID NO. 49;
- (c) CDR-L1 as depicted in SEQ ID NO. 58, CDR-L2 as depicted in SEQ ID NO. 59 and CDR-L3 as depicted in SEQ ID NO. 60;
- (d) CDR-L1 as depicted in SEQ ID NO. 69, CDR-L2 as depicted in SEQ ID NO. 70 and CDR-L3 as depicted in SEQ ID NO. 71;
- (e) CDR-L1 as depicted in SEQ ID NO. 80, CDR-L2 as depicted in SEQ ID NO. 81 and CDR-L3 as depicted in SEQ ID NO. 82;
- (f) CDR-L1 as depicted in SEQ ID NO. 91, CDR-L2 as depicted in SEQ ID NO. 92 and CDR-L3 as depicted in SEQ ID NO. 93;
- (g) CDR-L1 as depicted in SEQ ID NO. 102, CDR-L2 as depicted in SEQ ID NO. 103 and CDR-L3 as depicted in SEQ ID NO. 104;
- (h) CDR-L1 as depicted in SEQ ID NO. 113, CDR-L2 as depicted in SEQ ID NO. 114 and CDR-L3 as depicted in SEQ ID NO. 115;
- (i) CDR-L1 as depicted in SEQ ID NO. 124, CDR-L2 as depicted in SEQ ID NO. 125 and CDR-L3 as depicted in SEQ ID NO. 126;
- (j) CDR-L1 as depicted in SEQ ID NO. 135, CDR-L2 as depicted in SEQ ID NO. 136 and CDR-L3 as depicted in SEQ ID NO. 137;
- (k) CDR-L1 as depicted in SEQ ID NO. 146, CDR-L2 as depicted in SEQ ID NO. 147 and CDR-L3 as depicted in SEQ ID NO. 148;
- (l) CDR-L1 as depicted in SEQ ID NO. 157, CDR-L2 as depicted in SEQ ID NO. 158 and CDR-L3 as depicted in SEQ ID NO. 159;
- (m) CDR-L1 as depicted in SEQ ID NO. 168, CDR-L2 as depicted in SEQ ID NO. 169 and CDR-L3 as depicted in SEQ ID NO. 170;
- (n) CDR-L1 as depicted in SEQ ID NO. 179, CDR-L2 as depicted in SEQ ID NO. 180 and CDR-L3 as depicted in SEQ ID NO. 181;
- (o) CDR-L1 as depicted in SEQ ID NO. 190, CDR-L2 as depicted in SEQ ID NO. 191 and CDR-L3 as depicted in SEQ ID NO. 192;

- (p) CDR-L1 as depicted in SEQ ID NO. 201, CDR-L2 as depicted in SEQ ID NO. 202 and CDR-L3 as depicted in SEQ ID NO. 203;
- (q) CDR-L1 as depicted in SEQ ID NO. 212, CDR-L2 as depicted in SEQ ID NO. 213 and CDR-L3 as depicted in SEQ ID NO. 214;
- (r) CDR-L1 as depicted in SEQ ID NO. 223, CDR-L2 as depicted in SEQ ID NO. 224 and CDR-L3 as depicted in SEQ ID NO. 225;
- (s) CDR-L1 as depicted in SEQ ID NO. 234, CDR-L2 as depicted in SEQ ID NO. 235 and CDR-L3 as depicted in SEQ ID NO. 236;
- (t) CDR-L1 as depicted in SEQ ID NO. 245, CDR-L2 as depicted in SEQ ID NO. 246 and CDR-L3 as depicted in SEQ ID NO. 247;
- (u) CDR-L1 as depicted in SEQ ID NO. 256, CDR-L2 as depicted in SEQ ID NO. 257 and CDR-L3 as depicted in SEQ ID NO. 258;
- (v) CDR-L1 as depicted in SEQ ID NO. 267, CDR-L2 as depicted in SEQ ID NO. 268 and CDR-L3 as depicted in SEQ ID NO. 269;
- (w) CDR-L1 as depicted in SEQ ID NO. 278, CDR-L2 as depicted in SEQ ID NO. 279 and CDR-L3 as depicted in SEQ ID NO. 280;
- (x) CDR-L1 as depicted in SEQ ID NO. 289, CDR-L2 as depicted in SEQ ID NO. 290 and CDR-L3 as depicted in SEQ ID NO. 291;
- (y) CDR-L1 as depicted in SEQ ID NO. 300, CDR-L2 as depicted in SEQ ID NO. 301 and CDR-L3 as depicted in SEQ ID NO. 302;
- (z) CDR-L1 as depicted in SEQ ID NO. 311, CDR-L2 as depicted in SEQ ID NO. 312 and CDR-L3 as depicted in SEQ ID NO. 313;
- (aa) CDR-L1 as depicted in SEQ ID NO. 322, CDR-L2 as depicted in SEQ ID NO. 323 and CDR-L3 as depicted in SEQ ID NO. 324;
- (ab) CDR-L1 as depicted in SEQ ID NO. 333, CDR-L2 as depicted in SEQ ID NO. 334 and CDR-L3 as depicted in SEQ ID NO. 335;
- (ac) CDR-L1 as depicted in SEQ ID NO. 344, CDR-L2 as depicted in SEQ ID NO. 345 and CDR-L3 as depicted in SEQ ID NO. 346;
- (ad) CDR-L1 as depicted in SEQ ID NO. 355, CDR-L2 as depicted in SEQ ID NO. 356 and CDR-L3 as depicted in SEQ ID NO. 357;

- (ae) CDR-L1 as depicted in SEQ ID NO. 366, CDR-L2 as depicted in SEQ ID NO. 367 and CDR-L3 as depicted in SEQ ID NO. 368;
- (af) CDR-L1 as depicted in SEQ ID NO. 377, CDR-L2 as depicted in SEQ ID NO. 378 and CDR-L3 as depicted in SEQ ID NO. 379;
- (ag) CDR-L1 as depicted in SEQ ID NO. 388, CDR-L2 as depicted in SEQ ID NO. 389 and CDR-L3 as depicted in SEQ ID NO. 390;
- (ah) CDR-L1 as depicted in SEQ ID NO. 399, CDR-L2 as depicted in SEQ ID NO. 400 and CDR-L3 as depicted in SEQ ID NO. 401;
- (ai) CDR-L1 as depicted in SEQ ID NO. 410, CDR-L2 as depicted in SEQ ID NO. 411 and CDR-L3 as depicted in SEQ ID NO. 412;
- (aj) CDR-L1 as depicted in SEQ ID NO. 421, CDR-L2 as depicted in SEQ ID NO. 422 and CDR-L3 as depicted in SEQ ID NO. 423;
- (ak) CDR-L1 as depicted in SEQ ID NO. 432, CDR-L2 as depicted in SEQ ID NO. 433 and CDR-L3 as depicted in SEQ ID NO. 434;
- (al) CDR-L1 as depicted in SEQ ID NO. 443, CDR-L2 as depicted in SEQ ID NO. 444 and CDR-L3 as depicted in SEQ ID NO. 445;
- (am) CDR-L1 as depicted in SEQ ID NO. 454, CDR-L2 as depicted in SEQ ID NO. 455 and CDR-L3 as depicted in SEQ ID NO. 456;
- (an) CDR-L1 as depicted in SEQ ID NO. 465, CDR-L2 as depicted in SEQ ID NO. 466 and CDR-L3 as depicted in SEQ ID NO. 467;
- (ao) CDR-L1 as depicted in SEQ ID NO. 476, CDR-L2 as depicted in SEQ ID NO. 477 and CDR-L3 as depicted in SEQ ID NO. 478;
- (ap) CDR-L1 as depicted in SEQ ID NO. 487, CDR-L2 as depicted in SEQ ID NO. 488 and CDR-L3 as depicted in SEQ ID NO. 489;
- (aq) CDR-L1 as depicted in SEQ ID NO. 498, CDR-L2 as depicted in SEQ ID NO. 499 and CDR-L3 as depicted in SEQ ID NO. 500;
- (ar) CDR-L1 as depicted in SEQ ID NO. 509, CDR-L2 as depicted in SEQ ID NO. 510 and CDR-L3 as depicted in SEQ ID NO. 511; and
- (as) CDR-L1 as depicted in SEQ ID NO. 520, CDR-L2 as depicted in SEQ ID NO. 521 and CDR-L3 as depicted in SEQ ID NO. 522; wherein preferred are

- (c) CDR-L1 as depicted in SEQ ID NO. 58, CDR-L2 as depicted in SEQ ID NO. 59 and CDR-L3 as depicted in SEQ ID NO. 60;
 - (n) CDR-L1 as depicted in SEQ ID NO. 179, CDR-L2 as depicted in SEQ ID NO. 180 and CDR-L3 as depicted in SEQ ID NO. 181;
 - (ac) CDR-L1 as depicted in SEQ ID NO. 344, CDR-L2 as depicted in SEQ ID NO. 345 and CDR-L3 as depicted in SEQ ID NO. 346; and
 - (aj) CDR-L1 as depicted in SEQ ID NO. 421, CDR-L2 as depicted in SEQ ID NO. 422 and CDR-L3 as depicted in SEQ ID NO. 423.
23. The bispecific antibody construct according to any of the preceding claims, 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. 40 and a VH region as depicted in SEQ ID NO. 39;
 - (b) a VL region as depicted in SEQ ID NO. 51 and a VH region as depicted in SEQ ID NO. 50;
 - (c) a VL region as depicted in SEQ ID NO. 62 and a VH region as depicted in SEQ ID NO. 61;
 - (d) a VL region as depicted in SEQ ID NO. 73 and a VH region as depicted in SEQ ID NO. 72;
 - (e) a VL region as depicted in SEQ ID NO. 84 and a VH region as depicted in SEQ ID NO. 83;
 - (f) a VL region as depicted in SEQ ID NO. 95 and a VH region as depicted in SEQ ID NO. 94;
 - (g) a VL region as depicted in SEQ ID NO. 106 and a VH region as depicted in SEQ ID NO. 105;
 - (h) a VL region as depicted in SEQ ID NO. 117 and a VH region as depicted in SEQ ID NO. 116;
 - (i) a VL region as depicted in SEQ ID NO. 128 and a VH region as depicted in SEQ ID NO. 127;
 - (j) a VL region as depicted in SEQ ID NO. 139 and a VH region as depicted in SEQ ID NO. 138;
 - (k) a VL region as depicted in SEQ ID NO. 150 and a VH region as depicted in SEQ ID NO. 149;
 - (l) a VL region as depicted in SEQ ID NO. 161 and a VH region as depicted in SEQ ID NO. 160;
 - (m) a VL region as depicted in SEQ ID NO. 172 and a VH region as depicted in SEQ ID NO. 171;
 - (n) a VL region as depicted in SEQ ID NO. 183 and a VH region as depicted in SEQ ID NO. 182;
 - (o) a VL region as depicted in SEQ ID NO. 194 and a VH region as depicted in SEQ ID NO. 193;
 - (p) a VL region as depicted in SEQ ID NO. 205 and a VH region as depicted in SEQ ID NO. 204;
 - (q) a VL region as depicted in SEQ ID NO. 216 and a VH region as depicted in SEQ ID NO. 215;
 - (r) a VL region as depicted in SEQ ID NO. 227 and a VH region as depicted in SEQ ID NO. 226;

- (s) a VL region as depicted in SEQ ID NO. 238 and a VH region as depicted in SEQ ID NO. 237;
- (t) a VL region as depicted in SEQ ID NO. 249 and a VH region as depicted in SEQ ID NO. 248;
- (u) a VL region as depicted in SEQ ID NO. 260 and a VH region as depicted in SEQ ID NO. 259;
- (v) a VL region as depicted in SEQ ID NO. 271 and a VH region as depicted in SEQ ID NO. 270;
- (w) a VL region as depicted in SEQ ID NO. 282 and a VH region as depicted in SEQ ID NO. 281;
- (x) a VL region as depicted in SEQ ID NO. 293 and a VH region as depicted in SEQ ID NO. 292;
- (y) a VL region as depicted in SEQ ID NO. 304 and a VH region as depicted in SEQ ID NO. 303;
- (z) a VL region as depicted in SEQ ID NO. 315 and a VH region as depicted in SEQ ID NO. 314;
- (aa) a VL region as depicted in SEQ ID NO. 326 and a VH region as depicted in SEQ ID NO. 325;
- (ab) a VL region as depicted in SEQ ID NO. 337 and a VH region as depicted in SEQ ID NO. 336;
- (ac) a VL region as depicted in SEQ ID NO. 348 and a VH region as depicted in SEQ ID NO. 347;
- (ad) a VL region as depicted in SEQ ID NO. 359 and a VH region as depicted in SEQ ID NO. 358;
- (ae) a VL region as depicted in SEQ ID NO. 370 and a VH region as depicted in SEQ ID NO. 369;
- (af) a VL region as depicted in SEQ ID NO. 381 and a VH region as depicted in SEQ ID NO. 380;
- (ag) a VL region as depicted in SEQ ID NO. 392 and a VH region as depicted in SEQ ID NO. 391;
- (ah) a VL region as depicted in SEQ ID NO. 403 and a VH region as depicted in SEQ ID NO. 402;
- (ai) a VL region as depicted in SEQ ID NO. 414 and a VH region as depicted in SEQ ID NO. 413;
- (aj) a VL region as depicted in SEQ ID NO. 425 and a VH region as depicted in SEQ ID NO. 424;
- (ak) a VL region as depicted in SEQ ID NO. 436 and a VH region as depicted in SEQ ID NO. 435;
- (al) a VL region as depicted in SEQ ID NO. 447 and a VH region as depicted in SEQ ID NO. 446;
- (am) a VL region as depicted in SEQ ID NO. 458 and a VH region as depicted in SEQ ID NO. 457;
- (an) a VL region as depicted in SEQ ID NO. 469 and a VH region as depicted in SEQ ID NO. 468;
- (ao) a VL region as depicted in SEQ ID NO. 480 and a VH region as depicted in SEQ ID NO. 479;
- (ap) a VL region as depicted in SEQ ID NO. 491 and a VH region as depicted in SEQ ID NO. 490;
- (aq) a VL region as depicted in SEQ ID NO. 502 and a VH region as depicted in SEQ ID NO. 501;
- (ar) a VL region as depicted in SEQ ID NO. 513 and a VH region as depicted in SEQ ID NO. 512; and
- (as) a VL region as depicted in SEQ ID NO. 524 and a VH region as depicted in SEQ ID NO. 523;

24. The bispecific antibody construct according to any of the preceding claims, wherein the antibody construct comprises a sequence selected from an amino acid sequence as depicted in any of SEQ ID NOs: 41, 52, 63, 74, 85, 96, 107, 118, 129, 140, 151, 162, 173, 184, 195, 206, 217, 228, 239, 250, 261, 272, 283, 294, 305, 316, 327, 338, 349, 360, 371, 382, 393, 404, 415, 426, 437, 448, 459, 470, 481, 492, 503, 514, and 525.
25. The bispecific antibody construct according to any one of the preceding claims, 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: 41, 52, 63, 74, 85, 96, 107, 118, 129, 140, 151, 162, 173, 184, 195, 206, 217, 228, 239, 250, 261, 272, 283, 294, 305, 316, 327, 338, 349, 360, 371, 382, 393, 404, 415, 426, 437, 448, 459, 470, 481, 492, 503, 514, and 525;
 - (b) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-3;
 - (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: 15
26. The bispecific antibody construct according to 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: 1, 2, 3, 9, 10, 11 and 12.
 - (e) the first polypeptide monomer of the third domain having a polypeptide sequence selected from the group consisting of SEQ ID NOs: 17-24;
 - (f) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 6, 7 and 8; and
 - (g) the second polypeptide monomer of the third domain having a polypeptide sequence selected from the group consisting of SEQ ID NOs: 17-24.

27. The bispecific antibody construct according to any of the preceding claims, having an amino acid sequence selected from the group consisting of:
- SEQ ID NOs: 42, 43, 53, 54, 64, 65, 75, 76, 86, 87, 97, 98, 108, 109, 119, 120, 130, 131, 141, 142, 152, 153, 163, 164, 174, 175, 185, 186, 196, 197, 207, 208, 218, 219, 229, 230, 240, 241, 251, 252, 262, 263, 273, 274, 284, 285, 295, 296, 306, 307, 317, 318, 328, 329, 339, 340, 350, 351, 361, 362, 372, 373, 383, 384, 394, 395, 405, 406, 416, 417, 427, 428, 438, 439, 449, 450, 460, 461, 471, 472, 482, 483, 493, 494, 504, 505, 515, 516, 526 and 527, or having an amino acid having at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identity to said sequences.
28. A polynucleotide encoding an antibody construct as defined in any one of the preceding claims.
29. A vector comprising a polynucleotide as defined in claim 28.
30. A host cell transformed or transfected with the polynucleotide as defined in claim 28 or with the vector as defined in claim 29.
31. A process for the production of the bispecific antibody construct according to any one of claims 1 to 27, said process comprising culturing a host cell as defined in claim 30 under conditions allowing the expression of the antibody construct as defined in any one of claims 1 to 27 and recovering the produced antibody construct from the culture.
32. A pharmaceutical composition comprising the bispecific antibody construct according to any one of claims 1 to 27, or produced according to the process of claim 31.
33. The pharmaceutical composition of claim 32, which is stable for at least four weeks at about -20°C.
34. The bispecific antibody construct according to any one of claims 1 to 27, or produced according to the process of claim 31, for use in therapy.

35. Use of the bispecific antibody construct according to any one of claims 1 to 27, or produced according to the process of claim 31 in the manufacture of a medicament for the treatment of a proliferative disease, a tumorous disease, cancer, or an immunological disorder, wherein the disease preferably is gastrointestinal cancer or pancreatic cancer, most preferably gastric cancer.
36. A kit comprising the bispecific antibody construct according to any one of claims 1 to 27, or produced according to the process of claim 31, a polynucleotide as defined in claim 28, a vector as defined in claim 29, and/or a host cell as defined in claim 30.
37. Use of the bispecific antibody construct directed against MUC17 and CD3 in the manufacture of a medicament for the treatment or amelioration of gastrointestinal cancer.
38. A bispecific antibody construct directed against MUC17 and CD3 for use in therapy.