

Claims

1. A bispecific antibody construct comprising at least three domains in an amino to carboxyl order, wherein:
 - a first domain binds to a target cell surface antigen,
 - a second domain binds to an extracellular epitope of the human and/or the *Macaca* CD3ε chain; and
 - a third domain comprises two polypeptide monomers, each comprising a hinge, a CH2 and a CH3 domain, wherein said two polypeptide monomers are fused to each other via a peptide linker, wherein said third domain comprises in an amino to carboxyl order:

hinge-CH2-CH3-linker-hinge-CH2-CH3.
2. The antibody construct of claim 1, wherein the antibody construct is a single chain antibody construct.
3. The antibody construct of any one of claims 1 or 2, 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.
4. The antibody construct of claim 3, wherein each of said polypeptide monomers has an amino acid sequence selected from SEQ ID NO: 17-24.
5. The antibody construct of any one of claims 1 to 4, wherein the CH2 domain comprises an intra domain cysteine disulfide bridge.
6. The antibody construct of any one of claims 1 to 5, 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.

7. The antibody construct of any one of claims 1 to 6, wherein the first and second domain are fused to the third domain via a peptide linker.
8. The antibody construct according to claims 1 to 7, 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;
 - (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.
9. The antibody construct according to any one of the preceding claims, wherein the target cell surface antigen is a tumor antigen, an antigen specific for an immunological disorder or a viral antigen.
10. The antibody construct according to claim 9, wherein the tumor antigen is selected from the group consisting of CDH19, MSLN, DLL3, FLT3, EGFRvIII, CD33, CD19, CD20, and CD70.
11. The 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: 52, 70, 58, 76, 88, 106, 124, 94, 112, 130, 142, 160, 178, 148, 166, 184, 196, 214, 232, 202, 220, 238, 250, 266, 282, 298, 255, 271, 287, 303, 322, 338, 354, 370, 386, 402, 418, 434, 450, 466, 482, 498, 514, 530, 546, 327, 343, 359, 375, 391, 407, 423, 439, 455, 471, 487, 503, 519, 353, 551, 592, 608, 624, 640, 656, 672, 688, 704, 720, 736, 752, 768, 784, 800, 816, 832, 848, 864, 880, 896, 912, 928, 944, 960, 976, 992, 1008, 1024, 1040, 1056, 1072, 1088, 1104, 1120, 1136, 1152, 1168, 1184, 597, 613, 629, 645, 661, 677, 693, 709, 725, 741, 757, 773, 789, 805, 821, 837, 853,

869, 885, 901, 917, 933, 949, 965, 981, 997, 1013, 1029, 1045, 1061, 1077, 1093, 1109, 1125, 1141, 1157, 1173, 1189, 1277, 1289, 1301, 1313, 1325, 1337, 1349, 1361, 1373, 1385, 1397, 1409, 1421, 1433, 1445;

- (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: 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 of SEQ ID NO: 15;
- (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.

12. The antibody construct according to claim 11, having an amino acid sequence selected from the group consisting of:

- (a) SEQ ID NOs: 54, 55, 60, and 61;
- (b) SEQ ID NOs: 72, 73, 78, and 79;
- (c) SEQ ID NOs: 90, 91, 96, 97, 108, 109, 114, and 115;
- (d) SEQ ID NOs: 144, 145, 150, 151, 162, 163, 168, 169, 180, 181, 186, and 187;
- (e) SEQ ID NOs: 198, 199, 204, 205, 216, 217, 222, 223, 234, 235, 240, and 241;
- (f) SEQ ID NOs: 252, 306, 257, 307, 268, 308, 273, 309, 284, 310, 289, 311, 300, 312, 305, and 313;
- (g) SEQ ID NOs: 324, 554, 329, 555, 340, 556, 345, 557, 356, 558, 361, 559, 372, 560, 377, 561, 388, 562, 393, 563, 404, 564, 409, 565, 420, 566, 425, 567, 436, 568, 441, 569, 452, 570, 457, 571, 468, 572, 473, 573, 484, 574, 489, 575, 500, 576, 505, 577, 516, 578, 521, 579, 532, 580, 537, 581, 548, 582, 553, and 583;
- (h) SEQ ID NOs: 594, 610, 626, 642, 658, 674, 690, 706, 722, 738, 754, 77, 786, 802, 818, 834, 850, 866, 882, 898, 914, 930, 946, 962, 978, 994, 1010, 1026, 1042, 1058, 1074, 1090, 1106, 1122, 1138, 1154, 1170, 1186, 599, 615, 631, 647, 663, 679, 695, 711, 727, 743, 759, 775, 791, 807, 823, 839, 855, 871, 887, 903, 919, 935, 951, 967,

983, 999, 1015, 1031, 1047, 1063, 1079, 1095, 1111, 1127, 1143, 1159, 1175, 1191, and 1192-1267;

(i) SEQ ID NO: 43; and

(j) SEQ ID Nos: 1279, 1280, 1291, 1292, 1303, 1304, 1315, 1316, 1327, 1328, 1339, 1340, 1351, 1352, 1363, 1364, 1375, 1376, 1387, 1388, 1399, 1400, 1411, 1412, 1423, 1424, 1435, 1436, 1447, 1448.

13. A polynucleotide encoding an antibody construct as defined in any one of claims 1 to 12.
14. A vector comprising a polynucleotide as defined in claim 13.
15. A host cell transformed or transfected with the polynucleotide as defined in claim 13 or with the vector as defined in claim 14.
16. A process for the production of an antibody construct according to any one of claims 1 to 12, said process comprising culturing a host cell as defined in claim 13 under conditions allowing the expression of the antibody construct as defined in any one of claims 1 to 12 and recovering the produced antibody construct from the culture.
17. A pharmaceutical composition comprising an antibody construct according to any one of claims 1 to 12, or produced according to the process of claim 16.
18. The pharmaceutical composition of claims 17, which is stable for at least four weeks at about -20°C.
19. The antibody construct according to any one of claims 1 to 12, for use in the prevention, treatment or amelioration of a disease selected from a proliferative disease, a tumorous disease, a viral disease or an immunological disorder.
20. Use of the antibody construct according to any one of claims 1 to 13 in the manufacture of a medicament for the treatment or amelioration of a proliferative disease, a tumorous disease, a viral disease or an immunological disorder.

21. A kit comprising an antibody construct according to any one of claims 1 to 12, a polynucleotide as defined in claim 13, a vector as defined in claim 14, and/or a host cell as defined in claim 15.