

Claims

1. ~~A nucleic acid encoding a bispecific antibody construct comprising a first binding domain which binds to human delta-like 3 (DLL3) on the surface of a target cell and a second binding domain which binds to human and macaque CD3 on the surface of a T-cell and at least macaque CD3, wherein the first binding domain binds to an epitope of DLL3 which is comprised within the region as depicted in amino acid sequence of SEQ_ID NO: 260 258.~~
2. ~~The antibody construct according to nucleic acid of claim_1, wherein the first binding domain further binds to macaque DLL3, preferably to _~~
3. ~~The nucleic acid of claim 2, wherein the macaque DLL3 is Macaca fascicularis DLL3.~~
- 3.4. ~~The antibody construct according to nucleic acid of claim_1 or 2, wherein the second binding domain binds to human CD3 epsilon and to Callithrix jacchus, Saguinus Oedipus or Saimiri sciureus CD3 epsilon.~~
- 4.5. ~~The antibody construct according to any one nucleic acid of the preceding claims claim 1, wherein the antibody construct is in a format selected from the group consisting of: (scFv)₂, scFv-single domain mAb, diabodies and oligomers of the foregoing formats.~~
5. ~~The antibody construct according to any one of the preceding claims, wherein the first binding domain binds to an epitope of DLL3 which is comprised within the region as depicted in SEQ ID NO: 258.~~
6. ~~The antibody construct according to claim 56. The nucleic acid of claim 1,~~ wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from the group consisting of:
 - a) ~~CDR-H1 as depicted in comprising the amino acid sequence of SEQ_ID NO:-_31,~~ CDR-H2 ~~as depicted in comprising the amino acid sequence of SEQ_ID NO:-_32,~~ CDR-H3 ~~as depicted in comprising the amino acid sequence of SEQ_ID NO:-_33,~~ CDR-L1 ~~as depicted in comprising the amino acid sequence of SEQ_ID NO:-_34,~~ CDR-L2 ~~as depicted in comprising the amino acid sequence of SEQ_ID NO:-_35~~ and CDR-L3 ~~as depicted in comprising the amino acid sequence of SEQ_ID NO:-_36;~~

CDR-H3 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_103, CDR-L1 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_104, CDR-L2 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_105, and CDR-L3 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_106; and i) ~~—~~CDR-H1 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_111, CDR-H2 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_112, CDR-H3 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_113, CDR-L1 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_114, CDR-L2 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_115, and CDR-L3 ~~as depicted in~~comprising the amino acid sequence of SEQ_ID NO:-_116.

- 7._ The antibody construct according to ~~nucleic acid of claim 5 or 6~~, wherein the first binding domain comprises a ~~VH-VL region~~ comprising CDR-H1, CDR-H2 and CDR-H3 and a VH region comprising CDR-L1, CDR-L2 and CDR-L3 selected from the group consisting of ~~those depicted in~~:

a) CDR-L1 comprising the amino acid sequence of SEQ_ID NO: 342, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 343, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 344; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 345, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 346, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 347;

b) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 351, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 352, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 353; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 354, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 355, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 356;

c) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 360, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 361, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 362; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 363, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 364, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 365;

d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 369, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 370, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 371; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 372, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 373, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 374;

e) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 378, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 379, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 380; CDR-H1 comprising the amino acid sequence of

SEQ ID NO: 381, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 382, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 383;

f) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 387, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 388, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 389; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 392;

g) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 397, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 398; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 399, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 400, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 401;

h) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 405, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 406, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 407; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 408, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 409, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 410; and

i) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 414, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 415, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 416; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 417, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 418, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 419; and

j) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 423, CDR-L2 comprising the amino acid sequence of SEQ ID NO: 424, CDR-L3 comprising the amino acid sequence of SEQ ID NO: 425; CDR-H1 comprising the amino acid sequence of SEQ ID NO: 426, CDR-H2 comprising the amino acid sequence of SEQ ID NO: 427, and CDR-H3 comprising the amino acid sequence of SEQ ID NO: 428.

8. The nucleic acid of claim 6, wherein the second binding domain comprises a VH region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 348, SEQ ID NO: 357, SEQ ID NO: 366, SEQ ID NO: 375, SEQ ID NO: 384, SEQ ID NO: 393, SEQ ID NO: 402, SEQ ID NO: 411, SEQ ID NO: 420, and SEQ ID NO: 429.

9. The nucleic acid of claim 6, wherein the second binding domain comprises a VL region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO: 349, SEQ ID NO: 358, SEQ ID NO: 367, SEQ ID NO: 376, SEQ ID NO: 385, SEQ ID NO: 394, SEQ ID NO: 403, SEQ ID NO: 412, SEQ ID NO: 421, and SEQ ID NO: 430.

10. The nucleic acid of claim 6, wherein the second binding domain comprises a VH region and a VL region comprising the pair of amino acid sequences, respectively, selected from the group consisting of: SEQ ID NOs: 348 and 349; SEQ ID NOs: 357 and 358; SEQ ID NOs: 366 and 367; SEQ ID NOs: 375 and 376; SEQ ID NOs: 384 and 385; SEQ ID NOs: 393 and 394; SEQ ID NOs: 402 and 403; SEQ ID NOs: 411 and 412; SEQ ID NOs: 420 and 421; and SEQ ID NOs: 429 and 430.
11. The nucleic acid of claim 6, wherein the second binding domain comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 350, SEQ ID NO: 359, SEQ ID NO: 368, SEQ ID NO: 377, SEQ ID NO: 386, SEQ ID NO: 395, SEQ ID NO: 404, SEQ ID NO: 413, SEQ ID NO: 422, and SEQ ID NO: 431.
12. The nucleic acid of claim 6, wherein the first binding domain comprises a VH region comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 31, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 32, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 33, and a VL region comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 36, and wherein the second binding domain comprises a VL domain comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 423, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 424, a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 425, and a VH domain comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 426, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 427, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 428.
13. The nucleic acid of claim 12, wherein the first binding domain comprises a VH region comprising the amino acid sequence of SEQ ID NO: 435 and a VL region comprising the amino acid sequence of SEQ ID NO: 436, and wherein the second binding domain comprises a VH region comprising the amino acid sequence of SEQ ID NO: 429 and a VL region comprising the amino acid sequence of SEQ ID NO: 430.
14. The nucleic acid of claim 13, wherein the first binding domain comprises the amino acid sequence of SEQ ID NO: 437, and wherein the second binding domain comprises the amino acid sequence of SEQ ID NO: 431.
- 15.- The nucleic acid of claim 1, wherein the first binding domain comprises a VH region comprising the amino acid sequence selected from the group consisting of: SEQ ID NO:

37, SEQ_ID NO:-_47, SEQ_ID NO:-_57, SEQ_ID NO:-_67, SEQ_ID NO:-_77, SEQ_ID NO:-_87, SEQ_ID NO:-_97, SEQ_ID NO:-_107, SEQ_ID NO:-_117, SEQ_ID NO:-_435, and SEQ_ID NO:-_529.

~~8.16.~~ The antibody construct according to any one nucleic acid of ~~claims 5 to 7~~claim 1, wherein the first binding domain comprises a VL-region comprising the amino acid sequence selected from the group consisting of ~~those depicted in:~~ SEQ_ID NO:-_38, SEQ_ID NO:-_48, SEQ_ID NO:-_58, SEQ_ID NO:-_68, SEQ_ID NO:-_78, SEQ_ID NO:-_88, SEQ_ID NO:-_98, SEQ_ID NO:-_108, SEQ_ID NO:-_118, SEQ ID NO:-_436, and SEQ_ID NO:-_530.

~~9.17.~~ The antibody construct according to any one nucleic acid of ~~claims 5 to 8~~claim 1, wherein the first binding domain comprises a VH region and a VL region comprising the pair of amino acid sequences, respectively, selected from the group consisting of ~~pairs of a VH region and a VL region as depicted in:~~ SEQ_ID NOS:-_37+38; SEQ_ID NOS:-_47+48; SEQ_ID NOS:-_57+58; SEQ_ID NOS:-_67+68; SEQ_ID NOS:-_77+78; SEQ_ID NOS:-_87+88; SEQ_ID NOS:-_97+98; SEQ_ID NOS:-_107+108; SEQ_ID NOS:-_117+118; SEQ_ID NOS:-_435+436; and SEQ_ID NOS:-_529+530.

~~10.18.~~ The antibody construct according to any one nucleic acid of ~~claims 5 to 9~~claim 1, wherein the first binding domain comprises a polypeptide comprising the amino acid sequence selected from the group consisting of ~~those depicted in:~~ SEQ_ID NO:-_39, SEQ_ID NO:-_49, SEQ_ID NO:-_59, SEQ_ID NO:-_69, SEQ_ID NO:-_79, SEQ_ID NO:-_89, SEQ_ID NO:-_99, SEQ_ID NO:-_109, SEQ_ID NO:-_119, SEQ ID NO:-_437, and SEQ ID NO:-_531.

~~11.~~ The antibody construct according to any one of claims 5 to 10, comprising ~~19.~~ The nucleic acid of claim 1, wherein the nucleic acid comprises a nucleotide sequence encoding a polypeptide comprising the amino acid sequence selected from the group consisting of ~~those depicted in:~~ SEQ_ID NO:-_40, SEQ_ID NO:-_50, SEQ_ID NO:-_60, SEQ_ID NO:-_70, SEQ_ID NO:-_80, SEQ_ID NO:-_90, SEQ_ID NO:-_100, SEQ_ID NO:-_110, SEQ_ID NO:-_120, SEQ_ID NO:-_211, SEQ_ID NO:-_212, SEQ_ID NO:-_213, SEQ_ID NO:-_214, SEQ_ID NO:-_215, SEQ_ID NO:-_216, SEQ_ID NO:-_217, SEQ_ID NO:-_438, and SEQ_ID NO:-_532.

~~12.20.~~ The antibody construct according to any one nucleic acid of ~~claims~~claim 1 to 4, wherein the first binding domain binds to an epitope of DLL3 which is comprised within the region as depicted in SEQ ID NO: 259nucleic acid.

~~13.~~ The antibody construct according to claim 12, wherein the first binding domain comprises a VH region comprising CDR H1, CDR H2 and CDR H3 and a VL region comprising CDR L1, CDR L2 and CDR L3 selected from the group consisting of:

a) CDR H1 as depicted in SEQ ID NO: 121, CDR H2 as depicted in SEQ ID NO: 122, CDR H3 as depicted in SEQ ID NO: 123, 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;

b) CDR H1 as depicted in SEQ ID NO: 131, CDR H2 as depicted in SEQ ID NO: 132, CDR H3 as depicted in SEQ ID NO: 133, CDR L1 as depicted in SEQ ID NO: 134, CDR L2 as depicted in SEQ ID NO: 135 and CDR L3 as depicted in SEQ ID NO: 136;

c) CDR H1 as depicted in SEQ ID NO: 141, CDR H2 as depicted in SEQ ID NO: 142, CDR H3 as depicted in SEQ ID NO: 143, 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;

d) CDR H1 as depicted in SEQ ID NO: 151, CDR H2 as depicted in SEQ ID NO: 152, CDR H3 as depicted in SEQ ID NO: 153, CDR L1 as depicted in SEQ ID NO: 154, CDR L2 as depicted in SEQ ID NO: 155 and CDR L3 as depicted in SEQ ID NO: 156;

e) CDR H1 as depicted in SEQ ID NO: 161, CDR H2 as depicted in SEQ ID NO: 162, CDR H3 as depicted in SEQ ID NO: 163, CDR L1 as depicted in SEQ ID NO: 164, CDR L2 as depicted in SEQ ID NO: 165 and CDR L3 as depicted in SEQ ID NO: 166;

f) CDR H1 as depicted in SEQ ID NO: 131, CDR H2 as depicted in SEQ ID NO: 439, CDR H3 as depicted in SEQ ID NO: 133, CDR L1 as depicted in SEQ ID

NO: 134, CDR-L2 as depicted in SEQ ID NO: 135 and CDR-L3 as depicted in SEQ ID NO: 136;

g) ~~CDR-H1 as depicted in SEQ ID NO: 131, CDR-H2 as depicted in SEQ ID NO: 440, CDR-H3 as depicted in SEQ ID NO: 133, CDR-L1 as depicted in SEQ ID NO: 134, CDR-L2 as depicted in SEQ ID NO: 135 and CDR-L3 as depicted in SEQ ID NO: 136;~~

h) ~~CDR-H1 as depicted in SEQ ID NO: 131, CDR-H2 as depicted in SEQ ID NO: 132, CDR-H3 as depicted in SEQ ID NO: 133, CDR-L1 as depicted in SEQ ID NO: 441, CDR-L2 as depicted in SEQ ID NO: 135 and CDR-L3 as depicted in SEQ ID NO: 136;~~

i) ~~CDR-H1 as depicted in SEQ ID NO: 131, CDR-H2 as depicted in SEQ ID NO: 132, CDR-H3 as depicted in SEQ ID NO: 133, CDR-L1 as depicted in SEQ ID NO: 442, CDR-L2 as depicted in SEQ ID NO: 135 and CDR-L3 as depicted in SEQ ID NO: 136;~~

j) ~~CDR-H1 as depicted in SEQ ID NO: 131, CDR-H2 as depicted in SEQ ID NO: 132, CDR-H3 as depicted in SEQ ID NO: 133, CDR-L1 as depicted in SEQ ID NO: 443, CDR-L2 as depicted in SEQ ID NO: 135 and CDR-L3 as depicted in SEQ ID NO: 136;~~

k) ~~CDR-H1 as depicted in SEQ ID NO: 131, CDR-H2 as depicted in SEQ ID NO: 132, CDR-H3 as depicted in SEQ ID NO: 133, CDR-L1 as depicted in SEQ ID NO: 444, CDR-L2 as depicted in SEQ ID NO: 135 and CDR-L3 as depicted in SEQ ID NO: 136;~~

l) ~~CDR-H1 as depicted in SEQ ID NO: 131, CDR-H2 as depicted in SEQ ID NO: 439, CDR-H3 as depicted in SEQ ID NO: 133, CDR-L1 as depicted in SEQ ID NO: 441, CDR-L2 as depicted in SEQ ID NO: 135 and CDR-L3 as depicted in SEQ ID NO: 136; and~~

m) ~~CDR-H1 as depicted in SEQ ID NO: 131, CDR-H2 as depicted in SEQ ID NO: 440, CDR-H3 as depicted in SEQ ID NO: 133, CDR-L1 as depicted in SEQ ID NO: 442, CDR-L2 as depicted in SEQ ID NO: 135 and CDR-L3 as depicted in SEQ ID NO: 136~~nucleotide sequence encoding;

~~14. The antibody construct according to claim 12 or 13, wherein the first binding domain comprises a VH region selected from the group consisting of those depicted in SEQ ID NO: 127, SEQ ID NO: 137, SEQ ID NO: 147, SEQ ID NO: 157, SEQ ID NO: 167, SEQ ID NO: 445, SEQ ID NO: 446, SEQ ID NO: 447, SEQ ID NO: 448, SEQ ID NO: 449, SEQ ID NO: 450, SEQ ID NO: 451, SEQ ID NO: 452, SEQ ID NO: 453, SEQ ID NO: 454, and SEQ ID NO: 455.~~

~~15. The antibody construct according to any one of claims 12 to 14, wherein the first binding domain comprises a VL region selected from the group consisting of those depicted in SEQ ID NO: 128, SEQ ID NO: 138, SEQ ID NO: 148, SEQ ID NO: 158, SEQ ID NO: 168, SEQ ID NO: 456, SEQ ID NO: 457, SEQ ID NO: 458, SEQ ID NO: 459, SEQ ID NO: 460, SEQ ID NO: 461, SEQ ID NO: 462, SEQ ID NO: 463, SEQ ID NO: 464, SEQ ID NO: 465, SEQ ID NO: 466, SEQ ID NO: 467, SEQ ID NO: 468, SEQ ID NO: 469, and SEQ ID NO: 470.~~

~~16. The antibody construct according to any one of claims 12 to 15, wherein the first binding domain comprises a VH region and a VL region selected from the group consisting of pairs of a VH region and a VL region as depicted in SEQ ID NOs: 127+128; SEQ ID NOs: 137+138; SEQ ID NOs: 147+148; SEQ ID NOs: 157+158; SEQ ID NOs: 167+168; SEQ ID NOs: 137+456; SEQ ID NOs: 137+457; SEQ ID NOs: 137+458; SEQ ID NOs: 137+459; SEQ ID NOs: 137+460; SEQ ID NOs: 445+138; SEQ ID NOs: 446+138; SEQ ID NOs: 447+138; SEQ ID NOs: 445+460; SEQ ID NOs: 448+461; SEQ ID NOs: 449+462; SEQ ID NOs: 450+463; SEQ ID NOs: 450+464; SEQ ID NOs: 450+465; SEQ ID NOs: 450+466; SEQ ID NOs: 450+467; SEQ ID NOs: 450+468; SEQ ID NOs: 451+463; SEQ ID NOs: 452+463; SEQ ID~~

~~NOs 453+463; SEQ ID NOs 451+468; SEQ ID NOs 454+469; and SEQ ID NOs 455+470.~~

~~17. The antibody construct according to any one of claims 12 to 16, wherein the first binding domain comprises a polypeptide selected from the group consisting of those depicted in SEQ ID NO: 129, SEQ ID NO: 139, SEQ ID NO: 149, SEQ ID NO: 159, SEQ ID NO: 169, SEQ ID NO: 471, SEQ ID NO: 472, SEQ ID NO: 473, SEQ ID NO: 474, SEQ ID NO: 475, SEQ ID NO: 476, SEQ ID NO: 477, SEQ ID NO: 478, SEQ ID NO: 479, SEQ ID NO: 480, SEQ ID NO: 481, SEQ ID NO: 482, SEQ ID NO: 483, SEQ ID NO: 484, SEQ ID NO: 485, SEQ ID NO: 486, SEQ ID NO: 487, SEQ ID NO: 488, SEQ ID NO: 489, SEQ ID NO: 490, SEQ ID NO: 491, SEQ ID NO: 492, and SEQ ID NO: 493.~~

~~18. The antibody construct according to any one of claims 12 to 17, comprising a polypeptide comprising the amino acid sequence selected from the group consisting of those depicted in SEQ ID NO: 130, SEQ ID NO: 140, SEQ ID NO: 150, SEQ ID NO: 160, SEQ ID NO: 170, SEQ ID NO: 218, SEQ ID NO: 219, SEQ ID NO: 220, SEQ ID NO: 494, SEQ ID NO: 495, SEQ ID NO: 496, SEQ ID NO: 497, SEQ ID NO: 498, SEQ ID NO: 499, SEQ ID NO: 500, SEQ ID NO: 501, SEQ ID NO: 502, SEQ ID NO: 503, SEQ ID NO: 504, SEQ ID NO: 505, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508, SEQ ID NO: 509, SEQ ID NO: 510, SEQ ID NO: 511, SEQ ID NO: 512, SEQ ID NO: 513, SEQ ID NO: 514, SEQ ID NO: 515, and SEQ ID NO: 516.~~

~~19. The antibody construct according to any one of claims 5-11, comprising or consisting of a polypeptide selected from the group consisting of those depicted in SEQ ID NO: ;~~

SEQ ID NO: 517, SEQ_ID NO:-_518, SEQ_ID NO:-_519, SEQ_ID NO:-_520, SEQ_ID NO:-_521, SEQ_ID NO:-_522, SEQ_ID NO:-_523, and SEQ_ID NO:-_524.

20. ~~A polynucleotide encoding an antibody construct as defined in any one of the preceding claims.~~

21. ~~A vector comprising a polynucleotide as defined in~~ the nucleic acid of claim 20_1.

22. ~~A~~ An isolated host cell transformed or transfected with the ~~polynucleotide as defined in claim 20 or with the vector as defined in claim~~ vector of claim 21.

23. ~~A process for the production of an~~ producing a bispecific antibody construct according to any one of claims 1 to 19, said process comprising culturing ~~at the~~ the host cell as defined ~~in of claim_22~~ under conditions allowing the expression of ~~said the~~ the antibody construct and, optionally, recovering the ~~produced~~ antibody construct from the culture.

24. ~~A pharmaceutical composition comprising an antibody construct according to any one of claims 1 to 18, or produced according to the process of claim 23.~~

25. ~~The antibody construct according to any one of claims 1 to 19, or produced according to the process of claim 23, for use in the prevention, treatment or amelioration of a tumor or cancer disease or a metastatic cancer disease.~~

26. ~~A method for the treatment or amelioration of a tumor or cancer disease or a metastatic cancer disease, comprising the step of administering to a subject in need thereof the antibody construct according to any one of claims 1 to 19, or produced according to the process of claim 23.~~

27. ~~The method according to claim 26 or the antibody construct according to claim 24, wherein the tumor or cancer disease is selected from the group consisting of lung~~

~~cancer, preferably SCLC, breast, cervical, colon, colorectal, endometrial, head and neck, liver, ovarian, pancreatic, prostate, skin, gastric, testis, thyroid, adrenal, renal, bladder, uterine, esophageal, urothelial and brain tumor or cancer, lymphoma, carcinoma, and sarcoma, and a metastatic cancer disease derived from any of the foregoing.~~

~~28. A kit comprising an antibody construct according to any one of claims 1 to 19, an antibody construct produced according to the process of claim 23, a polynucleotide as defined in claim 20, a vector as defined in claim 21, and/or a host cell as defined in claim 22.~~

24. An isolated host cell transformed or transfected with the nucleic acid of claim 1.

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