

Claims

1. A bispecific antibody construct comprising a first binding domain which binds to human CD70 on the surface of a target cell and a second binding domain which binds to human CD3 on the surface of a T cell ~~and at least macaque CD3.~~

2. ~~The antibody construct according to 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, wherein~~
 - ~~• said CDR-H1 has the amino acid sequence X₁YX₂MX₃ (SEQ ID NO: 1869), wherein X₁ is S, T or V, X₂ is A or S, and X₃ is S or N;~~
 - ~~• said CDR-H2 has the amino acid sequence X₁ISX₂SGGX₃X₄X₅X₆AESVX₇G (SEQ ID NO: 1870), wherein X₁ is A, Y, V, L, or T, X₂ is G or S, X₃ is R, Y, S, G or I, X₄ is T, I, P, or A, X₅ is F, Y, N, Q or D, X₆ is Y or F, and X₇ is E, K or Q;~~
 - ~~• said CDR-H3 has the amino acid sequence X₁DYSNYX₂X₃FDY (SEQ ID NO: 1871), wherein X₁ is H, G or V, X₂ is P, A, L or F, and X₃ is Y or F;~~
 - ~~• said CDR-L1 has the amino acid sequence RAX₁QX₂X₃X₄X₅X₆LX₈ (SEQ ID NO: 1872), wherein X₁ is S or G, X₂ is S or G, X₃ is I or V, X₄ is R, S or no amino acid, X₅ is S or G, X₆ is S, N, T or D, X₇ is Y or no amino acid, and X₈ is A or G;~~
 - ~~• said CDR-L2 has the amino acid sequence X₁X₂SX₃X₄X₅X₆ (SEQ ID NO: 1873), wherein X₁ is G or A, X₂ is A or S, X₃ is S, T, N or I, X₄ is R or L, X₅ is A or Q, and X₆ is T or S; and~~
 - ~~• said CDR-L3 has the amino acid sequence QQYX₁X₂XPX₄X₅ (SEQ ID NO: 1874), wherein X₁ is G, Y or F, X₂ is D, S, Y, I or A, X₃ is L, T, S or Y, X₄ is F, L, P or I, and X₅ is T or P.~~

3. ~~The antibody construct according to claim 1 or 2, 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, wherein~~
 - ~~• said CDR-H1 has the amino acid sequence SYSMN (SEQ ID NO: 1422) or X₁YAMS (SEQ ID NO: 1875), wherein X₁ is S, T or V;~~
 - ~~• said CDR-H2 has an amino acid sequence selected from the group consisting of YISSSGGYIYYAESVKG (SEQ ID NO: 1423), VISGSGGITDFAESVKG (SEQ ID~~

- NO: 1367) and X_1 ISGSGGX $X_2X_3X_4$ YAESVX X_5 G (SEQ ID NO: 1876), wherein X_1 is A, V, L or T, X_2 is R, S, or G, X_3 is T, P or A, X_4 is F, N, Y or Q, and X_5 is E, K, or Q;
- ~~said CDR-H3 has an amino acid sequence selected from the group consisting of GDYSNYAYFDY (SEQ ID NO: 1424), HDYSNYFFFDY (SEQ ID NO: 1368), and X_1 DYSNYX X_2X_3 FDY (SEQ ID NO: 1877), wherein X_1 is H or V, X_2 is P, L or A, and X_3 is Y or F;~~
 - ~~said CDR-L1 has the amino acid sequence RASQGISNYLA (SEQ ID NO: 1425) or RAX X_1 QX $X_2X_3X_4X_5X_6$ YLX X_7 (SEQ ID NO: 1878), wherein X_1 is S or G, X_2 is S or G, X_3 is I or V, X_4 is R or S, X_5 is S or G, X_6 is S, T, N or D, and X_7 is A or G;~~
 - ~~said CDR-L2 has the amino acid sequence AASXLQS (SEQ ID NO: 1879), wherein X is T or I, or GX X_1 SX X_2 RAT (SEQ ID NO: 1880), wherein X_1 is A or S, and X_2 is S or N; and~~
 - ~~said CDR-L3 has an amino acid sequence selected from the group consisting of QQYYSTPLT (SEQ ID NO: 1427), QQYFAYPIT (SEQ ID NO: 1371), and QQYGX X_1X_2 PX X_3X_4 (SEQ ID NO: 1881), wherein X_1 is D, Y, S or I, X_2 is L, S or T, X_3 is F or P, and X_4 is T or P.~~
4. ~~The antibody construct according any one of the preceding claims, 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, wherein~~
- ~~said CDR-H1 has the amino acid sequence X_1 YAMS (SEQ ID NO: 1875), wherein X_1 is S, T or V;~~
 - ~~said CDR-H2 has the amino acid sequence X_1 ISGSGGX $X_2X_3X_4$ YAESVX X_5 G (SEQ ID NO: 1876), wherein X_1 is A, V, L or T, X_2 is R, S, or G, X_3 is T, P or A, X_4 is F, N, Y or Q, and X_5 is E, K, or Q;~~
 - ~~said CDR-H3 has the amino acid sequence X_1 DYSNYX X_2X_3 FDY (SEQ ID NO: 1877), wherein X_1 is H or V, X_2 is P, L or A, and X_3 is Y or F;~~
 - ~~said CDR-L1 has the amino acid sequence RAX X_1 QX $X_2X_3X_4X_5X_6$ YLX X_7 (SEQ ID NO: 1878), wherein X_1 is S or G, X_2 is S or G, X_3 is I or V, X_4 is R or S, X_5 is S or G, X_6 is S, T, N or D, and X_7 is A or G;~~
 - ~~said CDR-L2 has the amino acid sequence GX X_1 SX X_2 RAT (SEQ ID NO: 1880), wherein X_1 is A or S, and X_2 is S or N; and~~
 - ~~said CDR-L3 has the amino acid sequence QQYGX X_1X_2 PX X_3X_4 (SEQ ID NO: 1881), wherein X_1 is D, Y, S or I, X_2 is L, S or T, X_3 is F or P, and X_4 is T or P.~~

5. ~~The antibody construct according to any one of the preceding claims, 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, wherein~~
- ~~• said CDR-H1 has an amino acid sequence selected from the group consisting of SYAMS (SEQ ID NO: 1044), TYAMS (SEQ ID NO: 1142), VYAMS (SEQ ID NO: 1436), and SYSMN (SEQ ID NO: 1422);~~
 - ~~• said CDR-H2 has an amino acid sequence selected from the group consisting of AISGSGGRTFYAESVEG (SEQ ID NO: 1087), VISGSGGRPNYAESVKG (SEQ ID NO: 1045), AISGSGGSTFYAESVKG (SEQ ID NO: 1171), AISGSGGSTFYAESVQG (SEQ ID NO: 1213), AISGSGGGTFYAESVKG (SEQ ID NO: 1227), LISGSGGRTYYAESVKG (SEQ ID NO: 1241), AISGSGGRAQYAESVQG (SEQ ID NO: 1255), TISGSGGSTFYAESVKG (SEQ ID NO: 1437), YISSSGGYIYYAESVKG (SEQ ID NO: 1423), and VISGSGGITDFAESVKG (SEQ ID NO: 1367);~~
 - ~~• said CDR-H3 has an amino acid sequence selected from the group consisting of HDYSNYPYFDY (SEQ ID NO: 1088), VDYSNYLFFDY (SEQ ID NO: 1046), HDYSNYAYFDY (SEQ ID NO: 1438), GDYSNYAYFDY (SEQ ID NO: 1424), and HDYSNYFFFDY (SEQ ID NO: 1368);~~
 - ~~• said CDR-L1 has an amino acid sequence selected from the group consisting of RASQSIRSSYLA (SEQ ID NO: 1089), RASQSVRSTYLA (SEQ ID NO: 1145), RAGQSVRSSYLG (SEQ ID NO: 1047), RASQSVRSSYLA (SEQ ID NO: 1173), RASQSVRSNYLA (SEQ ID NO: 1187), RASQSVRGNYLA (SEQ ID NO: 1215), RASQSIRSNYLA (SEQ ID NO: 1229), RASQSVSSNLA (SEQ ID NO: 1257), RASQGVRSDYLA (SEQ ID NO: 1271), RASQGVRSSYLA (SEQ ID NO: 1341), and RASQGISNYLA (SEQ ID NO: 1369);~~
 - ~~• said CDR-L2 has an amino acid sequence selected from the group consisting of GASSRAT (SEQ ID NO: 1048), GASNRAT (SEQ ID NO: 1244), GSSSRAT (SEQ ID NO: 1258), AASTLQS (SEQ ID NO: 1426), and AASILQS (SEQ ID NO: 1370); and~~
 - ~~• said CDR-L3 has an amino acid sequence selected from the group consisting of QQYGDLPFT (SEQ ID NO: 1091), QQYGYSPPT (SEQ ID NO: 1049), QQYGYSPFT (SEQ ID NO: 1217), QQYGSSPFT (SEQ ID NO: 1231), QQYGISPPT (SEQ ID NO: 1245), QQYGSSPPP (SEQ ID NO: 1259), QQYGSTPPT (SEQ ID NO: 1273), QQYGSSPPT (SEQ ID NO: 1343), QQYYSTPLT (SEQ ID NO: 1427), and QQYFAYPIT (SEQ ID NO: 1371).~~

6. ~~The antibody construct according to any one of the preceding claims,~~ 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, wherein said CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2 and CDR-L3 are selected from the group consisting of those depicted in:

- ~~16)~~1) SEQ: ID NOs: 1044-1049;
- ~~17)~~2) SEQ: ID NOs: 1086-1091;
- ~~18)~~3) SEQ: ID NOs: 1142-1147;
- ~~19)~~4) SEQ: ID NOs: 1170-1175;
- ~~20)~~5) SEQ: ID NOs: 1184-1189;
- ~~21)~~6) SEQ: ID NOs: 1212-1217;
- ~~22)~~7) SEQ: ID NOs: 1226-1231;
- ~~23)~~8) SEQ: ID NOs: 1240-1245;
- ~~24)~~9) SEQ: ID NOs: 1254-1259;
- ~~25)~~10) SEQ: ID NOs: 1268-1273;
- ~~26)~~11) SEQ: ID NOs: 1338-1343;
- ~~27)~~12) SEQ: ID NOs: 1352-1357;
- ~~28)~~13) SEQ: ID NOs: 1366-1371;
- ~~29)~~14) SEQ: ID NOs: 1422-1427; and
- ~~30)~~15) SEQ: ID NOs: 1436-1441;

~~27.~~ The antibody construct according to claim 1 ~~any one of the preceding claims,~~ wherein the first binding domain comprises a VH region selected from the group consisting of those depicted in SEQ ID NO: 1050, SEQ ID NO: 1092, SEQ ID NO: 1148, SEQ ID NO: 1176, SEQ ID NO: 1190, SEQ ID NO: 1218, SEQ ID NO: 1232, SEQ ID NO: 1246, SEQ ID NO: 1260, SEQ ID NO: 1274, SEQ ID NO: 1344, SEQ ID NO: 1358, SEQ ID NO: 1372, SEQ ID NO: 1428, and SEQ ID NO: 1442.

~~38.~~ The antibody construct according to claim 1 or 2 ~~any one of the preceding claims,~~ wherein the first binding domain comprises a VL region selected from the group consisting of those depicted in SEQ ID NO: 1051, SEQ ID NO: 1093, SEQ ID NO: 1149, SEQ ID NO: 1177, SEQ ID NO: 1191, SEQ ID NO: 1219, SEQ ID NO: 1233, SEQ ID NO: 1247, SEQ ID NO: 1261, SEQ ID NO: 1275, SEQ ID NO: 1345, SEQ ID NO: 1359, SEQ ID NO: 1373, SEQ ID NO: 1429, and SEQ ID NO: 1443.

49. The antibody construct according to any one of the preceding claims, 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: 1050+1051, SEQ ID NOs: 1092+1093, SEQ ID NOs: 1148+1149, SEQ ID NOs: 1176+1177, SEQ ID NOs: 1190+1191, SEQ ID NOs: 1218+1219, SEQ ID NOs: 1232+1233, SEQ ID NOs: 1246+1247, SEQ ID NOs: 1260+1261, SEQ ID NOs: 1274+1275, SEQ ID NOs: 1344+1345, SEQ ID NOs: 1358+1359, NOs: 1372+1373, SEQ ID NOs: 1428+1429, and SEQ ID NOs: 1442+1443.
510. The antibody construct according to any one of the preceding claims, wherein the first binding domain comprises a polypeptide selected from the group consisting of those depicted in SEQ ID NO: 1052, SEQ ID NO: 1094, SEQ ID NO: 1150, SEQ ID NO: 1178, SEQ ID NO: 1192, SEQ ID NO: 1220, SEQ ID NO: 1234, SEQ ID NO: 1248, SEQ ID NO: 1262, SEQ ID NO: 1276, SEQ ID NO: 1346, SEQ ID NO: 1360, SEQ ID NO: 1374, SEQ ID NO: 1430, and SEQ ID NO: 1444.
611. The antibody construct according to any one of the preceding claims, comprising a polypeptide selected from the group consisting of those depicted in SEQ ID NO: 1053, SEQ ID NO: 1095, SEQ ID NO: 1151, SEQ ID NO: 1179, SEQ ID NO: 1193, SEQ ID NO: 1221, SEQ ID NO: 1235, SEQ ID NO: 1249, SEQ ID NO: 1263, SEQ ID NO: 1277, SEQ ID NO: 1347, SEQ ID NO: 1361, SEQ ID NO: 1375, SEQ ID NO: 1431, and SEQ ID NO: 1445.
712. The antibody construct according to any one of the preceding claims, comprising or consisting of a polypeptide selected from the group consisting of those depicted in SEQ ID NO: 1696, SEQ ID NO: 1702, SEQ ID NO: 1710, SEQ ID NO: 1714, SEQ ID NO: 1716, SEQ ID NO: 1720, SEQ ID NO: 1722, SEQ ID NO: 1724, SEQ ID NO: 1726, SEQ ID NO: 1728, SEQ ID NO: 1738, SEQ ID NO: 1740, SEQ ID NO: 1742, SEQ ID NO: 1750, and SEQ ID NO: 1752.
813. The antibody construct according to any one of the preceding claims, wherein the first binding domain further binds to macaque CD70, preferably to *Macaca fascicularis* CD70.

- ~~9~~14. The antibody construct according to any one of the preceding claims, wherein the second binding domain binds to human CD3 epsilon and to *Callithrix jacchus*, *Saguinus Oedipus* or *Saimiri sciureus* CD3 epsilon.
- ~~10~~15. The antibody construct according to any one of the preceding claims, 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.
- ~~11~~16. A polynucleotide encoding an antibody construct as defined in any one of the preceding claims.
- ~~12~~17. A vector comprising the polynucleotide as defined in claim ~~11~~16.
- ~~13~~18. A host cell transformed or transfected with the polynucleotide as defined in claim ~~11~~16 or with the vector as defined in claim ~~12~~17.
- ~~14~~19. A process for the production of an antibody construct according to any one of claims 1 to ~~10~~15, said process comprising culturing a host cell as defined in claim ~~13~~18 under conditions allowing the expression of said antibody construct and recovering the produced antibody construct from the culture.
- ~~15~~20. A pharmaceutical composition comprising an antibody construct according to any one of claims 1 to ~~10~~15 or produced according to the process of claim ~~14~~19.
- ~~16~~21. The antibody construct according to any one of claims 1 to ~~10~~15, or produced according to the process of claim ~~14~~19, for use in the prevention, treatment ~~or amelioration~~ of a tumor or cancer disease or of a metastatic cancer disease.
- ~~22~~. ~~A method for the treatment or amelioration of a tumor or cancer disease or of 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 15, or produced according to the process of claim 19.~~
- ~~17~~23. The ~~method according to claim 22 or the~~ antibody construct according to claim ~~16~~21, wherein the tumor or cancer disease is selected from the group consisting of renal, lung,

pancreatic, ovarian, breast, colon, head and neck, stomach, rectal, thymic, and brain tumor or cancer, leukemia, lymphoma, melanoma, Kaposi's Sarcoma, embryonal carcinoma, and a metastatic cancer disease derived from any of the foregoing.

1824. A kit comprising an antibody construct according to any one of claims 1 to 1045, an antibody construct produced according to the process of claim 1419, a polynucleotide as defined in claim 1146, a vector as defined in claim 1217, and/or a host cell as defined in claim 1318.