Claims

1. A polypeptide comprising a binding domain, which is an antibody capable of binding to an epitope of human and Callithrix jacchus, Saguinus oedipus or Saimiri sciureus CD3ε chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs:2, 4, 6, or 8 and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu, wherein the first binding domain comprises a VL region comprising CDR-L1 GSSTGAVTSGNYPN (SEQ ID NO:153), CDR-L2 GTKFLAP (SEQ ID NO:154) and CDR-L3 VLWYSNRWV (SEQ ID NO:155) and a VH region comprising CDR-H 1 KYAMN (SEQ ID NO:174), CDR-H2 RIRSKYNNYATYYADSVKD (SEQ ID NO:175) and CDR-H3 HGNFGNSYISYWAY (SEQ ID NO:176), and
wherein the polypeptide further comprises a second binding domain capable of binding to a cell surface antigen which is CD33. ~~capable of binding to an epitope of human and non-chimpanzee primate CD3ε (epsilon) chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID Nos. 2, 4, 6, or 8.~~

~~1. The polypeptide of claim 1, wherein said binding domain capable of binding to an epitope of the human and non-chimpanzee primate CD3ε (epsilon) chain is of human origin.~~

2. The polypeptide as defined in claim 1, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs:2, 4, 6, and 8 and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu.

~~2. The polypeptide according to any one of claims 1 to 2, wherein the polypeptide comprises a first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain and a second binding domain capable of binding to a cell surface antigen.~~

3. The polypeptide of claim 1 or 2, wherein the first binding domain comprises a VL region selected from the group consisting of a VL region as depicted in SEQ ID NO: 179 or 183.

~~3. The polypeptide according to claim 3, wherein the second binding domain binds to a cell surface antigen of a human and a non-chimpanzee primate.~~

4. The polypeptide of claim 1 or 2, wherein the first binding domain comprises a VH region selected from the group consisting of a VH region as depicted in SEQ ID NO: 177 or 181.

~~4. The polypeptide according to any one of claims 1 to 4, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VL region comprising CDR-Ll, CDR-L2 and CDR-L3 selected from:~~

~~(a) CDR-Ll as depicted in SEQ ID NO. 27, CDR-L2 as depicted in SEQ ID NO. 28 and CDR-L3 as depicted in SEQ ID NO. 29;~~

~~(b) CDR-Ll as depicted in SEQ ID NO. 117, CDR-L2 as depicted in SEQ ID NO. 118 and CDR-L3 as depicted in SEQ ID NO. 119; and~~

~~(c) CDR-Ll as depicted in SEQ ID NO. 153, CDR-L2 as depicted in SEQ ID NO. 154 and CDR-L3 as depicted in SEQ ID NO. 155.~~

5. The polypeptide of any one of claims 1 to 4, wherein the first binding comprises a VL region as depicted in SEQ ID NO:179 or 183 and a VH region as depicted in SEQ ID NO:177 or 181.

6. The polypeptide according to claim 5, wherein the first binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 185 or 187.

~~5. The polypeptide according to any one of claims 1 to 4, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VH region comprising CDR-H 1, CDR-H2 and CDR-H3 selected from:~~

~~(a) CDR-HI as depicted in SEQ ID NO. 12, CDR-H2 as depicted in SEQ ID NO. 13 and CDR-H3 as depicted in SEQ ID NO. 14;~~

~~(b) CDR-HI as depicted in SEQ ID NO. 30, CDR-H2 as depicted in SEQ ID NO. 31 and CDR-H3 as depicted in SEQ ID NO. 32;~~

~~(c) CDR-HI as depicted in SEQ ID NO. 48, CDR-H2 as depicted in SEQ ID NO. 49 and CDR-H3 as depicted in SEQ ID NO. 50;~~

~~(d) CDR-HI 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-HI as depicted in SEQ ID NO. 84, CDR-H2 as depicted in SEQ ID NO. 85 and CDR-H3 as depicted in SEQ ID NO. 86;

(f) CDR-HI as depicted in SEQ ID NO. 102, CDR-H2 as depicted in SEQ ID NO. 103 and CDR-H3 as depicted in SEQ ID NO. 104;

(g) CDR-HI as depicted in SEQ ID NO. 120, CDR-H2 as depicted in SEQ ID NO. 121 and CDR-H3 as depicted in SEQ ID NO. 122;

(h) CDR-HI as depicted in SEQ ID NO. 138, CDR-H2 as depicted in SEQ ID NO. 139 and CDR-H3 as depicted in SEQ ID NO. 140;

(i) CDR-HI as depicted in SEQ ID NO. 156, CDR-H2 as depicted in SEQ ID NO. 157 and CDR-H3 as depicted in SEQ ID NO. 158; and

(j) CDR-HI as depicted in SEQ ID NO. 174, CDR-H2 as depicted in SEQ ID NO. 175 and CDR-H3 as depicted in SEQ ID NO. 176.

6. The polypeptide according to any one of claims 1 to 5, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VL region selected from the group consisting of a VL region as depicted in SEQ ID NO. 35, 39, 125, 129, 161 or 165.

7. The polypeptide according to any one of claims 1 to 4 and 6, wherein the binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VH region selected from the group consisting of a VH region as depicted in SEQ ID NO. 15, 19, 33, 37, 51, 55, 69, 73, 87, 91, 105, 109, 123, 127, 141, 145, 159, 163, 177 or 181.

7. The polypeptide of any one of claims 1 to 6, wherein said polypeptide is a bispecific single chain antibody molecule.

8. The polypeptide according to any one of claims 1 to 8, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises a VL region and a VH region selected from the group consisting of:

(a) a VL region as depicted in SEQ ID NO. 17 or 21 and a VH region as depicted in SEQ ID NO. 15 or 19;

(b) a VL region as depicted in SEQ ID NO. 35 or 39 and a VH region as depicted in SEQ ID NO. 33 or 37;

(c) a VL region as depicted in SEQ ID NO. 53 or 57 and a VH region as depicted in SEQ ID NO. 51 or 55;

(d) a VL region as depicted in SEQ ID NO. 71 or 75 and a VH region as depicted in SEQ ID NO. 69 or 73;

(e) a VL region as depicted in SEQ ID NO. 89 or 93 and a VH region as depicted in SEQ ID NO. 87 or 91;

(f) a VL region as depicted in SEQ ID NO. 107 or 1 11 and a VH region as depicted in SEQ ID NO. 105 or 109;

(g) a VL region as depicted in SEQ ID NO. 125 or 129 and a VH region as depicted in SEQ ID NO. 123 or 127;

(h) a VL region as depicted in SEQ ID NO. 143 or 147 and a VH region as depicted in SEQ ID NO. 141 or 145;

(i) a VL region as depicted in SEQ ID NO. 161 or 165 and a VH region as depicted in SEQ ID NO. 159 or 163; and

(j) a VL region as depicted in SEQ ID NO. 179 or 183 and a VH region as depicted in SEQ ID NO. 177 or 181.

8. The polypeptide of claim 7, wherein the bispecific single chain molecule comprises a group of the following sequences as CDR H1, CDR H2, CDR H3, CDR L1, CDR L2 and CDR L3 in the second binding domain selected from the group consisting of SEQ ID Nos: SEQ ID NOs:382-384 and 387-389, SEQ ID NOs:400-402 and 405-407, SEQ ID NOs:418-420 and 423-425, SEQ ID NOs:436-438 and 441-443, SEQ ID NOs:454-456 and 459-461, SEQ ID NOs:472-474 and 477-479, SEQ ID NOs:490-492 and 495-497, SEQ ID NOs:508-510 and 513-515.

9. The polypeptide according to claim 9, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3ε chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 23, 25, 41, 43, 59, 61, 77, 79, 95, 97, 1 13, 1 15, 131, 133, 149, 151, 167 .169, 185 or 187.

9. The polypeptide of claim 8, wherein the bispecific single chain antibody molecule comprises a sequence selected from:

(a) an amino acid sequence as depicted in any of SEQ ID NOs: 393, 395, 397, 411, 413, 415, 429, 431, 433, 447, 449, 451, 465, 467, 469, 483, 485, 487, 501, 503, 505, 519, 521, 523; and

(b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID NOs: 394, 396, 398, 412, 414, 416, 430, 432, 434, 448, 450, 452, 466, 468, 470, 484, 486, 488, 502, 504, 506, 520, 522, 524.

10. A nucleic acid sequence encoding a polypeptide as defined in any of claims 1 to 9.

~~10. The polypeptide according to any one of claims 3 to 10, wherein the cell surface antigen is a tumor antigen.~~

~~11. The polypeptide according to any one of claims 3 to 10, wherein the cell surface antigen is selected from EGFR, EGFRvIII, MCSP, Carbonic anhydrase CD30, CD33, CD44v6, EpCAM, Her2/neu, MUC1, IgE, HBV and HCV.~~

11. A vector, which comprises a nucleic acid sequence as defined in claim 10.

~~12. The polypeptide of any one of claims 3 to 12, wherein said polypeptide is a bispecific single chain antibody molecule.~~

12. A pharmaceutical composition comprising a polypeptide according to any one of claims 1 to 9.

~~13. The polypeptide according to claim 13, wherein the bispecific single chain antibody molecule comprises a group of the following sequences as CDR H1, CDR H2, CDR H3, CDR L1 , CDR L2 and CDR L3 in the second binding domain selected from the group consisting of:~~

~~SEQ ID NOs: 189-194, SEQ ID NOs: 201-206, SEQ ID NOs: 219-224, SEQ ID NOs: 237-242, SEQ ID NOs:255-260, SEQ ID NOs:273-279, SEQ ID NOs: 382384 and 387-389, SEQ ID NOs: 400-402 and 405-407, SEQ ID NOs: 418-420 and 423-425, SEQ ID NOs: 436-438 and 441-443, SEQ ID NOs: 454-456 and 459-461, SEQ ID NOs: 472-474~~

and 477-479, SEQ ID NOs: 490-492 and 495497, SEQ ID NOs: and 508-510 and 513-515,

SEQ ID NOs: 530-532 and 1568 to 1570, SEQ ID NOs: 545-547 and 550-552,

SEQ ID NOs: 559-561 and 564-566,

SEQ ID NOs: 577-579 and 582-584,

SEQ ID NOs: 615-617 and 620-622, SEQ ID NOs: 633-635, 638, 639 and 1571 ,

SEQ ID NOs: 650-652 and 655-657, SEQ ID NOS. 668-670 and 673-675, SEQ ID NOs: 682-684 and 687-689, SEQ ID NOs: 696-698 and 701-703, SEQ ID NOs: 710-712 and 715-717, SEQ ID NOs: 724-726 and 729-731, SEQ ID NOs:

738-740 and 743-745, SEQ ID NOs: 752-754 and 757-759, SEQ ID NOs: 766768 and 771-773, SEQ ID NOs: 780-782 and 785-787, SEQ ID NOs: 794-796 and 799-801, SEQ ID NOs: 808-810 and 813-815, SEQ ID NOs: 822-824 and 827-829, SEQ ID NOs: 836-838 and 841-843, SEQ ID NOs: 850-852 and 855857,

SEQ ID NOs: 866-868 and 871-873, SEQ ID NOs: 884-886 and 889-891, SEQ ID NOs: 902-904 and 907-909, SEQ ID NOs: 920-922 and 925-927, SEQ ID NOs: 938-940 and 943-945, SEQ ID NOs: 956-958 and 961-963, SEQ ID NOs:

974-976 and 979-981, SEQ ID NOs: 992-994 and 997-999, SEQ ID NOs: 10061008 and 1011-1013, SEQ ID NOs: 1020-1022 and 1025-1027, SEQ ID NOs: 1034-1036 and 1039-1041, SEQ ID NOs: 1048-1050 and 1053-1055, SEQ ID NOs: 1062-1064 and 1067-1069, SEQ ID NOs: 1076-1078 and 1081-1083, SEQ

ID NOs: 1090-1092 and 1095-1097,

SEQ ID NOs: 1114-1116 and 1119-1121, SEQ ID NOs: 1128-1 130 and 1 1331 135,

SEQ ID NOs: 1141-1143 and 1146-1148, SEQ ID NOs: 1155-1157 and 1 1601162, SEQ ID NOs: 1169-1171 and 1174-1176, SEQ ID NOs: 1 183-1 185 and 1188-1190, SEQ ID NOs: 1197-1199 and 1202-1204, SEQ ID NOs: 1211-1213 and 1216-1218, SEQ ID NOs: 1125-1227 and 1230-1232, SEQ ID NOs: 12391241 and 1244-1246, SEQ ID NOs:, 1253-1255 and 1258-1260, SEQ ID NOs: 1267-1269 and 1272-1274, SEQ ID NOs: 1281-1283 and 1286-1288, SEQ ID NOs: 1295-1297 and 1300-1302, SEQ ID NOs: 1309-1311 and 1314-1316, SEQ

ID NOs: 1323-1325 and 1328-1330,

SEQ ID NOs:1343-1345 and 1348-1350, SEQ ID NOs: 1361-1363 and 13661368, SEQ ID NOs:1375-1377 and 1380-1382, SEQ ID NOs: 1389- 1391 and 1394-1396, SEQ ID NOs:1403-1405 and 1408-1410, SEQ ID NOs: 1417-1419 and 1422-1424, SEQ ID NOs:

1431-1433 and 1436-1438, SEQ ID NOs:14451447 and 1450-1452, SEQ ID NOs:1459-1461 and 1464-1466, SEQ ID NOs.•

1473-1475 and 1478-1480,

SEQ ID NOs: 1486-1491, SEQ ID NOs: 1492-1497,

SEQ ID NOs: 1505-1507 and 1510-1512, SEQ ID NOs: 1531-1533 and 15361538,

SEQ ID NOs: 1573-1575 and 1578-1580, SEQ ID NOs: 1591-1593 and 15961598, SEQ ID NOs: 1605-1607 and 1610-1612, SEQ ID NOs: 1619-1621 and

1624-1626, SEQ ID NOs: 1634-1636 and 1639-1641 and SEQ ID NOs: 16521654, SEQ ID NOs•. 1657-1659 and SEQ ID NOs: 1669-1674.

13. The pharmaceutical composition of claim 12 for use in a method for the prevention, treatment or amelioration of a proliferative disease.

14. The polypeptide according to claim 13, wherein the bispecific single chain antibody molecule comprises a sequence selected from:

(a) an amino acid sequence as depicted in any of SEQ ID NOS. 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 393, 395, 397, 411, 413, 415, 429, 431, 433, 447, 449, 451, 465, 467, 469, 483, 485, 487, 501, 503, 505, 519, 521, 523, 1336, 1338, 1340, 538, 540 ,542, 556, 570, 572, 574, 588, 590, 592, 626, 628, 630, 643, 645, 647 ,661 , 663, 665, 679, 693, 707, 721, 735, 749, 763, 777, 791, 805, 819 ,833, 847, 861, 863, 877, 879, 881, 895, 897, 899, 913, 915, 917, 931, 933, 935, 949, 951, 953, 967, 969, 971, 985, 987, 989, 1003, 1017, 1031, 1045, 1059, 1073, 1087, 1101, 1125, 1138, 1152, 1166, 1180, 1194, 1208, 1222, 1236, 1250, 1264, 1278, 1292, 1306, 1320, 1334, 1354, 1356, 1358, 1372, 1386, 1400, 1414, 1428, 1442, 1456, 1470, 1484,

~~1500, 1502, 1518, 1520, 1522, 1524, 1526, 1528, 1544, 1546, 1548, 1550, 1552, 1554, 1556, 1558, 1562, 1564, 1566, 1586, 1588, 1602, 1616, 1630, 1647, 1649 or 1663; and~~

~~(b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID Nos. 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 394, 396, 398, 412, 414, 416, 430, 432, 434, 448, 450, 452, 466, 468, 470, 484, 486, 488, 502, 504, 506, 520, 522, 524, 1337, 1339, 1341, 539, 541, 543, 557, 571, 573, 575, 589, 591 , 593, 627, 629, 631, 644, 646, 648, 662, 664, 666, 680, 694, 708, 722, 736, 750, 764, 778, 792, 806, 820, 834, 848, 862, 864, 878, 880, 882, 896, 898, 900, 914, 916, 918, 932, 934, 936, 950, 952, 954, 968, 970, 972, 986, 988, 990, 1004, 1018, 1032, 1046, 1060, 1074, 1088, 1 102, 1 126, 1139, 1153, 1167, 1181, 1195, 1209, 1223, 1237, 1251, 1265, 1279, 1293, 1307, 1321, 1335, 1355, 1357, 1359, 1373, 1387, 1401, 1415, 1429, 1443, 1457, 1471, 1485, 1501, 1503, 1519, 1521, 1523, 1525, 1527, 1529, 1545, 1547, 1549, 1551, 1553, 1555, 1557, 1559, 1561 , 1563, 1565, 1567, 1587, 1589, 1603, 1617, 1631, 1648, 1650 or 1664.~~

14. The pharmaceutical composition for the use of claim 13, wherein said pharmaceutical composition is suitable to be administered in combination with an additional drug.

15. The pharmaceutical composition for the use of claim 14, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.

~~15. A nucleic acid sequence encoding a polypeptide as defined in any of claims 1 to 15.~~

~~16. A vector, which comprises a nucleic acid sequence as defined in claim 16.~~

~~17. The vector of claim 17, wherein said vector further comprises a regulatory sequence, which is operably linked to said nucleic acid sequence defined in claim 16.~~

~~18. The vector of claim 18, wherein said vector is an expression vector.~~

~~19. A host transformed or transfected with a vector defined in any of claims 17 to 19.~~

~~20. A process for the production of a polypeptide according to any of claims 1 to 15, said process comprising culturing a host defined in claim 20 under conditions allowing the expression of the polypeptide as defined in any of claims 1 to 15 and recovering the produced polypeptide from the culture.~~

~~22. A pharmaceutical composition comprising a polypeptide according to any one of claims 1 to 15, or produced according to the process of claim 21.~~

~~23. The pharmaceutical composition of claim 22, which is further comprising suitable formulations of carriers, stabilizers and/or excipients.~~

~~24. A pharmaceutical composition comprising a polypeptide according to any one of claims 1 to 15, or produced according to the process of claim 21 for the prevention, treatment or amelioration of a disease selected from a proliferative disease, a tumorous disease, or an immunological disorder.~~

~~25. The pharmaceutical composition of claim 24, which is further comprising suitable formulations of carriers, stabilizers and/or excipients.~~

~~26. Use of a polypeptide as defined in any of claims 1 to 15, or produced according to claim 21, for the preparation of a pharmaceutical composition for the prevention, treatment or amelioration of a disease selected from a proliferative disease, a tumorous disease, or an immunological disorder.~~

~~27. The use according to claim 26, wherein said tumorous disease is a malignant disease.~~

~~28. The use according to claim 26 or 27, wherein said pharmaceutical composition is suitable to be administered in combination with an additional drug.~~

~~29. The use of claim 28, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.~~

~~30. The use of claim 29, wherein said proteinaceous compound or nonproteinaceous compound is administered simultaneously or non-simultaneously with a pharmaceutical composition according to claim 22 or 23.~~

~~31. A method for the prevention, treatment or amelioration of a disease in a subject in the need thereof, said method comprising the step of administration of an effective amount of a pharmaceutical composition of claim 22 or 23.~~

~~32. The method of claim 31, wherein said disease is a proliferative disease, a tumorous disease, or an immunological disorder.~~

~~33. The method of claim 32, wherein said tumorous disease is a malignant disease.~~

~~34. The method of any of claims 31 to 33, wherein said pharmaceutical composition is administered in combination with an additional drug.~~

~~35. The method of claim 34, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.~~

36. The method of claim 35, wherein said proteinaceous compound or nonproteinaceous compound is administered simultaneously or non-simultaneously with a pharmaceutical composition according to claim 22 or 23.

37. The method of any one of claims 31 to 36, wherein said subject is a human.

38. A kit comprising a polypeptide as defined in any of claims 1 to 15, a nucleic acid molecule as defined in claim 16, a vector as defined in any of claims 17 to 19, or a host as defined in claim 20.

39. A method for the identification of (a) polypeptide(s) comprising a cross-species specific binding domain capable of binding to an epitope of human and nonchimpanzee primate CD3ε (CD3 epsilon), the method comprising the steps of:

(a) contacting the polypeptide(s) with an N-terminal fragment of the extracellular domain of CD3ε of maximal 27 amino acids comprising the amino acid sequence Gin-Asp-Gly-Asn-Glu-Glu-Met-Gly (SEQ ID NO. 381) or Gln-Asp-Gly-Asn-Glu-Glu-Ile-Gly (SEQ ID NO. 382), fixed via its C-terminus to a solid phase;

(b) eluting the bound polypeptide(s) from said fragment; and

(c) isolating the polypeptide(s) from the eluate of (b).

40. The method of claim 1, wherein the polypeptide(s) comprise(s) the identified binding domain as a first binding domain and a second binding domain binding to a cell surface antigen.