Claims

1. A bispecific single chain antibody molecule comprising a first binding domain which is an antigen-interaction site, capable of binding to an epitope of human and Callithrix jacchus, Saguinis oedipus or Saimiri sciureus 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, and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu (QDGNE), and a second binding domain capable of binding to prostate-specific membrane antigen (PSMA).

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.

3. The bispecific single chain antibody molecule of claim 1, wherein at least one of said first or second binding domain is CDR-grafted, humanized or human.

4. The bispecific single chain antibody molecule according to any one of claims 1 to 3, 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-L1, CDR-L2 and CDR-L3 selected from:
   (a) CDR-L1 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-L1 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-L1 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 bispecific single chain antibody molecule according to any one of claims 1 to 3, 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-H1 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-H1 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-H1 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-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. 84, CDR-H2 as depicted in SEQ ID NO. 85 and CDR-H3 as depicted in SEQ ID NO. 86;

(f) CDR-H1 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-H1 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-H1 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-H1 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-H1 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 bispecific single chain antibody molecule 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 selected from the group consisting of a VL region as depicted in SEQ ID NO. 35, 39, 125, 129, 161 or 165.

7. The bispecific single chain antibody molecule according to any one of claims 1 or 3 and 5, wherein the first 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.

8. The bispecific single chain antibody molecule according to any one of claims 1 to 7, 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 111 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.

9. The bispecific single chain antibody molecule according to claim 8, 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, 113, 115, 131, 133, 149, 151, 167, 169, 185 or 187.

10. The bispecific single chain antibody molecule according to any one of claims 1 to 9, wherein the second binding domain is capable of binding to human PSMA and/or a non-Chimpanzee primate PSMA.

11. The bispecific single chain antibody molecule according to claim 10, 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:

a) CDR H1-3 of SEQ ID NO: 226-228 and CDR L1-3 of SEQ ID NO: 231-233;

b) CDR H1-3 of SEQ ID NO: 240-242 and CDR L1-3 of SEQ ID NO: 245-247;

c) CDR H1-3 of SEQ ID NO: 254-256 and CDR L1-3 of SEQ ID NO: 259-261;

d) CDR H1-3 of SEQ ID NO: 268-270 and CDR L1-3 of SEQ ID NO: 273-275;

e) CDR H1-3 of SEQ ID NO: 618-620 and CDR L1-3 of SEQ ID NO: 623-625;

f) CDR H1-3 of SEQ ID NO: 282-284 and CDR L1-3 of SEQ ID NO: 287-289;

g) CDR H1-3 of SEQ ID NO: 296-298 and CDR L1-3 of SEQ ID NO: 301-303;

h) CDR H1-3 of SEQ ID NO: 310-312 and CDR L1-3 of SEQ ID NO: 315-317;

i) CDR H1-3 of SEQ ID NO: 324-326 and CDR L1-3 of SEQ ID NO: 329-331;

j) CDR H1-3 of SEQ ID NO: 338-340 and CDR L1-3 of SEQ ID NO: 343-345;

k) CDR H1-3 of SEQ ID NO: 352-354 and CDR L1-3 of SEQ ID NO: 357-359;

l) CDR H1-3 of SEQ ID NO: 366-368 and CDR L1-3 of SEQ ID NO: 371-373;

m) CDR H1-3 of SEQ ID NO: 380-382 and CDR L1-3 of SEQ ID NO: 385-387;

n) CDR H1-3 of SEQ ID NO: 394-396 and CDR L1-3 of SEQ ID NO: 399-401;

o) CDR H1-3 of SEQ ID NO: 408-410 and CDR L1-3 of SEQ ID NO: 413-415;

p) CDR H1-3 of SEQ ID NO: 422-424 and CDR L1-3 of SEQ ID NO: 427-429;

q) CDR H1-3 of SEQ ID NO: 436-438 and CDR L1-3 of SEQ ID NO: 441-443;

r) CDR H1-3 of SEQ ID NO: 450-452 and CDR L1-3 of SEQ ID NO: 455-457;

s) CDR H1-3 of SEQ ID NO: 464-466 and CDR L1-3 of SEQ ID NO: 469-471;

t) CDR H1-3 of SEQ ID NO: 478-480 and CDR L1-3 of SEQ ID NO: 483-485;

u) CDR H1-3 of SEQ ID NO: 492-494 and CDR L1-3 of SEQ ID NO: 497-499;

v) CDR H1-3 of SEQ ID NO: 506-508 and CDR L1-3 of SEQ ID NO: 511-513;

w) CDR H1-3 of SEQ ID NO: 520-522 and CDR L1-3 of SEQ ID NO: 525-527;

x) CDR H1-3 of SEQ ID NO: 534-536 and CDR L1-3 of SEQ ID NO: 539-541;

y) CDR H1-3 of SEQ ID NO: 548-550 and CDR L1-3 of SEQ ID NO: 553-555;

z) CDR H1-3 of SEQ ID NO: 562-564 and CDR L1-3 of SEQ ID NO: 567-569;

aa) CDR H1-3 of SEQ ID NO: 576-578 and CDR L1-3 of SEQ ID NO: 581-583;

ab) CDR H1-3 of SEQ ID NO: 590-592 and CDR L1-3 of SEQ ID NO: 595-597; and

ac) CDR H1-3 of SEQ ID NO: 604-606 and CDR L1-3 of SEQ ID NO: 609-611.

12. The bispecific single chain antibody molecule of claim 11, wherein the binding domains are arranged in the order VH PSMA-VL PSMA-VH CD3-VL CD3 or VL PSMA-VH PSMA-VH CD3-VL CD3.

13. The bispecific single chain antibody molecule according to claim 12, 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: 237, 251, 265, 279, 629, 293, 307, 321, 335, 349, 363, 377, 391, 405, 419, 433, 447, 461, 475, 489, 503, 517, 531, 545, 559, 573, 587, 601 or 615; and

(b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID NOs: 238, 252, 266, 280, 630, 294, 308, 322, 336, 350, 364, 378, 392, 406, 420, 434, 448, 462, 476, 490, 504, 518, 532, 546, 560, 574, 588, 602 or 616.

14. A nucleic acid sequence encoding a bispecific single chain antibody molecule as defined in any of claims 1 to 13.

15. A vector, which comprises a nucleic acid sequence as defined in claim 14.

16. The vector of claim 15, wherein said vector further comprises a regulatory sequence, which is operably linked to said nucleic acid sequence defined in claim 14.

17. The vector of claim 16, wherein said vector is an expression vector.

18. A host transformed or transfected with a vector defined in any of claims 15 to 17.

19. A process for the production of a bispecific single chain antibody molecule according to any of claims 1 to 13, said process comprising culturing a host defined in claim 18 under conditions allowing the expression of the bispecific single chain antibody molecule as defined in any of claims 1 to 13 and recovering the produced polypeptide from the culture.

20. A pharmaceutical composition comprising a bispecific single chain antibody molecule according to any one of claims 1 to 13, or produced according to the process of claim 19.

21. The pharmaceutical composition of claim 20 for use in the prevention, treatment or amelioration of cancer.

22. A bispecific single chain antibody molecule according to any one of claims 1 to 13, or produced according to the process of claim 19, for use in the prevention, treatment or amelioration of cancer.

23. The pharmaceutical composition of claim 21 or the bispecific single chain antibody molecule of claim 22, wherein said cancer is a solid tumor, preferably a carcinoma or prostate cancer.

24. The pharmaceutical composition of claim 20, 21 or 23 or the bispecific single chain antibody molecule of claim 22 or 23 which, optionally further comprises suitable formulations of carriers, stabilizers and/or excipients.

25. The pharmaceutical composition of claim 20, 21, 23 or 24 or the bispecific single chain antibody molecule of claim 22, 23 or 24, wherein said bispecific single chain antibody molecule or pharmaceutical composition is suitable to be administered in combination with an additional drug.

26. The pharmaceutical composition or bispecific single chain antibody molecule of claim 25, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.

27. The pharmaceutical composition or the bispecific single chain antibody molecule of claim 26, wherein said proteinaceous compound or non-proteinaceous compound is administered simultaneously or non-simultaneously with the bispecific single chain antibody molecule of claim 22, 23, or 24, or the pharmaceutical composition according to claim 20 or 21.

28. Use of a bispecific single chain antibody molecule as defined in any of claims 1 to 13, or produced according to claim 19, for the preparation of a pharmaceutical composition for the prevention, treatment or amelioration of a disease.

29. 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 20 or 21.

30. The method of claim 29 or the use of claim 28, wherein said disease is cancer.

31. The method or use of claim 30, wherein said cancer is a solid tumor, preferably a carcinoma or prostate cancer.

32. The method of any of claims 29 to 31 or the use of claim 28, 30 or 31, wherein said pharmaceutical composition is administered in combination with an additional drug.

33. The method or use of claim 32, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.

34. The method or use of claim 33, wherein said proteinaceous compound or non-proteinaceous compound is administered simultaneously or non-simultaneously with a pharmaceutical composition according to claim 20 or 21.

35. The method of any one of claims 29 to 34 or the use of claim 28, or 30 to 34, wherein said subject is a human.

36. A kit comprising a bispecific single chain antibody molecule as defined in any of claims 1 to 13, a nucleic acid molecule as defined in claim 14, a vector as defined in any of claims 15 to 17, or a host as defined in claim 18.

Claims

1. A bispecific single chain antibody molecule comprising a first binding domain which is an antigen-interaction site, capable of binding to an epitope of human and Callithrix jacchus, Saguinis oedipus or Saimiri sciureus 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, and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu (QDGNE), and a second binding domain capable of binding to human prostate-specific membrane antigen (PSMA) and/or to a non-Chimpanzee primate PSMA, and 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:

   a) CDR H1-3 of SEQ ID NO: 226-228 and CDR L1-3 of SEQ ID NO: 231-233;

   b) CDR H1-3 of SEQ ID NO: 240-242 and CDR L1-3 of SEQ ID NO: 245-247;

   c) CDR H1-3 of SEQ ID NO: 254-256 and CDR L1-3 of SEQ ID NO: 259-261;

   d) CDR H1-3 of SEQ ID NO: 268-270 and CDR L1-3 of SEQ ID NO: 273-275;

   e) CDR H1-3 of SEQ ID NO: 618-620 and CDR L1-3 of SEQ ID NO: 623-625;

   f) CDR H1-3 of SEQ ID NO: 282-284 and CDR L1-3 of SEQ ID NO: 287-289;

   g) CDR H1-3 of SEQ ID NO: 296-298 and CDR L1-3 of SEQ ID NO: 301-303;

   h) CDR H1-3 of SEQ ID NO: 310-312 and CDR L1-3 of SEQ ID NO: 315-317;

   i) CDR H1-3 of SEQ ID NO: 324-326 and CDR L1-3 of SEQ ID NO: 329-331;

   j) CDR H1-3 of SEQ ID NO: 338-340 and CDR L1-3 of SEQ ID NO: 343-345;

k) CDR H1-3 of SEQ ID NO: 352-354 and CDR L1-3 of SEQ ID NO: 357-359;

l) CDR H1-3 of SEQ ID NO: 366-368 and CDR L1-3 of SEQ ID NO: 371-373;

m) CDR H1-3 of SEQ ID NO: 380-382 and CDR L1-3 of SEQ ID NO: 385-387;

n) CDR H1-3 of SEQ ID NO: 394-396 and CDR L1-3 of SEQ ID NO: 399-401;

o) CDR H1-3 of SEQ ID NO: 408-410 and CDR L1-3 of SEQ ID NO: 413-415;

p) CDR H1-3 of SEQ ID NO: 422-424 and CDR L1-3 of SEQ ID NO: 427-429;

q) CDR H1-3 of SEQ ID NO: 436-438 and CDR L1-3 of SEQ ID NO: 441-443;

r) CDR H1-3 of SEQ ID NO: 450-452 and CDR L1-3 of SEQ ID NO: 455-457;

s) CDR H1-3 of SEQ ID NO: 464-466 and CDR L1-3 of SEQ ID NO: 469-471;

t) CDR H1-3 of SEQ ID NO: 478-480 and CDR L1-3 of SEQ ID NO: 483-485;

u) CDR H1-3 of SEQ ID NO: 492-494 and CDR L1-3 of SEQ ID NO: 497-499;

v) CDR H1-3 of SEQ ID NO: 506-508 and CDR L1-3 of SEQ ID NO: 511-513;

w) CDR H1-3 of SEQ ID NO: 520-522 and CDR L1-3 of SEQ ID NO: 525-527;

x) CDR H1-3 of SEQ ID NO: 534-536 and CDR L1-3 of SEQ ID NO: 539-541;

y) CDR H1-3 of SEQ ID NO: 548-550 and CDR L1-3 of SEQ ID NO: 553-555;

z) CDR H1-3 of SEQ ID NO: 562-564 and CDR L1-3 of SEQ ID NO: 567-569;

aa) CDR H1-3 of SEQ ID NO: 576-578 and CDR L1-3 of SEQ ID NO: 581-583;

ab) CDR H1-3 of SEQ ID NO: 590-592 and CDR L1-3 of SEQ ID NO: 595-597; and

ac) CDR H1-3 of SEQ ID NO: 604-606 and CDR L1-3 of SEQ ID NO: 609-611.

2. The bispecific single chain antibody molecule of claim 1, wherein the binding domains are arranged in the order VH PSMA-VL PSMA-VH CD3-VL CD3 or VL PSMA-VH PSMA-VH CD3-VL CD3.

3. The bispecific single chain antibody molecule according to claim 2, 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: 237, 251, 265, 279, 629, 293, 307, 321, 335, 349, 363, 377, 391, 405, 419, 433, 447, 461, 475, 489, 503, 517, 531, 545, 559, 573, 587, 601 or 615; and

(b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID NOs: 238, 252, 266, 280, 630, 294, 308, 322, 336, 350, 364, 378, 392, 406, 420, 434, 448, 462, 476, 490, 504, 518, 532, 546, 560, 574, 588, 602 or 616.

4. The bispecific single chain antibody molecule according to any one of claims 1 to 3, wherein the bispecific single chain antibody contains a tag.

5. The bispecific single chain antibody molecule according to claim 4 wherein the tag is a C-terminal His-tag.

6. A nucleic acid sequence encoding a bispecific single chain antibody molecule as defined in any of claims 1 to 5.

7. A vector, which comprises a nucleic acid sequence as defined in claim 6.

8. The vector of claim 7, wherein said vector further comprises a regulatory sequence, which is operably linked to said nucleic acid sequence defined in claim 6.

9. The vector of claim 8, wherein said vector is an expression vector.

10. A host cell transformed or transfected with a vector defined in any of claims 7 to 9.

11. A process for the production of a bispecific single chain antibody molecule according to any of claims 1 to 5, said process comprising culturing a host cell defined in claim 10 under conditions allowing the expression of the bispecific single chain antibody molecule as defined in any of claims 1 to 5 and recovering the produced polypeptide from the culture.

12. A pharmaceutical composition comprising a bispecific single chain antibody molecule according to any one of claims 1 to 5, or produced according to the process of claim 11.

13. The pharmaceutical composition of claim 12 for use in the prevention, treatment or amelioration of cancer.

14. A bispecific single chain antibody molecule according to any one of claims 1 to 5, or produced according to the process of claim 11, for use in the prevention, treatment or amelioration of cancer.

15. The pharmaceutical composition of claim 13 or the bispecific single chain antibody molecule of claim 14, wherein said cancer is a solid tumor, preferably a carcinoma or prostate cancer.

16. The pharmaceutical composition of claim 12, 13 or 15 or the bispecific single chain antibody molecule of claim 12 or 13 which, optionally further comprises suitable formulations of carriers, stabilizers and/or excipients.

17. The pharmaceutical composition of claim 12, 13, 15 or 16 or the bispecific single chain antibody molecule of claim 14, 15 or 16, wherein said bispecific single chain antibody molecule or pharmaceutical composition is suitable to be administered in combination with an additional drug.

18. The pharmaceutical composition or bispecific single chain antibody molecule of claim 17, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.

19. The pharmaceutical composition or the bispecific single chain antibody molecule of claim 18, wherein said proteinaceous compound or non- proteinaceous compound is administered simultaneously or non-simultaneously with the bispecific single chain antibody molecule of claim 14, 15, or 16, or the pharmaceutical composition according to claim 12 or 13.

20. Use of a bispecific single chain antibody molecule as defined in any of claims 1 to 5, or produced according to claim 11, for the preparation of a pharmaceutical composition for the prevention, treatment or amelioration of a disease.

21. A kit comprising a bispecific single chain antibody molecule as defined in any of claims 1 to 5, a nucleic acid molecule as defined in claim 6, a vector as defined in any of claims 7 to 9, or a host cell as defined in claim 10.