SEQ ID Nos.: 51, 54, and 63-101. In some embodiments, said protein comprises a CDR2 comprising a sequence set forth in any one of SEQ ID Nos.: 52, 55, and 102-140. In some embodiments, said protein comprises a CDR3 comprising a sequence set forth in any one of SEQ ID Nos.: 53, 56, and 141-179. In some embodiments, said protein comprises a framework region 1 (f1) comprising a sequence as set forth in any one of SEQ ID Nos.: 180-218. In some embodiments, said protein comprises a framework region 2 (f2) comprising a sequence as set forth in any one of SEQ ID Nos.: 219-257. In some embodiments, said protein comprises a framework region 3 (f3) comprising a sequence as set forth in any one of SEQ ID Nos.: 258-296. In some embodiments, said protein comprises a framework region 4 (f4) comprising a sequence as set forth in any one of SEQ ID Nos.: 297-335. In some embodiments, said protein comprises an amino acid sequence as set forth in any one of SEQ ID Nos.: 1-40, and 58.

[0009a] One embodiment provides a single domain mesothelin binding protein, wherein said protein comprises the following formula:

*f*1-*r*1-*f*2-*r*2-*f*3-*r*3-*f*4

wherein, r1 is CDR1; r2 is CDR2; and r3 CDR3; and wherein f1, f2, f3 and f4 are framework residues, and wherein: (i) the CDR1 comprises the sequence GSTFSIRAMR (SEQ ID Nos.: 88, and 96-98), the CDR2 comprises the sequence VIYGSSTYYADAVKGRFT (SEQ ID Nos.: 127, 135-137), and the CDR3 comprises the sequence DTIGTARDY (SEQ ID Nos.: 166, 174-176); (ii) the CDR1 comprises the sequence GRTSTIDTMY (SEQ ID Nos.: 89, 99-101), the CDR2 comprises YVTSRGTSNVADSVKGRFT (SEQ ID Nos.: 128, 138-140), and the CDR3 comprises the sequence RTTSYPVDF (SEQ ID Nos.: 167, 177-179); (iii) the CDR1 comprises the sequence GSTSSINTMY (SEQ ID Nos.: 82, 86, 90, 93-95), the CDR2 comprises the sequence FISSGGSTNVRDSVKGRFT (SEQ ID Nos. 132-134), the CDR3 comprises the sequence YIPYGGTLHDF (SEQ ID Nos.: 164, 168, 171-173); (iv) the CDR1 comprises the sequence GGDWSANFMY (SEQ ID Nos.: 54, 91-92), the CDR2 comprises the sequence RISGRGVVDYVESVKGRFT (SEQ ID Nos.: 130-131), the CDR3 comprises the sequence ASY (SEQ ID Nos.: 169-170); or (v) the CDR1 comprises the sequence GSTFRIRVMR (SEQ ID NO: 79), the CDR2 comprises the sequence VISGSSTYYADSVKGRFT (SEQ ID NO: 118), and the CDR3 comprises the sequence DDSGIARDY (SEQ ID NO: 157).

[0010] One embodiment provides a polynucleotide encoding a single domain mesothelin binding protein according to any one of the above embodiments. A further embodiment provides a vector comprising the polynucleotide of the above embodiment. A further embodiment provides a host cell transformed with the vector according to the above embodiment.

[0010a] One embodiment provides a single domain mesothelin binding protein comprising an amino acid sequence as set forth in any one of SEQ ID Nos.: 17, 26, 27, 32-40, 58 and 60-62.

[0011] One embodiment provides a pharmaceutical composition comprising (i) a single domain meosthelin binding protein according to any one of the above embodiments, the polynucleotide according to any one of the above embodiments, the vector according to any one of the above embodiments, or the host cell according to any one of the above embodiments, and (ii) a pharmaceutically acceptable carrier.

[0012] A further embodiment provides a process for the production of a single domain mesothelin binding protein according to any one of the above embodiments, said process comprising culturing a host transformed or transfected with a vector comprising a nucleic acid sequence encoding a single domain mesothelin binding protein according to any one of the above embodiments under conditions allowing the expression of the mesothelin binding protein and recovering and purifying the produced protein from the culture.

[0012a] One embodiment provides the single domain mesothelin binding protein as described herein for use in therapy.

[0012b] One embodiment provides a use of the single domain mesothelin binding protein as described herein in the manufacture of a medicament for the treatment or amelioration of a proliferative disease, or a tumorous disease, that expresses mesothelin, wherein the medicament is to be administered to a subject in need thereof.

[0013] One embodiment provides a method for the treatment or amelioration of a proliferative disease, or a tumorous disease, comprising the administration of the mesothelin binding protein any one of the above embodiments, to a subject in need thereof. In some embodiments, the subject is human. In some embodiments, the method further comprises administration of an agent in combination with the single domain mesothelin binding protein according to any one of the above embodiments. In some embodiments, the single domain mesothelin binding protein selectively binds to tumor cells expressing mesothelin. In some embodiments, the single domain mesothelin binding protein mediates T cell killing of tumor cells expressing mesothelin. In some embodiments, the tumorous disease comprises a solid tumor disease. In some embodiments, the

CLAIMS

WHAT IS CLAIMED IS:

1. A single domain mesothelin binding protein, wherein said protein comprises the following formula:

*f*1-*r*1-*f*2-*r*2-*f*3-*r*3-*f*4

wherein, r1 is CDR1; r2 is CDR2; and r3 CDR3; and wherein f1, f2, f3 and f4 are framework residues, and wherein:

(i) the CDR1 comprises the sequence GSTFSIRAMR (SEQ ID Nos.: 88, and 96-98), the CDR2 comprises the sequence VIYGSSTYYADAVKGRFT (SEQ ID Nos.: 127, 135-137), and the CDR3 comprises the sequence DTIGTARDY (SEQ ID Nos.: 166, 174-176);

(ii) the CDR1 comprises the sequence GRTSTIDTMY (SEQ ID Nos.: 89, 99-101), the CDR2 comprises YVTSRGTSNVADSVKGRFT (SEQ ID Nos.: 128, 138-140), and the CDR3 comprises the sequence RTTSYPVDF (SEQ ID Nos.: 167, 177-179);

(iii) the CDR1 comprises the sequence GSTSSINTMY (SEQ ID Nos.: 82, 86, 90, 93-95), the CDR2 comprises the sequence FISSGGSTNVRDSVKGRFT (SEQ ID Nos. 132-134), the CDR3 comprises the sequence YIPYGGTLHDF (SEQ ID Nos.: 164, 168, 171-173);

(iv) the CDR1 comprises the sequence GGDWSANFMY (SEQ ID Nos.: 54, 91-92), the CDR2 comprises the sequence RISGRGVVDYVESVKGRFT (SEQ ID Nos.: 130-131), the CDR3 comprises the sequence ASY (SEQ ID Nos.: 169-170); or

(v) the CDR1 comprises the sequence GSTFRIRVMR (SEQ ID NO: 79), the CDR2 comprises the sequence VISGSSTYYADSVKGRFT (SEQ ID NO: 118), and the CDR3 comprises the sequence DDSGIARDY (SEQ ID NO: 157).

2. The single domain mesothelin binding protein of claim 1, wherein said protein binds to an epitope of mesothelin, wherein said epitope is located in region I, comprising amino acid residues 296-390 of SEQ ID NO: 57, region II comprising amino acid residue 391-486 of SEQ ID NO: 57, or region III comprising amino acid residues 487-598 of SEQ ID NO: 57.

3. The single domain mesothelin binding protein of claim 1, wherein said protein comprises an amino acid sequence as set forth in any one of SEQ ID Nos.: 17, 26, 27, 32-40, 58 and 60-62.

4. The single domain mesothelin binding protein of claim 1, wherein f1 comprises a sequence as set forth in any one of SEQ ID Nos.: 196, 205, and 208-218.

5. The single domain mesothelin binding protein of claim 1, wherein f2 comprises a sequence as set forth in any one of SEQ ID Nos.: 235, 244 and 247-257.

6. The single domain mesothelin binding protein of claim 1, wherein f3 comprises a sequence as set forth in any one of SEQ ID Nos.: 274, 283, and 286-296.

7. The single domain mesothelin binding protein of claim 1, wherein f4 comprises a sequence as set forth in any one of SEQ ID Nos.: 313, 322, and 325-335.

8. A single domain mesothelin binding protein comprising an amino acid sequence as set forth in any one of SEQ ID Nos.: 17, 26, 27, 32-40, 58 and 60-62.

9. Use of the single domain mesothelin binding protein of claim 1 in the manufacture of a medicament for the treatment or amelioration of a proliferative disease, or a tumorous disease, that expresses mesothelin, wherein the medicament is to be administered to a subject in need thereof.

10. The use of claim 9, wherein the medicament is to be administered at a dose of up to 10 mg/kg.

11. The use of claim 10, wherein the medicament is to be administered once a week, twice per week, every other day, or every three weeks.

12. The use of claim 11, wherein the subject is human.

13. The use of claim 9, wherein an agent is to be further administered in combination with the medicament.

14. The use of claim 9, wherein the single domain mesothelin binding protein selectively binds to tumor cells expressing mesothelin.

15. The use of claim 14, wherein the single domain mesothelin binding protein mediates T cell killing of tumor cells expressing mesothelin.

16. The use of claim 15, wherein the tumorous disease comprises a solid tumor disease.

17. The use of claim 16, wherein the solid tumor disease comprises mesothelioma, lung cancer, gastric cancer, ovarian cancer, or triple negative breast cancer.

18. The use of claim 17, wherein the solid tumor disease is metastatic.

19. The single domain mesothelin binding protein of claim 1 for use in therapy.