

CLAIMS

WHAT IS CLAIMED IS:

1. A single domain mesothelin binding protein, wherein the single domain mesothelin protein comprises a sequence of SEQ ID NO: 31.
2. A single domain mesothelin binding protein, wherein the single domain mesothelin protein comprises a sequence selected from the group consisting of SEQ ID NOs: 1-16, 18-25 and 28-29.
3. A single domain mesothelin binding protein, wherein the single domain mesothelin protein comprises the following formula:

fl-r1-f2-r2-f3-r3-f4

wherein, r1 is CDR1; r2 is CDR2; and r3 CDR3; and

wherein fl, f2, f3 and f4 are framework residues, and

wherein:

- (i) the CDR1 comprises the sequence GSTSSINTMY (SEQ ID NO: 82), the CDR2 comprises the sequence FISSGGSTNVRDSVKGRFS (SEQ ID NO: 121), and the CDR3 comprises the sequence YIPLRGTLHDY (SEQ ID NO: 160);
- (ii) the CDR1 comprises the sequence GSTSSINTMY (SEQ ID NO: 82), the CDR2 comprises TINRGGSTNVRDSVKGRFS (SEQ ID NO: 125), and the CDR3 comprises the sequence YIPYGGTLHDF (SEQ ID NO: 164);
- (iii) the CDR1 comprises the sequence TTFSINSMS (SEQ ID NO: 87), the CDR2 comprises the sequence VITNRGTTSYADSVKGRFT (SEQ ID NO: 126), the CDR3 comprises the sequence IADWRGY (SEQ ID NO: 153);
- (iv) the CDR1 comprises the sequence AIGSINSMS (SEQ ID NO: 85), the CDR2 comprises the sequence VITDRGSTSYADSVKGRFT (SEQ ID NO: 114), the CDR3 comprises the sequence IADWRGY (SEQ ID NO: 153);
- (v) the CDR1 comprises the sequence GLTFGVYGME (SEQ ID NO: 74), the CDR2 comprises the sequence SHTSTGYVYYRDSVKGRFT (SEQ ID NO: 113), and the CDR3 comprises the sequence NRGSYEY (SEQ ID NO: 152);

- (vi) the CDR1 comprises the sequence GSTSNINNMR (SEQ ID NO: 66), the CDR2 comprises the sequence VITRGGYAIYLDVKGGRFT (SEQ ID NO: 105), and the CDR3 comprises the sequence DRVEGTSGGPQLRDY (SEQ ID NO: 144); or
 - (vii) the CDR1 comprises the sequence GTTYTFDLMS (SEQ ID NO: 65), the CDR2 comprises the sequence SISSDGRTSYADSVRGRFT (SEQ ID NO: 104), and the CDR3 comprises the sequence QRSGVRAF (SEQ ID NO: 143).
4. The single domain mesothelin binding protein of claim 3, wherein the single domain mesothelin binding protein comprises a sequence selected from the group consisting of SEQ ID NOs: 3, 4, 12, 20, 23, 24 and 25.
 5. The single domain mesothelin binding protein of claim 3 or 4, wherein
 - (i) f1 comprises a sequence as set forth in any one of SEQ ID NOs: 180-218;
 - (ii) f2 comprises a sequence as set forth in any one of SEQ ID NOs: 219-257;
 - (iii) f3 comprises a sequence as set forth in any one of SEQ ID NOs: 258-296; and/or
 - (iv) f4 comprises a sequence as set forth in any one of SEQ ID NOs: 297-335.
 6. A polynucleotide encoding the single domain mesothelin binding protein of any one of claims 1-5.
 7. A polynucleotide encoding a single domain mesothelin binding protein, wherein the single domain mesothelin binding protein comprises the following formula:

$$f1-r1-f2-r2-f3-r3-f4$$
 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 NO: 88), the CDR2 comprises the sequence VIYGSSTYYADAVKGGRFT (SEQ ID NO: 127), and the CDR3 comprises the sequence DTIGTARDY (SEQ ID NO: 166);
 - (ii) the CDR1 comprises the sequence GRTSTIDTMY (SEQ ID NO: 89), the CDR2 comprises YVTSRGTSNVADSVKGRFT (SEQ ID NO: 128), and the CDR3 comprises the sequence RTTSYPVDF (SEQ ID NO: 167);
 - (iii) the CDR1 comprises the sequence GSTSSINTMY (SEQ ID NO: 82), the CDR2 comprises the sequence FISSGGSTNVRDSVKGRFT (SEQ ID NO: 132), the CDR3 comprises the sequence YIPYGGTLHDF (SEQ ID NO: 164);

- (iv) the CDR1 comprises the sequence GGDWSANFMY (SEQ ID NO: 54), the CDR2 comprises the sequence RISGRGVVDYVESVKGRFT (SEQ ID NO: 130), the CDR3 comprises the sequence ASY (SEQ ID NO: 169); 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).
8. The polynucleotide of claim 7, wherein the CDR1 comprises the sequence GSTFSIRAMR (SEQ ID NO: 88), the CDR2 comprises the sequence VIYGSSTYYADAVKGRFT (SEQ ID NO: 127), and the CDR3 comprises the sequence DTIGTARDY (SEQ ID NO: 166).
 9. The polynucleotide of claim 7, wherein the single domain mesothelin binding 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.
 10. The polynucleotide of claim 9, wherein the single domain mesothelin binding protein comprises an amino acid sequence as set forth in SEQ ID NO: 58.
 11. The single domain mesothelin binding protein of any one of claims 1-5 for use in therapy.
 12. The polynucleotide of any one of claims 6-10 for use in therapy.
 13. Use of the single domain mesothelin binding protein of any one of claims 1-5 in the manufacture of a medicament for the treatment or amelioration of a proliferative disease, or a tumorous disease.
 14. Use of the polynucleotide of any one of claims 6-10 in the manufacture of a medicament for use the treatment or amelioration of a proliferative disease, or a tumorous disease.
 15. The use of claim 13 or 14, wherein the single domain mesothelin binding protein or the polynucleotide is to be administered to a subject in need thereof.
 16. The use of claim 15, wherein the single domain mesothelin binding protein is to be administered at a dose of up to 10 mg/kg.
 17. The use of claim 16, wherein the single domain mesothelin binding protein is to be administered once a week, twice per week, every other day, or every three weeks.
 18. The use of any one of claims 13-17, wherein the tumorous disease comprises a solid tumor disease.
 19. The use of claim 18, wherein the solid tumor disease comprises mesothelioma, lung cancer, gastric cancer, ovarian cancer, or triple negative breast cancer.

20. The use of claim 18 or 19, wherein the solid tumor disease is metastatic.