Claims

1. A bispecific antibody construct comprising a first binding domain which binds to human MSLN on the surface of a target cell and a second binding domain which binds to human CD3 on the surface of a T cell, wherein the first binding domain binds to an epitope of MSLN which is comprised within the region as depicted in SEQ ID NO: 245;

   wherein the first binding domain which binds human MSLN comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 and a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from the group consisting of:

   a) CDR-H1 as depicted in SEQ ID NO: 161, CDR-H2 as depicted in SEQ ID NO: 162, CDR-H3 as depicted in SEQ ID NO: 163, CDR-L1 as depicted in SEQ ID NO: 164, CDR-L2 as depicted in SEQ ID NO: 165 and CDR-L3 as depicted in SEQ ID NO: 166;
   b) CDR-H1 as depicted in SEQ ID NO: 171, CDR-H2 as depicted in SEQ ID NO: 172, CDR-H3 as depicted in SEQ ID NO: 173, CDR-L1 as depicted in SEQ ID NO: 174, CDR-L2 as depicted in SEQ ID NO: 175 and CDR-L3 as depicted in SEQ ID NO: 176;
   c) CDR-H1 as depicted in SEQ ID NO: 181, CDR-H2 as depicted in SEQ ID NO: 182, CDR-H3 as depicted in SEQ ID NO: 183, CDR-L1 as depicted in SEQ ID NO: 184, CDR-L2 as depicted in SEQ ID NO: 185 and CDR-L3 as depicted in SEQ ID NO: 186;
   d) CDR-H1 as depicted in SEQ ID NO: 191, CDR-H2 as depicted in SEQ ID NO: 192, CDR-H3 as depicted in SEQ ID NO: 193, CDR-L1 as depicted in SEQ ID NO: 194, CDR-L2 as depicted in SEQ ID NO: 195 and CDR-L3 as depicted in SEQ ID NO: 196; and
   e) CDR-H1 as depicted in SEQ ID NO: 201, CDR-H2 as depicted in SEQ ID NO: 202, CDR-H3 as depicted in SEQ ID NO: 203, CDR-L1 as depicted in SEQ ID NO: 204, CDR-L2 as depicted in SEQ ID NO: 205 and CDR-L3 as depicted in SEQ ID NO: 206.

2. The antibody construct according to claim 1, wherein the second binding domain binds to human CD3 epsilon and to *Callithrix jacchus, Saguinus Oedipus* or *Saimiri sciureus* CD3 epsilon.

3. 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 those formats.

4. The antibody construct according to 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: 167, SEQ ID NO: 177, SEQ ID NO: 187, SEQ ID NO: 197, and SEQ ID NO: 207, and/or wherein the first binding domain comprises a VL region selected from the group consisting of those depicted in SEQ ID NO: 168, SEQ ID NO: 178, SEQ ID NO: 188, SEQ ID NO: 198, and SEQ ID NO: 208.

5. 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 NO: 167+168, SEQ ID NO: 177+178, SEQ ID NO: 187+188, SEQ ID NO: 197+198, and SEQ ID NO: 207+208.

6. 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: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209.

7. The antibody construct according to any one of claims 1 to 4, comprising:
   (a) a polypeptide comprising in the following order starting from the N-terminus:
      - a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209;
      - a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-9; and
      - a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 37, SEQ ID NO: 46, SEQ ID NO: 55, SEQ ID NO: 64, SEQ ID NO: 73, SEQ ID NO: 82, SEQ ID NO: 91, SEQ ID NO: 100, and SEQ ID NO: 103; and
      - optionally a His-tag, such as the one depicted in SEQ ID NO 10;
   (b) a polypeptide comprising in following order starting from the N-terminus:
      - a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209;

- a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-9;
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 37, SEQ ID NO: 46, SEQ ID NO: 55, SEQ ID NO: 64, SEQ ID NO: 73, SEQ ID NO: 82, SEQ ID NO: 91, SEQ ID NO: 100, and SEQ ID NO: 103;
- optionally a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-9;
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NOs: 104-134; and
- optionally a His-tag, such as the one depicted in SEQ ID NO 10;

(c) a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having the amino acid sequence QRFVTGHFGGLX$_1$PANG (SEQ ID NO: 135) whereas X_1 is Y or H; and
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209;
- a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-9;
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 37, SEQ ID NO: 46, SEQ ID NO: 55, SEQ ID NO: 64, SEQ ID NO: 73, SEQ ID NO: 82, SEQ ID NO: 91, SEQ ID NO: 100, and SEQ ID NO: 103;
- a polypeptide having the amino acid sequence QRFVTGHFGGLHPANG (SEQ ID NO: 137) or QRFCTGHFGGLHPCNG (SEQ ID NO: 139); and
- optionally a His-tag, such as the one depicted in SEQ ID NO 10;

(d) a polypeptide comprising in the following order starting from the N-terminus
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 17, SEQ ID NO: 26, SEQ ID NO: 35, SEQ ID NO: 44, SEQ ID NO: 53, SEQ ID NO: 62, SEQ ID NO: 71, SEQ ID NO: 80, SEQ ID NO: 89, SEQ ID NO: 98, and SEQ ID NO: 101;
- a peptide linker having the amino acid sequence depicted in SEQ ID NO: 8;
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 168, SEQ ID NO: 178, SEQ ID NO: 188, SEQ ID NO: 198, and SEQ ID NO: 208 and a serine residue at the C-terminus;

- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 140;and

a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 167, SEQ ID NO: 177, SEQ ID NO: 187, SEQ ID NO: 197, and SEQ ID NO: 207;
- a peptide linker having the amino acid sequence depicted in SEQ ID NO: 8;
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 18, SEQ ID NO: 27, SEQ ID NO: 36, SEQ ID NO: 45, SEQ ID NO: 54, SEQ ID NO: 63, SEQ ID NO: 72, SEQ ID NO: 81, SEQ ID NO: 90, SEQ ID NO: 99, and SEQ ID NO: 102 and a serine residue at the C-terminus;
- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 141;

(e) a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 17, SEQ ID NO: 26, SEQ ID NO: 35, SEQ ID NO: 44, SEQ ID NO: 53, SEQ ID NO: 62, SEQ ID NO: 71, SEQ ID NO: 80, SEQ ID NO: 89, SEQ ID NO: 98, and SEQ ID NO: 101;
- a peptide linker having the amino acid sequence depicted in SEQ ID NO: 8;
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 168, SEQ ID NO: 178, SEQ ID NO: 188, SEQ ID NO: 198, and SEQ ID NO: 208;
- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 142;and

a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 167, SEQ ID NO: 177, SEQ ID NO: 187, SEQ ID NO: 197, and SEQ ID NO: 207;
- a peptide linker having an amino acid sequence depicted in SEQ ID NO: 8;
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 18, SEQ ID NO: 27, SEQ ID NO: 36, SEQ ID NO: 45, SEQ ID NO: 54, SEQ ID NO: 63, SEQ ID NO: 72, SEQ ID NO: 81, SEQ ID NO: 90, SEQ ID NO: 99, and SEQ ID NO: 102 and a serine residue at the C-terminus;
- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 143;

(f) a polypeptide comprising in the following order starting from the N-terminus:

- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209;
- a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-9; and
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 37, SEQ ID NO: 46, SEQ ID NO: 55, SEQ ID NO: 64, SEQ ID NO: 73, SEQ ID NO: 82, SEQ ID NO: 91, SEQ ID NO: 100, and SEQ ID NO: 103; and
- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 144; and

a polypeptide having the amino acid sequence depicted in SEQ ID NO: 145;

(g) a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209; and
- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 146;and

a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 37, SEQ ID NO: 46, SEQ ID NO: 55, SEQ ID NO: 64, SEQ ID NO: 73, SEQ ID NO: 82, SEQ ID NO: 91, SEQ ID NO: 100, and SEQ ID NO: 103; and
- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 147;

(h) a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209; and
- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 148;and

a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 37, SEQ ID NO: 46, SEQ ID NO: 55, SEQ ID NO: 64, SEQ ID NO: 73, SEQ ID NO: 82, SEQ ID NO: 91, SEQ ID NO: 100, and SEQ ID NO: 103; and

- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 149; or

(i) a polypeptide comprising in the following order starting from the N-terminus:
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209;
- a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-9; and
- a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 37, SEQ ID NO: 46, SEQ ID NO: 55, SEQ ID NO: 64, SEQ ID NO: 73, SEQ ID NO: 82, SEQ ID NO: 91, SEQ ID NO: 100, and SEQ ID NO: 103; and
- a polypeptide having the amino acid sequence depicted in SEQ ID NO: 150.

8. The antibody construct according to any one of claims 1 to 6 comprising in an N- to C-terminal order:
- the first binding domain having an amino acid sequence selected from the group consisting of SEQ ID NO: 169, SEQ ID NO: 179, SEQ ID NO: 189, SEQ ID NO: 199, and SEQ ID NO: 209;
- a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 8 and 9;
- the second binding domain having an amino acid sequence selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 37, SEQ ID NO: 46, SEQ ID NO: 55, SEQ ID NO: 64, SEQ ID NO: 73, SEQ ID NO: 82, SEQ ID NO: 91, SEQ ID NO: 100, and SEQ ID NO: 103 (see also SEQ ID NOs: 23, 25, 41, 43, 59, 61, 77, 79, 95, 97, 113, 115, 131, 133, 149, 151, 167, 169, 185 or 187 of WO 2008/119567);
- a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 4, 5, 6, 8 and 9; and
- the third domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 260-267.

9. The antibody construct according to claim 8, comprising a sequence selected from the group consisting of SEQ ID NOs: 276 to 287

10. A polynucleotide encoding an antibody construct as defined in any one of the preceding claims.

11. A host cell transformed or transfected with the polynucleotide as defined in claim 10.

12. A pharmaceutical composition comprising an antibody construct according to any one of claims 1 to 9.

13. An antibody construct according to any one of claims 1 to 9 for use in the prevention or treatment of a solid tumor disease or a metastatic cancer disease.

14. A kit comprising an antibody construct according to any one of claims 1 to 9, a polynucleotide as defined in claim 10, and/or a host cell as defined in claim 11.