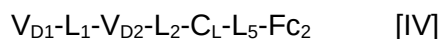
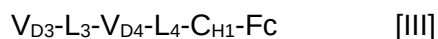


CLAIMS

1. An antibody-like binding protein that binds specifically to human CD3ε and human CD123 comprising two polypeptide chains that form two antigen-binding sites, wherein a first polypeptide chain has a structure represented by the formula [IV]:



and a second polypeptide chain has a structure represented by the formula [III]:



wherein:

a) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 71, wherein:

V_{D1} has an amino acid sequence of SEQ ID NO: 54,

L_1 has an amino acid sequence of SEQ ID NO: 56,

V_{D2} has an amino acid sequence of SEQ ID NO: 10,

L_2 has an amino acid sequence of SEQ ID NO: 56,

C_L has an amino acid sequence of SEQ ID NO: 18,

L_5 consists of no amino acid residues, and

Fc_2 has an amino acid sequence of SEQ ID NO: 70; and

wherein V_{D1} comprises a CDR1-L having an amino acid sequence of SEQ ID NO: 48, a CDR2-L having an amino acid sequence WAS, and a CDR3-L having an amino acid sequence of SEQ ID NO: 49; and

V_{D2} comprises a CDR4-L having an amino acid sequence of SEQ ID NO: 11, a CDR5-L having an amino acid sequence KVS, and a CDR6-L having an amino acid sequence of SEQ ID NO: 8;

b) the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 67, wherein:

V_{D3} has an amino acid sequence of SEQ ID NO: 9,

L_3 which consists of no amino acids residues,

V_{D4} has an amino acid sequence of SEQ ID NO: 52,

L₄ which consists of no amino acid residues,

C_{H1} has an amino acid sequence of SEQ ID NO: 19, and

Fc has an amino acid sequence of SEQ ID NO: 68; and

wherein V_{D3} comprises a CDR1-H having an amino acid sequence of SEQ ID NO: 5, a CDR2-H having an amino acid sequence of SEQ ID NO: 6, and a CDR3-H having an amino acid sequence of SEQ ID NO: 7; and

VD₄ comprises a CDR4-H having an amino acid sequence of SEQ ID NO: 50, a CDR5-H having an amino acid sequence of SEQ ID NO: 53, and a CDR6-H having an amino acid sequence of SEQ ID NO: 51;

and wherein the polypeptide of formula [IV] and the polypeptide of formula [III] form a cross-over light chain-heavy chain pair.

2. The antibody-like binding protein according to claim 1, wherein the polypeptide of formula [III] comprises a Fc having an amino acid sequence of SEQ ID NO: 68, wherein:

- a) X₁ is Y, X₂ is S, X₃ is T, X₄ is L, X₅ is Y, or X₁ is C, X₂ is S, X₃ is S, X₄ is A, X₅ is V, and
- b) X₆ is H and X₇ is Y, or X₆ is R and X₇ is F.

3. The antibody-like binding protein according to either claim 1 or 2, wherein:

a) the polypeptide of formula [IV] comprises a Fc domain (Fc₂) having an amino acid sequence of SEQ ID NO: 81, and

the polypeptide of formula [III] comprises a Fc domain having an amino acid sequence of SEQ ID NO: 60, or

b) the polypeptide of formula [IV] comprises a Fc domain (Fc₂) having an amino acid sequence of SEQ ID NO: 73, and

the polypeptide of formula [III] comprises a Fc domain having an amino acid sequence of SEQ ID NO: 75, or

c) the polypeptide of formula [IV] comprises a Fc domain (Fc₂) having an amino acid sequence of SEQ ID NO: 77, and

the polypeptide of formula [III] comprises a Fc domain having an amino acid sequence of SEQ ID NO: 75, or

d) the polypeptide of formula [IV] comprises a Fc domain (Fc₂) having an amino acid sequence of SEQ ID NO: 77, and

the polypeptide of formula [III] comprises a Fc domain having an amino acid sequence of SEQ ID NO: 79.

4. The antibody-like binding protein according to any one of claims 1 to 3, wherein:

a) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 80, or

an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 80 in which the 3 CDRs of amino acid sequences of SEQ ID NO: 48, WAS, and SEQ ID NO: 49 of V_{D1} having an amino acid sequence of SEQ ID NO: 54, and the 3 CDRs of amino acid sequences of SEQ ID NO: 11, KVS, and SEQ ID NO: 8 of V_{D2} having an amino acid sequence of SEQ ID NO: 10, and the amino acid positions 481, 486, 498, 500, 539, 567, and 568 of the amino acid sequence of SEQ ID NO: 80 are unaltered; and

the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 59, or

an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 59 in which the 3 CDRs of amino acid sequences of SEQ ID NO: 50, SEQ ID NO: 53, and SEQ ID NO: 51 of V_{D4} having an amino acid sequence of SEQ ID NO: 52, and the 3 CDRs of amino acid sequences of SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7 of V_{D3} having an amino acid sequence of SEQ ID NO: 9, and the amino acid positions 473, 492, 531, 559, 560, 478, and 490 of the amino acid sequence of SEQ ID NO: 59 are unaltered; or

b) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 72, or

an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 72 in which the 3 CDRs of amino acid sequences of SEQ ID NO: 48, WAS, and SEQ ID NO: 49 of V_{D1} having an amino acid sequence of SEQ ID NO: 54, and the 3 CDRs of amino acid sequences of SEQ ID NO: 11, KVS, and SEQ ID NO: 8 of V_{D2} having an amino acid sequence of SEQ ID NO: 10, and the amino acid positions 481, 486, 498, 500, 539, 567, and 568 of the amino acid sequence of SEQ ID NO: 72 are unaltered; and

the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 74,
or

an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 74 in which the 3 CDRs of amino acid sequences of SEQ ID NO: 50, SEQ ID NO: 53, and SEQ ID NO: 51 of V_{D4} having an amino acid sequence of SEQ ID NO: 52, and the 3 CDRs of amino acid sequences of SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7 of V_{D3} having an amino acid sequence of SEQ ID NO: 9, and the amino acid positions 473, 492, 531, 559, 560, 478, and 490 of the amino acid sequence of SEQ ID NO: 74 are unaltered; or

c) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 76, or

an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 76 in which the 3 CDRs of amino acid sequences of SEQ ID NO: 48, WAS, and SEQ ID NO: 49 of V_{D1} having an amino acid sequence of SEQ ID NO: 54, and the 3 CDRs of amino acid sequences of SEQ ID NO: 11, KVS, and SEQ ID NO: 8 of V_{D2} having an amino acid sequence of SEQ ID NO: 10, and the amino acid positions 481, 486, 498, 500, 539, 567, and 568 of the amino acid sequence of SEQ ID NO: 76 are unaltered; and

the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 74,
or

an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 74 in which the 3 CDRs of amino acid sequences of SEQ ID NO: 50, SEQ ID NO: 53, and SEQ ID NO: 51 of V_{D4} having an amino acid sequence of SEQ ID NO: 52, and the 3 CDRs of amino acid sequences of SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7 of V_{D3} having an amino acid sequence of SEQ ID NO: 9, and the amino acid positions 473, 492, 531, 559, 560, 478, and 490 of the amino acid sequence of SEQ ID NO: 74 are unaltered; or

d) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 76, or

an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 76 in which the 3 CDRs of amino acid sequences of SEQ ID NO: 48, WAS, and SEQ ID NO: 49 of V_{D1} having an amino acid sequence of SEQ ID NO: 54, and the 3 CDRs of amino acid sequences of SEQ ID NO: 11, KVS, and SEQ ID NO: 8 of V_{D2} having an amino acid sequence of SEQ ID NO: 10, and the amino acid positions 481, 486, 498, 500, 539, 567, and 568 of the amino acid sequence of SEQ ID NO: 76 are unaltered; and

the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 78,
or

an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 78 in which the 3 CDRs of amino acid sequences of SEQ ID NO: 50, SEQ ID NO: 53, and SEQ ID NO: 51 of V_{D4} having an amino acid sequence of SEQ ID NO: 52, and the 3 CDRs of amino acid sequences of SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7 of V_{D3} having an amino acid sequence of SEQ ID NO: 9, and the amino acid positions 473, 492, 531, 559, 560, 478, and 490 of the amino acid sequence of SEQ ID NO: 78 are unaltered.

5. The antibody-like binding protein according to any one of claims 1 to 4, wherein:

a) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 80; and

the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 59,

b) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 72, and

the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 74,

c) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 76; and

the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 74, or

d) the polypeptide of formula [IV] consists of the amino acid sequence of SEQ ID NO: 76; and

the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 78.

6. An antibody-like binding protein that binds specifically to human CD3 ϵ and human CD123 comprising three polypeptide chains that form two antigen-binding sites, wherein a first polypeptide has a structure represented by the formula [I]:

V_{D1} -L₁- V_{D2} -L₂-C_L [I]

and a second polypeptide chain has a structure represented by the formula [III]:

V_{D3} -L₃- V_{D4} -L₄-C_{H1}-Fc [III];

and a third polypeptide Fc_3 which is the immunoglobulin hinge region and C_{H2} , C_{H3} immunoglobulin heavy chain constant domains of an immunoglobulin;

wherein:

a) the polypeptide of formula [I] consists of the amino acid sequence of SEQ ID NO: 55, wherein:

V_{D1} has an amino acid sequence of SEQ ID NO: 54,

L_1 has an amino acid sequence of SEQ ID NO: 56,

V_{D2} has an amino acid sequence of SEQ ID NO: 10,

L_2 has an amino acid sequence of SEQ ID NO: 56,

C_L has an amino acid sequence of SEQ ID NO: 18,

wherein V_{D1} comprises a CDR1-L having an amino acid sequence of SEQ ID NO: 48, a CDR2-L having an amino acid sequence WAS, and a CDR3-L having an amino acid sequence of SEQ ID NO: 49; and

V_{D2} comprises a CDR4-L having an amino acid sequence of SEQ ID NO: 11, a CDR5-L having an amino acid sequence KVS, and a CDR6-L having an amino acid sequence of SEQ ID NO: 8;

b) the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 67, wherein:

V_{D3} has an amino acid sequence of SEQ ID NO: 9,

L_3 which consists of no amino acid residues,

V_{D4} has an amino acid sequence of SEQ ID NO: 52,

L_4 which consists of no amino acid residues,

C_{H1} of has an amino acid sequence of SEQ ID NO: 19, and

Fc has an amino acid sequence of SEQ ID NO: 68 wherein X_1 is Y, X_2 is C, X_3 is W, X_4 is L, X_5 is Y, and X_6 is H and X_7 is Y, or X_6 is R and X_7 is F,

wherein V_{D3} comprises a CDR1-H having an amino acid sequence of SEQ ID NO: 5, a CDR2-H having an amino acid sequence of SEQ ID NO: 6, and a CDR3-H having an amino acid sequence of SEQ ID NO: 7; and

VD₄ comprises a CDR4-H having an amino acid sequence of SEQ ID NO: 50, a CDR5-H having an amino acid sequence of SEQ ID NO: 53, and a CDR6-H having an amino acid sequence of SEQ ID NO: 51;

and wherein:

- the polypeptide of formula [I] and the polypeptide of formula [III] form a cross-over light chain-heavy chain pair,
- the polypeptide of formula [III] heterodimerizes with the third polypeptide through its Fc domain,
- the third polypeptide Fc₃ consists of the amino acid sequence of SEQ ID NO: 69 or an amino acid sequence that is at least 85% identical to the amino acid sequence of SEQ ID NO: 69, wherein the amino acid positions 129, 146, 148, 187, 215, and 216 of the amino acid sequence of SEQ ID NO: 69 are unaltered.

7. The antibody-like binding protein according to claim 6, comprising:

- the polypeptide of formula [I] consists of the amino acid sequence of SEQ ID NO: 55,
- the polypeptide of formula [III] consists of the amino acid sequence of SEQ ID NO: 65, and
- Fc₃ consists of the amino acid sequence of SEQ ID NO: 69.

8. A pharmaceutical composition comprising an antibody-like binding protein according to any one of claims 1 to 7 and a pharmaceutically acceptable carrier.

9. An isolated nucleic acid comprising a nucleotide sequence encoding an antibody-like binding protein according to any one of claims 1 to 7.

10. A host cell which has been transformed by a nucleic acid according to claim 9.