CLAIMS

1. A polypeptide complex which comprises:

(1) a cancer antigen-binding domain, wherein said antigen is not CD3;

(2) any one of the Fc domains of SEQ ID NOs: 23, 24, 25, and 26 in which an amino acid(s) forming the Fc domain is mutated, wherein the Fc domain mutant has reduced Fcγ receptor-binding activity by said mutation as compared with control polypeptide complex comprising the Fc domain of the same isotype selected from SEQ ID NOs: 23, 24, 25, and 26, and wherein the Fc domain mutant has reduced binding activity to FcγRI, FcγRIIA, FcγRIIB, FcγRIIIA, and/or FcγRIIIB; and

(3) a CD3-binding domain,

wherein the polypeptide complex is any one selected from the group consisting of:

(i) the polypeptide complex which comprises two cancer antigen-binding domains, wherein the cancer antigen-binding domains are individually linked to either of the two polypeptides forming an Fc domain, and wherein the CD3-binding domain is linked to either or both of the two CH3s forming the Fc domain;

(ii) the polypeptide complex which comprises two cancer antigen-binding domains, wherein the cancer antigen-binding domains are individually linked to either of the two polypeptides forming an Fc domain, and wherein the CD3-binding domain is linked to either or both of the two cancer antigen-binding domains; and

(iii) the polypeptide complex which comprises one cancer antigen-binding domain and one CD3-binding domain, wherein the cancer antigen-binding domain is linked to one of the polypeptides forming the Fc domain, and wherein the CD3-binding domain is linked to the other polypeptide forming the Fc domain.

2. The polypeptide complex of claim 1, wherein the antigen-binding domain and CD3-binding domain are each a monovalent Fab.

3. The polypeptide complex of claim 2, in which the heavy chain Fv fragment of a monovalent Fab forming the antigen-binding domain is linked to one of the polypeptides forming the Fc domain *via* a CH1 domain and the light chain Fv fragment of the Fab is linked to a CL domain; and the heavy chain Fv fragment of Fab forming the CD3-binding domain is linked to the other polypeptide forming the Fc domain *via* a CH1 domain and the light chain Fv fragment of the Fab is linked to a CL domain.

4. The polypeptide complex of claim 2 comprising:

(1) an antigen-binding domain in which the heavy chain Fv fragment of a monovalent Fab structure that binds to an antigen is linked *via* a CH1 domain to one of the polypeptides forming the Fc domain, and the light chain Fv fragment of the Fab structure is linked to a CL domain; and

(2) a CD3-binding domain in which the heavy chain Fv fragment of a monovalent Fab structure that binds to a CD3 is linked *via* a CH1 domain to the other polypeptide forming the Fc domain, and the light chain Fv fragment of the Fab structure is linked to a CL domain;

wherein electric charges of the CH1 and CL domains are controlled so that the heavy chain Fv fragment of the antigen-binding domain assembles with the light chain Fv fragment of the antigen-binding domain, or the heavy chain Fv fragment of the CD3-binding domain assembles with the light chain Fv fragment of the CD3-binding domain.

5. The polypeptide complex of claim 4, wherein the amino acid residues in the CH1 and CL domains are one, two, or more combinations of amino acid residues selected from the group consisting of the combinations of:

(a) the amino acid residue at position 147 (EU numbering) in the CH1 domain, and the amino acid residue at position 180 (EU numbering) in the CL domain;

(b) the amino acid residue at position 147 (EU numbering) in the CH1 domain, and the amino acid residue at position 131 (EU numbering) in the CL domain;

(c) the amino acid residue at position 147 (EU numbering) in the CH1 domain, and the amino acid residue at position 164 (EU numbering) in the CL domain;

(d) the amino acid residue at position 147 (EU numbering) in the CH1 domain, and the amino acid residue at position 138 (EU numbering) in the CL domain;

(e) the amino acid residue at position 147 (EU numbering) in the CH1 domain, and the amino acid residue at position 123 (EU numbering) in the CL domain; and

(f) the amino acid residue at position 175 (EU numbering) in the CH1 domain, and the amino acid residue at position 160 (EU numbering) in the CL domain; or

(g) optionally comprising the amino acid residue at position 213 (EU numbering) in the CH1 domain, and the amino acid residue at position 123 (EU numbering) in the CL domain of any one, two or more combinations of (a) to (f),

and in which the amino acid residue in the CH1 domain has an electric charge opposite to that of the amino acid residue in the CL domain,

and wherein the amino acid residue having an opposite electric charge is selected from an amino acid residue in either group:

(X) glutamic acid (E) and aspartic acid (D); or

(Y) lysine (K), arginine (R), and histidine (H);

particularly
i) wherein the amino acid residues having an opposite electric charge are:
Lys at position 175 (EU numbering) in the CH1 domain, and Glu at positions 131, 160, and 180 (EU numbering) in the CL domain;
or,
ii) wherein the amino acid residues having an opposite electric charge are:
Glu at positions 147 and 175 (EU numbering) in the CH1 domain, and Lys at positions 131, 160, and 180 (EU numbering) in the CL domain, especially
wherein the amino acid residue at position 213 (EU numbering) in the CH1 domain is Glu, and the amino acid residue of position 123 (EU numbering) in the CL domain is Lys.

6. The polypeptide complex of any one of claims 1 to 5, wherein the Fc domain comprises any one of the amino acids below:
the amino acid sequence of positions 118 to 260 (EU numbering) is the sequence of SEQ ID NO: 24; or
the amino acid sequence at positions 261 to 447 (EU numbering) is the sequence of SEQ ID NO: 26.

7. The polypeptide complex of any one of claims 1 to 5, wherein the Fc domain comprises a mutation in the amino acids of SEQ ID NO: 23 forming the Fc domain and wherein the amino acids forming the Fc domain comprises a mutation at any one of the following positions:
220, 226, 229, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 264, 265, 266, 267, 269, 270, 295, 296, 297, 298, 299, 300, 325, 327, 328, 329, 330, 331, and 332 (EU numbering).

8. The polypeptide complex of claim 7,
i) wherein the Fc domain is an Fc domain comprising a substitution of the amino acid at position 233, 234, 235, 236, 237, 327, 330, or 331 (EU numbering) by the amino acid at a corresponding position (EU numbering) in the corresponding IgG2 or IgG4;
or
ii) wherein the Fc domain comprises an amino acid mutation at position 234, 235, or 297 (EU numbering) and the amino acid(s) at position(s) 234, 235, and/or 297 is substituted with alanine.

9. The polypeptide complex of any one of claims 6 to 8,
i) wherein the sequences of two polypeptides forming the Fc domain are different from

each other and wherein the amino acid at position 349 is substituted with cysteine and the amino acid at position 366 (EU numbering) is substituted with tryptophan among the amino acid residues of one of the two polypeptides forming the Fc domain; and wherein the amino acid at position 356 is substituted with cysteine, the amino acid at position 366 is substituted with serine, the amino acid at position 368 is substituted with alanine, and the amino acid at position 407 (EU numbering) is substituted with valine among the amino acid residues of the other polypeptide;

or

ii) wherein the sequences of two polypeptides forming the Fc domain are different from each other and wherein the amino acid at position 356 (EU numbering) is substituted with lysine among the amino acid residues of one of the two polypeptides forming the Fc domain; the amino acid at position 439 (EU numbering) is substituted with glutamic acid in the other polypeptide; and the amino acid at position 435 (EU numbering) is substituted with arginine among the amino acid residues of either of the two polypeptides.

10. The polypeptide complex of claim 9, wherein the sequence GK is deleted from the carboxyl termini of two polypeptides forming the Fc domain.

11. A polynucleotide encoding the polypeptide complex of any one of claims 1 to 10, a vector comprising the said polynucleotide, or a cell comprising the said vector.

12. A method for producing a polypeptide complex, which comprises culturing the cell of claim 11 and isolating the polypeptide complex from the culture supernatant.

13. A therapeutic agent for cancer, which comprises as an active ingredient the polypeptide complex of any one of claims 1 to 10.