Patent Claims

1. A multispecific antibody, comprising:

    a) a first light chain and a first heavy chain of a first antibody which specifically binds to a first antigen; and
    b) a second light chain and a second heavy chain of a second antibody which specifically binds to a second antigen, and wherein the variable domains VL and VH in the second light chain and second heavy chain of the second antibody are replaced by each other; and

wherein

in the constant domain CL of the first light chain under a) the amino acid at position 124, numbering according to Kabat, is substituted independently by lysine (K), arginine (R) or histidine (H), and wherein in the constant domain CH1 of the first heavy chain under a) the amino acid at position 147, numbering according to Kabat EU index, or the amino acid at position 213, numbering according to Kabat EU index, is substituted independently by glutamic acid (E) or aspartic acid (D).

2. The multispecific antibody according to claim 1,

wherein in the constant domain CL of the first light chain under a) the amino acid at position 124, numbering according to Kabat, is substituted independently by lysine (K), arginine (R) or histidine (H), and wherein in the constant domain CH1 of the first heavy chain under a) the amino acid at position 147, numbering according to Kabat EU index, is substituted independently by glutamic acid (E) or aspartic acid (D).

3. The multispecific antibody according to claim 1,

wherein in the constant domain CL of the first light chain under a) the amino acid at position 124, numbering according to Kabat, is substituted independently by lysine (K) or arginine (R), and wherein in the constant domain CH1 of the first heavy chain under a) the amino acid at position 213, numbering according to Kabat EU index, is substituted independently by glutamic acid (E) or aspartic acid (D).

4. The multispecific antibody according to claim 1,

wherein in the constant domain CL of the first light chain under a) the amino acid at position 124, numbering according to Kabat, is substituted independently by lysine (K), arginine (R) or histidine (H) and the amino acid at position 123, numbering according to Kabat, is substituted independently by lysine (K), arginine (R) or histidine (H), and wherein in the constant domain CH1 of the first heavy chain under a) the amino acid at position 147, numbering according to Kabat EU index, is substituted independently by glutamic acid (E) or aspartic acid (D)

and the amino acid at position 213, numbering according to Kabat EU index, is substituted independently by glutamic acid (E) or aspartic acid (D).

5. The multispecific antibody according to claim 4, wherein in the constant domain CL of the first light chain under a) the amino acid at position 124, numbering according to Kabat, is substituted independently by lysine (K) or arginine (R).

6. The multispecific antibody according to claim 1,

wherein in the constant domain CL of the first light chain under a) the amino acid at position 124, numbering according to Kabat, is substituted by lysine (K) and the amino acid at position 123, numbering according to Kabat, is substituted by lysine (K),

and wherein in the constant domain CH1 of the first heavy chain under a) the amino acid at position 147, numbering according to Kabat EU index, is substituted by glutamic acid (E) and the amino acid at position 213, numbering according to Kabat EU index, is substituted by glutamic acid (E).

7. The antibody according to any one of the preceding claims, characterized in that

a first CH3 domain of the first heavy chain of the antibody under a) and a second CH3 domain of the second heavy chain of the antibody under b) each meet at an interface which comprises an original interface between the antibody CH3 domains,

wherein said interface is altered to promote the formation of the multispecific antibody, wherein the alteration is characterized in that:

i) the CH3 domain of one heavy chain is altered,
so that within the original interface of the CH3 domain of the one heavy chain that meets the original interface of the CH3 domain of the other heavy chain within the multispecific antibody,
an amino acid residue is replaced with an amino acid residue having a larger side chain volume, thereby generating a protuberance within the interface of the CH3 domain of the one heavy chain which is positionable in a cavity within the interface of the CH3 domain of the other heavy chain;

and

ii) the CH3 domain of the other heavy chain is altered,
so that within the original interface of the CH3 domain of the other heavy chain that meets the original interface of the CH3 domain of the one heavy chain within the multispecific antibody,
an amino acid residue is replaced with an amino acid residue having a smaller side chain volume, thereby generating a cavity within the interface of the CH3 domain of the other heavy chain within which a protuberance within the interface of the CH3 domain of the one heavy chain is positionable,

wherein

the said amino acid residue having a larger side chain volume is selected from the group consisting of arginine (R), phenylalanine (F), tyrosine (Y) and tryptophan (W); and said amino acid residue having a smaller side chain volume is selected from the group consisting of alanine (A), serine (S), threonine (T) and valine (V).

8. The antibody according to claim 7, characterized in that

both CH3 domains are further altered by the introduction of cysteine (C) as amino acid in the corresponding positions of each CH3 domain such that a disulfide bridge between both CH3 domains can be formed.

9. A multispecific antibody according to any one of the preceding claims that specifically binds to human TWEAK and that specifically binds to human IL17, wherein

A) the multispecific antibody comprises
a variable heavy chain domain (VH) of SEQ ID NO:24, and a variable light chain domain (VL) of SEQ ID NO:25; and

B) the multispecific antibody comprises
a variable heavy chain domain (VH) of SEQ ID NO:26, and a variable light chain domain (VL) of SEQ ID NO:27.

10. A method for the preparation of the multispecific antibody according to any one of claims 1 to 9,

comprising the steps of

A) transforming a host cell with vectors comprising nucleic acid molecules encoding
a) the first light chain and the first heavy chain of the multispecific antibody according to any one of claims 1 to 9; and
b) the second light chain and the second heavy chain of the multispecific antibody according to any one of claims 1 to 9;

B) culturing the host cell under conditions that allow synthesis of said antibody molecule; and

C) recovering said antibody molecule from said culture.

11. A nucleic acid encoding the amino acid sequences of a multispecific antibody according to any one of claims 1 to 9.

12. An expression vector containing the nucleic acid according to claim 11 capable of expressing said nucleic acid in a host cell.

13. A composition comprising the antibody according to any one of claims 1 to 9.

14. A pharmaceutical composition comprising an antibody according to any one of claims 1 to 9 and at least one pharmaceutically acceptable excipient.