Claims

1. A ~~humanized or chimeric~~bispecific antibody comprising:

a first antigen binding region for specifically binding to human CD3, ~~wherein said antibody comprises a binding region~~ comprising a heavy chain variable (VH) region ~~CDR1, CDR2, and CDR3~~ having the ~~sequences~~sequence as set forth in SEQ ID ~~NOs: 1, 2~~NO: 6, and ~~3, respectively, and~~a light chain variable (VL) region ~~CDR1, CDR2, and CDR3~~ having the ~~sequences as set forth in SEQ ID NO: 4, the sequence GTN, and the~~ sequence as set forth in SEQ ID NO: ~~5, respectively.~~10; and

a second antigen binding region for specifically binding to human CD20.

2. The bispecific antibody according to claim 1, wherein said ~~VH region has at least 90%, at least 95%, at least 97%, or at least 99% amino acid sequence identity to the amino acid sequence as set forth in the VH sequences selected from the group consisting of;~~

~~a) a VH sequence as set forth in SEQ ID NO:6;~~

~~b) a VH sequence as set forth in SEQ ID NO:8;~~

~~c) a VH sequence as set forth in SEQ ID NO:7; and~~

~~d) a VH sequence as set forth in SEQ ID NO:9.~~

~~3. The antibody according to any one of the preceding claims, wherein said VL region has at least 90%, at least 95%, at least 97%, or at least 99% amino acid sequence identity to the amino acid sequence as set forth in the VL sequences selected from the group consisting of;~~

~~a) a VL sequence as set forth in SEQ ID NO:10;~~

~~b) a VL sequence as set forth in SEQ ID NO:11; and~~

~~c) a VL sequence as set forth in SEQ ID NO:12.~~

~~4. The antibody according to any one of the preceding claims, wherein said VH region is selected from the group consisting of;~~

~~a) a VH sequence as set forth in SEQ ID NO:6;~~

~~b) a VH sequence as set forth in SEQ ID NO:8;~~

~~c) a VH sequence as set forth in SEQ ID NO:7; and~~

~~d) a VH sequence as set forth in SEQ ID NO:9.~~

~~5. The antibody according to any one of the preceding claims, wherein said VL region is selected from the group consisting of;~~

~~a) a VL sequence as set forth in SEQ ID NO:10;~~

~~b) a VL sequence as set forth in SEQ ID NO:11; and~~

~~c) a VL sequence as set forth in SEQ ID NO:12.~~

~~6. The antibody according to any one of the preceding claims, wherein said VH and VL regions are selected from the group consisting of;~~

~~a) a VH sequence as set forth in SEQ ID NO:6, and a VL sequence as set forth in SEQ ID NO:10;~~

~~b) a VH sequence as set forth in SEQ ID NO:8, and a VL sequence as set forth in SEQ ID NO:10;~~

~~c) a VH sequence as set forth in SEQ ID NO:9, and a VL sequence as set forth in SEQ ID NO:10;~~

~~d) a VH sequence as set forth in SEQ ID NO:6, and a VL sequence as set forth in SEQ ID NO:11;~~

~~e) a VH sequence as set forth in SEQ ID NO:6, and a VL sequence as set forth in SEQ ID NO:12;~~

~~f) a VH sequence as set forth in SEQ ID NO:7, and a VL sequence as set forth in SEQ ID NO:10;~~

~~g) a VH sequence as set forth in SEQ ID NO:7, and a VL sequence as set forth in SEQ ID NO:11;~~

~~h) a VH sequence as set forth in SEQ ID NO:7, and a VL sequence as set forth in SEQ ID NO:12;~~

~~i) a VH sequence as set forth in SEQ ID NO:8, and a VL sequence as set forth in SEQ ID NO:11;~~

~~j) a VH sequence as set forth in SEQ ID NO:8, and a VL sequence as set forth in SEQ ID NO:12;~~

~~k) a VH sequence as set forth in SEQ ID NO:9, and a VL sequence as set forth in SEQ ID NO:11; and~~

~~l) a VH sequence as set forth in SEQ ID NO:9, and a VL sequence as set forth in SEQ ID NO:12.~~

~~7. The antibody according to any one of the preceding claims, wherein said binding region comprises a VH sequence and a VL sequence selected from the group consisting of;~~

a) a VH sequence as set forth in SEQ ID NO:6, and a VL sequence as set forth in SEQ ID NO:10;

b) a VH sequence as set forth in SEQ ID NO:8, and a VL sequence as set forth in SEQ ID NO:10; and

c) a VH sequence as set forth in SEQ ID NO:9, and a VL sequence as set forth in SEQ ID NO:10.

8. The antibody according to any one of the preceding claims, wherein the antibody is a humanized antibody.

9. The antibody according to claim 1, wherein the antibody is a chimeric antibody.

10. The antibody according to any one of the preceding claims, wherein the antibody is a full-length antibody.

11. The antibody according to any one of the preceding claims, wherein said antibody comprises an Fc region comprising a first and a second bispecific antibody comprises a first immunoglobulin heavy chain.

12. The antibody according to any one of the preceding claims, wherein said first and said second heavy chains are of an isotype selected from the group consisting of IgG1, IgG2, IgG3, and IgG4.

13. The antibody according to any one of the preceding claims, wherein said antibody comprises an Fc region which has been modified so that binding of C1q to said antibody is reduced compared to a wild-type antibody by at least 70%, at least 80%, at least 90%, at least 95%, at least 97%, or 100%, wherein C1q binding is determined by ELISA.

14. The antibody according to any one of the preceding claims, wherein said antibody comprises an Fc region which has been modified so that said antibody mediates reduced Fc-mediated T-cell proliferation compared to a wild-type antibody by at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 99% or 100%, wherein said T-cell proliferation is measured in a peripheral blood mononuclear cell (PBMC)-based functional assay.

15. The antibody according to any one of the preceding claims, wherein said antibody comprises an Fc region which has been modified so that said antibody reduces Fc-mediated CD69 expression by at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 99% or 100% when compared to a wild-type antibody wherein said Fc-mediated CD69 expression is determined in a PBMC-based functional assay.

16. The antibody according to any one of the preceding claims, wherein said antibody comprises a first and and a second immunoglobulin heavy chain, wherein in at least one of said first and second immunoglobulin heavy chains one or more amino acids in the positions corresponding to positions L234, L235, D265, N297, and P331 in a human IgG1 heavy chain, are not L, L, D, N, and P, respectively. .

17. The antibody according to claim 16, wherein in at least one of said first and second heavy chains the amino acids in the positions corresponding to positions L234 and L235 in a human IgG1 heavy chain, are F and E; or A and A, respectively. , wherein the amino acid positions are numbered according to the EU numbering system.

18. The antibody according to claim 16, wherein in at least one of said first and second heavy chains the amino acid in the position corresponding to position N297 in a human IgG1 heavy chain, is not N.

19. The antibody according to claim 16, wherein in at least one of said first and second heavy chains the amino acids in the positions corresponding to positions L234 and L235 in a human IgG1 heavy chain, are not L and L, respectively.

20. The antibody according to any of claims 16 and 19, wherein in at least one of said first and second heavy chains the amino acids in the positions corresponding to positions L234 and L235 in a human IgG1 heavy chain, are F and E; or A and A, respectively. , wherein the amino acid positions are numbered according to the EU numbering system.

21. The antibody according to claim 16, wherein in at least one of said first and second heavy chains the amino acids in the positions corresponding to positions L234, L235, and D265 in a human IgG1 heavy chain, are not L, LF, E, and DA, respectively. , wherein the amino acid positions are numbered according to the EU numbering system.

~~33. The~~8. A bispecific antibody ~~according to any of claims 28 to 32, wherein said~~comprising:

a first immunoglobulin heavy chain and a first immunoglobulin light chain, which are connected via disulfide bridges forming a first antigen binding region ~~is according to any of claims 1 to 7, and said second~~ for specifically binding to human CD3, comprising a heavy chain variable (VH) region ~~binds~~ having the sequence as set forth in SEQ ID NO: 6, and a light chain variable (VL) region having the sequence as set forth in SEQ ID NO: 10, and

a second immunoglobulin heavy chain and a second immunoglobulin light chain, which are connected via disulfide bridges forming a second antigen binding region for specifically binding to a different target than said first antigen binding region~~.~~;

~~34. A nucleic acid construct encoding one or more amino acid sequences set out in Table 1.~~

~~35. An expression vector comprising~~

~~(i) a nucleic acid sequence encoding a heavy chain sequence of a humanized or chimeric antibody according to any one of claims 1 to 33;~~

~~(ii) a nucleic acid sequence encoding a light chain sequence of~~wherein in at least one of the first and the second heavy chains, the amino acids in the positions corresponding to position L234, L235, and D265 in a human IgG1 heavy chain are F, E, and A, respectively, the amino acid in the position corresponding to F405 in a human IgG1 heavy chain is L in the first heavy chain, and the amino acid in the position corresponding to K409 in a human IgG1 heavy chain is R in the second heavy chain, wherein the amino acid positions are numbered according to the EU numbering system.

9. The bispecific antibody of claim 8, wherein in both the first and the second heavy chains the amino acids in the positions corresponding to position L234, L235, and D265 in a human IgG1 heavy chain are F, E, and A, respectively.

10. The bispecific antibody of claims 8 or 9, wherein the first heavy chain comprises a heavy chain constant region of SEQ ID NO:25.

11. The bispecific antibody of any one of claims 8 to 22, wherein the second heavy chain comprises a ~~humanized or chimeric~~heavy chain constant region of SEQ ID NO:26.

12. The bispecific antibody according to any one of claims ~~1 to 33; or~~8 to 11, wherein the second antigen binding region is for specifically binding to human CD20.
~~(iii) both (i) and (ii).~~

~~36. A host cell comprising an expression vector of claim 35.~~

~~37. The host cell according to claim 36, wherein said host cell is a recombinant eukaryotic, recombinant prokaryotic, or recombinant microbial host cell.~~

~~38~~
13. The bispecific antibody according to claim 12, wherein the second antigen binding region comprises a heavy chain comprising a heavy chain variable region having the sequence as set forth in SEQ ID NO: 29, and a light chain comprising a light chain variable region having the sequence as set forth in SEQ ID NO: 30.

14. The bispecific antibody according to claim 9, wherein the second heavy chain comprises a heavy chain variable region having the sequence as set forth in SEQ ID NO: 29, and a light chain comprising a light chain variable region having the sequence as set forth in SEQ ID NO: 30.

15. The bispecific antibody according to claim 14, wherein the bispecific antibody is a full-length antibody.

16. A composition comprising ~~an antibody according to~~ the bispecific antibody as defined in any one of claims 1 to 12 together with an excipient, diluent or carrier.

17. A composition comprising the bispecific antibody as defined in any one of claims ~~1 to 27 or a bispecific antibody according to any one of claims 28 to 33~~13 to 15; together with an excipient, diluent or carrier.

~~39~~18. A pharmaceutical composition comprising the bispecific antibody ~~according to~~as defined in any one of claims 1 to ~~27 or bispecific antibody according to any one of claims 28 to 33~~13 and a pharmaceutical acceptable carrier.

~~40. The antibody according to any one of claims 1 to 27, said bispecific antibody according to any one of claims 28 to 33, said composition according to claim 38, or said pharmaceutical composition according to claim 39 for use as a medicament.~~

~~41. The antibody according to any one of claims 1 to 27, said~~ 19. A pharmaceutical composition comprising the bispecific antibody as defined in any one of claims 13 to 15 and a pharmaceutical acceptable carrier.

20. The bispecific antibody ~~according to~~ as defined in any one of claims ~~28~~1 to ~~33, said~~12, the composition ~~according to~~as defined in claim ~~38~~16, or ~~said~~the pharmaceutical composition ~~according to~~ as defined in claim ~~39,~~18 for use ~~in~~ as a medicament.

21. The bispecific antibody as defined in any one of claims 13 to 15, the composition as defined in claim 17, or the pharmaceutical composition as defined in claim 19 for use as a medicament.

22. A use of the bispecific antibody as defined in any one of claims 1 to 12, the composition as defined in claim 16, or the pharmaceutical composition as defined in claim 18 for preparation of a medicament for the treatment of a ~~disease.~~

~~42. A method of treatment of a disease comprising administering said antibody according to any one of claims 1 to 27, said bispecific antibody according to any one of claims 28 to 33, said composition according to claim 38, or said pharmaceutical composition according to claim 39, to a subject in need thereof.~~

~~43. The use or method according to any one of claims 40 to 42, wherein the disease is~~ cancer, an infectious disease, or an autoimmune disease.

~~44~~23. A ~~method of diagnosing a disease characterized by involvement or accumulation of CD3-expressing cells, comprising administering said antibody according to any one of claims 1 to 27, said~~ use of the bispecific antibody ~~according to~~ as defined in any one of

claims ~~28~~13 to ~~33, said~~15, the composition ~~according to~~ as defined in claim ~~38~~17, or ~~said~~the pharmaceutical composition ~~according to~~as defined in claim ~~39 to a subject, optionally wherein said antibody or said bispecific antibody is labeled with a detectable agent.~~

~~45. A method~~19, for ~~producing an antibody according to any one of claims 1 to 27, or a bispecific antibody according to any one of claims 28 to 33, comprising the steps of~~

~~a) culturing a host cell according to any one of claims 36 to 37; and~~

~~b) purifying said antibody from the culture media.~~

~~46. A diagnostic composition comprising an antibody according to any one of claims 1 to 27, or a bispecific antibody according to any one of claims 28 to 33.~~

~~47. A method~~preparation of a medicament for ~~detecting the presence of CD3 antigen, or a cell expressing CD3, in a sample comprising~~ the ~~steps of;~~ treatment of a cancer, an infectious disease, or an autoimmune disease.

~~a) contacting the sample with an antibody according to any one of claims 1 to 27 or a bispecific antibody according to any one of claims 28 to 33, under conditions that allow for formation of a complex between said antibody or bispecific antibody and CD3; and~~
~~b) analyzing whether a complex has been formed.~~

~~48. A kit for detecting the presence of CD3 antigen, or a cell expressing CD3, in a sample comprising~~
~~i) an antibody according to any one of claims 1 to 27, or a bispecific antibody according to any one of claims 28 to 33; and~~
~~ii) instructions for use of said kit.~~

~~49. An anti-idiotypic antibody which binds to an antibody of any one of claims 1 to 27.~~