

Claims

1. A humanized or chimeric antibody binding to human CD3, wherein said antibody comprises a binding region comprising a heavy chain variable (VH) region and a variable light chain region, wherein said VH region comprises the CDR1, CDR2 and CDR3 sequences set forth in SEQ ID NO: 1, 2, 176 [H101G], and wherein said VL region comprises CDR1, CDR2, and CDR3 regions having the CDR sequences as set forth in SEQ ID NO:6, GTN.
2. The antibody according to claim 1, wherein said binding region comprises a variable light chain (VL) region, wherein said VL region is selected from the group consisting of;
 - a) a VL sequence as set forth in SEQ ID NO:8;
 - b) a VL sequence as set forth in SEQ ID NO:10 or
 - c) a VL sequence having at least 90%, at least 95%, at least 97% or at least 99% amino acid sequence identity to any one of the sequences as set forth in a) to b).
3. The antibody according to claim 1 or claim 2, wherein human CD3 is human CD3 epsilon as specified in SEQ ID NO: 399.
4. The antibody according to any one of the preceding claims, wherein the antibody has a binding affinity to human CD3 epsilon peptide with SEQ ID NO: 402 corresponding to a K_D value from 1.0×10^{-7} to 9.9×10^{-7} M as determined by Bio-Layer Interferometry.
5. The antibody according to any one of the preceding claims, wherein the antibody is a humanized antibody.
6. The antibody according to any one of the preceding claims, wherein the antibody is a full-length antibody.
7. The antibody according to any one of the preceding claims, wherein the antibody is of an isotype selected from the group consisting of IgG1, IgG2, IgG3, and IgG4.
8. The antibody according to any one of the preceding claims, wherein the antibody is monovalent, bivalent or multivalent.
9. The antibody according to any one of the preceding claims, wherein said antibody comprises an Fc region comprising a first and a second immunoglobulin heavy chain.
10. The antibody according to any one of the preceding claims, wherein said antibody comprises a first 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 according to EU numbering, are not L, L, D, N, and P, respectively.

11. The antibody according to claim 10, wherein in at least one of said first and second immunoglobulin heavy chains the amino acid in the position corresponding to position D265 in a human IgG1 heavy chain, is not D.
12. The antibody according to claim 10, 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.
13. The antibody according to claim 10, 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.
14. The antibody according to any one of claims 10 to 13, 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.
15. The antibody according to claim 14, 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, respectively.
16. The antibody according to claim 14, 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 A and A, respectively.
17. The antibody according to claim 9, 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, L, and D, respectively.
18. The antibody according to claim 17, 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 F, E, and A; or A, A, and A, respectively.
19. The antibody according to claim 17 or claim 18, 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 F, E, and A, respectively.
20. The antibody according to claim 17 or claim 18, 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 A, A, and A, respectively.
21. The antibody according to claim 10, wherein in at least one of said first and second heavy chains the amino acids in the positions corresponding to positions L234, L235, D265, N297, and P331 in a human IgG1 heavy chain, are F, E, A, Q, and S, respectively.

22. A bispecific antibody comprising a first binding region of an antibody according to any one of claims 1 to 21, and a second binding region which binds a different target than said first antigen binding region.
23. The bispecific antibody according to claim 22 wherein said antibody comprises a first and a second heavy chain.
24. The bispecific antibody according to claim 22 or claim 23, wherein each of said first and second heavy chain comprises at least a hinge region, a CH2 and CH3 region, wherein in said first heavy chain at least one of the amino acids in the positions corresponding to a positions selected from the group consisting of T366, L368, K370, D399, F405, Y407, and K409 in a human IgG1 heavy chain has been substituted, and in said second heavy chain at least one of the amino acids in the positions corresponding to a position selected from the group consisting of T366, L368, K370, D399, F405, Y407, and K409 in a human IgG1 heavy chain has been substituted, and wherein said first and said second heavy chains are not substituted in the same positions.
25. The bispecific antibody according to claim 24, wherein the amino acid in the position corresponding to F405 in a human IgG1 heavy chain is L in said first heavy chain, and the amino acid in the position corresponding to K409 in a human IgG1 heavy chain is R in said second heavy chain, or vice versa.
26. The bispecific antibody according to any one of claims 22 to 25, wherein said first binding region is according to any one of claims 1 to 9, and said second binding region binds a different target than said first binding region.
27. A method of reducing the binding affinity of an antibody binding to human CD3 compared to a reference antibody comprising a heavy chain variable (VH) region, wherein said VH region comprises the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NO: 1, 2, 3, which method comprises introducing a mutation in one of the CDR3 sequence of the said reference antibody, wherein said mutation in the VH CDR3 region is H101G, wherein the positions are numbered according to the reference sequence of the SEQ ID NO: 4.
28. The method according to claim 27, wherein antibody has a binding affinity to human CD3 epsilon peptide with SEQ ID NO: 402 corresponding to a K_D value from 1.0×10^{-7} to 9.9×10^{-7} M as determined by Bio-Layer Interferometry.
29. The method according to claim 27 or claim 28, wherein the human CD3 epsilon is expressed on a T cell.
30. The method according to any one of claims 27 to 29, wherein the human CD3 epsilon is in isolated form, e.g. an isolated human CD3 epsilon-peptide.
31. A nucleic acid construct encoding one or more amino acid sequences of any of claims 1 to 26.
32. An expression vector comprising

- (i) a nucleic acid sequence encoding a heavy chain sequence of a humanized or chimeric antibody according to claim 1;
- (ii) a nucleic acid sequence encoding a light chain sequence of a humanized or chimeric antibody according to claim 2; or
- (iii) both (i) and (ii).

33. A host cell comprising an expression vector of claim 32.

34. The host cell according to claim 33, wherein said host cell is a recombinant eukaryotic, recombinant prokaryotic, or recombinant microbial host cell.

35. A composition comprising an antibody according to any one of claims 1 to 9 or a bispecific antibody according to claims 10 to 26.

36. A pharmaceutical composition comprising the antibody according to any one of claims 1 to 9, or the bispecific antibody according to any one of claims 10 to 26 and a pharmaceutical acceptable carrier.

37. The antibody according to any one of claims 1 to 26, the composition according to claim 35, or the pharmaceutical composition according to claim 36 for use as a medicament.

38. The antibody according to any one of claims 1 to 9, the bispecific antibody according to claims 10 to 26, the composition according to claim 35, or the pharmaceutical composition according to claim 36, for use in the treatment of a disease.

39. Use of the antibody according to any one of claims 1 to 9, the bispecific antibody according to claims 10 to 26, the composition according to claim 35, or the pharmaceutical composition according to claim 36, in the manufacture of a medicament for the treatment of cancer, an infectious disease, or an autoimmune disease in a subject.

40. The use of claim 39, wherein said antibody is labeled with a detectable agent.

41. A method for producing an antibody according to any one of claims 1 to 9 comprising the steps of

- a) culturing a host cell according to claim 33 or claim 34; and
- b) purifying said antibody from the culture media.

42. A diagnostic composition comprising an antibody according to any one of claims 1 to 9 or a bispecific antibody according to any one of claims 10 to 26.

43. A method for detecting the presence of CD3 antigen, or a cell expressing CD3, in a sample comprising the steps of;

- a) contacting the sample with an antibody according to any one of claims 1 to 9 or a bispecific antibody according to any one of claims 10 to 26, 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.
44. 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 9 or a bispecific antibody according to any one of claims 10 to 26; and
 - ii) instructions for use of said kit.
45. An anti-idiotypic antibody which binds to an antibody of any one of claims 1 to 9 or a bispecific antibody according to any one of claims 10 to 26.