

CLAIMS

1. A bispecific antibody comprising a first antigen-binding arm comprising a first antigen-binding region binding to human CD3 ϵ (epsilon) and a second binding arm comprising a second antigen-binding region binding to human CD20, wherein:
 - (i) said first binding arm comprises a first heavy chain comprising a first heavy chain variable sequence (VH) as set forth in SEQ ID NO:6, and a first heavy chain constant sequence (CH), and a first light chain comprising a first light chain variable sequence (VL) as set forth in SEQ ID NO:10 and a first light chain constant sequence (CL), and
said second binding arm comprises a second heavy chain comprising a second heavy chain variable sequence (VH) as set forth in SEQ ID NO:27 and a second heavy chain constant sequence (CH), and a second light chain comprising a second light chain variable sequence (VL) as set forth in SEQ ID NO:28 and a second light chain constant sequence (CL);
 - (ii) said first and second heavy chain constant sequences are IgG1 constant sequences, wherein in both the first and second heavy chain 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,
the amino acid in the position corresponding to F405 in a human IgG1 heavy chain is L in said first heavy chain,
the amino acid in the position corresponding to K409 in a human IgG1 heavy chain is R in said second heavy chain,
the amino acid positions are according to EU-numbering, and
 - (iii) the bispecific antibody comprises a light chain constant sequence (CL) as set forth in SEQ ID NO: 29.
2. The bispecific antibody according to claim 1, which is a full-length antibody.
3. The bispecific antibody according to any one of the preceding claims, which is a full length IgG1 antibody.
4. The bispecific antibody according to any one of the preceding claims, wherein the bispecific antibody is of the IgG1m(f) isotype.

5. The bispecific antibody according to any of the preceding claims, wherein the bispecific antibody comprises a lambda light chain constant region and a kappa light chain constant region.
6. The bispecific antibody according to any of the preceding claims, wherein the first binding arm comprises a human lambda light chain constant region.
7. The bispecific antibody according to any of the preceding claims, wherein the second binding arm comprises a human kappa light chain constant region.
8. The bispecific antibody according to any of the preceding claims, wherein the first binding arm comprises a human lambda light chain constant region and the second binding arm comprises a human kappa light chain constant region.
9. The bispecific antibody according to any of the preceding claims, wherein the first binding arm comprises a light chain constant sequence (CL) as set forth in SEQ ID NO: 29 and the second binding arm comprises a human kappa light chain constant region.
10. A nucleic acid construct encoding a bispecific antibody as defined in any of claims 1-9.
11. An expression vector comprising:
 - (i) a nucleic acid sequence encoding a heavy chain sequence of a first binding arm as defined in claim 1;
 - (ii) a nucleic acid sequence encoding a light chain sequence of a first binding arm as defined in any one of the preceding claims 1, 6, 8 and 9;
 - (iii) a nucleic acid sequence encoding a heavy chain sequence of a second binding arm as defined in claim 1; and
 - (iv) a nucleic acid sequence encoding a light chain sequence of a second binding arm as defined in any one of the preceding claims 1, 7, 8 and 9.
12. A host cell comprising an expression vector of claim 11.
13. The host cell according to claim 12, wherein said host cell is a recombinant eukaryotic, recombinant prokaryotic, or recombinant microbial host cell.

14. A composition comprising a bispecific antibody according to any one of the preceding claims 1-9.
15. A pharmaceutical composition comprising the bispecific antibody according to any one of the preceding claims 1-9 and a pharmaceutically acceptable carrier.
16. The bispecific antibody according to any one of the preceding claims 1-9, the composition according to claim 14, or the pharmaceutical composition according to claim 15 for use as a medicament.
17. The bispecific antibody according to any one of the preceding claims 1-9, the composition according to claim 14, or the pharmaceutical composition according to claim 15 for use in the treatment of cancer.
18. The bispecific antibody for use according to claim 17, wherein the use is for treating B cell malignancies.
19. The bispecific antibody for use according to claim 17 or 18, wherein the use is for treating NHL or B cell leukemia.
20. The bispecific antibody for use according to any one of claims 17-19, wherein the use is in combination with one or more further therapeutic agents.
21. The bispecific antibody for use according to claim 20, wherein the use is in combination with a chemotherapeutic agent.
22. Use of a bispecific antibody according to any one of the preceding claims 1-9 for the manufacture of a medicament for the treatment of cancer.
23. The use according to claim 22, wherein the use is for treating B cell malignancies.
24. The use according to claims 22 or 23, wherein the use is for treating NHL or B cell leukemia.
25. The use according to any of claims 22-24, wherein the bispecific antibody is used in combination with one or more further therapeutic agent.

26. The use according to any of claims 22-25, wherein the bispecific antibody is used in combination with a chemotherapeutic agent.
27. A method for producing a bispecific antibody according to any one of the preceding claims 1-9, comprising the steps of
- a) culturing a host cell comprising an expression vector comprising a nucleic acid sequence encoding a heavy chain sequence of a first binding arm as defined in claim 1 and a nucleic acid sequence encoding a light chain sequence of a first binding arm as defined in any of claims 1, 6, 8 and 9, and purifying a first antibody from the culture media;
 - b) culturing a host cell comprising an expression vector comprising a nucleic acid sequence encoding a heavy chain sequence of a second binding arm as defined in claim 1, and a nucleic acid sequence encoding a light chain sequence of a second binding arm as defined in any one of claims 1, 7, 8 and 9, and purifying a second antibody from the culture media;
 - c) incubating said first antibody together with said second antibody under reducing conditions sufficient to allow the cysteines in the hinge region to undergo disulfide-bond isomerization, and
 - d) obtaining said bispecific antibody.
28. A diagnostic composition comprising a bispecific antibody according to any one of the preceding claims 1-9.
29. A method for detecting whether cross-linking between CD3- and CD20-expressing cells occurs in a sample derived from a patient such as a blood sample, lymph node sample or bone marrow sample, upon administration of a bispecific antibody according to any one of the preceding claims 1-9, comprising the steps of:
- a. contacting the sample with a bispecific antibody according to any one of the preceding claims 1-9, under conditions that allow for formation of a complex between said bispecific antibody and the CD3- and CD20-expressing cells; and
 - b. analyzing whether a complex has been formed.
30. A kit for detecting cross-linking between CD3- and CD20-expressing cells, in a sample derived from a patient such as a blood sample, lymph node sample or bone marrow sample, comprising

- i) a bispecific antibody according to any one of the preceding claims 1-9; and
- ii) instructions for use of said kit.