Claims

1. A modified anti-CD20 antibody, wherein said modified antibody induces higher levels of apoptosis when complexed with CD20 as compared to when the chimeric B-Ly1 antibody is complexed with CD20, and wherein said modified antibody comprises:

   a first polypeptide comprising a heavy chain variable region sequence of SEQ ID NO: 128 and a second polypeptide comprising a light chain variable region sequence of SEQ ID NO: 48; or

   a first polypeptide comprising a heavy chain variable region sequence of SEQ ID NO: 129 and a second polypeptide comprising a light chain variable region sequence of SEQ ID NO: 48.

2. The antibody of claim 1, wherein said antibody comprises an Fc region that has been glycoengineered to have an increase in the amount of bisected complex oligosaccharides.

3. The antibody of claim 1 or 2, wherein said antibody comprises an Fc region that has been glycoengineered to have a decrease in the amount of fucose residues.

4. The antibody of any one of claims 1-3, said antibody having an Fc region with modified oligosaccharides.

5. The antibody of claim 4, wherein at least 20% of the oligosaccharides in the Fc region are bisected, nonfucosylated.

6. The antibody of claim 4, wherein at least 50% of the oligosaccharides in the Fc region are nonfucosylated.

7. A host cell expressing at least one nucleic acid encoding a first polypeptide having β(1,4)-N-acetylglucosaminyltransferase III activity in an amount sufficient to glycoengineer the Fc

region of a second polypeptide produced by said host cell, wherein said second polypeptide is the antibody of any one of claims 1-6.

8. The host cell of claim 7, wherein said host cell further expresses a nucleic acid encoding a polypeptide having mannosidase II activity.

9. The host cell of claim 7 or 8, wherein said antibody produced by said host cell exhibits increased Fc receptor binding affinity as a result of said glycoengineering.

10. The host cell of claim 9, wherein said Fc receptor is FcγRIIIA receptor.

11. The host cell of claim 7 or 8, wherein said antibody produced by said host cell exhibits increased effector function as a result of said glycoengineering.

12. The host cell of claim 11, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

13. The host cell of claim 11 or 12, wherein said increased effector function is increased antibody-dependent cellular cytotoxicity.

14. The host cell of claim 7 or 8, further comprising at least one transfected polynucleotide encoding the first and second polypeptides according to claim 1, and wherein said polynucleotide further comprises a sequence encoding a region equivalent to the Fc region of a human immunoglobulin.

15. A pharmaceutical composition comprising the antibody of any one of claims 1-6 and a pharmaceutically acceptable carrier.

16. Use of the antibody of any one of claims 1-6 for the manufacture of a medicament to treat a haematological malignancy, wherein said haematological malignancy is B-cell lymphoma, non-Hodgkin's lymphoma, or B-cell chronic lymphocytic leukaemia.

17. Use of the antibody of any one of claims 1-6 for the manufacture of a medicament to treat an autoimmune disease, wherein said autoimmune disease is rheumatoid arthritis or lupus.

18. Use of the antibody according to claim 16, wherein said haematological malignancy is B-cell lymphoma.

19. An antibody according to any one of claims 1-6 for use as a medicament to treat B-cell lymphoma.

20. An isolated polynucleotide comprising a sequence that encodes a light chain variable region sequence of SEQ ID NO: 48.

21. The isolated polynucleotide of claim 20, wherein said isolated polynucleotide further comprises a sequence that encodes a heavy chain variable region sequence of SEQ ID NO: 128.

22. The isolated polynucleotide of claim 20, wherein said isolated polynucleotide further comprises a sequence that encodes a heavy chain variable region sequence of SEQ ID NO: 129.

23. An expression vector comprising the polynucleotide of any one of claims 20-22.

24. A host cell comprising the expression vector of claim 23.

25. A method for producing in a host cell an anti-CD20 antibody having an Fc region with modified oligosaccharides and engineered to have increased effector function, said method comprising:

a. culturing a host cell engineered to express at least one nucleic acid encoding a polypeptide having β(1,4)-N-acetylglucosaminyltransferase III activity under

conditions which permit the production of said antibody, and which permit the modification of the oligosaccharides present on the Fc region of said antibody; and

b. isolating said antibody;

wherein said antibody is the modified antibody of any one of claims 1-6.

26. The method of claim 25, wherein said host cell is further engineered to express a nucleic acid encoding a polypeptide having mannosidase II activity.

27. The method of claim 25 or 26, wherein said modified oligosaccharides have reduced fucosylation as compared to non-modified oligosaccharides.

28. The method of any one of claims 25-27, wherein said antibody produced by said host cell has an increased proportion of bisected, non-fucosylated oligosaccharides in the Fc region of said polypeptide.

CLAIMS

1. A modified anti-CD20 antibody, wherein said modified antibody induces higher levels of apoptosis when complexed with CD20 as compared to when the chimeric B-Ly1 antibody is complexed with CD20, and wherein said modified antibody comprises:

   a first polypeptide comprising a heavy chain variable region sequence of SEQ ID NO: 128 and a second polypeptide comprising a light chain variable region sequence of SEQ ID NO: 48; or

   a first polypeptide comprising a heavy chain variable region sequence of SEQ ID NO: 129 and a second polypeptide comprising a light chain variable region sequence of SEQ ID NO: 48.

2. The antibody of claim 1, wherein said antibody comprises an Fc region that has been glycoengineered to have an increase in the amount of bisected complex oligosaccharides.

3. The antibody of claim 1 or 2, wherein said antibody comprises an Fc region that has been glycoengineered to have a decrease in the amount of fucose residues.

4. The antibody of any of claims 1-3, said antibody having an Fc region with modified oligosaccharides.

5. The antibody of claim 4, wherein at least 20% of the oligosaccharides in the Fc region are bisected, nonfucosylated.

6. The antibody of claim 4, wherein at least 50% of the oligosaccharides in the Fc region are nonfucosylated.

7. A host cell expressing at least one nucleic acid encoding a polypeptide having β(1,4)-N-acetylglucosaminyltransferase III activity in an amount sufficient to glycoengineer the Fc

region of a polypeptide produced by said host cell, wherein said polypeptide is the antibody of any one of claims 1-6.

8. The host cell of claim 7, wherein said host cell further expresses a nucleic acid encoding a polypeptide having mannosidase II activity.

9. The host cell of claim 7 or 8, wherein said antibody produced by said host cell exhibits increased Fc receptor binding affinity as a result of said glycoengineering.

10. The host cell of claim 9, wherein said Fc receptor is FcγRIIIA receptor.

11. The host cell of claim 7 or 8, wherein said antibody produced by said host cell exhibits increased effector function as a result of said glycoengineering.

12. The host cell of claim 11, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

13. The host cell of claim 11 or 12, wherein said increased effector function is increased antibody-dependent cellular cytotoxicity.

14. The host cell of claim 7 or 8, further comprising at least one transfected polynucleotide encoding the first and second polypeptides according to claim 1, and wherein said polynucleotide further comprises a sequence encoding a region equivalent to the Fc region of a human immunoglobulin.

15. A pharmaceutical composition comprising the antibody of any one of claims 1-6 and a pharmaceutically acceptable carrier.

16. Use of the antibody of any one of claims 1-6 for the manufacture of a medicament to treat a disorder treatable by B-cell depletion.

17. Use of the antibody according to claim 16, wherein said disorder is a haematological malignancy or an autoimmune disease.

18. Use of the antibody according to claim 17, wherein said haematological malignancy is B-cell lymphoma, non-Hodgkin's lymphoma, or B-cell chronic lymphocytic leukaemia.

19. Use of the antibody according to claim 17, wherein said autoimmune disease is rheumatoid arthritis or lupus.

20. Use of the antibody according to claim 17, wherein said haematological malignancy is B-cell lymphoma.

21. An antibody according to any one of claims 1-6 for use as a medicament to treat B-cell lymphoma.

22. An isolated polynucleotide comprising a sequence that encodes a light chain variable region sequence of SEQ ID NO: 48.

23. The isolated polynucleotide of claim 22, wherein said isolated polynucleotide further comprises a sequence that encodes a heavy chain variable region sequence of SEQ ID NO: 128.

24. The isolated polynucleotide of claim 22, wherein said isolated polynucleotide further comprises a sequence that encodes a heavy chain variable region sequence of SEQ ID NO: 129.

25. An expression vector comprising the polynucleotide of any one of claims 22-24.

26. A host cell comprising the expression vector of claim 25.

27. A method for producing in a host cell an anti-CD20 antibody having an Fc region with modified oligosaccharides and engineered to have increased effector function, said method comprising:

a. culturing a host cell engineered to express at least one nucleic acid encoding a polypeptide having β(1,4)-N-acetylglucosaminyltransferase III activity under

conditions which permit the production of said antibody, and which permit the modification of the oligosaccharides present on the Fc region of said antibody; and

b. isolating said antibody;

wherein said antibody is the modified antibody of any one of claims 1-6.

28. The method of claim 27, wherein said host cell is further engineered to express a nucleic acid encoding a polypeptide having mannosidase II activity.

29. The method of claim 27 or 28, wherein said modified oligosaccharides have reduced fucosylation as compared to non-modified oligosaccharides.

30. The method of any one of claims 27-29, wherein said antibody produced by said host cell has an increased proportion of bisected, non-fucosylated oligosaccharides in the Fc region of said polypeptide.