CLAIMS

1. An isolated antibody or a functional protein comprising an antigen-binding portion of an antibody for a target BAFFR polypeptide (SEQ ID NO: 87), characterized in that the antibody or functional protein comprises a V_H polypeptide having at least 90 percent sequence identity to anyone of SEQ ID NOs: 50-56 and a V_L polypeptide sequence having at least 90 percent sequence identity to anyone of SEQ ID NOs: 43-49 and wherein said antibody or functional protein binds to the BAFFR polypeptide with a K_D of 100nM or less and inhibits BLyS induced human B cell proliferation with an IC_{50} of 10nM or less and depletes B cells *in vivo* or *in vitro*.

2. The antibody or functional protein of claim 1 comprising a V_H polypeptide sequence of SEQ ID NO: 51 and a V_L polypeptide sequence of SEQ ID NO: 44.

3. The antibody or functional protein of claim 1 comprising a V_H polypeptide sequence of SEQ ID NO: 52 and a V_L polypeptide sequence of SEQ ID NO: 45.

4. The antibody or functional protein of claim 1 comprising a V_H polypeptide sequence of SEQ ID NO: 53 and a V_L polypeptide sequence of SEQ ID NO: 46.

5. The antibody or functional protein of claim 1 comprising a V_H polypeptide sequence of SEQ ID NO: 54 and a V_L polypeptide sequence of SEQ ID NO: 47.

6. The antibody or functional protein of claim 1 comprising a V_H polypeptide sequence of SEQ ID NO: 55 and a V_L polypeptide sequence of SEQ ID NO: 48.

7. The antibody or functional protein of claim 1 comprising a V_H polypeptide sequence of SEQ ID NO: 56 and a V_L polypeptide sequence of SEQ ID NO: 49.

8. An isolated antibody or a functional protein comprising an antigen-binding portion of an antibody for a target BAFFR polypeptide (SEQ ID NO: 87), characterized in that the antibody or functional protein comprises

(a) a heavy chain variable region CDR1 amino acid sequence selected from the group consisting of SEQ ID NOs: 1-7;

(b) a heavy chain variable region CDR2 amino acid sequence selected from the group consisting of SEQ ID NOs: 8-14;

(c) a heavy chain variable region CDR3 amino acid sequences are selected from the group consisting of SEQ ID NOs: 15-21;

(d) a light chain variable region CDR1 amino acid sequence selected from the group consisting of SEQ ID NOs: 22-28

(e) a light chain variable region CDR2 amino acid sequence selected from the group consisting of SEQ ID NOs: 29-35; and

(f) a light chain variable region of CDR3 amino acid sequence selected from the group consisting of SEQ ID NOs: 36-42

and wherein said antibody or functional protein binds to the BAFFR polypeptide with a K_D of 100nM or less and inhibits BLyS induced human B cell proliferation with an IC_{50} of 10nM or less and depletes B cells *in vivo* or *in vitro*.

9. The antibody or functional protein according to claim 8 comprising a heavy chain variable region CDR1 of SEQ ID NO: 2; a heavy chain variable region CDR2 of SEQ ID NO: 9; a heavy chain variable region CDR3 of SEQ ID NO: 16; a light chain variable region CDR1 of SEQ ID NO: 23; a light chain variable region CDR2 of SEQ ID NO: 30; and a light chain variable region CDR3 of SEQ ID NO: 37.

10. The antibody or functional protein according to claim 8 comprising a heavy chain variable region CDR1 of SEQ ID NO: 3; a heavy chain variable region CDR2 of SEQ ID NO: 10; a heavy chain variable region CDR3 of SEQ ID NO: 17; a light chain variable region CDR1 of SEQ ID NO: 24; a light chain variable region CDR2 of SEQ ID NO: 31; and a light chain variable region CDR3 of SEQ ID NO: 38.

11. The antibody or functional protein according to claim 8 comprising a heavy chain variable region CDR1 of SEQ ID NO: 4; a heavy chain variable region CDR2 of SEQ ID NO: 11; a heavy chain variable region CDR3 of SEQ ID NO: 18; a light chain variable region CDR1 of SEQ ID NO: 25; a light chain variable region CDR2 of SEQ ID NO: 32; and a light chain variable region CDR3 of SEQ ID NO: 39

12. The antibody or functional protein according to claim 8 comprising a heavy chain variable region CDR1 of SEQ ID NO: 5; a heavy chain variable region CDR2 of SEQ ID NO: 12; a heavy chain variable region CDR3 of SEQ ID NO: 19; a light chain variable region CDR1 of

SEQ ID NO: 26; a light chain variable region CDR2 of SEQ ID NO: 33; and a light chain variable region CDR3 of SEQ ID NO: 40.

13. The antibody or functional protein according to claim 8 comprising a heavy chain variable region CDR1 of SEQ ID NO: 6; a heavy chain variable region CDR2 of SEQ ID NO: 13; a heavy chain variable region CDR3 of SEQ ID NO: 20; a light chain variable region CDR1 of SEQ ID NO: 27; a light chain variable region CDR2 of SEQ ID NO: 34; and a light chain variable region CDR3 of SEQ ID NO: 41.

14. The antibody or functional protein according to claim 8 comprising a heavy chain variable region CDR1 of SEQ ID NO: 7; a heavy chain variable region CDR2 of SEQ ID NO: 14; a heavy chain variable region CDR3 of SEQ ID NO: 21; a light chain variable region CDR1 of SEQ ID NO: 28; a light chain variable region CDR2 of SEQ ID NO: 35; and a light chain variable region CDR3 of SEQ ID NO: 42.

15. The antibody or functional protein according to any one of claims 1-14, comprising a full length heavy chain comprising an amino acid sequence that is at least 95% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs 75-78 and a full length light chain comprising an amino acid sequence that is at least 95% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs 71-74.

16. An antibody comprising a heavy chain sequence of SEQ ID NO: 75 and a light chain sequence of SEQ ID NO: 71.

17. An antibody comprising a heavy chain sequence of SEQ ID NO:76 and a light chain sequence of SEQ ID NO:72.

18. An antibody comprising a heavy chain sequence of SEQ ID NO:77 and a light chain sequence of SEQ ID NO:73.

19. An antibody comprising a heavy chain sequence of SEQ ID NO:78 and a light chain sequence of SEQ ID NO:74.

20. The isolated antibody or functional protein of any one of claims 1-14 and 16-19, wherein said antibody or functional protein depletes B cells *in vitro* with an EC_{50} of 10nM or less as measured in a human B cell depleting ADCC assay.

21. The antibody or functional protein of any of claims 1-14 and 16-19, wherein said antibody or functional protein is capable of reducing *in vivo* the percentage of B cells up to 90% as

compared to untreated control, as measured by Fluorescent Activated Cell Sorting (FACS) of B cells.

22. The antibody or functional protein of any of claims 1-14 and 16-19, wherein said antibody or functional protein has no agonistic activity.

23. The antibody or functional protein according to any of claims 1-14 and 16-19, which is a fully human or humanized IgG1 antibody.

24. The antibody or functional protein of any one of claims 1-14 and 16-19, which comprises a mutated or chemically modified amino acid Fc region, wherein said mutated or chemically modified Fc region provides increased ADCC activity when compared with wild type Fc region.

25. The antibody or functional protein of any one of claims 1-14 and 16-19, wherein said antibody or protein is hypofucosylated or non-fucosylated and has reduced amounts of or no fucosyl residues.

26. The antibody of claim 25, which is produced by recombinant expression in a mammalian cell line with deficient expression of the FUT8 gene encoding fucosyltransferase, thereby increasing ADCC activity of antibodies produced therein as compared with a cell line expressing the wild type FUT8 gene.

27. The antibody or functional protein according to any one of claims 1-14 and 16-19, for use as a medicament.

28. The antibody or functional protein according to any one of claims 1-14 and 16-19, for the treatment of a pathological disorder that is mediated by BAFF Receptor or that can be treated by killing or depleting B cells.

29. The antibody or functional protein according to any one of claims 1-14 and 16-19, for the treatment of autoimmune diseases.

30. The antibody or functional protein according to claim 29 for the treatment of rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, pemphigus vulgaris or multiple sclerosis.

31. The antibody or functional protein according to any one of claims 1-14 and 16-19, for the treatment of B cell neoplasm.

32. The antibody of functional protein according to claim 31, wherein the B cell neoplasm is lymphoma, leukemia or myeloma.

33. The antibody or functional protein according to claim 31 for the treatment of B-cell Non-Hodgkin's lymphomas.

34. The antibody or functional protein according to claim 33, wherein the B-cell Non-Hodgkin's lymphomas is small lymphocytic lymphoma, lymphoplasmacytoid lymphoma, mantle cell lymphoma, follicular lymphoma, mucosa-associated lymphoid tissue lymphoma, diffuse large cell lymphoma, and Burkitt's lymphoma; precursor B-lymphoblastic leukemia; and B-cell chronic lymphocytic leukemia, and multiple myeloma.

35. A pharmaceutical composition for the treatment of rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, multiple sclerosis, pemphigus vulgaris, lymphoma, leukemia or myeloma comprising an antibody or functional protein according to any one of claims 1-14 and 16-19.

36. An isolated nucleic acid encoding the antibody or functional protein according to any one of claims 1-14 and 16-19.

37. A cloning or expression vector comprising one or more nucleic acids according to claim 36.

38. A host cell comprising one or more cloning or expression vectors according to claim 37.

39. A process for the production of an antibody or functional protein of any one of claims 1-14 and 16-19, comprising culturing the host cell comprising one or more nucleic acids encoding the antibody or functional protein according to anyone of claims 1-14 and 16-19.

40. The process of claim 39, wherein said host cell is a cell line lacking fucosyltransferase expression.

41. The process of claim 40, wherein said cell line is a mammalian cell deficient for the expression of a gene encoding fucosyltransferase.

42. The process of claim 41, wherein the mammalian cell deficient for the expression of a gene encoding fucosyltransferase is a CHO cell line deficient for the FUT8 gene.

Claims

1. An isolated antibody, or a protein comprising the antigen binding portion of said antibody, said antibody or protein comprising an HCDR1 of SEQ ID NO: 3, an HCDR2 of SEQ ID NO: 10, an HCDR3 of SEQ ID NO: 17, an LCDR1 of SEQ ID NO: 24, an LCDR2 of SEQ ID NO: 31 and an LCDR3 of SEQ ID NO: 38, wherein said antibody or protein binds to BAFFR.

2. The isolated antibody or protein of claim 1, wherein said antibody or protein depletes B cells in vitro with an EC_{50} of 10 nM or less, as measured in a human B cell depleting ADCC assay.

3. The isolated antibody or protein of claim 1 or claim 2, wherein said antibody or protein is capable of reducing *in vivo* the percentage of B cells up to 90% as compared to untreated control, as measured by Fluorescent Activated Cell Sorting (FACS) of B cells.

4. The isolated antibody or protein of claim 1, wherein said antibody or protein has no agonistic activity.

5. The isolated antibody or protein according to claim 1, which is a fully human or humanized IgG1 antibody.

6. The isolated antibody or protein of claim 5, which comprises a mutated or chemically modified amino acid Fc region, wherein said mutated or chemically modified Fc region provides increased ADCC activity when compared with wild type Fc region.

7. An isolated antibody or protein comprising a heavy chain sequence of SEQ ID NO:75 and a light chain sequence of SEQ ID NO:71.

8. An isolated antibody or a protein comprising the antigen binding portion of said antibody, said antibody or antigen binding portion comprising a variable heavy chain (VH) of SEQ ID NO: 52 and variable light chain (VL) of SEQ ID NO: 45.

9. The isolated antibody or protein of claim 5, wherein said antibody or protein is hypofucosylated or non-fucosylated and has reduced amounts of or no fucosyl residues.

10. The isolated antibody or protein of claim 9, which is produced by recombinant expression in a cell line with deficient expression of the FUT8 gene encoding fucosyltransferase, thereby increasing ADCC activity of antibodies produced therein as compared with a cell line expressing the wild type FUT8 gene.

11. A pharmaceutical composition comprising an antibody or protein according to claim 1, 2, 5, 6, 10 or 9, further comprising a pharmaceutically acceptable carrier.

12. A method of killing or depleting B cells in a subject comprising the step of administering to a subject the composition of claim 11.

13. A method of killing or depleting B cells comprising the step of contacting a B cell with the composition of claim 11.