

CLAIMS

1. An antibody or antigen-binding fragment thereof, comprising:

(a) aCD38-b-329-HCDR3 amino acid sequence (SEQ ID NO: 3) as variable heavy chain complementarity determining region 3;

5 (b) aCD38-b-329-HCDR1 amino acid sequence (SEQ ID NO: 1) as variable heavy chain complementarity determining region 1;

(c) aCD38-b-329-HCDR2 amino acid sequence (SEQ ID NO: 2) as variable heavy chain complementarity determining region 2;

10 (d) aCD38-b-329-LCDR1 amino acid sequence (SEQ ID NO: 5) as variable light chain complementarity determining region 1;

(e) aCD38-b-329-LCDR2 amino acid sequence (SEQ ID NO: 6) as variable light chain complementarity determining region 2; and

15 (f) a sequence selected from the group consisting of aCD38-b-329-LCDR3 amino acid sequence (SEQ ID NO: 7), QQDEAVFT (SEQ ID NO: 10) and QQDSAVFT (SEQ ID NO: 11) as variable light chain complementarity determining region 3.

2. An antibody or antigen-binding fragment thereof according to Claim 1, in which the antibody or antigen-binding fragment thereof comprises a variable heavy chain comprising aCD38-b-329-HCDR123 amino acid sequence (SEQ ID NO: 4).

20 3. An antibody or antigen-binding fragment thereof according to Claim 1 or 2, in which the antibody or antigen-binding fragment thereof further comprises a variable light chain sequence selected from aCD38-b-329-LCDR123 amino acid sequence (SEQ ID NO: 8), SEQ ID NO: 16 and SEQ ID NO: 17.

25 4. An antibody or antigen-binding fragment thereof according to Claim 1, 2 or 3, in which the antibody or antigen-binding fragment thereof is mutated to remove the DG motif in the LCDR3 region.

5. An antibody or antigen-binding fragment thereof according to any preceding claim, in which the antibody or an antigen-binding fragment thereof is selected from the group consisting of:

- 5 (a) an antibody or antigen binding fragment thereof comprising an HCDR1 comprising the sequence of SEQ ID NO: 1, an HCDR2 comprising the sequence of SEQ ID NO: 2, an HCDR3 comprising the sequence of SEQ ID NO 3, an LCDR1 comprising the sequence of SEQ ID NO: 5, an LCDR2 comprising the sequence of SEQ ID NO: 6, and an LCDR3 comprising the sequence of SEQ ID NO: 7;
- 10 (b) an antibody or antigen binding fragment thereof comprising an HCDR1 comprising the sequence of SEQ ID NO: 1, an HCDR2 comprising the sequence of SEQ ID NO: 2, an HCDR3 comprising the sequence of SEQ ID NO 3, an LCDR1 comprising the sequence of SEQ ID NO: 5, an LCDR2 comprising the sequence of SEQ ID NO: 6, and an LCDR3 comprising the sequence of SEQ ID NO: 10;
- 15 (c) an antibody or antigen binding fragment thereof comprising an HCDR1 comprising the sequence of SEQ ID NO: 1, an HCDR2 comprising the sequence of SEQ ID NO: 2, an HCDR3 comprising the sequence of SEQ ID NO 3, an LCDR1 comprising the sequence of SEQ ID NO: 5, an LCDR2 comprising the sequence of SEQ ID NO: 6, and an LCDR3 comprising the sequence of SEQ ID NO: 11;
- (d) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 4 and a light chain variable region comprising the sequence of SEQ ID NO: 8;
- 20 (e) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 4 and a light chain variable region comprising the sequence of SEQ ID NO: 16;
- (f) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 4 and a light chain variable region comprising the sequence of SEQ ID NO: 17;
- 25 (g) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 12 and a light chain variable region comprising the sequence of SEQ ID NO: 15;
- 30 (h) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 12 and a light chain variable region comprising the sequence of SEQ ID NO: 13; and

(i) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 12 and a light chain variable region comprising the sequence of SEQ ID NO: 14.

6. An antibody or an antigen-binding fragment thereof according to any preceding claim,
5 in which the antibody or antigen-binding fragment thereof is a-fucosylated.

7. An antibody or antigen-binding fragment thereof according to any preceding claim, in
which the antibody or antigen-binding fragment thereof is a monoclonal antibody, a domain
antibody, a single chain antibody, a Fab fragment, a F(ab')₂ fragment, a single chain variable
fragment (scFv), a scFv-Fc fragment, a single chain antibody (scAb), an aptamer, or a
10 nanobody.

8. An antibody or antigen-binding fragment thereof according to any preceding claim, in
which the antibody or antigen-binding fragment thereof is a rabbit, mouse, chimeric,
humanized or fully human antigen-binding antibody.

9. An antibody or antigen-binding fragment thereof according to any preceding claim, in
15 which the antibody is selected from the group consisting of IgG1, IgG2, IgG3, and IgG4
isotype antibodies.

10. An antibody or antigen-binding fragment thereof according to any preceding claim, in
which the antibody or antigen-binding fragment thereof is comprised in a bispecific antibody,
a multispecific antibody, or an immunoconjugate further comprising a therapeutic or
20 diagnostic agent.

11. An antibody or antigen-binding fragment thereof according to any preceding claim, in
which the antibody or antigen-binding fragment thereof binds the extracellular domain of
human CD38.

12. An antibody or antigen-binding fragment thereof according to any preceding claim, in
25 which the antibody or antigen-binding fragment thereof binds cells expressing human CD38
on their surface and is a CD38 Modulating Antibody Agent.

13. A nucleic acid molecule encoding an antibody or antigen-binding fragment thereof
according to any preceding claim.

14. A nucleic acid vector comprising a nucleic acid molecule according to Claim 13.

15. A host cell comprising a nucleic acid vector according to Claim 14.
16. A method for producing an antibody or antigen-binding fragment thereof according to any of Claims 1 to 12 by culturing a host cell according to Claim 15.
17. A composition comprising an antibody or antigen-binding fragment thereof according to
5 any of Claims 1 to 12 and a pharmaceutically acceptable carrier or excipient.
18. A composition according to Claim 17, in which the composition is for use in the treatment of cancer.
19. Use of an antibody or antigen-binding fragment thereof according to any of Claims 1 to 12 in the manufacture of a medicament for treating a cancer.
- 10 20. A composition for use according to Claim 18 or a use according to Claim 19, in which the antibody is to be administered simultaneously or sequentially in any order, with a second agent.
21. A composition for use according to Claim 18 or 20 or a use according to Claim 19 or 20 for use in which the subject has a solid tumor or a haematological cancer.

CLAIMS

1. An antibody or antigen-binding fragment thereof, comprising:
 - (a) aCD38-b-329-HCDR3 amino acid sequence (SEQ ID NO: 3) as variable heavy chain complementarity determining region 3;
 - 5 (b) aCD38-b-329-HCDR1 amino acid sequence (SEQ ID NO: 1) as variable heavy chain complementarity determining region 1;
 - (c) aCD38-b-329-HCDR2 amino acid sequence (SEQ ID NO: 2) as variable heavy chain complementarity determining region 2;
 - (d) aCD38-b-329-LCDR1 amino acid sequence (SEQ ID NO: 5) as variable light chain complementarity determining region 1;
 - 10 (e) aCD38-b-329-LCDR2 amino acid sequence (SEQ ID NO: 6) as variable light chain complementarity determining region 2; and
 - (f) a sequence selected from the group consisting of aCD38-b-329-LCDR3 amino acid sequence (SEQ ID NO: 7), QQDEAVFT (SEQ ID NO: 10) and QQDSAVFT (SEQ ID NO: 11) as variable light chain complementarity determining region 3.
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2. An antibody or antigen-binding fragment thereof according to Claim 1, in which the antibody or antigen-binding fragment thereof comprises a variable heavy chain comprising aCD38-b-329-HCDR123 amino acid sequence (SEQ ID NO: 4).
3. An antibody or antigen-binding fragment thereof according to Claim 1 or 2, in which the antibody or antigen-binding fragment thereof further comprises a variable light chain sequence selected from aCD38-b-329-LCDR123 amino acid sequence (SEQ ID NO: 8), SEQ ID NO: 16 and SEQ ID NO: 17.
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4. An antibody or antigen-binding fragment thereof according to Claim 1, 2 or 3, in which the antibody or antigen-binding fragment thereof is mutated to remove the DG motif in the LCDR3 region.
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5. An antibody or antigen-binding fragment thereof according to any preceding claim, in which the antibody or an antigen-binding fragment thereof is selected from the group consisting of:

- 5 (a) an antibody or antigen binding fragment thereof comprising an HCDR1 comprising the sequence of SEQ ID NO: 1, an HCDR2 comprising the sequence of SEQ ID NO: 2, an HCDR3 comprising the sequence of SEQ ID NO 3, an LCDR1 comprising the sequence of SEQ ID NO: 5, an LCDR2 comprising the sequence of SEQ ID NO: 6, and an LCDR3 comprising the sequence of SEQ ID NO: 7;
- 10 (b) an antibody or antigen binding fragment thereof comprising an HCDR1 comprising the sequence of SEQ ID NO: 1, an HCDR2 comprising the sequence of SEQ ID NO: 2, an HCDR3 comprising the sequence of SEQ ID NO 3, an LCDR1 comprising the sequence of SEQ ID NO: 5, an LCDR2 comprising the sequence of SEQ ID NO: 6, and an LCDR3 comprising the sequence of SEQ ID NO: 10;
- 15 (c) an antibody or antigen binding fragment thereof comprising an HCDR1 comprising the sequence of SEQ ID NO: 1, an HCDR2 comprising the sequence of SEQ ID NO: 2, an HCDR3 comprising the sequence of SEQ ID NO 3, an LCDR1 comprising the sequence of SEQ ID NO: 5, an LCDR2 comprising the sequence of SEQ ID NO: 6, and an LCDR3 comprising the sequence of SEQ ID NO: 11;
- (d) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 4 and a light chain variable region comprising the sequence of SEQ ID NO: 8;
- 20 (e) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 4 and a light chain variable region comprising the sequence of SEQ ID NO: 16;
- (f) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 4 and a light chain variable region comprising the sequence of SEQ ID NO: 17;
- 25 (g) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 12 and a light chain variable region comprising the sequence of SEQ ID NO: 15;
- (h) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 12 and a light chain variable region comprising the sequence of SEQ ID NO: 13; and
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- (i) an antibody or antigen binding fragment thereof comprising a heavy chain variable region comprising the sequence of SEQ ID NO: 12 and a light chain variable region comprising the sequence of SEQ ID NO: 14.
6. An antibody or an antigen-binding fragment thereof according to any preceding claim,
5 in which the antibody or antigen-binding fragment thereof is a-fucosylated.
7. An antibody or antigen-binding fragment thereof according to any preceding claim, in which the antibody or antigen-binding fragment thereof is a monoclonal antibody, a Fab fragment, a F(ab')₂ fragment, a single chain variable fragment (scFv), a scFv-Fc fragment or a single chain antibody (scAb).
- 10 8. An antibody or antigen-binding fragment thereof according to any preceding claim, in which the antibody or antigen-binding fragment thereof is a rabbit, mouse, chimeric, humanized or fully human antigen-binding antibody.
9. An antibody or antigen-binding fragment thereof according to any preceding claim, in which the antibody is selected from the group consisting of IgG1, IgG2, IgG3, and IgG4
15 isotype antibodies.
10. An antibody or antigen-binding fragment thereof according to any preceding claim, in which the antibody or antigen-binding fragment thereof is comprised in a bispecific antibody, a multispecific antibody, or an immunoconjugate further comprising a therapeutic or diagnostic agent.
- 20 11. An antibody or antigen-binding fragment thereof according to any preceding claim, in which the antibody or antigen-binding fragment thereof binds the extracellular domain of human CD38.
12. An antibody or antigen-binding fragment thereof according to any preceding claim, in which the antibody or antigen-binding fragment thereof binds cells expressing human CD38
25 on their surface.
13. A nucleic acid molecule encoding an antibody or antigen-binding fragment thereof according to any preceding claim.
14. A nucleic acid vector comprising a nucleic acid molecule according to Claim 13.
15. A host cell comprising a nucleic acid vector according to Claim 14.

16. A method for producing an antibody or antigen-binding fragment thereof according to any of Claims 1 to 12 by culturing a host cell according to Claim 15.
17. A composition comprising an antibody or antigen-binding fragment thereof according to any of Claims 1 to 12 and a pharmaceutically acceptable carrier or excipient.
- 5 18. A composition according to Claim 17, in which the composition is for use in the treatment of cancer in a subject.
19. Use of an antibody or antigen-binding fragment thereof according to any of Claims 1 to 12 in the manufacture of a medicament for treating a cancer in a subject.
20. A composition for use according to Claim 18 or a use according to Claim 19, in which
10 the antibody is to be administered to the subject, simultaneously or sequentially in any order, with a second agent.
21. A composition for use according to Claim 18 or 20 or a use according to Claim 19 or 20, in which the subject has a solid tumor or a haematological cancer.