

Claims

1. A bispecific antigen binding molecule, comprising
(a) a first antigen binding moiety that binds to a first antigen,
5 wherein the first antigen is GPRC5D and the first antigen binding moiety comprises a
- (i) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 83, a HCDR 2 of SEQ ID NO: 84, and a HCDR 3 of SEQ ID NO: 86, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 87, a LCDR 2 of SEQ ID NO: 88 and a LCDR 3
10 of SEQ ID NO: 89;
- (ii) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 83, a HCDR 2 of SEQ ID NO: 85, and a HCDR 3 of SEQ ID NO: 86, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 87, a LCDR 2 of SEQ ID NO: 88 and a LCDR 3
15 of SEQ ID NO: 89,
- (iii) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 90, a HCDR 2 of SEQ ID NO: 91, and a HCDR 3 of SEQ ID NO: 93, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 94, a LCDR 2 of SEQ ID NO: 95 and a LCDR 3
20 of SEQ ID NO: 97;
- (iv) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 90, a HCDR 2 of SEQ ID NO: 91, and a HCDR 3 of SEQ ID NO: 93, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 94, a LCDR 2 of SEQ ID NO: 96 and a LCDR 3
25 of SEQ ID NO: 97; or
- (v) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 90, a HCDR 2 of SEQ ID NO: 92, and a HCDR 3 of SEQ ID NO: 93, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 94, a LCDR 2 of SEQ ID NO: 95 and a LCDR 3
30 of SEQ ID NO: 97; and

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(b) a second antigen binding moiety that binds to a second antigen, wherein the second antigen is CD3 and the second antigen binding moiety comprises

(i) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 29, a HCDR 2 of SEQ ID NO: 30, and a HCDR 3 of SEQ ID NO: 31, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 32, a LCDR 2 of SEQ ID NO: 33 and a LCDR 3 of SEQ ID NO: 34;

(i) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 98, a HCDR 2 of SEQ ID NO: 99, and a HCDR 3 of SEQ ID NO: 100, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 101, a LCDR 2 of SEQ ID NO: 102 and a LCDR 3 of SEQ ID NO: 103; or

(ii) a heavy chain variable region (VH) comprising a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 106, a HCDR 2 of SEQ ID NO: 107, and a HCDR 3 of SEQ ID NO: 108, and a light chain variable region (VL) comprising a light chain complementarity determining region (LCDR) 1 of SEQ ID NO: 109, a LCDR 2 of SEQ ID NO: 110 and a LCDR 3 of SEQ ID NO: 111.

2. The bispecific antigen binding molecule of claim 1,

(i) wherein the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 13, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 14; or

(ii) wherein the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 15, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 16; or

(iii) wherein the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 48, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 53; or

(iv) wherein the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 49, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 52; or

(v) wherein the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 57, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 64; or

(vi) wherein the VH of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 58, and wherein the VL of the first antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 63.

3. The bispecific antigen binding molecule of claim 1 or 2, wherein the VH of the second antigen binding moiety comprises an amino acid sequence

(i) that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 35, and the VL of the second antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 36;

(ii) that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 104, and the VL of the second antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 105; or

- (iii) that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 112, and the VL of the second antigen binding moiety comprises an amino acid sequence that is at least about 95%, 96%, 97%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 113.
- 5 4. The bispecific antigen binding molecule of any one of claims 1 to 3, wherein the first and/or the second antigen binding moiety is a Fab molecule.
5. The bispecific antigen binding molecule of any one of claims 1 to 4, wherein the second antigen binding moiety is a Fab molecule wherein the variable domains VL and VH or the constant domains CL and CH1, particularly the variable domains VL and VH, of the Fab light chain and the Fab heavy chain are replaced by each other.
- 10 6. The bispecific antigen binding molecule of any one of claims 1 to 5, wherein the first antigen binding moiety is a Fab molecule wherein in the constant domain the amino acid at position 124 is substituted independently by lysine (K), arginine (R) or histidine (H) (numbering according to Kabat) and the amino acid at position 123 is substituted independently by lysine (K), arginine
- 15 (R) or histidine (H) (numbering according to Kabat), and in the constant domain CH1 the amino acid at position 147 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index) and the amino acid at position 213 is substituted independently by glutamic acid (E), or aspartic acid (D) (numbering according to Kabat EU index).
- 20 7. The bispecific antigen binding molecule of any one of claims 1 to 6, wherein the first and the second antigen binding moiety are fused to each other, optionally via a peptide linker.
8. The bispecific antigen binding molecule of any one of claims 1 to 7, wherein the first and the second antigen binding moiety are each a Fab molecule and wherein either (i) the second antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab
- 25 heavy chain of the first antigen binding moiety, or (ii) the first antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the second antigen binding moiety.
9. The bispecific antigen binding molecule of any one of claims 1 to 8, comprising a third antigen binding moiety.

10. The bispecific antigen binding molecule of claim 9, wherein the third antigen moiety is identical to the first antigen binding moiety.
11. The bispecific antigen binding molecule of any one of claims 1 to 10, comprising an Fc domain composed of a first and a second subunit.
- 5 12. The bispecific antigen binding molecule of claim 11, wherein the first, the second and, where present, the third antigen binding moiety are each a Fab molecule;
and wherein either (i) the second antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the first antigen binding moiety and the first antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus
10 of the first subunit of the Fc domain, or (ii) the first antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the second antigen binding moiety and the second antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain;
and wherein the third antigen binding moiety, where present, is fused at the C-terminus of the
15 Fab heavy chain to the N-terminus of the second subunit of the Fc domain.
13. The bispecific antigen binding molecule of claim 11 or 12, wherein the Fc domain is an IgG Fc domain.
14. The bispecific antigen binding molecule of claim 13, wherein the Fc domain is an IgG₁ Fc domain.
- 20 15. The bispecific antigen binding molecule of any one of claims 11 to 14, wherein the Fc domain is a human Fc domain.
16. The bispecific antigen binding molecule of any one of claims 11 to 15, wherein an amino acid residue in the CH3 domain of the first subunit of the Fc domain is replaced with an amino acid residue having a larger side chain volume, thereby generating a protuberance within the
25 CH3 domain of the first subunit which is positionable in a cavity within the CH3 domain of the second subunit, and an amino acid residue in the CH3 domain of the second subunit of the Fc domain is replaced with an amino acid residue having a smaller side chain volume, thereby generating a cavity within the CH3 domain of the second subunit within which the protuberance within the CH3 domain of the first subunit is positionable.

17. The bispecific antigen binding molecule of any one of claims 11 to 16, wherein the Fc domain comprises one or more amino acid substitution that reduces binding to an Fc receptor and/or effector function.
18. One or more isolated polynucleotide encoding the bispecific antigen binding molecule of any
5 one of claims 1 to 17.
19. One or more vector, particularly expression vector, comprising the polynucleotide(s) of claim 18.
20. A host cell comprising the polynucleotide(s) of claim 18 or the vector(s) of claim 19.
21. A method of producing a bispecific antigen binding molecule that binds to GPRC5D,
10 comprising the steps of a) culturing the host cell of claim 20 under conditions suitable for the expression of the bispecific antigen binding molecule and b) optionally recovering the bispecific antigen binding molecule.
22. A bispecific antigen binding molecule that binds to GPRC5D, produced by the method of claim 21.
- 15 23. A pharmaceutical composition comprising the bispecific antigen binding molecule of any one of claims 1 to 17 or 22 and a pharmaceutically acceptable carrier.
24. The bispecific antigen binding molecule of any one of claims 1 to 17 or 22 or the pharmaceutical composition of claim 23 for use as a medicament.
25. The bispecific antigen binding molecule of any one of claims 1 to 17 or 22 or the
20 pharmaceutical composition of claim 23 for use in the treatment of a disease.
26. The bispecific antigen binding molecule or pharmaceutical composition of claim 25, wherein the disease is cancer or an autoimmune disease.
27. The bispecific antigen binding molecule or pharmaceutical composition of claim 25, wherein the disease is multiple myeloma.
- 25 28. Use of the bispecific antigen binding molecule of any one of claims 1 to 17 or 22 in the manufacture of a medicament for the treatment of a disease.

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29. A method of treating a disease in an individual, comprising administering to said individual a therapeutically effective amount of a composition comprising the bispecific antigen binding molecule of any one of claims 1 to 17 or 22 in a pharmaceutically acceptable form.
30. The use of claim 28 or the method of claim 29, wherein said disease is cancer or an autoimmune
5 disease.
31. The use of claim 28 or the method of claim 29, wherein said disease is multiple myeloma.
32. The invention as described herein.