

Claim

1. An isolated antibody, or an antigen-binding fragment thereof, that binds specifically to G protein-coupled receptor class C group 5 member D (GPRC5D),
wherein the antibody or antigen-binding fragment thereof comprises a variable heavy chain (VH) region of SEQ ID NO: 55 and a variable light chain (VL) region of SEQ ID NO: 58.
2. The isolated antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment is a human antibody or antigen-binding fragment.
3. The isolated antibody or antigen-binding fragment of claim 1 or claim 2, wherein the antibody or antigen-binding fragment is recombinant.
4. The isolated antibody or antigen-binding fragment of any one of claim 1 to 3, wherein the antigen binding fragment is a Fab fragment, a Fab2 fragment, or a single chain antibody.
5. The isolated antibody or antigen-binding fragment of any one of claim 1 to 4, wherein the antibody or antigen-binding fragment thereof are of IgG1, IgG2, IgG3, or IgG4 isotype.
6. The isolated antibody or antigen-binding fragment of any one of claim 1 to 5, wherein the antibody or antigen-binding fragment is of IgG1 or an IgG4 isotype, optionally wherein;
 - i. the IgG1 has a K409R substitution in its Fc region;
 - ii. the IgG1 has an F405L substitution in its Fc region; or
 - iii. the IgG4 has an F405L substitution and an R409K substitution in its Fc region.
7. An isolated bispecific GPRC5D x CD3 antibody comprising:
 - a) a first heavy chain (HC1);
 - b) a second heavy chain (HC2);
 - c) a first light chain (LC1); and
 - d) a second light chain (LC2),wherein the HC1 and the LC1 pair to form a first antigen-binding site that specifically binds CD3, and the HC2 and the LC2 pair to form a second antigen-binding site that specifically binds GPRC5D,

wherein HC1 comprises SEQ ID NO: 25 and LC1 comprises SEQ ID NO: 26, and wherein HC2 comprises of SEQ ID NO: 55 and LC2 comprises SEQ ID NO: 58.

8. The GPRC5D x CD3 bispecific antibody of claim 7, wherein the antibody is of IgG1, IgG2, IgG3, or IgG4 isotype.
9. The GPRC5D x CD3 bispecific antibody of claim 8, wherein, the antibody is of IgG4 isotype.
10. The GPRC5D x CD3 bispecific antibody of any one of claims 7 to 9, wherein the antibody binds GPRC5D on the surface of human myeloma cells.
11. The GPRC5D x CD3 bispecific antibody of any one of claims 7 to 10, wherein the antibody binds GPRC5D on the surface of human multiple myeloma cells.
12. The GPRC5D x CD3 bispecific antibody of any one of claims 7 to 11, wherein the HC1 comprises SEQ ID NO: 99, and LC1 comprises SEQ ID NO: 100.
13. An isolated cell expressing the GPRC5D x CD3 bispecific antibody of any one of claims 7 to 12.
14. The isolated cell of claim 13, wherein the cell is a hybridoma.
15. The isolated cell of claim 13, wherein the antibody is recombinantly produced.
16. Use of the GPRC5D x CD3 bispecific antibody of any one of claims 7 to 12 for the manufacture of a medicament for treating cancer.
17. The use of claim 16, wherein the cancer is a hematological cancer.
18. The use of claim 17, wherein the hematological cancer is a GPRC5D-expressing B cell cancer.
19. The use of claim 18, wherein the GPRC5D-expressing B cell cancer is multiple

myeloma.

20. The use of any one of claims 16 to 19, wherein the medicament is adapted to be administrable with a second therapeutic agent.
21. The use of claim 33, wherein the second therapeutic agent is a chemotherapeutic agent or a targeted anti-cancer therapy.
22. The use of claim 21, wherein the chemotherapeutic agent is cytarabine, an anthracycline, histamine dihydrochloride, or interleukin 2.
23. The use of claim 21, wherein the second therapeutic agent is adapted to be administered to said subject simultaneously with, sequentially, or separately from the medicament.
24. A pharmaceutical composition comprising the GPRC5D x CD3 bispecific antibody of any one of claims 7 to 12 and a pharmaceutically acceptable carrier.
25. A method for generating the GPRC5D x CD3 bispecific antibody of any one of claims 7 to 12 by culturing the isolated cell any one of claims 13 to 15.
26. One or more isolated synthetic polynucleotides encoding the HC1, the HC2, the LC1, and the LC2 of the GPRC5D x CD3 bispecific antibody of any one of claims 7 to 12.
27. A kit comprising the GPRC5D x CD3 bispecific antibody of any one of claims 7 to 12 and/or the one or more polynucleotides as defined in claim 26, and packaging for the same.
28. An isolated antibody that binds specifically to GPRC5D comprising:
 - a heavy chain comprising a variable heavy (VH) chain region comprising the amino acid sequence of SEQ ID NO: 55, and
 - a light chain comprising a variable light (VL) chain region comprising the amino acid sequence of SEQ ID NO: 58,wherein the antibody is an IgG4 isotype.

29. The isolated antibody of claim 28, wherein the heavy chain further comprises the amino acid sequence of SEQ ID NO: 59.
30. An isolated GPRC5D x CD3 bispecific antibody comprising:
a GPRC5D binding portion comprising:
a heavy chain comprising a variable heavy (VH) chain region comprising the amino acid sequence of SEQ ID NO: 55, and
a light chain comprising a variable light (VL) chain region comprising the amino acid sequence of SEQ ID NO: 58; and
a CD3 binding portion comprising a heavy chain comprising SEQ ID NO: 99 and a light chain comprising SEQ ID NO: 100,
wherein the antibody is an IgG4 isotype.
31. The isolated GPRC5D x CD3 bispecific antibody of claim 30, wherein the GPRC5D heavy chain further comprises the amino acid sequence of SEQ ID NO: 59.