

CLAIMS

1. An anti-ceramide antibody or antigen-binding fragment thereof comprising an immunoglobulin heavy chain variable region (VH) comprising a heavy chain complementarity determining region (CDR) 1 (HCDR1), a heavy chain CDR2 (HCDR2), and a heavy chain CDR3 (HCDR3), and an immunoglobulin light chain variable region (VL) comprising a light chain complementarity determining region (CDR) 1 (LCDR1), a light chain CDR2 (LCDR2), and a light chain CDR3 (LCDR3), wherein:

- (a) the HCDR1 comprises an amino acid sequence selected from SEQ ID NO: 1 and 2;
- (b) the HCDR2 comprises an amino acid sequence selected from SEQ ID NO: 3, 4, 5, and 6;
- (c) the HCDR3 comprises the amino acid sequence of SEQ ID NO: 7;
- (d) the LCDR1 comprises the amino acid sequence of SEQ ID NO: 8;
- (e) the LCDR2 comprises the amino acid sequence of SEQ ID NO: 9; and
- (f) the LCDR3 comprises the amino acid sequence of SEQ ID NO: 10.

2. The anti-ceramide antibody or antigen-binding fragment thereof of claim 1, wherein the HCDR1 comprises SEQ ID NO: 1 and the HCDR2 comprises SEQ ID NO: 3.

3. The anti-ceramide antibody or antigen-binding fragment thereof of claim 1, wherein:

- (i) the HCDR1 comprises SEQ ID NO: 1 and the HCDR2 comprises SEQ ID NO: 4;
- (ii) the HCDR1 comprises SEQ ID NO: 1 and the HCDR2 comprises SEQ ID NO: 5;
- (iii) the HCDR1 comprises SEQ ID NO: 1 and the HCDR2 comprises SEQ ID NO: 6;
- (iv) the HCDR1 comprises SEQ ID NO: 2 and the HCDR2 comprises SEQ ID NO: 3;
- (v) the HCDR1 comprises SEQ ID NO: 2 and the HCDR2 comprises SEQ ID NO: 4;
- (vi) the HCDR1 comprises SEQ ID NO: 2 and the HCDR2 comprises SEQ ID NO: 5; or
- (vii) the HCDR1 comprises SEQ ID NO: 2 and the HCDR2 comprises SEQ ID NO: 6.

4. The anti-ceramide antibody or antigen-binding fragment thereof of claim 2, wherein the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 18 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 22.

5. The anti-ceramide antibody or antigen-binding fragment thereof of claim 3, wherein:
- (i) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 17 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 22;
 - (ii) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 17 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 23;
 - (iii) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 17 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 24;
 - (iv) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 18 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 23;
 - (v) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 18 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 24
 - (vi) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 19 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 22;
 - (vii) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 19 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 23;
 - (viii) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 19 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 24
 - (ix) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 20 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 22; or

(x) the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 21 and the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to SEQ ID NO: 22.

6. The anti-ceramide antibody or antigen-binding fragment thereof any one of claims 1-5, wherein the VH comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to a sequence selected from SEQ ID NO: 17, 18, 19, 20, and 21; and wherein the VL comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to a sequence selected from SEQ ID NO: 22, 23 and 24.

7. The anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the antibody or antigen-binding fragment is humanized.

8. The anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the antibody or antigen-binding fragment is fully human.

9. The anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein the anti-ceramide antibody comprises one or more point mutations in the Fc domain of the antibody.

10. The anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the anti-ceramide antibody or antigen-binding fragment thereof is a single chain variable fragment (scFv).

11. The anti-ceramide antibody or antigen-binding fragment thereof of claim 10, wherein the scFv comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100% identical to a sequence selected from the group consisting of SEQ ID NOs: 48-61, or the scFv consists of a sequence selected from the group consisting of SEQ ID NOs: 48-61.

12. The anti-ceramide antibody or antigen-binding fragment thereof of claim 10, wherein the scFv comprises an amino acid sequence that is at least 90%, at least 95%, at least 97%, or 100%

identical to SEQ ID NO: 48 or 51, or the scFv consists of the amino acid sequence of SEQ ID NO: 48 or 51.

13. The anti-ceramide antibody or antigen-binding fragment thereof of claim 10, wherein the light chain variable region of said scFv is carboxy-terminal to the heavy chain variable region of said scFv.

14. The anti-ceramide antibody or antigen-binding fragment thereof of claim 10, wherein the light chain variable region of said scFv is amino-terminal to the heavy chain variable region of said scFv.

15. The anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 10-14, wherein the scFv comprises a linker polypeptide.

16. The anti-ceramide antibody or antigen-binding fragment thereof of claim 15, wherein the linker polypeptide is between the light chain variable region and the heavy chain variable region of the said scFv.

17. The anti-ceramide antibody or antigen-binding fragment thereof of claim 15 or 16, wherein the linker polypeptide comprises a Gly₄Ser linker or the formula (Gly₄Ser)_n, wherein n = 1-5.

18. A polynucleotide encoding the anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-17.

19. An expression vector comprising the polynucleotide of claim 18.

20. A host cell comprising the polynucleotide of claim 18 or the expression vector of claim 19.

21. A method of manufacturing the anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-17, comprising introducing an expression vector comprising a

polynucleotide encoding the anti-ceramide antibody or antigen-binding fragment thereof into a host cell.

22. Use of a therapeutically effective amount of the anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-17 in the manufacture of a medicament for inhibiting apoptosis in a subject in need thereof, wherein said medicament is to be administered to the subject.

23. The use of claim 22, wherein the apoptosis is associated with a disease selected from the group consisting of graft versus host disease, radiation disease, GI syndrome, and autoimmune disease.

24. The use of claim 23, wherein the disease is radiation disease or GI syndrome and the anti-ceramide antibody or antigen-binding fragment thereof is to be administered before the subject is exposed to radiation.

25. The use of claim 23, wherein the disease is graft versus host disease and the anti-ceramide antibody or antigen-binding fragment thereof is to be administered before the subject receives a transplant.

26. The use of claim 25, wherein the transplant is a bone marrow transplant.

27. The use of claim 22, wherein the anti-ceramide antibody or antigen-binding fragment thereof is to be administered intravenously, intramuscularly, intraperitoneally, intracerebrospinally, subcutaneously, intrasynovially, intrathecally, orally, topically, or via inhalation.

28. Use of an effective amount of the anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-17 in the manufacture of a medicament for mitigating apoptosis in a subject with GI syndrome, after the subject is exposed to penetrating radiation, wherein said medicament is to be administered to the subject.

29. The use of claim 28, wherein the anti-ceramide antibody or antigen-binding fragment thereof is to be administered immediately after the subject is exposed to penetrating radiation.
30. The use of claim 28, wherein the anti-ceramide antibody or antigen-binding fragment thereof is to be administered within 24 hours after the subject is exposed to penetrating radiation.
31. Use of an effective amount of anti-ceramide antibody or antigen binding fragment thereof of any one of claims 1-17 in the manufacture of a medicament for inhibiting apoptosis in a subject with GvHD, either before the subject receives a transplant or after the subject receives a transplant prior to the onset of GvHD.
32. The use of claim 31, wherein the transplant is a bone marrow transplant.
33. The anti-ceramide antibody or antigen-binding fragment thereof of any one of claims 1-17 for use as a medicament.