

Claims

1. An anti-triggering expression on myeloid cells 2 (TREM2) antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region complementarity determining region (CDR)1 comprising SEQ ID NO: 7; a heavy chain variable region CDR2 comprising SEQ ID NO: 5; a heavy chain variable region CDR3 comprising SEQ ID NO: 6; a light chain variable region CDR1 comprising SEQ ID NO: 17; a light chain variable region CDR2 comprising SEQ ID NO: 18; and a light chain variable region CDR3 comprising SEQ ID NO: 19, wherein the CDR numbering is as defined by the Kabat numbering system.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) polypeptide sequence having at least 95% sequence identity to SEQ ID NO: 13, and a light chain variable region (VL) polypeptide sequence having at least 95% sequence identity to SEQ ID NO: 24.

3. The antibody or antigen-binding fragment thereof of claim 2, wherein the VH comprises the amino acid sequence of SEQ ID NO: 13 and wherein the VL comprises the amino acid sequence of SEQ ID NO: 24.

4. The antibody or antigen-binding fragment of any one of claims 1-3, wherein the antibody or antigen-binding fragment comprises a human IgG1 heavy chain constant region.

5. The antibody or antigen-binding fragment of claim 4, wherein the antibody or antigen-binding fragment comprises a modified Fc domain that has reduced antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC) activity compared to the parental antibody.

6. The antibody or antigen-binding fragment of any one of claims 1-5, wherein the antibody or antigen-binding fragment comprises a heavy chain that is at least 95% identical to

the amino acid sequence of SEQ ID NO: 37, and a light chain that is at least 95% identical to the amino acid sequence of SEQ ID NO: 26.

7. An anti-TREM2 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 37, and a light chain comprising the amino acid sequence of SEQ ID NO: 26.8.

8. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-7 and a pharmaceutically acceptable carrier.

9. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-8 in the manufacture of a medicament for the treatment of a neuroinflammatory or neurodegenerative, wherein a therapeutically effective amount of the medicament is to be administered to the subject.

10. The use of claim 9, wherein the neuroinflammatory or neurodegenerative disease is Alzheimer's disease, frontotemporal dementia, Parkinson's disease, amyotrophic lateral sclerosis, Nasu-Hakola disease, multiple sclerosis, amyotrophic lateral sclerosis (ALS), anti-NMDA receptor encephalitis, autism, brain lupus (NP-SLE), chemo-induced peripheral neuropathy (CIPN), posttherapeutic neuralgia, chronic inflammatory demyelinating polyneuropathy (CIDP), epilepsy, Guillain-Barré Syndrom (GBS), inclusion body myositis, lysosomal storage diseases, sphingomyelinlipidose (Niemann-Pick C), mucopolysaccharidose II/IIIB, metachromatic leukodystrophy, multifocal motor neuropathy, Myasthenia Gravis, Neuro-Behcet's Disease, neuromyelitis optica (NMO), optic neuritis, polymyositis, dermatomyositis, Rasmussen's encephalitis, Rett's Syndrome, stroke, transverse myelitis, traumatic brain injury, spinal cord injury, viral encephalitis, or bacterial meningitis.

11. The use of claim 10, wherein the neuroinflammatory or neurodegenerative disease is Alzheimer's disease.

12. The use of claim 10, wherein the neuroinflammatory or neurodegenerative disease is multiple sclerosis.

13. The use of claim 10, wherein the neuroinflammatory or neurodegenerative disease is amyotrophic lateral sclerosis.

14. An antibody or antigen-binding fragment thereof that binds to the immunoglobulin superfamily (IgSF) domain of human triggering expression on myeloid cells 2 (hTREM2) comprising:

a) a heavy chain sequence comprising SEQ ID NO: 15 and a light chain sequence comprising SEQ ID NO: 26;

b) a heavy chain sequence comprising SEQ ID NO: 29 and a light chain sequence comprising SEQ ID NO: 26;

c) a heavy chain sequence comprising SEQ ID NO: 33 and a light chain sequence comprising SEQ ID NO: 26;

d) a heavy chain sequence comprising SEQ ID NO: 35 and a light chain sequence comprising SEQ ID NO: 26;

e) a heavy chain sequence comprising SEQ ID NO: 37 and a light chain sequence comprising SEQ ID NO: 26;

f) a heavy chain sequence comprising SEQ ID NO: 39 and a light chain sequence comprising SEQ ID NO: 26;

g) a heavy chain sequence comprising SEQ ID NO: 52 and a light chain sequence comprising SEQ ID NO: 63;

h) a heavy chain sequence comprising SEQ ID NO: 66 and light chain sequence comprising SEQ ID NO: 63;

i) a heavy chain sequence comprising SEQ ID NO: 70 and light chain sequence comprising SEQ ID NO: 63;

j) a heavy chain sequence comprising SEQ ID NO: 72 and light chain sequence comprising SEQ ID NO: 63;

k) a heavy chain sequence comprising SEQ ID NO: 74 and light chain sequence comprising SEQ ID NO: 63;

l) a heavy chain sequence comprising SEQ ID NO: 76 and light chain sequence comprising SEQ ID NO: 63;

m) a heavy chain sequence comprising SEQ ID NO: 15 and light chain sequence comprising SEQ ID NO: 82; or

n) a heavy chain sequence comprising SEQ ID NO: 95 and light chain sequence comprising SEQ ID NO: 106.