CLAIMS

[Claim 1]

An anti-gpNMB antibody or its fragment or a derivative thereof which binds specifically to at least one site in a region from a PMEL-CAF-like (PMEL core amyloid fragment-like) domain to a PKD domain of human gpNMB (glycoprotein nonmetastatic melanoma protein B).

[Claim 2]

The anti-gpNMB antibody or its fragment or a derivative thereof according to claim 1, which binds specifically to a region containing amino acid residue(s) D287 and/or H301 of human gpNMB having the amino acid sequence defined in SEQ ID NO 209.

[Claim 3]

The anti-gpNMB antibody or its fragment or a derivative thereof according to claim 1 or 2, which binds specifically to a region containing amino acid residue(s) R214 and/or R215 of human gpNMB having the amino acid sequence defined in SEQ ID NO 209.

[Claim 4]

The anti-gpNMB antibody or its fragment or a derivative thereof according to claim 2 or 3, which also binds specifically to one or more regions selected from of a region containing amino acid residue(s) K257 and/or D258, a region containing amino acid residue(s) H268 and/or D269, a region containing an amino acid residue K282, a region containing an amino acid residue K316, and a region containing amino acid residue(s) H216 and/or R218, of human gpNMB having the amino acid sequence defined in SEQ ID NO 209.

[Claim 5]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 4, which also binds specifically to at least one site in a region from a PMEL-CAF-like domain to a PKD domain of mouse gpNMB.

[Claim 6]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 5, having one or more activities selected from: an activity to reduce the number of mal-functional microglia; an activity to remove amyloid beta oligomers; an activity to increase the number of synapses; and an activity to restore cognitive function.

[Claim 7]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 6, which is a monoclonal antibody or its fragment or a derivative thereof.

[Claim 8]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 7, which comprises at least a heavy chain variable region comprising:
(1) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 1, or an amino acid sequence derived from SEQ ID NO 1 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 1,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 3, or an amino acid sequence derived from SEQ ID NO 3 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 3, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 5, or an amino acid sequence derived from SEQ ID NO 5 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 75.0 % or higher, 83.3 % or higher, or 91.6 % or higher to SEQ ID NO 5, or
(2) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 17, or an amino acid sequence derived from SEQ ID NO 17 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 17,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 19, or an amino acid sequence derived from SEQ ID NO 19 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 19, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 21, or an amino acid sequence derived from SEQ ID NO 21 via substitution, deletion, or insertion of any one, two, three, four, five, or six amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 66.6 % or higher, 73.3 % or higher, 80.0 % or higher, 86.6 % or higher, or 93.3 % or higher to SEQ ID NO 21, or
(3) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 33, or an amino acid sequence derived from SEQ ID NO 33 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology

(preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 33,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 35, or an amino acid sequence derived from SEQ ID NO 35 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 35, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 37, or an amino acid sequence derived from SEQ ID NO 37 via substitution, deletion, or insertion of any one, two, three, four, five, or six amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 66.6 % or higher, 73.3 % or higher, 80.0 % or higher, 86.6 % or higher, or 93.3 % or higher to SEQ ID NO 37, or
(4) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 49, or an amino acid sequence derived from SEQ ID NO 49 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 49,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 51, or an amino acid sequence derived from SEQ ID NO 51 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 51, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 53, or an amino acid sequence derived from SEQ ID NO 53 via substitution, deletion, or insertion of any one, two, three, four, five, or six amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 68.7 % or higher, 75.0 % or higher, 81.2 % or higher, 87.5 % or higher, or 93.7 % or higher to SEQ ID NO 53, or
(5) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 65, or an amino acid sequence derived from SEQ ID NO 65 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 65,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 67, or an amino acid sequence derived from SEQ ID NO 67 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 67, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 69, or an amino acid sequence derived from SEQ ID NO 69 via substitution, deletion, or insertion of any one, two, three, four, or five amino acid residues, or an amino acid sequence having a

homology (preferably identity) of 64.2 % or higher, 71.4 % or higher, 78.5 % or higher, 85.7 % or higher, or 92.8 % or higher to SEQ ID NO 69, or
(6) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 81, or an amino acid sequence derived from SEQ ID NO 81 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 70.0 % or higher, 80.0 % or higher, or 90.0 % or higher to SEQ ID NO 81,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 83, or an amino acid sequence derived from SEQ ID NO 83 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 71.4 % or higher or 85.7 % or higher to SEQ ID NO 83, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 85, or an amino acid sequence derived from SEQ ID NO 85 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 64.2 % or higher, 71.4 % or higher, 81.8 % or higher, or 90.9 % or higher to SEQ ID NO 85, or
(7) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 97, or an amino acid sequence derived from SEQ ID NO 97 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 97,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 99, or an amino acid sequence derived from SEQ ID NO 99 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 99, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 101, or an amino acid sequence derived from SEQ ID NO 101 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher or 80.0 % or higher to SEQ ID NO 101, or
(8) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 113, or an amino acid sequence derived from SEQ ID NO 113 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 70.0 % or higher, 80.0 % or higher, or 90.0 % or higher to SEQ ID NO 113,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 115, or an amino acid sequence derived from SEQ ID NO 115 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 71.4 % or higher or 85.7 % or higher to SEQ ID NO 115, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 117, or an amino

acid sequence derived from SEQ ID NO 117 via substitution, deletion, or insertion of any one, two, three, four, five, or six amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 66.6 % or higher, 73.3 % or higher, 80.0 % or higher, 86.6 % or higher, or 93.3 % or higher to SEQ ID NO 117, or
(9) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 129, or an amino acid sequence derived from SEQ ID NO 129 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 70.0 % or higher, 80.0 % or higher, or 90.0 % or higher to SEQ ID NO 129,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 131, or an amino acid sequence derived from SEQ ID NO 131 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 71.4 % or higher or 85.7 % or higher to SEQ ID NO 131, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 133, or an amino acid sequence derived from SEQ ID NO 133 via substitution, deletion, or insertion of any one, two, three, four, five, or six amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 66.6 % or higher, 73.3 % or higher, 80.0 % or higher, 86.6 % or higher, or 93.3 % or higher to SEQ ID NO 133, or
(10) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 145, or an amino acid sequence derived from SEQ ID NO 145 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 145,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 147, or an amino acid sequence derived from SEQ ID NO 147 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, or 87.5 % or higher to SEQ ID NO 147, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 149, or an amino acid sequence derived from SEQ ID NO 149 via substitution, deletion, or insertion of any one, two, three, four, five, or six amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 66.6 % or higher, 73.3 % or higher, 80.0 % or higher, 86.6 % or higher, or 93.3 % or higher to SEQ ID NO 149, or
(11) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 161, or an amino acid sequence derived from SEQ ID NO 161 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 70.0 % or higher, 80.0 % or higher, or 90.0 % or higher to SEQ ID NO 161,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 163, or an amino acid sequence derived from SEQ ID NO 163 via substitution, deletion, or insertion of any

one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 71.4 % or higher or 85.7 % or higher to SEQ ID NO 163, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 165, or an amino acid sequence derived from SEQ ID NO 165 via substitution, deletion, or insertion of any one, two, three, four, five, or six amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 66.6 % or higher, 73.3 % or higher, 80.0 % or higher, 86.6 % or higher, or 93.3 % or higher to SEQ ID NO 165,
(12) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 287, or an amino acid sequence derived from SEQ ID NO 287 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 62.5 % or higher, 75.0 % or higher, 87.5 % or higher, or 90.0 % or higher to SEQ ID NO 287,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 289, or an amino acid sequence derived from SEQ ID NO 289 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 71.4 % or higher or 85.7 % or higher to SEQ ID NO 289, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 291, or an amino acid sequence derived from SEQ ID NO 291 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher or 83.3 % or higher to SEQ ID NO 291, or
(13) as a CDR-H1 sequence, the amino acid sequence defined in SEQ ID NO 17, or an amino acid sequence derived from SEQ ID NO 17 via substitution, deletion, or insertion of any one, two, three, four, five, or six amino acid residues other than asparagine at position 32 and tryptophan at position 33,
as a CDR-H2 sequence, the amino acid sequence defined in SEQ ID NO 19, or an amino acid sequence derived from SEQ ID NO 19 via substitution, deletion, or insertion of any one, two, three, four, or five amino acid residues other than aspartic acid at position 55, phenylalanine at position 57, and threonine at position 58, and
as a CDR-H3 sequence, the amino acid sequence defined in SEQ ID NO 21, or an amino acid sequence derived from SEQ ID NO 21 via substitution, deletion, or insertion of any one, two, three, four, five, six, seven, eight, nine, ten, eleven, or twelve amino acid residues arginine at position 98, glycine at position 100, and glycine at position 109.

[Claim 9]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 7, which comprises at least a heavy chain variable region comprising:
(1) the amino acid sequence defined in SEQ ID NO 13, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 13, or
(2) the amino acid sequence defined in SEQ ID NO 29, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 29, or

(3) the amino acid sequence defined in SEQ ID NO 45, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 45, or
(4) the amino acid sequence defined in SEQ ID NO 61, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 61, or
(5) the amino acid sequence defined in SEQ ID NO 77, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 77, or
(6) the amino acid sequence defined in SEQ ID NO 93, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 93, or
(7) the amino acid sequence defined in SEQ ID NO 109, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 109, or
(8) the amino acid sequence defined in SEQ ID NO 125, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 125, or
(9) the amino acid sequence defined in SEQ ID NO 141, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 141, or
(10) the amino acid sequence defined in SEQ ID NO 157, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 157, or
(11) the amino acid sequence defined in SEQ ID NO 173, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 173, or
(12) the amino acid sequence defined in SEQ ID NO 299, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 299.

[Claim 10]

The anti-gpNMB antibody or its fragment or a derivative thereof according to claim 8 or 9, wherein the heavy chain variable region comprises, as a framework sequence, a framework sequence of any class of human immunoglobulin.

[Claim 11]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 8 to 10, which further comprises a heavy chain constant region having an amino acid sequence of a heavy chain constant region of any class of human immunoglobulin.

[Claim 12]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 11, which comprises at least a light chain variable region comprising:
(1) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 7, or an amino acid sequence derived from SEQ ID NO 7 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher or 83.3 % or higher to SEQ ID NO 7,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 9, or an amino acid

sequence derived from SEQ ID NO 9 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 9, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 11, or an amino acid sequence derived from SEQ ID NO 11 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 11, or
(2) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 23, or an amino acid sequence derived from SEQ ID NO 23 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher or 80.0 % or higher to SEQ ID NO 23,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 25, or an amino acid sequence derived from SEQ ID NO 25 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 25, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 27, or an amino acid sequence derived from SEQ ID NO 27 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 27, or
(3) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 39, or an amino acid sequence derived from SEQ ID NO 39 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher or 80.0 % or higher to SEQ ID NO 39,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 41, or an amino acid sequence derived from SEQ ID NO 41 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 41, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 43, or an amino acid sequence derived from SEQ ID NO 43 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 43, or
(4) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 55, or an amino acid sequence derived from SEQ ID NO 55 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher or 83.3 % or higher to SEQ ID NO 55,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 57, or an amino acid sequence derived from SEQ ID NO 57 via substitution, deletion, or insertion of any one

amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 57, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 59, or an amino acid sequence derived from SEQ ID NO 59 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 59, or
(5) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 71, or an amino acid sequence derived from SEQ ID NO 71 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher or 80.0 % or higher to SEQ ID NO 71,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 73, or an amino acid sequence derived from SEQ ID NO 73 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 73, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 75, or an amino acid sequence derived from SEQ ID NO 75 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 70.0 % or higher, 80.0 % or higher, or 90.0 % or higher to SEQ ID NO 75, or
(6) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 87, or an amino acid sequence derived from SEQ ID NO 87 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher or 83.3 % or higher to SEQ ID NO 87,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 89, or an amino acid sequence derived from SEQ ID NO 89 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 89, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 91, or an amino acid sequence derived from SEQ ID NO 91 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 91, or
(7) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 103, or an amino acid sequence derived from SEQ ID NO 103 via substitution, deletion, or insertion of any one or two amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher or 83.3 % or higher to SEQ ID NO 103,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 105, or an amino acid sequence derived from SEQ ID NO 105 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of

66.6 % or higher to SEQ ID NO 105, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 107, or an amino acid sequence derived from SEQ ID NO 107 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 107, or
(8) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 119, or an amino acid sequence derived from SEQ ID NO 119 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 64.2 % or higher, 71.4 % or higher, 81.8 % or higher, or 90.9 % or higher to SEQ ID NO 119,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 121, or an amino acid sequence derived from SEQ ID NO 121 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 121, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 123, or an amino acid sequence derived from SEQ ID NO 123 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 123, or
(9) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 135, or an amino acid sequence derived from SEQ ID NO 135 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 64.2 % or higher, 71.4 % or higher, 81.8 % or higher, or 90.9 % or higher to SEQ ID NO 135,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 137, or an amino acid sequence derived from SEQ ID NO 137 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 137, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 139, or an amino acid sequence derived from SEQ ID NO 139 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 139, or
(10) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 151, or an amino acid sequence derived from SEQ ID NO 151 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 60.0 % or higher, 70.0 % or higher, 80.0 % or higher, or 90.0 % or higher to SEQ ID NO 151,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 153, or an amino acid

sequence derived from SEQ ID NO 153 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 153, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 155, or an amino acid sequence derived from SEQ ID NO 155 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 155, or
(11) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 167, or an amino acid sequence derived from SEQ ID NO 167 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 64.2 % or higher, 71.4 % or higher, 81.8 % or higher, or 90.9 % or higher to SEQ ID NO 167,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 169, or an amino acid sequence derived from SEQ ID NO 169 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 169, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 171, or an amino acid sequence derived from SEQ ID NO 171 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 171, or
(12) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 293, or an amino acid sequence derived from SEQ ID NO 293 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues, or an amino acid sequence having a homology (preferably identity) of 64.2 % or higher, 71.4 % or higher, 81.8 % or higher or 90.9 % or higher to SEQ ID NO 293,
as a CDR-L2, the amino acid sequence defined in SEQ ID NO 295, or an amino acid sequence derived from SEQ ID NO 295 via substitution, deletion, or insertion of any one amino acid residue, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher to SEQ ID NO 295, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 297, or an amino acid sequence derived from SEQ ID NO 297 via substitution, deletion, or insertion of any one, two, or three amino acid residues, or an amino acid sequence having a homology (preferably identity) of 66.6 % or higher, 77.7 % or higher, or 88.8 % or higher to SEQ ID NO 297, or
(13) as a CDR-L1, the amino acid sequence defined in SEQ ID NO 23, or an amino acid sequence derived from SEQ ID NO 23 via substitution, deletion, or insertion of any one, two, or three amino acid residues other than isoleucine at position 29 and tyrosine at position 31,

as a CDR-L2, the amino acid sequence defined in SEQ ID NO 25, or an amino acid sequence derived from SEQ ID NO 25 via substitution, deletion, or insertion of any one or two amino acid residues other than threonine at No. 50, and
as a CDR-L3, the amino acid sequence defined in SEQ ID NO 27, or an amino acid sequence derived from SEQ ID NO 27 via substitution, deletion, or insertion of any one, two, three, or four amino acid residues other than histidine at position 88, glutamine at position 89, tryptophan at position 90, serine at position 92, and tyrosine at position 93.

[Claim 13]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 11, which comprises at least a light chain variable region comprising:
(1) the amino acid sequence defined in SEQ ID NO 15, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 15, or
(2) the amino acid sequence defined in SEQ ID NO 31, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 31, or
(3) the amino acid sequence defined in SEQ ID NO 47, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 47, or
(4) the amino acid sequence defined in SEQ ID NO 63, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 63, or
(5) the amino acid sequence defined in SEQ ID NO 79, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 79, or
(6) the amino acid sequence defined in SEQ ID NO 95, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 95, or
(7) the amino acid sequence defined in SEQ ID NO 111, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 111, or
(8) the amino acid sequence defined in SEQ ID NO 127, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 127, or
(9) the amino acid sequence defined in SEQ ID NO 143, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 143, or
(10) the amino acid sequence defined in SEQ ID NO 159, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 159, or
(11) the amino acid sequence defined in SEQ ID NO 175, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 175, or
(12) the amino acid sequence defined in SEQ ID NO 301, or an amino acid sequence having a homology of 60 % or higher to SEQ ID NO 301.

[Claim 14]

The anti-gpNMB antibody or its fragment or a derivative thereof according to claim 12 or 13, wherein the light chain variable region comprises, as a framework sequence, a framework sequence of any class of human immunoglobulin.

[Claim 15]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 12 to 14, which further comprises a light chain constant region having an amino acid sequence of a light chain constant region of any class of human immunoglobulin.

[Claim 16]

The anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 15, which is a Fab, scFv, Diabody, Nanobody, VHH, bispecific antibody, or multispecific antibody, or a derivative thereof.

[Claim 17]

An anti-gpNMB antibody or its fragment or a derivative thereof which binds to at least one site in a region from a PMEL-CAF-like domain to a PKD domain competitively with an anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 16.

[Claim 18]

A nucleic acid molecule comprising a polynucleotide sequence encoding an anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 17.

[Claim 19]

A cloning vector or expression vector carrying at least one nucleic acid molecule according to claim 18.

[Claim 20]

A recombinant cell transformed with a vector according to claim 19.

[Claim 21]

A method for producing an anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 17, comprising culturing a recombinant cell according to claim 20.

[Claim 22]

A method for producing an anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 17, comprising: administering to an animal a polypeptide having the same amino acid sequence as a region containing amino acid residue(s) D287 and/or H301 and /or a region containing amino acid residue(s) R214 and /or R215 of human gpNMB having the amino acid sequence defined in SEQ ID NO 209;

and collecting an antibody or its fragment or a derivative thereof produced in the body of the animal.

[Claim 23]

A vaccine having an activity to stimulate the production of an anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 17, comprising a polypeptide having the same amino acid sequence as a region containing amino acid residue(s) D287 and/or H301 and /or a region containing amino acid residue(s) R214 and /or R215 of human gpNMB having the amino acid sequence defined in SEQ ID NO 209.

[Claim 24]

A pharmaceutical composition comprising, as an active ingredient, one or more selected from the group consisting of an anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 17, a nucleic acid molecule according to claim 18, a vector according to claim 19, and a recombinant cell according to claim 20.

[Claim 25]

Use of the pharmaceutical composition according to claim 24 in the manufacture of a medicament for decreasing the number of mal-functional microglia in a subject and/or removing amyloid β oligomers in a subject and/or increasing the number of synapses in a subject and/or treating or preventing neurodegenerative disease in a subject.

[Claim 26]

Use of a pharmaceutical composition in the manufacture of a medicament for removing amyloid β oligomers in a subject and/or increasing the number of synapses in a subject and/or treating or preventing neurodegenerative disease in a subject, wherein the pharmaceutical composition comprises an agent for decreasing the number of mal-functional microglia as an active ingredient.

[Claim 27]

The use according to claim 25 or 26, wherein the neurodegenerative disease is Alzheimer’s disease.

[Claim 28]

The use according to claim 27, wherein the pharmaceutical composition further comprises a second active ingredient.

[Claim 29]

The use according to claim 28, wherein the second active ingredient is one or more selected from an anti-Tau antibody, anti-amyloid β antibody, anti-CD33 antibody, anti-semaphorin 4D antibody, anti-TNFα antibody, anti-sortilin antibody, anti-galactose-specific lectin (galectin) 3 antibody, and anti-TREM2 (triggering receptor expressed on myeloid cells 2) antibody.

[Claim 30]

The use according to claim 28, wherein the second active ingredient is a vaccine comprising a full-length or partial-length polypeptide of one or more proteins selected from Tau, amyloid β, CD33, semaphorin 4D, TNFα, sortilin, galactose-specific lectin (galectin) 3, and TREM2 (triggering receptor expressed on myeloid cells 2), or a nucleic acid encoding the polypeptide.

[Claim 31]

The pharmaceutical composition of claim 24 for use in therapy.