

CLAIM

1. A one-armed anti-human NR1 antibody selected from any of the following (a) to (e):

(a) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 31 to 35 of SEQ ID NO: 10, CDR2 comprising the amino acid sequences of amino acids 50 to 66 of SEQ ID NO: 10, and CDR3 comprising the amino acid sequences of amino acids 99 to 111 of SEQ ID NO: 10, a light chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 24 to 34 of SEQ ID NO: 12, CDR2 comprising the amino acid sequences of amino acids 50 to 56 of SEQ ID NO: 12, and CDR3 comprising the amino acid sequences of amino acids 89 to 97 of SEQ ID NO: 12;

(b) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 26 to 34 of SEQ ID NO: 2, CDR2 comprising the amino acid sequences of amino acids 52 to 58 of SEQ ID NO: 2, and CDR3 comprising the amino acid sequences of amino acids 97 to 109 of SEQ ID NO: 2, a light chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 26 to 33 of SEQ ID NO: 4, CDR2 comprising the amino acid sequences of amino acids 51 to 53 of SEQ ID NO: 4, and CDR3 comprising the amino acid sequences comprising amino acids 92 to 100 of SEQ ID NO: 4;

(c) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 31 to 35 of SEQ ID NO: 6, CDR2 comprising the amino acid sequences of amino acids 50 to 66 of SEQ ID NO: 6, and CDR3 comprising the amino acid sequences of amino acids 99 to 110 of SEQ ID NO: 6, a light chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 24 to 34 of SEQ ID NO: 8, CDR2 comprising the amino acid sequences of amino acids 50 to 56 of SEQ ID NO: 8, and CDR3 comprising the amino acid sequences of amino acids 89 to 98 of SEQ ID NO: 8;

(d) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 31 to 36 of SEQ ID NO: 14, CDR2 comprising the amino acid sequences of amino acids 51 to 66 of SEQ ID NO: 14, and CDR3 comprising the amino acid sequences of amino acids 99 to 108 of SEQ ID NO: 14, a light chain

variable region comprising CDR1 comprising the amino acid sequences of amino acids 24 to 34 of SEQ ID NO: 16, CDR2 comprising the amino acid sequences of amino acids 50 to 56 of SEQ ID NO: 16, and CDR3 comprising the amino acid sequences of amino acids 89 to 97 of SEQ ID NO: 16;

(e) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 31 to 36 of SEQ ID NO: 18, CDR2 comprising the amino acid sequences of amino acids 51 to 66 of SEQ ID NO: 18, and CDR3 comprising the amino acid sequences of amino acids 99 to 108 of SEQ ID NO: 18, a light chain variable region comprising CDR1 comprising the amino acid sequences of amino acids 24 to 34 of SEQ ID NO: 20, CDR2 comprising the amino acid sequences of amino acids 50 to 56 of SEQ ID NO: 20, and CDR3 comprising the amino acid sequences of amino acids 89 to 97 of SEQ ID NO: 20.

2. The one-armed anti-human NR1 antibody according to claim 1, which is selected from any of the following (a) to (e):

(a) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising the amino acid sequences shown in SEQ ID NO: 10, and a light chain variable region comprising the amino acid sequences shown in SEQ ID NO: 12;

(b) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising the amino acid sequences shown in SEQ ID NO: 2, and a light chain variable region comprising the amino acid sequences shown in SEQ ID NO: 4;

(c) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising the amino acid sequences shown in SEQ ID NO: 6, and a light chain variable region comprising the amino acid sequences shown in SEQ ID NO: 8;

(d) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising the amino acid sequence shown in SEQ ID NO: 14, and a light chain variable region comprising the amino acid sequence shown in SEQ ID NO: 16;

(e) a one-armed anti-human NR1 antibody comprising a heavy chain variable region comprising the amino acid sequence shown in SEQ ID NO: 18, and a light chain variable region comprising the amino acid sequence shown in SEQ ID NO: 20.

3. The one-armed anti-human NR1 antibody according to claim 1 or 2, further comprising an Fc region, wherein the Fc region comprises a Fc polypeptide.
4. The one-armed anti-human NR1 antibody according to any one of claims 1 to 3, wherein the Fc region comprises a LALA mutation (L234A and L235A), according to Eu numbering.
5. The one-armed anti-human NR1 antibody according to any one of claims 1 to 3, wherein the Fc region comprises a Knobs-into-holes mutation.
6. The one-armed anti-human NR1 antibody according to any one of claims 1 to 3, wherein the Fc region comprises a LALA mutation (L234A and L235A), according to Eu numbering, and a Knobs-into-holes mutation.
7. The one-armed anti-human NR1 antibody according to any one of claims 1 to 6, wherein the one-armed anti-human NR1 antibody is a human antibody or a humanized antibody.
8. A one-armed anti-human NR1 antibody comprising:
 - (a) a heavy chain comprising the amino acid sequences shown in SEQ ID NO: 30, a light chain comprising the amino acid sequences shown in SEQ ID NO: 32, and an Fc polypeptide comprising the amino acid sequences shown in SEQ ID NO: 42;
 - (b) a heavy chain comprising the amino acid sequences shown in SEQ ID NO: 22, a light chain comprising the amino acid sequences shown in SEQ ID NO: 24, and an Fc polypeptide comprising the amino acid sequences shown in SEQ ID NO: 42;
 - (c) a heavy chain comprising the amino acid sequences shown in SEQ ID NO: 26, a light chain comprising the amino acid sequences shown in SEQ ID NO: 28, and an Fc polypeptide comprising the amino acid sequences shown in SEQ ID NO: 42;
 - (d) a heavy chain comprising the amino acid sequences shown in SEQ ID NO: 34, a light chain comprising the amino acid sequences shown in SEQ ID NO: 36, and an Fc polypeptide comprising the amino acid sequences shown in SEQ ID NO: 42; or
 - (e) a heavy chain comprising the amino acid sequences shown in SEQ ID NO: 38, a light chain comprising the amino acid sequences shown in SEQ ID NO: 40, and an Fc polypeptide comprising the amino acid sequences shown in SEQ ID NO: 42.
9. A one-armed anti-human NR1 antibody that binds to human NR1 competitively with an anti-human NR1 antibody and inhibits the intracellular internalization of NMDAR by a patient-derived pathogenic anti-human NR1 antibody from Anti-NMDAR encephalitis comprising a heavy chain

variable region comprising the amino acid sequences shown in SEQ ID NO: 2, and a light chain variable region comprising the amino acid sequences shown in SEQ ID NO: 4.

10. The one-armed anti-human NR1 antibody according to any one of claims 1 to 9, which is produced by post-translational modification.
11. The one-armed anti-human NR1 antibody according to claim 10, wherein the post-translational modification is polyglutamylation at the N-terminal of the heavy chain and/or deletion of the lysine at the C-terminal of the heavy chain.
12. A polynucleotide comprising the nucleotide sequence of any one of claims 1-11.
13. An expression vector comprising the polynucleotide of claim 12.
14. Host cells transformed with the expression vector of claim 13.
15. A method for producing a one-armed anti-human NR1 antibody, which comprises a step of culturing the host cell according to claim 14 to express a polypeptide constituting the one-armed anti-human NR1 antibody.
16. A pharmaceutical composition comprising the one-armed anti-human NR1 antibody according to any one of claims 1 to 11 and a pharmaceutically acceptable excipient.
17. Use of the one-armed anti-human NR1 antibody according to any one of claims 1 to 11 or the pharmaceutical composition according to claim 16 in the manufacture of a medicament for the treatment of anti-NMDAR encephalitis.
18. The one-armed anti-human NR1 antibody according to any one of claims 1 to 11 or the pharmaceutical composition according to claim 16 for use in therapy.