Disclosure of the Invention

[Problems to be Solved by the Invention]

The present invention was achieved in view of the circumstances described above. An objective of the present invention is to provide anti-NR10 antibodies, and pharmaceutical compositions comprising an anti-NR10 antibody.

[Summary]

According to a first aspect, there is provided an anti-NR10 antibody that recognizes domain 1, which is any one of:

(1) an antibody comprising a heavy chain variable region comprising CDR1 of SEQ ID NO: 196, CDR2 of SEQ ID NO: 197, and CDR3 of SEQ ID NO: 184 (H28, H42) and a light chain variable region comprising CDR1 of SEQ ID NO: 202, CDR2 of SEQ ID NO: 170, and CDR3 of SEQ ID NO: 193 (L17);

(2) an antibody comprising a heavy chain variable region comprising CDR1 of SEQ ID NO: 9, CDR2 of SEQ ID NO: 197, and CDR3 of SEQ ID NO: 184 (H30, H44) and a light chain variable region comprising CDR1 of SEQ ID NO: 202, CDR2 of SEQ ID NO: 170, and CDR3 of SEQ ID NO: 193 (L17);

(3) an antibody comprising a heavy chain variable region comprising CDR1 of SEQ ID NO: 176, CDR2 of SEQ ID NO: 197, CDR3 of SEQ ID NO: 184 (H34, H46) and a light chain variable region comprising CDR1 of SEQ ID NO: 202, CDR2 of SEQ ID NO: 170, and CDR3 of SEQ ID NO: 193 (L17);

(4) an antibody comprising a heavy chain variable region comprising CDR1 of SEQ ID NO: 9, CDR2 of SEQ ID NO: 198, and CDR3 of SEQ ID NO: 184 (H57, H78) and a light chain variable region comprising CDR1 of SEQ ID NO: 202, CDR2 of SEQ ID NO: 170, and CDR3 of SEQ ID NO: 193 (L17);

(5) an antibody comprising a heavy chain variable region comprising CDR1 of SEQ ID NO: 176, CDR2 of SEQ ID NO: 198, and CDR3 of SEQ ID NO: 184 (H71, H92) and a light chain variable region comprising CDR1 of SEQ ID NO: 202, CDR2 of SEQ ID NO: 170, and CDR3 of SEQ ID NO: 193 (L17); or

(6) an antibody comprising a heavy chain variable region comprising CDR1 of SEQ ID NO: 9, CDR2 of SEQ ID NO: 199, and CDR3 of SEQ ID NO: 184 (H97, H98) and a light chain variable region comprising CDR1 of SEQ ID NO: 203, CDR2 of SEQ ID NO: 170, and CDR3 of SEQ ID NO: 193 (L50).

According to a second aspect, there is provided an anti-NR10 antibody that recognizes domain 1, which is any one of: (1) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 206 (H28) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H28L17);

(2) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 207 (H30) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H30L17);

(3) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 208 (H34) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H34L17);

(4) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 209 (H42) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H42L17);

(5) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 210 (H44) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H44L17);

(6) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 211 (H46) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H46L17);

(7) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 212 (H57) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H57L17);

(8) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 213 (H71) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H71L17);

(9) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 214 (H78) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H78L17);

(10) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 215 (H92) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 220 (L17) (H92L17);

(11) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 216 (H97) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 221 (L50) (H97L50); or

(12) an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 217 (H98) and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 221 (L50) (H98L50).

According to a third aspect, there is provided an anti-NR10 antibody that recognizes domain 1, which is any one of:

(1) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 224 (H28) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H28L17);

(2) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 225 (H30) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H30L17);

(3) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 226 (H34) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H34L17);

(4) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 227 (H42) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H42L17);

(5) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 228 (H44) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H44L17);

(6) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 229 (H46) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H46L17);

(7) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 230 (H57) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H57L17);

(8) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 231 (H71) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H71L17);

(9) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 232 (H78) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H78L17);

(10) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 233 (H92) and a light chain comprising the amino acid sequence of SEQ ID NO: 238 (L17) (H92L17);

(11) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 234 (H97) and a light chain comprising the amino acid sequence of SEQ ID NO: 239 (L50) (H97L50); or

(12) an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 235 (H98) and a light chain comprising the amino acid sequence of SEQ ID NO: 239 (L50) (H98L50).

According to a fourth aspect, there is provided a pharmaceutical composition comprising the antibody as defined above.

According to a fifth aspect, there is provided an antibody as defined above for use in the treatment of an inflammatory disease.

According to a sixth aspect, there is provided the use of the antibody as defined above in the preparation of a therapeutic agent for an inflammatory disease.

[Means for Solving the Problems]

The present inventors conducted dedicated studies to achieve the objective described above. The present inventors succeeded in obtaining anti-NR10 antibodies having an effective neutralizing activity against NR10. Furthermore, the present inventors succeeded in humanizing the antibodies while maintaining their activity. The present inventors also successfully produced antibodies with improved pharmacokinetics, enhanced antigen-binding activity, improved stability, and/or reduced risk of immunogenicity. These antibodies are useful as therapeutic agents for inflammatory diseases.

The present invention relates to anti-NR10 antibodies, and pharmaceutical compositions comprising an anti-NR10 antibody. More specifically, the present invention includes:

[1] an antibody that recognizes domain 1 of NR10;

[2] the antibody of [1], which has a neutralizing activity;

[3] the antibody of [1] or [2], which is a humanized antibody;

[4] an anti-NR10 antibody which is any one of:

(1) an antibody comprising a heavy chain variable region which comprises CDR1 comprising the amino acid sequence of SEQ ID NO: 1, CDR2 comprising the amino acid sequence of SEQ ID NO: 2, and CDR3 comprising the amino acid sequence of SEQ ID NO: 3;

(2) an antibody comprising the heavy chain variable region of SEQ ID NO: 4;

(3) an antibody comprising a light chain variable region which comprises CDR1 comprising the amino acid sequence of SEQ ID NO: 5, CDR2 comprising the amino acid sequence of SEQ ID NO: 6, and CDR3 comprising the amino acid sequence of SEQ ID NO: 7;

(4) an antibody comprising the light chain variable region of SEQ ID NO: 8;

(5) an antibody comprising the heavy chain variable region of (1) and the light chain variable region of (3);

(6) an antibody comprising the heavy chain variable region of (2) and the light chain variable region of (4);

(7) an antibody in which one or more amino acids are substituted, deleted, added, and/or inserted in the antibody of any one of (1) to (6), which has an activity equivalent to that of the antibody of any one of (1) to (6); and