

CLAIMS

1. Use of an RGMa inhibiting substance in manufacture of an agent for preventing or treating dementia selected from diabetic dementia and vascular dementia.
2. The use according to claim 1, wherein the RGMa inhibiting substance is an anti-RGMa neutralizing antibody or an antigen-binding fragment thereof.
3. The use according to claim 2, wherein the anti-RGMa neutralizing antibody is a humanized antibody.
4. The use according to claim 2 or 3, wherein the anti-RGMa neutralizing antibody is an antibody recognizing an amino acid sequence selected from SEQ ID NOS: 16, 36, 37, 38 and 39.
5. The use according to any one of claims 2 to 4, wherein the anti-RGMa neutralizing antibody is an antibody selected from the following (a) to (l):
 - (a) an anti-RGMa neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 5, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 6, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 7, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 8, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 9, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 10;
 - (b) an anti-RGMa neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 11, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 12, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 13, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 14, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 15, and an HCDR3 comprising an amino acid sequence comprising SFG;
 - (c) an anti-RGMa neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO:

17, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 18, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 19, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 20, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 21, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 22;

(d) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 23, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 24, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 25, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 26, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 27, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 28;

(e) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 29, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 30, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 31, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 32, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 33, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 34;

(f) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 29, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 30, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 35, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 32, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 33, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 34;

(g) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO:

29, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 30, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 40, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 32, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 33, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 34;

(h) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 29, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 30, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 41, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 32, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 33, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 34;

(i) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 29, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 30, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 42, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 32, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 33, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 34;

(j) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 29, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 30, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 43, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 32, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 33, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 34;

(k) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO:

29, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 30, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 44, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 32, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 33, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 34; and

(l) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 29, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 30, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 45, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 32, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 33, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 34.

6. The use according to any one of claims 2 to 5, wherein the anti-RGMA neutralizing antibody is an antibody represented by the following (a):

(a) an anti-RGMA neutralizing antibody comprising a light chain variable region comprising an LCDR1 comprising the amino acid sequence represented by SEQ ID NO: 5, an LCDR2 comprising the amino acid sequence represented by SEQ ID NO: 6, and an LCDR3 comprising the amino acid sequence represented by SEQ ID NO: 7, and a heavy chain variable region comprising an HCDR1 comprising the amino acid sequence represented by SEQ ID NO: 8, an HCDR2 comprising the amino acid sequence represented by SEQ ID NO: 9, and an HCDR3 comprising the amino acid sequence represented by SEQ ID NO: 10.