CLAIMS

[Claim 1]

Use of an RGMa inhibiting substance in manufacturing an agent for inhibiting abnormal protein aggregate accumulation.

[Claim 2]

Use of an RGMa inhibiting substance in manufacturing an agent for inhibiting the uptake of an abnormal protein into a neuron.

[Claim 3]

The use according to claim 1 or 2, wherein the agent for inhibiting abnormal protein aggregate accumulation or the agent for inhibiting the uptake of an abnormal protein into a neuron is an agent for preventing or treating a disease associated with accumulation of abnormal protein aggregates.

[Claim 4]

The use according to claim 3, wherein the disease associated with accumulation of abnormal protein aggregates is a disease selected from spinocerebellar degeneration, spinocerebellar ataxia, dentatorubropallidoluysian atrophy, fragile X-associated tremor/ataxia syndrome, spinobulbar muscular atrophy, fragile X syndrome, fragile XE syndrome, myotonic dystrophy (type 1), lethal insomnia, frontotemporal dementia or frontotemporal lobar degeneration, Pick disease, primary progressive aphasia, primary progressive nonfluent-variant aphasia, progressive supranuclear palsy, corticobasal degeneration, argyrophilic grain dementia, globular glial tauopathy, and dementia with Lewy body.

[Claim 5]

The use according to claim 3 or 4, wherein the disease associated with accumulation of abnormal protein aggregates is frontotemporal dementia (FTD) or frontotemporal lobar degeneration (FTLD).

[Claim 6]

The use according to any one of claims 1 to 5, wherein the RGMa inhibiting substance is an anti-RGMa neutralizing antibody or an antigen-binding fragment thereof.

[Claim 7]

The use according to claim 6, wherein the anti-RGMa neutralizing antibody is

a humanized antibody.

[Claim 8]

The use according to claim 6 or 7, 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.

[Claim 9]

The use according to any one of claims 6 to 8, 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.