

Patent Document 1: WO2005/087268

Patent Document 2: Japanese Translated PCT Patent Application Laid-open No.  
2010-537655

Patent Document 3: Japanese Translated PCT Patent Application Laid-open No.  
5 2009-510002

Patent Document 4: WO2011/071059

Patent Document 5: Japanese Translated PCT Patent Application Laid-open No.  
2011-512806

Patent Document 6: Japanese Translated PCT Patent Application Laid-open No.  
10 2004-525875

#### NON-PATENT DOCUMENTS

[0007]

Non-Patent Document 1: Neuron 5, 735-743 (1990)

15 Non-Patent Document 2: J. Cell Biol. 173, 47-58 (2006)

Non-Patent Document 3: Cell Reports 10, 1-12 (2015)

#### SUMMARY

[0007a]

20 In a first aspect of the present disclosure, there is provided an isolated RGMa-binding protein, which does not inhibit binding between Repulsive Guidance Molecule a (RGMa) and neogenin but neutralizes the neurite outgrowth inhibiting activity of RGMa.

[0007b]

25 In a second aspect of the present disclosure, there is provided a nucleic acid molecule coding for the protein portion of the RGMa-binding protein according to the first aspect.

[0007c]

In a third aspect of the present disclosure, there is provided a recombinant vector comprising the nucleic acid molecule according to the second aspect.

[0007d]

- 5 In a fourth aspect of the present disclosure, there is provided a host cell containing the recombinant vector according to the third aspect.

[0007e]

- In a fifth aspect of the present disclosure, there is provided a method for producing the RGMa-binding protein according to the first aspect, the method comprising a step  
10 of culturing the host cell according to the fourth aspect.

[0007f]

In a sixth aspect of the present disclosure, there is provided a pharmaceutical composition comprising the RGMa-binding protein according to the first aspect.

[0007g]

- 15 In a seventh aspect of the present disclosure, there is provided the pharmaceutical composition according to the sixth aspect for use in preventing, treating, or preventing the relapse of neurological or immunological diseases.

[0007h]

- In an eighth aspect of the present disclosure, there is provided an isolated anti-RGMa  
20 antibody, or an antigen-binding fragment thereof, wherein the amino acid sequence of each of the light chain complementarity determining region 1 (LCDR1), the light chain complementarity determining region 2 (LCDR2), the light chain complementarity determining region 3 (LCDR3), the heavy chain complementarity

determining region 1 (HCDR1), the heavy chain complementarity determining region 2 (HCDR2) and the heavy chain complementarity determining region 3 (HCDR3) comprises the following:

LCDR1: RASQDISSYLN (SEQ ID NO: 30 in Sequence Listing),

5 LCDR2: YTSRLHS (SEQ ID NO: 31 in Sequence Listing),

LCDR3: QQLNTLP (SEQ ID NO: 32 in Sequence Listing),

HCDR1: DAWMD (SEQ ID NO: 33 in Sequence Listing),

HCDR2: EIRSKANNHATYYAESVKG (SEQ ID NO: 34 in Sequence Listing) and

HCDR3: RDGAY (SEQ ID NO: 35 in Sequence Listing);

10 or

LCDR1: RSSQSLVHSNGNTYLH (SEQ ID NO: 36 in Sequence Listing)

LCDR2: KVSNRFS (SEQ ID NO: 37 in Sequence Listing)

LCDR3: SQSTHVP (SEQ ID NO: 38 in Sequence Listing)

HCDR1: TSYAWN (SEQ ID NO: 39 in Sequence Listing)

15 HCDR2: YISYDGTNNYNPSLKN (SEQ ID NO: 40 in Sequence Listing) and

HCDR3: SFG, and

wherein in each of the CDR sequences one or several amino acids may be substituted, deleted, and/or added.

[0007i]

20 In a ninth aspect of the present disclosure, there is provided an RGMa-binding protein, which competes with the anti-RGMa antibody according to the eighth aspect for binding to RGMa.

[0007j]

In a tenth aspect of the present disclosure, there is provided a nucleic acid molecule  
25 coding for the protein portion of the anti-RGMa antibody or an antigen-binding

fragment thereof according to the eighth aspect.

[0007k]

In a eleventh aspect of the present disclosure, there is provided a recombinant vector comprising the nucleic acid molecule according to the tenth aspect.

5 [0007l]

In a twelfth aspect of the present disclosure, there is provided a host cell containing the recombinant vector according to the eleventh aspect.

[0007m]

10 In a thirteenth aspect of the present disclosure, there is provided a method for producing the anti-RGMA antibody or an antigen-binding fragment thereof according to the eighth aspect, the method comprising a step of culturing the host cell according to the twelfth aspect.

[0007n]

15 In a fourteenth aspect of the present disclosure, there is provided a pharmaceutical composition comprising the anti-RGMA antibody or an antigen-binding fragment thereof according to the eighth aspect.

[0007o]

20 In a fifteenth aspect of the present disclosure, there is provided the pharmaceutical composition according to the fourteenth aspect for use in preventing, treating, or preventing the relapse of neurological or immunological diseases.

TECHNICAL PROBLEM

[0008]

Therapeutic uses of anti-RGMa antibody against neurological and immunological diseases are disclosed as described above, but conventional antibodies have problems such as insufficient activity, possibility of impairing intrinsic functions of RGMa, and side effects. In particular, conventional antibodies  
5 may inhibit binding between RGMa and neogenin, thereby also inhibiting favorable effects such as apoptosis suppression exerted by neogenin bound to RGMa.

Thus, an object of the present invention is to provide an RGMa-binding protein which does not inhibit RGMa/neogenin interaction but neutralizes the neurite