as pharmaceutical compositions for inducing an immune response in a subject infected with a foreign biological species or affected with cancer when administered to the subject. The present inventors have also elucidated that the antigen-binding molecules of the present disclosure are useful as pharmaceutical compositions that, when administered to a subject infected with a foreign biological species or affected with cancer, induce an immune response in the subject and also have cytotoxicity or antiproliferative effect against the cancer cells and foreign biological species. Methods for producing these pharmaceutical compositions have also been discovered.

In one apect, there is provided a pharmaceutical composition that induces an immune response to an antigen, which comprises as an active ingredient an antibody, wherein the antibody comprises an antigen-binding domain whose binding activity to the antigen changes depending on an ion concentration condition and comprises an FcRn-binding domain having binding activity to FcRn in a neutral pH range, wherein the antigen-binding domain comprises: (i) an antibody variable region in which at least one or more amino acids selected from the group consisting of amino acids at positions 95, 96, 100a and 101 according to Kabat numbering in the antibody heavy chain variable region and amino acids at positions 30, 31, 32, 50 and 92 according to Kabat numbering in the antibody light chain variable region are amino acids having a metal-chelating activity and the antigen-binding activity is higher under a high calcium ion concentration condition than under a low calcium ion concentration condition; or (ii) antibody ~~variable region~~CDRs in which at least one or more amino acids are His and the antigen-binding activity is higher in a neutral pH range than in an acidic pH range, and wherein the FcRn-binding domain comprises an antibody Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 257, 308, 428, and 434 according to EU numbering in the Fc region are different from amino acids at corresponding positions in a naturally-occurring human IgG Fc region.

In one aspect, there is provided the use of the antibody as defined herein in the manufacture of a medicament for inducing an immune response in a living organism.

In one aspect, there is provided a method for producing an antibody that induces an immune response, which comprises imparting FcRn-binding activity in a neutral pH range to an FcRn-binding domain that is contained in an antibody containing an antigen-binding domain whose antigen-binding activity changes depending on an ion concentration condition, wherein the antigen-binding domain comprises: (i) an antibody variable region in which at least one or more amino acids selected from the group consisting of amino acids at positions 95, 96, 100a and 101 according to Kabat numbering in the antibody heavy chain variable region and amino acids at positions 30, 31, 32, 50 and 92 according to Kabat numbering in the antibody light chain variable region are amino acids having a metal-chelating activity and the antigen-binding activity is higher under a high calcium ion concentration condition than under a low calcium ion concentration condition; or (ii) antibody ~~variable region~~ CDRs in which at least one or more amino acids are His and the antigen-binding activity is higher in a neutral pH range than in an acidic pH range, and wherein the FcRn-binding domain comprises an antibody Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 257, 308, 428, and

434 according to EU numbering in the Fc region are different from amino acids at corresponding positions in a naturally-occurring human IgG Fc region.

More specifically, the present disclosure provides [1] to [47] below:

[1] a pharmaceutical composition that induces an immune response to an antigen, which comprises as an active ingredient an antigen-binding molecule, wherein the antigen-binding molecule comprises an antigen-binding domain whose binding activity to the antigen changes depending on an ion concentration condition and comprises an FcRn-binding domain having binding activity to FcRn in a neutral pH range;

[2] the pharmaceutical composition of [1], wherein the ion concentration is a calcium ion concentration;

[3] the pharmaceutical composition of [2], wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity is higher under a high calcium ion concentration condition than under a low calcium ion concentration condition;

[4] the pharmaceutical composition of [1], wherein the ion concentration condition is a pH condition;

[5] the pharmaceutical composition of [4], wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity is higher in a neutral pH range than under an acidic pH range;

[6] the pharmaceutical composition of any one of [1] to [5], wherein the antigen-binding molecule has neutralizing activity against the antigen;

[7] the pharmaceutical composition of any one of [1] to [6], wherein the antigen-binding molecule has cytotoxic activity against a cell expressing the antigen;

[8] the pharmaceutical composition of any one of [1] to [7], wherein the FcRn-binding domain comprises an antibody Fc region;

[9] the pharmaceutical composition of [8], wherein the Fc region is an Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 257, 308, 428, and 434 according to EU numbering in the Fc region are different from amino acids at corresponding positions in a naturally-occurring Fc region;

[10] the pharmaceutical composition of [8] or [9], wherein the Fc region comprises at least one or more amino acids selected from the group consisting of:

CLAIMS

1. A pharmaceutical composition that induces an immune response to an antigen, which comprises as an active ingredient an antibody, wherein the antibody comprises an antigen-binding domain whose binding activity to the antigen changes depending on an ion concentration condition and comprises an FcRn-binding domain having binding activity to FcRn in a neutral pH range, wherein the antigen-binding domain comprises:
(i) an antibody variable region in which at least one or more amino acids selected from the group consisting of amino acids at positions 95, 96, 100a and 101 according to Kabat numbering in the antibody heavy chain variable region and amino acids at positions 30, 31, 32, 50 and 92 according to Kabat numbering in the antibody light chain variable region are amino acids having a metal-chelating activity and the antigen-binding activity is higher under a high calcium ion concentration condition than under a low calcium ion concentration condition; or (ii) antibody CDRs in which at least one or more amino acids are His and the antigen-binding activity is higher in a neutral pH range than in an acidic pH range, and wherein the FcRn-binding domain comprises an antibody Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 257, 308, 428, and 434 according to EU numbering in the Fc region are different from amino acids at corresponding positions in a naturally-occurring human IgG Fc region.

2. The pharmaceutical composition of claim 1, wherein the antibody has neutralizing activity against the antigen.

3. The pharmaceutical composition of claim 1 or 2, wherein the antibody has cytotoxic activity against a cell expressing the antigen.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein the Fc region comprises at least one or more amino acids selected from the group consisting of:
Ala at amino acid position 257;
Pro at amino acid position 308;
Leu at amino acid position 428; and
Tyr at amino acid position 434,
according to EU numbering in the Fc region.

5. The pharmaceutical composition of any one of claims 1 to 4, wherein the Fcγ receptor-binding activity of the Fc region is higher than that of a naturally-occurring human IgG Fc region in which the sugar chain attached at position 297 according to EU numbering is a fucose-containing sugar chain.

6. The pharmaceutical composition of claim 5, wherein the Fcγ receptor is FcγRIa, FcγRIIa(R), FcγRIIa(H), FcγRIIb, FcγRIIIa(V), or FcγRIIIa(F).

7. The pharmaceutical composition of claim 5 or 6, wherein the Fc region is an Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 221, 222, 223, 224, 225, 227, 228, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 243, 244, 245, 246, 247, 249, 250, 251, 254, 255, 256, 258, 260, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 278, 279, 280, 281, 282, 283, 284, 285, 286, 288, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 311, 313, 315, 317, 318, 320, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 339, 376, 377, 378, 379, 380, 382, 385, 392, 396, 421, 427, 428, 429, 434, 436, and 440 according to EU numbering in the Fc region are different from amino acids at corresponding positions in a naturally-occurring human IgG Fc region.

8. The pharmaceutical composition of any one of claims 5 to 7, wherein the Fc region comprises at least one or more amino acids selected from the group consisting of:
either Lys or Tyr at amino acid position 221;
any one of Phe, Trp, Glu, and Tyr at amino acid position 222;
any one of Phe, Trp, Glu, and Lys at amino acid position 223;
any one of Phe, Trp, Glu, and Tyr at amino acid position 224;
any one of Glu, Lys, and Trp at amino acid position 225;
any one of Glu, Gly, Lys, and Tyr at amino acid position 227;
any one of Glu, Gly, Lys, and Tyr at amino acid position 228;
any one of Ala, Glu, Gly, and Tyr at amino acid position 230;
any one of Glu, Gly, Lys, Pro, and Tyr at amino acid position 231;
any one of Glu, Gly, Lys, and Tyr at amino acid position 232;
any one of Ala, Asp, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 233;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 234;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and

Tyr at amino acid position 235;
any one of Ala, Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 236;
any one of Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 237;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 238;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Thr, Val, Trp, and Tyr at amino acid position 239;
any one of Ala, Ile, Met, and Thr at amino acid position 240;
any one of Asp, Glu, Leu, Arg, Trp, and Tyr at amino acid position 241;
any one of Leu, Glu, Leu, Gln, Arg, Trp, and Tyr at amino acid position 243;
His at amino acid position 244;
Ala at amino acid position 245;
any one of Asp, Glu, His, and Tyr at amino acid position 246;
any one of Ala, Phe, Gly, His, Ile, Leu, Met, Thr, Val, and Tyr at amino acid position 247;
any one of Glu, His, Gln, and Tyr at amino acid position 249;
either Glu or Gln at amino acid position 250;
Phe at amino acid position 251;
any one of Phe, Met, and Tyr at amino acid position 254;
any one of Glu, Leu, and Tyr at amino acid position 255;
any one of Ala, Met, and Pro at amino acid position 256;
any one of Asp, Glu, His, Ser, and Tyr at amino acid position 258;
any one of Asp, Glu, His, and Tyr at amino acid position 260;
any one of Ala, Glu, Phe, Ile, and Thr at amino acid position 262;
any one of Ala, Ile, Met, and Thr at amino acid position 263;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at amino acid position 264;
any one of Ala, Leu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Val, Trp, and Tyr at amino acid position 265;
any one of Ala, Ile, Met, and Thr at amino acid position 266;
any one of Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Thr, Val, Trp, and Tyr at amino acid position 267;
any one of Asp, Glu, Phe, Gly, Ile, Lys, Leu, Met, Pro, Gln, Arg, Thr, Val, and Trp at amino acid position 268;
any one of Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino

acid position 269;
any one of Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at amino acid position 270;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 271;
any one of Asp, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 272;
either Phe or Ile at amino acid position 273;
any one of Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 274;
either Leu or Trp at amino acid position 275;
any one of Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 276;
any one of Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, and Trp at amino acid position 278;
Ala at amino acid position 279;
any one of Ala, Gly, His, Lys, Leu, Pro, Gln, Trp, and Tyr at amino acid position 280;
any one of Asp, Lys, Pro, and Tyr at amino acid position 281;
any one of Glu, Gly, Lys, Pro, and Tyr at amino acid position 282;
any one of Ala, Gly, His, Ile, Lys, Leu, Met, Pro, Arg, and Tyr at amino acid position 283;
any one of Asp, Glu, Leu, Asn, Thr, and Tyr at amino acid position 284;
any one of Asp, Glu, Lys, Gln, Trp, and Tyr at amino acid position 285;
any one of Glu, Gly, Pro, and Tyr at amino acid position 286;
any one of Asn, Asp, Glu, and Tyr at amino acid position 288;
any one of Asp, Gly, His, Leu, Asn, Ser, Thr, Trp, and Tyr at amino acid position 290;
any one of Asp, Glu, Gly, His, Ile, Gln, and Thr at amino acid position 291;
any one of Ala, Asp, Glu, Pro, Thr, and Tyr at amino acid position 292;
any one of Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 293;
any one of Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 294;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 295;
any one of Ala, Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, and Val at amino acid position 296;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr

at amino acid position 297;
any one of Ala, Asp, Glu, Phe, His, Ile, Lys, Met, Asn, Gln, Arg, Thr, Val, Trp, and Tyr at amino acid position 298;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Val, Trp, and Tyr at amino acid position 299;
any one of Ala, Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, and Trp at amino acid position 300;
any one of Asp, Glu, His, and Tyr at amino acid position 301;
Ile at amino acid position 302;
any one of Asp, Gly, and Tyr at amino acid position 303;
any one of Asp, His, Leu, Asn, and Thr at amino acid position 304;
any one of Glu, Ile, Thr, and Tyr at amino acid position 305;
any one of Ala, Asp, Asn, Thr, Val, and Tyr at amino acid position 311;
Phe at amino acid position 313;
Leu at amino acid position 315;
either Glu or Gln at amino acid position 317;
any one of His, Leu, Asn, Pro, Gln, Arg, Thr, Val, and Tyr at amino acid position 318;
any one of Asp, Phe, Gly, His, Ile, Leu, Asn, Pro, Ser, Thr, Val, Trp, and Tyr at amino acid position 320;
any one of Ala, Asp, Phe, Gly, His, Ile, Pro, Ser, Thr, Val, Trp, and Tyr at amino acid position 322;
Ile at amino acid position 323;
any one of Asp, Phe, Gly, His, Ile, Leu, Met, Pro, Arg, Thr, Val, Trp, and Tyr at amino acid position 324;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 325;
any one of Ala, Asp, Glu, Gly, Ile, Leu, Met, Asn, Pro, Gln, Ser, Thr, Val, Trp, and Tyr at amino acid position 326;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Thr, Val, Trp, and Tyr at amino acid position 327;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 328;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 329;
any one of Cys, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 330;

any one of Asp, Phe, His, Ile, Leu, Met, Gln, Arg, Thr, Val, Trp, and Tyr at amino acid position 331;
any one of Ala, Asp, Glu, Phe, Gly, His, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 332;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Ser, Thr, Val, and Tyr at amino acid position 333;
any one of Ala, Glu, Phe, Ile, Leu, Pro, and Thr at amino acid position 334;
any one of Asp, Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Val, Trp, and Tyr at amino acid position 335;
any one of Glu, Lys, and Tyr at amino acid position 336;
any one of Glu, His, and Asn at amino acid position 337;
any one of Asp, Phe, Gly, Ile, Lys, Met, Asn, Gln, Arg, Ser, and Thr at amino acid position 339;
either Ala or Val at amino acid position 376;
either Gly or Lys at amino acid position 377;
Asp at amino acid position 378;
Asn at amino acid position 379;
any one of Ala, Asn, and Ser at amino acid position 380;
either Ala or Ile at amino acid position 382;
Glu at amino acid position 385;
Thr at amino acid position 392;
Leu at amino acid position 396;
Lys at amino acid position 421;
Asn at amino acid position 427;
either Phe or Leu at amino acid position 428;
Met at amino acid position 429;
Trp at amino acid position 434;
Ile at amino acid position 436; and
any one of Gly, His, Ile, Leu, and Tyr at amino acid position 440;
according to EU numbering in the Fc region.

9. The pharmaceutical composition of any one of claims 5 to 8, wherein the naturally-occurring human IgG Fc region is an Fc region of any one of human IgG1, human IgG2, human IgG3, and human IgG4 in which the sugar chain attached at position 297 according to EU numbering is a fucose-containing sugar chain.

10. The pharmaceutical composition of any one of claims 5 to 9, wherein the Fc region is

modified so that the percentage of the Fc region to which a fucose-deficient sugar chain is attached, or bisecting *N*-acetylglucosamine is added, at position 297 according to EU numbering in the Fc region, will become higher.

11. Use of the antibody of any one of claims 1 to 10 in the manufacture of a medicament for inducing an immune response in a living organism.

12. A method for producing an antibody that induces an immune response, which comprises imparting FcRn-binding activity in a neutral pH range to an FcRn-binding domain that is contained in an antibody containing an antigen-binding domain whose antigen-binding activity changes depending on an ion concentration condition, wherein the antigen-binding domain comprises: (i) an antibody variable region in which at least one or more amino acids selected from the group consisting of amino acids at positions 95, 96, 100a and 101 according to Kabat numbering in the antibody heavy chain variable region and amino acids at positions 30, 31, 32, 50 and 92 according to Kabat numbering in the antibody light chain variable region are amino acids having a metal-chelating activity and the antigen-binding acitivty is higher under a calcium ion concentration condition than under low calcium ion concentration condition; or (ii) antibody CDRs in which at least one or more amino acids are His and the antigen-binding activity is higher in a neutral pH range than in an acidic pH range, and
wherein the FcRn-binding domain comprises an antibody Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 257, 308, 428, and 434 according to EU numbering in the Fc region are different from amino acids at corresponding positions in a naturally-occurring human IgG Fc region.

13. The method of claim 12, wherein the antibody has neutralizing activity against the antigen.

14. The method of claim 12 or 13, wherein the antibody has cytotoxic activity against a cell expressing the antigen.

15. The method of any one of claims 12 to 14, comprising the step of performing at least one or more amino acid substitutions selected from the group consisting of:
amino acid substitution with Ala at position 257;
amino acid substitution with Pro at position 308;
amino acid substitution with Leu at position 428; and
amino acid substitution with Tyr at position 434,
according to EU numbering in the Fc region.

16. The method of any one of claims 12 to 15, comprising the step of enhancing the Fcγ receptor-binding activity of the Fc region as compared to that of a naturally-occurring human IgG Fc region in which the sugar chain attached at position 297 according to EU numbering is a fucose-containing sugar chain.

17. The method of claim 16, wherein the Fcγ receptor is FcγRIa, FcγRIIa(R), FcγRIIa(H), FcγRIIb, FcγRIIIa(V), or FcγRIIIa(F).

18. The method of claim 16 or 17, comprising the step of substituting at least one or more amino acids selected from the group consisting of amino acids at positions 221, 222, 223, 224, 225, 227, 228, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 243, 244, 245, 246, 247, 249, 250, 251, 254, 255, 256, 258, 260, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 278, 279, 280, 281, 282, 283, 284, 285, 286, 288, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 311, 313, 315, 317, 318, 320, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 339, 376, 377, 378, 379, 380, 382, 385, 392, 396, 421, 427, 428, 429, 434, 436, and 440 according to EU numbering in the Fc region.

19. The method of any one of claims 16 to 18, comprising the step of performing at least one or more amino acid substitutions selected from the group consisting of:
amino acid substitution with either Lys or Tyr at position 221;
amino acid substitution with any one of Phe, Trp, Glu, and Tyr at position 222;
amino acid substitution with any one of Phe, Trp, Glu, and Lys at position 223;
amino acid substitution with any one of Phe, Trp, Glu, and Tyr at position 224;
amino acid substitution with any one of Glu, Lys, and Trp at position 225;
amino acid substitution with any one of Glu, Gly, Lys, and Tyr at position 227;
amino acid substitution with any one of Glu, Gly, Lys, and Tyr at position 228;
amino acid substitution with any one of Ala, Glu, Gly, and Tyr at position 230;
amino acid substitution with any one of Glu, Gly, Lys, Pro, and Tyr at position 231;
amino acid substitution with any one of Glu, Gly, Lys, and Tyr at position 232;
amino acid substitution with any one of Ala, Asp, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 233;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 234;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln,

Arg, Ser, Thr, Val, Trp, and Tyr at position 235;
amino acid substitution with any one of Ala, Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 236;
amino acid substitution with any one of Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 237;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 238;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Thr, Val, Trp, and Tyr at position 239;
amino acid substitution with any one of Ala, Ile, Met, and Thr at position 240;
amino acid substitution with any one of Asp, Glu, Leu, Arg, Trp, and Tyr at position 241;
amino acid substitution with any one of Leu, Glu, Leu, Gln, Arg, Trp, and Tyr at position 243;
amino acid substitution with His at position 244;
amino acid substitution with Ala at position 245;
amino acid substitution with any one of Asp, Glu, His, and Tyr at position 246;
amino acid substitution with any one of Ala, Phe, Gly, His, Ile, Leu, Met, Thr, Val, and Tyr at position 247;
amino acid substitution with any one of Glu, His, Gln, and Tyr at position 249;
amino acid substitution with either Glu or Gln at position 250;
amino acid substitution with Phe at position 251;
amino acid substitution with any one of Phe, Met, and Tyr at position 254;
amino acid substitution with any one of Glu, Leu, and Tyr at position 255;
amino acid substitution with any one of Ala, Met, and Pro at position 256;
amino acid substitution with any one of Asp, Glu, His, Ser, and Tyr at position 258;
amino acid substitution with any one of Asp, Glu, His, and Tyr at position 260;
amino acid substitution with any one of Ala, Glu, Phe, Ile, and Thr at position 262;
amino acid substitution with any one of Ala, Ile, Met, and Thr at position 263;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at position 264;
amino acid substitution with any one of Ala, Leu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Val, Trp, and Tyr at position 265;
amino acid substitution with any one of Ala, Ile, Met, and Thr at position 266;
amino acid substitution with any one of Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Thr, Val, Trp, and Tyr at position 267;
amino acid substitution with any one of Asp, Glu, Phe, Gly, Ile, Lys, Leu, Met, Pro, Gln, Arg, Thr, Val, and Trp at position 268;

amino acid substitution with any one of Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 269;

amino acid substitution with any one of Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at position 270;

amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 271;

amino acid substitution with any one of Asp, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 272;

amino acid substitution with either Phe or Ile at position 273;

amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 274;

amino acid substitution with either Leu or Trp at position 275;

amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 276;

amino acid substitution with any one of Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, and Trp at position 278;

amino acid substitution with Ala at position 279;

amino acid substitution with any one of Ala, Gly, His, Lys, Leu, Pro, Gln, Trp, and Tyr at position 280;

amino acid substitution with any one of Asp, Lys, Pro, and Tyr at position 281;

amino acid substitution with any one of Glu, Gly, Lys, Pro, and Tyr at position 282;

amino acid substitution with any one of Ala, Gly, His, Ile, Lys, Leu, Met, Pro, Arg, and Tyr at position 283;

amino acid substitution with at position 284 is any one of Asp, Glu, Leu, Asn, Thr, and Tyr;

amino acid substitution with any one of Asp, Glu, Lys, Gln, Trp, and Tyr at position 285;

amino acid substitution with any one of Glu, Gly, Pro, and Tyr at position 286;

amino acid substitution with any one of Asn, Asp, Glu, and Tyr at position 288;

amino acid substitution with any one of Asp, Gly, His, Leu, Asn, Ser, Thr, Trp, and Tyr at position 290;

amino acid substitution with any one of Asp, Glu, Gly, His, Ile, Gln, and Thr at position 291;

amino acid substitution with any one of Ala, Asp, Glu, Pro, Thr, and Tyr at position 292;

amino acid substitution with any one of Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 293;

amino acid substitution with any one of Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 294;

amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Arg, Ser,

Thr, Val, Trp, and Tyr at position 295;
amino acid substitution with any one of Ala, Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, and Val at position 296;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 297;
amino acid substitution with any one of Ala, Asp, Glu, Phe, His, Ile, Lys, Met, Asn, Gln, Arg, Thr, Val, Trp, and Tyr at position 298;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Val, Trp, and Tyr at position 299;
amino acid substitution with any one of Ala, Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, and Trp at position 300;
amino acid substitution with any one of Asp, Glu, His, and Tyr at position 301;
amino acid substitution with Ile at position 302;
amino acid substitution with any one of Asp, Gly, and Tyr at position 303;
amino acid substitution with at position 304 is any one of Asp, His, Leu, Asn, and Thr;
amino acid substitution with any one of Glu, Ile, Thr, and Tyr at position 305;
amino acid substitution with any one of Ala, Asp, Asn, Thr, Val, and Tyr at position 311;
amino acid substitution with Phe at position 313;
amino acid substitution with Leu at position 315;
amino acid substitution with either Glu or Gln at position 317;
amino acid substitution with any one of His, Leu, Asn, Pro, Gln, Arg, Thr, Val, and Tyr at position 318;
amino acid substitution with any one of Asp, Phe, Gly, His, Ile, Leu, Asn, Pro, Ser, Thr, Val, Trp, and Tyr at position 320;
amino acid substitution with any one of Ala, Asp, Phe, Gly, His, Ile, Pro, Ser, Thr, Val, Trp, and Tyr at position 322;
amino acid substitution with Ile at position 323;
amino acid substitution with any one of Asp, Phe, Gly, His, Ile, Leu, Met, Pro, Arg, Thr, Val, Trp, and Tyr at position 324;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 325;
amino acid substitution with any one of Ala, Asp, Glu, Gly, Ile, Leu, Met, Asn, Pro, Gln, Ser, Thr, Val, Trp, and Tyr at position 326;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Thr, Val, Trp, and Tyr at position 327;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln,

Arg, Ser, Thr, Val, Trp, and Tyr at position 328;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 329;
amino acid substitution with any one of Cys, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 330;
amino acid substitution with any one of Asp, Phe, His, Ile, Leu, Met, Gln, Arg, Thr, Val, Trp, and Tyr at position 331;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 332;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Ser, Thr, Val, and Tyr at position 333;
amino acid substitution with any one of Ala, Glu, Phe, Ile, Leu, Pro, and Thr at position 334;
amino acid substitution with any one of Asp, Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Val, Trp, and Tyr at position 335;
amino acid substitution with any one of Glu, Lys, and Tyr at position 336;
amino acid substitution with any one of Glu, His, and Asn at position 337;
amino acid substitution with any one of Asp, Phe, Gly, Ile, Lys, Met, Asn, Gln, Arg, Ser, and Thr at position 339;
amino acid substitution with either Ala or Val at position 376;
amino acid substitution with either Gly or Lys at position 377;
amino acid substitution with Asp at position 378;
amino acid substitution with Asn at position 379;
amino acid substitution with any one of Ala, Asn, and Ser at position 380;
amino acid substitution with either Ala or Ile at position 382;
amino acid substitution with Glu at position 385;
amino acid substitution with Thr at position 392;
amino acid substitution with Leu at position 396;
amino acid substitution with Lys at position 421;
amino acid substitution with Asn at position 427;
amino acid substitution with either Phe or Leu at position 428;
amino acid substitution with Met at position 429;
amino acid substitution with Trp at position 434;
amino acid substitution with Ile at position 436; and
amino acid substitution with any one of Gly, His, Ile, Leu, and Tyr at position 440,
according to EU numbering in the Fc region.

20. The method of any one of claims 16 to 19, wherein the naturally-occurring human IgG Fc region is an Fc region of any one of human IgG1, human IgG2, human IgG3, and human IgG4 in which the sugar chain attached at position 297 according to EU numbering is a fucose-containing sugar chain.

21. The method of any one of claims 16 to 20, comprising the step of modifying the Fc region so that the percentage of the Fc region to which a fucose-deficient sugar chain is attached, or bisecting *N*-acetylglucosamine is added, at position 297 according to EU numbering in the Fc region, will become higher.

CLAIMS

1. A pharmaceutical composition that induces an immune response to an antigen, which comprises as an active ingredient an antibody, wherein the antibody comprises an antigen-binding domain whose binding activity to the antigen changes depending on an ion concentration condition and comprises an FcRn-binding domain having binding activity to FcRn in a neutral pH range, wherein the antigen-binding domain comprises an antibody variable region in which at least one or more amino acids selected from the group consisting of amino acids at positions 95, 96, 100a and 101 according to Kabat numbering in the antibody heavy chain variable region and amino acids at positions 30, 31, 32, 50 and 92 according to Kabat numbering in the antibody light chain variable region are amino acids having a metal-chelating activity or antibody variable region in
which at least one or more amino acids are His, and wherein the FcRn-binding domain comprises an antibody Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 257, 308, 428, and 434 according to EU numbering in the Fc region are different from amino acids.at corresponding positions in a naturally-occurring Fc region.

2. The pharmaceutical composition of claim 1, wherein the ion concentration is a calcium ion concentration.

3. The pharmaceutical composition of claim 2, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity is higher under a high calcium ion concentration condition than under a low calcium ion concentration condition.

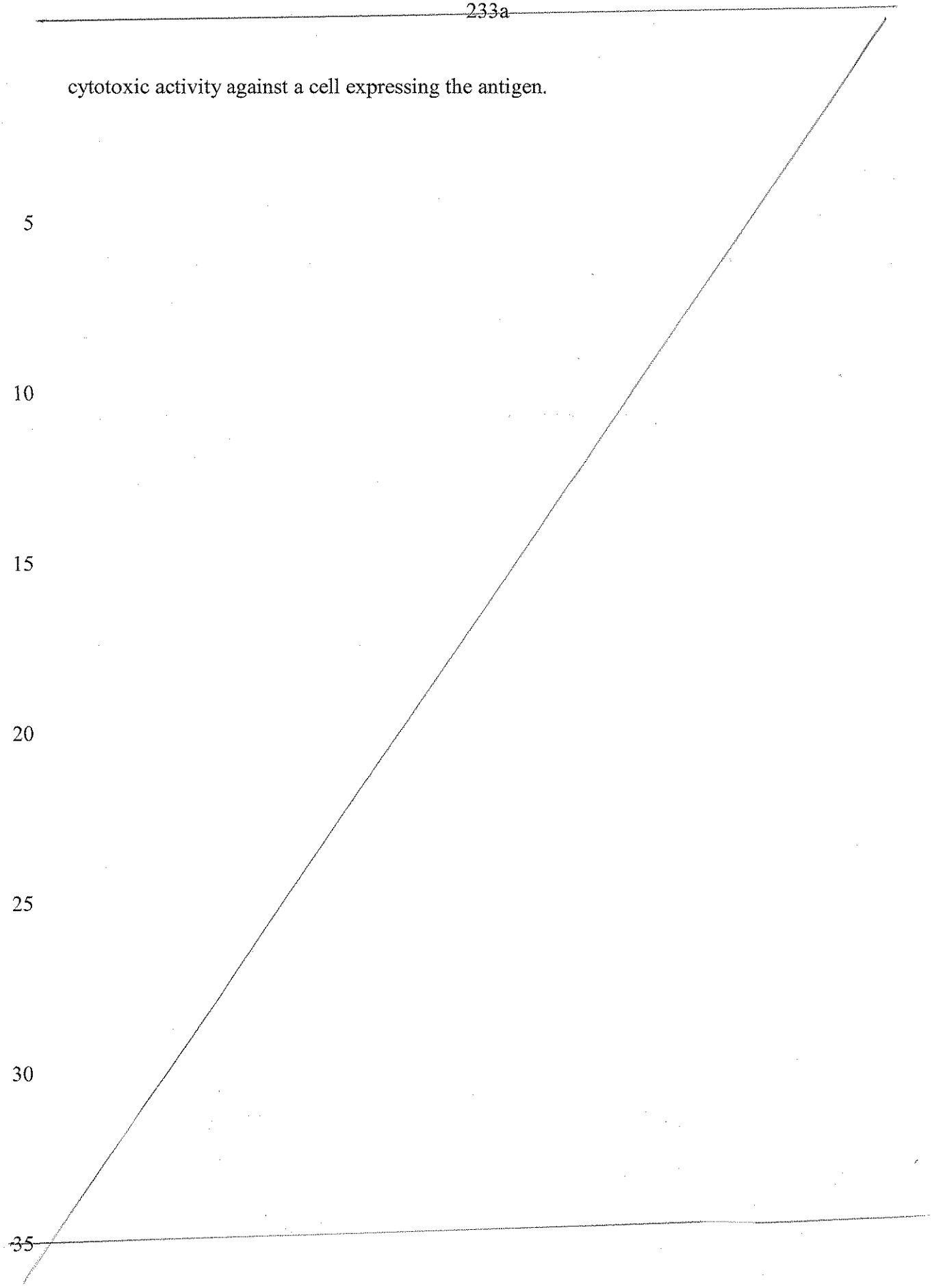
4. The pharmaceutical composition of claim 1, wherein the ion concentration condition is a pH condition.

5. The pharmaceutical composition of claim 4, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity is higher in a neutral pH range than under an acidic pH range.

6. The pharmaceutical composition of any one of claims 1 to 5, wherein the antibody has neutralizing activity against the antigen.

~~7. The pharmaceutical composition of any one of claims 1 to 6, wherein the antibody has~~

cytotoxic activity against a cell expressing the antigen.



8. The pharmaceutical composition of any one of claims 1 to 7, wherein the Fc region comprises at least one or more amino acids selected from the group consisting of:
Ala at amino acid position 257;
Pro at amino acid position 308;
Leu at amino acid position 428; and
Tyr at amino acid position 434,
according to EU numbering in the Fc region.

9. The pharmaceutical composition of any one of claims 1 to 8, wherein the Fcγ receptor-binding activity of the Fc region is higher than that of a naturally-occurring human IgG Fc region in which the sugar chain attached at position 297 according to EU numbering is a fucose-containing sugar chain.

10. The pharmaceutical composition of claim 9, wherein the Fcγ receptor is FcγRIa, FcγRIIa(R), FcγRIIa(H), FcγRIIb, FcγRIIIa(V), or FcγRIIIa(F).

11. The pharmaceutical composition of claim 9 or 10, wherein the Fc region is an Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 221, 222, 223, 224, 225, 227, 228, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 243, 244, 245, 246, 247, 249, 250, 251, 254, 255, 256, 258, 260, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 278, 279, 280, 281, 282, 283, 284, 285, 286, 288, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 311, 313, 315, 317, 318, 320, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 339, 376, 377, 378, 379, 380, 382, 385, 392, 396, 421, 427, 428, 429, 434, 436, and 440 according to EU numbering in the Fc region are different from amino acids at corresponding positions in a naturally-occurring Fc region.

12. The pharmaceutical composition of any one of claims 9 to 11, wherein the Fc region comprises at least one or more amino acids selected from the group consisting of:
either Lys or Tyr at amino acid position 221;
any one of Phe, Trp, Glu, and Tyr at amino acid position 222;
any one of Phe, Trp, Glu, and Lys at amino acid position 223;
any one of Phe, Trp, Glu, and Tyr at amino acid position 224;
any one of Glu, Lys, and Trp at amino acid position 225;
any one of Glu, Gly, Lys, and Tyr at amino acid position 227;
any one of Glu, Gly, Lys, and Tyr at amino acid position 228;

any one of Ala, Glu, Gly, and Tyr at amino acid position 230;
any one of Glu, Gly, Lys, Pro, and Tyr at amino acid position 231;
any one of Glu, Gly, Lys, and Tyr at amino acid position 232;
any one of Ala, Asp, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 233;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 234;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 235;
any one of Ala, Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 236;
any one of Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 237;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 238;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Thr, Val, Trp, and Tyr at amino acid position 239;
any one of Ala, Ile, Met, and Thr at amino acid position 240;
any one of Asp, Glu, Leu, Arg, Trp, and Tyr at amino acid position 241;
any one of Leu, Glu, Leu, Gln, Arg, Trp, and Tyr at amino acid position 243;
His at amino acid position 244;
Ala at amino acid position 245;
any one of Asp, Glu, His, and Tyr at amino acid position 246;
any one of Ala, Phe, Gly, His, Ile, Leu, Met, Thr, Val, and Tyr at amino acid position 247;
any one of Glu, His, Gln, and Tyr at amino acid position 249;
either Glu or Gln at amino acid position 250;
Phe at amino acid position 251;
any one of Phe, Met, and Tyr at amino acid position 254;
any one of Glu, Leu, and Tyr at amino acid position 255;
any one of Ala, Met, and Pro at amino acid position 256;
any one of Asp, Glu, His, Ser, and Tyr at amino acid position 258;
any one of Asp, Glu, His, and Tyr at amino acid position 260;
any one of Ala, Glu, Phe, Ile, and Thr at amino acid position 262;
any one of Ala, Ile, Met, and Thr at amino acid position 263;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at amino acid position 264;

any one of Ala, Leu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Val, Trp, and Tyr at amino acid position 265;

any one of Ala, Ile, Met, and Thr at amino acid position 266;

any one of Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Thr, Val, Trp, and Tyr at amino acid position 267;

any one of Asp, Glu, Phe, Gly, Ile, Lys, Leu, Met, Pro, Gln, Arg, Thr, Val, and Trp at amino acid position 268;

any one of Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 269;

any one of Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at amino acid position 270;

any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 271;

any one of Asp, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 272;

either Phe or Ile at amino acid position 273;

any one of Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 274;

either Leu or Trp at amino acid position 275;

any one of Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 276;

any one of Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, and Trp at amino acid position 278;

Ala at amino acid position 279;

any one of Ala, Gly, His, Lys, Leu, Pro, Gln, Trp, and Tyr at amino acid position 280;

any one of Asp, Lys, Pro, and Tyr at amino acid position 281;

any one of Glu, Gly, Lys, Pro, and Tyr at amino acid position 282;

any one of Ala, Gly, His, Ile, Lys, Leu, Met, Pro, Arg, and Tyr at amino acid position 283;

any one of Asp, Glu, Leu, Asn, Thr, and Tyr at amino acid position 284;

any one of Asp, Glu, Lys, Gln, Trp, and Tyr at amino acid position 285;

any one of Glu, Gly, Pro, and Tyr at amino acid position 286;

any one of Asn, Asp, Glu, and Tyr at amino acid position 288;

any one of Asp, Gly, His, Leu, Asn, Ser, Thr, Trp, and Tyr at amino acid position 290;

any one of Asp, Glu, Gly, His, Ile, Gln, and Thr at amino acid position 291;

any one of Ala, Asp, Glu, Pro, Thr, and Tyr at amino acid position 292;

~~any one of Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid~~

position 293;
any one of Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 294;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 295;
any one of Ala, Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, and Val at amino acid position 296;
any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 297;
any one of Ala, Asp, Glu, Phe, His, Ile, Lys, Met, Asn, Gln, Arg, Thr, Val, Trp, and Tyr at amino acid position 298;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Val, Trp, and Tyr at amino acid position 299;
any one of Ala, Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, and Trp at amino acid position 300;
any one of Asp, Glu, His, and Tyr at amino acid position 301;
Ile at amino acid position 302;
any one of Asp, Gly, and Tyr at amino acid position 303;
any one of Asp, His, Leu, Asn, and Thr at amino acid position 304;
any one of Glu, Ile, Thr, and Tyr at amino acid position 305;
any one of Ala, Asp, Asn, Thr, Val, and Tyr at amino acid position 311;
Phe at amino acid position 313;
Leu at amino acid position 315;
either Glu or Gln at amino acid position 317;
any one of His, Leu, Asn, Pro, Gln, Arg, Thr, Val, and Tyr at amino acid position 318;
any one of Asp, Phe, Gly, His, Ile, Leu, Asn, Pro, Ser, Thr, Val, Trp, and Tyr at amino acid position 320;
any one of Ala, Asp, Phe, Gly, His, Ile, Pro, Ser, Thr, Val, Trp, and Tyr at amino acid position 322;
Ile at amino acid position 323;
any one of Asp, Phe, Gly, His, Ile, Leu, Met, Pro, Arg, Thr, Val, Trp, and Tyr at amino acid position 324;
any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 325;
any one of Ala, Asp, Glu, Gly, Ile, Leu, Met, Asn, Pro, Gln, Ser, Thr, Val, Trp, and Tyr at amino acid position 326;

any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Thr, Val, Trp, and Tyr at amino acid position 327;

any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 328;

any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 329;

any one of Cys, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 330;

any one of Asp, Phe, His, Ile, Leu, Met, Gln, Arg, Thr, Val, Trp, and Tyr at amino acid position 331;

any one of Ala, Asp, Glu, Phe, Gly, His, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 332;

any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Ser, Thr, Val, and Tyr at amino acid position 333;

any one of Ala, Glu, Phe, Ile, Leu, Pro, and Thr at amino acid position 334;

any one of Asp, Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Val, Trp, and Tyr at amino acid position 335;

any one of Glu, Lys, and Tyr at amino acid position 336;

any one of Glu, His, and Asn at amino acid position 337;

any one of Asp, Phe, Gly, Ile, Lys, Met, Asn, Gln, Arg, Ser, and Thr at amino acid position 339;

either Ala or Val at amino acid position 376;

either Gly or Lys at amino acid position 377;

Asp at amino acid position 378;

Asn at amino acid position 379;

any one of Ala, Asn, and Ser at amino acid position 380;

either Ala or Ile at amino acid position 382;

Glu at amino acid position 385;

Thr at amino acid position 392;

Leu at amino acid position 396;

Lys at amino acid position 421;

Asn at amino acid position 427;

either Phe or Leu at amino acid position 428;

Met at amino acid position 429;

Trp at amino acid position 434;

Ile at amino acid position 436; and

~~any one of Gly, His, Ile, Leu, and Tyr at amino acid position 440;~~

according to EU numbering in the Fc region.

13. The pharmaceutical composition of any one of claims 9 to 12, wherein the naturally-occurring Fc region is an Fc region of any one of human IgG1, human IgG2, human IgG3, and human IgG4 in which the sugar chain attached at position 297 according to EU numbering is a fucose-containing sugar chain.

14. The pharmaceutical composition of any one of claims 9 to 13, wherein the Fc region is modified so that the percentage of the Fc region to which a fucose-deficient sugar chain is attached, or bisecting *N*-acetylglucosamine is added, at position 297 according to EU numbering in the Fc region, will become higher.

15. Use of the antibody of any one of claims 1 to 14 in the manufacture of a medicament for inducing an immune response in a living organism.

16. A method for producing an antibody that induces an immune response, which comprises imparting FcRn-binding activity in a neutral pH range to an FcRn-binding domain that is contained in an antibody containing an antigen-binding domain whose antigen-binding activity changes depending on an ion concentration condition, wherein the antigen-binding domain comprises an antibody variable region in which at least one or more amino acids selected from the group consisting of amino acids at positions 95, 96, 100a and 101 according to Kabat numbering in the antibody heavy chain variable region and amino acids at positions 30, 31, 32, 50 and 92 according to Kabat numbering in the antibody light chain variable region are amino acids having a metal-chelating activity or antibody variable region in which at least one or more amino acids are His, and
wherein the FcRn-binding domain comprises an antibody Fc region in which at least one or more amino acids selected from the group consisting of amino acids at positions 257, 308, 428, and 434 according to EU numbering in the Fc region are different from amino acids at corresponding positions in a naturally-occurring Fc region.

17. The method of claim 16, wherein the ion concentration is a calcium ion concentration.

18. The method of claim 17, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity is higher under a high calcium ion concentration condition than under a low calcium ion concentration condition.

19. The method of claim 16, wherein the ion concentration condition is a pH condition.

20. The method of claim 19, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity is higher in a neutral pH range than in an acidic pH range.

21. The method of any one of claims 16 to 20, wherein the antibody has neutralizing activity against the antigen.

22. The method of any one of claims 16 to 20, wherein the antibody has

cytotoxic activity against a cell expressing the antigen.

23. The method of any one of claims 16 to 22, comprising the step of performing at least one or more amino acid substitutions selected from the group consisting of:
amino acid substitution with Ala at position 257;
amino acid substitution with Pro at position 308;
amino acid substitution with Leu at position 428; and
amino acid substitution with Tyr at position 434,
according to EU numbering in the Fc region.

24. The method of any one of claims 16 to 23, comprising the step of enhancing the Fcγ receptor-binding activity of the Fc region as compared to that of a naturally-occurring human IgG Fc region in which the sugar chain attached at position 297 according to EU numbering is a fucose-containing sugar chain.

25. The method of claim 24, wherein the Fcγ receptor is FcγRIa, FcγRIIa(R), FcγRIIa(H), FcγRIIb, FcγRIIIa(V), or FcγRIIIa(F).

26. The method of claim 24 or 25, comprising the step of substituting at least one or more amino acids selected from the group consisting of amino acids at positions 221, 222, 223, 224, 225, 227, 228, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 243, 244, 245, 246, 247, 249, 250, 251, 254, 255, 256, 258, 260, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 278, 279, 280, 281, 282, 283, 284, 285, 286, 288, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 311, 313, 315, 317, 318, 320, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 339, 376, 377, 378, 379, 380, 382, 385, 392, 396, 421, 427, 428, 429, 434, 436, and 440 according to EU numbering in the Fc region.

27. The method of any one of claims 24 to 26, comprising the step of performing at least one

or more amino acid substitutions selected from the group consisting of:
amino acid substitution with either Lys or Tyr at position 221;
amino acid substitution with any one of Phe, Trp, Glu, and Tyr at position 222;
amino acid substitution with any one of Phe, Trp, Glu, and Lys at position 223;
amino acid substitution with any one of Phe, Trp, Glu, and Tyr at position 224;
amino acid substitution with any one of Glu, Lys, and Trp at position 225;
amino acid substitution with any one of Glu, Gly, Lys, and Tyr at position 227;
amino acid substitution with any one of Glu, Gly, Lys, and Tyr at position 228;
amino acid substitution with any one of Ala, Glu, Gly, and Tyr at position 230;
amino acid substitution with any one of Glu, Gly, Lys, Pro, and Tyr at position 231;
amino acid substitution with any one of Glu, Gly, Lys, and Tyr at position 232;
amino acid substitution with any one of Ala, Asp, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 233;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 234;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 235;
amino acid substitution with any one of Ala, Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 236;
amino acid substitution with any one of Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 237;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 238;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Thr, Val, Trp, and Tyr at position 239;
amino acid substitution with any one of Ala, Ile, Met, and Thr at position 240;
amino acid substitution with any one of Asp, Glu, Leu, Arg, Trp, and Tyr at position 241;
amino acid substitution with any one of Leu, Glu, Leu, Gln, Arg, Trp, and Tyr at position 243;
amino acid substitution with His at position 244;
amino acid substitution with Ala at position 245;
amino acid substitution with any one of Asp, Glu, His, and Tyr at position 246;
amino acid substitution with any one of Ala, Phe, Gly, His, Ile, Leu, Met, Thr, Val, and Tyr at position 247;
amino acid substitution with any one of Glu, His, Gln, and Tyr at position 249;
amino acid substitution with either Glu or Gln at position 250;
amino acid substitution with Phe at position 251;

amino acid substitution with any one of Phe, Met, and Tyr at position 254;
amino acid substitution with any one of Glu, Leu, and Tyr at position 255;
amino acid substitution with any one of Ala, Met, and Pro at position 256;
amino acid substitution with any one of Asp, Glu, His, Ser, and Tyr at position 258;
amino acid substitution with any one of Asp, Glu, His, and Tyr at position 260;
amino acid substitution with any one of Ala, Glu, Phe, Ile, and Thr at position 262;
amino acid substitution with any one of Ala, Ile, Met, and Thr at position 263;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at position 264;
amino acid substitution with any one of Ala, Leu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Val, Trp, and Tyr at position 265;
amino acid substitution with any one of Ala, Ile, Met, and Thr at position 266;
amino acid substitution with any one of Asp, Glu, Phe, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Thr, Val, Trp, and Tyr at position 267;
amino acid substitution with any one of Asp, Glu, Phe, Gly, Ile, Lys, Leu, Met, Pro, Gln, Arg, Thr, Val, and Trp at position 268;
amino acid substitution with any one of Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 269;
amino acid substitution with any one of Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at position 270;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 271;
amino acid substitution with any one of Asp, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 272;
amino acid substitution with either Phe or Ile at position 273;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 274;
amino acid substitution with either Leu or Trp at position 275;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 276;
amino acid substitution with any one of Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, and Trp at position 278;
amino acid substitution with Ala at position 279;
amino acid substitution with any one of Ala, Gly, His, Lys, Leu, Pro, Gln, Trp, and Tyr at position 280;
amino acid substitution with any one of Asp, Lys, Pro, and Tyr at position 281;

amino acid substitution with any one of Glu, Gly, Lys, Pro, and Tyr at position 282;
amino acid substitution with any one of Ala, Gly, His, Ile, Lys, Leu, Met, Pro, Arg, and Tyr at position 283;
amino acid substitution with at position 284 is any one of Asp, Glu, Leu, Asn, Thr, and Tyr;
amino acid substitution with any one of Asp, Glu, Lys, Gln, Trp, and Tyr at position 285;
amino acid substitution with any one of Glu, Gly, Pro, and Tyr at position 286;
amino acid substitution with any one of Asn, Asp, Glu, and Tyr at position 288;
amino acid substitution with any one of Asp, Gly, His, Leu, Asn, Ser, Thr, Trp, and Tyr at position 290;
amino acid substitution with any one of Asp, Glu, Gly, His, Ile, Gln, and Thr at position 291;
amino acid substitution with any one of Ala, Asp, Glu, Pro, Thr, and Tyr at position 292;
amino acid substitution with any one of Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 293;
amino acid substitution with any one of Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 294;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 295;
amino acid substitution with any one of Ala, Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, and Val at position 296;
amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 297;
amino acid substitution with any one of Ala, Asp, Glu, Phe, His, Ile, Lys, Met, Asn, Gln, Arg, Thr, Val, Trp, and Tyr at position 298;
amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Val, Trp, and Tyr at position 299;
amino acid substitution with any one of Ala, Asp, Glu, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, and Trp at position 300;
amino acid substitution with any one of Asp, Glu, His, and Tyr at position 301;
amino acid substitution with Ile at position 302;
amino acid substitution with any one of Asp, Gly, and Tyr at position 303;
amino acid substitution with at position 304 is any one of Asp, His, Leu, Asn, and Thr;
amino acid substitution with any one of Glu, Ile, Thr, and Tyr at position 305;
amino acid substitution with any one of Ala, Asp, Asn, Thr, Val, and Tyr at position 311;
amino acid substitution with Phe at position 313;
amino acid substitution with Leu at position 315;
amino acid substitution with either Glu or Gln at position 317;

amino acid substitution with any one of His, Leu, Asn, Pro, Gln, Arg, Thr, Val, and Tyr at position 318;

amino acid substitution with any one of Asp, Phe, Gly, His, Ile, Leu, Asn, Pro, Ser, Thr, Val, Trp, and Tyr at position 320;

amino acid substitution with any one of Ala, Asp, Phe, Gly, His, Ile, Pro, Ser, Thr, Val, Trp, and Tyr at position 322;

amino acid substitution with Ile at position 323;

amino acid substitution with any one of Asp, Phe, Gly, His, Ile, Leu, Met, Pro, Arg, Thr, Val, Trp, and Tyr at position 324;

amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 325;

amino acid substitution with any one of Ala, Asp, Glu, Gly, Ile, Leu, Met, Asn, Pro, Gln, Ser, Thr, Val, Trp, and Tyr at position 326;

amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Thr, Val, Trp, and Tyr at position 327;

amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Lys, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 328;

amino acid substitution with any one of Asp, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 329;

amino acid substitution with any one of Cys, Glu, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Pro, Arg, Ser, Thr, Val, Trp, and Tyr at position 330;

amino acid substitution with any one of Asp, Phe, His, Ile, Leu, Met, Gln, Arg, Thr, Val, Trp, and Tyr at position 331;

amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Lys, Leu, Met, Asn, Pro, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at position 332;

amino acid substitution with any one of Ala, Asp, Glu, Phe, Gly, His, Ile, Leu, Met, Pro, Ser, Thr, Val, and Tyr at position 333;

amino acid substitution with any one of Ala, Glu, Phe, Ile, Leu, Pro, and Thr at position 334;

amino acid substitution with any one of Asp, Phe, Gly, His, Ile, Leu, Met, Asn, Pro, Arg, Ser, Val, Trp, and Tyr at position 335;

amino acid substitution with any one of Glu, Lys, and Tyr at position 336;

amino acid substitution with any one of Glu, His, and Asn at position 337;

amino acid substitution with any one of Asp, Phe, Gly, Ile, Lys, Met, Asn, Gln, Arg, Ser, and Thr at position 339;

amino acid substitution with either Ala or Val at position 376;

amino acid substitution with either Gly or Lys at position 377;

amino acid substitution with Asp at position 378;
amino acid substitution with Asn at position 379;
amino acid substitution with any one of Ala, Asn, and Ser at position 380;
amino acid substitution with either Ala or Ile at position 382;
amino acid substitution with Glu at position 385;
amino acid substitution with Thr at position 392;
amino acid substitution with Leu at position 396;
amino acid substitution with Lys at position 421;
amino acid substitution with Asn at position 427;
amino acid substitution with either Phe or Leu at position 428;
amino acid substitution with Met at position 429;
amino acid substitution with Trp at position 434;
amino acid substitution with Ile at position 436; and
amino acid substitution with any one of Gly, His, Ile, Leu, and Tyr at position 440,
according to EU numbering in the Fc region.

28. The method of any one of claims 24 to 27, wherein the naturally-occurring Fc region is an Fc region of any one of human IgG1, human IgG2, human IgG3, and human IgG4 in which the sugar chain attached at position 297 according to EU numbering is a fucose-containing sugar chain.

29. The method of any one of claims 24 to 28, comprising the step of modifying the Fc region so that the percentage of the Fc region to which a fucose-deficient sugar chain is attached, or bisecting *N*-acetylglucosamine is added, at position 297 according to EU numbering in the Fc region, will become higher.