CLAIMS

1. Use of an antigen-binding molecule for eliminating antigen from plasma, wherein the antigen-binding molecule comprises an antigen-binding domain whose antigen-binding activity varies depending on ion concentration conditions, and an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering.

2. The use of claim 1, wherein the Fc region has an amino acid substitution at at least one or more positions selected from the group consisting of 233, 234, 237, 264, 265, 266, 267, 268, 269, 272, 274, 296, 326, 327, 330, 331, 332, 333, 355, 356, 358, 396, 409, and 419 as indicated by EU numbering.

3. The use of claim 2, wherein the amino acids of the Fc region include any one or more of the following amino acids indicated by EU numbering:
Asp at amino acid position 233;
Tyr at amino acid position 234;
Asp at amino acid position 237;
Ile at amino acid position 264;
Glu at amino acid position 265;
any one of Phe, Met, and Leu at amino acid position 266;
any one of Ala, Glu, Gly, and Gln at amino acid position 267;
any one of Asp, Glu, and Gln at amino acid position 268;
Asp at amino acid position 269;
Asp, Phe, Ile, Met, Asn, Pro, or Gln at amino acid position 272;
Gln at amino acid position 274;
Asp or Phe at amino acid position 296;
Ala or Asp at amino acid position 326;
Gly at amino acid position 327;
Lys or Arg at amino acid position 330;
Ser at amino acid position 331;
Thr at amino acid position 332;
any one of Thr, Lys, and Arg at amino acid position 333;
Gln at amino acid position 355;
Glu at amino acid position 356;
Met at amino acid position 358;
any one of Asp, Glu, Phe, Ile, Lys, Leu, Met, Gln, Arg, and Tyr at amino acid position 396;

Arg at amino acid position 409; and
Glu at amino acid position 419.

4. The use of any one of claims 1 to 3, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity varies depending on calcium ion concentration conditions.

5. The use of claim 4, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity varies such that the antigen-binding activity under a low calcium ion concentration condition is lower than an antigen-binding activity under a high calcium ion concentration condition.

6. The use of any one of claims 1 to 3, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity varies depending on pH conditions.

7. The use of claim 6, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity varies such that the antigen-binding activity under an acidic pH range condition is lower than an antigen-binding activity under a neutral pH range condition.

8. The use of any one of claims 1 to 7, wherein the antigen-binding domain is an antibody variable region.

9. The use of any one of claims 1 to 8, wherein the Fc region is an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering in the Fc region included in any one of SEQ ID NOs: 14, 15, 16, or 17.

10. The use of any one of claims 1 to 8, wherein the FcRn-binding activity of the Fc region under an acidic pH range condition is enhanced compared to the FcRn-binding activity of the Fc region included in any one of SEQ ID NO: 14, 15, 16, or 17.

11. The use of claim 10, wherein the Fc region with enhanced binding is an Fc region having an amino acid substitution at least one or more positions selected from the group consisting of 244, 245, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 260, 262, 265, 270, 272, 279, 283, 285, 286, 288, 293, 303, 305, 307, 308, 309, 311, 312, 314, 316, 317, 318, 332, 339, 340, 341, 343, 356, 360, 362, 375, 376, 377, 378, 380, 382, 385, 386, 387, 388, 389, 400, 413, 415, 423, 424, 427, 428, 430, 431, 433, 434, 435, 436, 438, 439, 440, 442, and 447, as indicated by EU

numbering, in the amino acid sequence of the Fc region included in any one of SEQ ID NO: 14, 15, 16, or 17.

12. The use of claim 11, wherein the Fc region with enhanced binding comprises at least one or more amino acids selected from the group consisting of:
Leu at amino acid position 244;
Arg at amino acid position 245;
Pro at amino acid position 249;
Gln or Glu at amino acid position 250;
any one of Arg, Asp, Glu, and Leu at amino acid position 251;
any one of Phe, Ser, Thr, and Tyr at amino acid position 252;
Ser or Thr at amino acid position 254;
any one of Arg, Gly, Ile, and Leu at amino acid position 255;
any one of Ala, Arg, Asn, Asp, Gln, Glu, Pro, and Thr at amino acid position 256;
any one of Ala, Ile, Met, Asn, Ser, and Val at amino acid position 257;
Asp at amino acid position 258;
Ser at amino acid position 260;
Leu at amino acid position 262;
Lys at amino acid position 270;
Leu or Arg at amino acid position 272;
any one of Ala, Asp, Gly, His, Met, Asn, Gln, Arg, Ser, Thr, Trp, and Tyr at amino acid position 279;
any one of Ala, Asp, Phe, Gly, His, Ile, Lys, Leu, Asn, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at amino acid position 283;
Asn at amino acid position 285;
Phe at amino acid position 286;
Asn or Pro at amino acid position 288;
Val at amino acid position 293;
any one of Ala, Glu, Gln, and Met at amino acid position 307;
any one of Ile, Pro, and Thr at amino acid position 308;
Pro at amino acid position 309;
any one of Ala, Glu, Ile, Lys, Leu, Met, Ser, Val, and Trp at amino acid position 311;
any one of Ala, Asp, and Pro at amino acid position 312;
Ala or Leu at amino acid position 314;
Lys at amino acid position 316;
Pro at amino acid position 317;

Asn or Thr at amino acid position 318;
any one of Phe, His, Lys, Leu, Met, Arg, Ser, and Trp at amino acid position 332;
any one of Asn, Thr, and Trp at amino acid position 339;
Pro at amino acid position 341;
any one of Glu, His, Lys, Gln, Arg, Thr, or Tyr at amino acid position 343;
Arg at amino acid position 375;
any one of Gly, Ile, Met, Pro, Thr, and Val at amino acid position 376;
Lys at amino acid position 377;
any one of Asp, Asn, and Val at amino acid position 378;
any one of Ala, Asn, Ser, and Thr at amino acid position 380;
any one of Phe, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 382;
any one of Ala, Arg, Asp, Gly, His, Lys, Ser, and Thr at amino acid position 385;
any one of Arg, Asp, Ile, Lys, Met, Pro, Ser, and Thr at amino acid position 386;
any one of Ala, Arg, His, Pro, Ser, and Thr at amino acid position 387;
any one of Asn, Pro, and Ser at amino acid position 389;
Asn at amino acid position 423;
Asn at amino acid position 427;
any one of Leu, Met, Phe, Ser, and Thr at amino acid position 428;
any one of Ala, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, and Tyr at amino acid position 430;
His or Asn at amino acid position 431;
any one of Arg, Gln, His, Ile, Lys, Pro, and Ser at amino acid position 433;
any one of Ala, Gly, His, Phe, Ser, Trp, and Tyr at amino acid position 434;
any one of Arg, Asn, His, Ile, Leu, Lys, Met, and Thr at amino acid position 436;
any one of Lys, Leu, Thr, and Trp at amino acid position 438;
Lys at amino acid position 440; and
Lys at amino acid position 442
as indicated by EU numbering, in the amino acid sequence of the Fc region included in any one of SEQ ID NO: 14, 15, 16, or 17.

13. The use of any one of claims 1 to 12, wherein the antigen-binding molecule is an antibody.

14. A pharmaceutical composition comprising an antigen-binding molecule which comprises an antigen-binding domain whose antigen-binding activity varies depending on ion concentration conditions, and an Fc region in which the amino acid at position 238 is Asp and the amino acid at

position 271 is Gly as indicated by EU numbering.

15. The pharmaceutical composition of claim 14, wherein the Fc region has an amino acid substitution at at least one or more positions selected from the group consisting of 233, 234, 237, 264, 265, 266, 267, 268, 269, 272, 274, 296, 326, 327, 330, 331, 332, 333, 355, 356, 358, 396, 409, and 419 as indicated by EU numbering.

16. The pharmaceutical composition of claim 15, wherein the amino acids of the Fc region include any one or more of the following amino acids indicated by EU numbering:
Asp at amino acid position 233;
Tyr at amino acid position 234;
Asp at amino acid position 237;
Ile at amino acid position 264;
Glu at amino acid position 265;
any one of Phe, Met, and Leu at amino acid position 266;
any one of Ala, Glu, Gly, and Gln at amino acid position 267;
any one of Asp, Glu, and Gln at amino acid position 268;
Asp at amino acid position 269;
any one of Asp, Phe, Ile, Met, Asn, Pro, and Gln at amino acid position 272;
Gln at amino acid position 274;
Asp or Phe at amino acid position 296;
Ala or Asp at amino acid position 326;
Lys or Arg at amino acid position 330;
Gly at amino acid position 327;
Ser at amino acid position 331;
Thr at amino acid position 332;
any one of Thr, Lys, and Arg at amino acid position 333;
Gln at amino acid position 355;
Glu at amino acid position 356;
Met at amino acid position 358;
any one of Asp, Glu, Phe, Ile, Lys, Leu, Met, Gln, Arg, and Tyr at amino acid position 396;
Arg at amino acid position 409; and
Glu at amino acid position 419.

17. A method of producing an antigen-binding molecule, comprising the steps of (a) to (e) below:

(a) obtaining an antigen-binding domain whose antigen-binding activity varies depending on ion concentration conditions;

(b) obtaining a gene encoding the antigen-binding domain selected in step (a);

(c) operably linking the gene obtained in step (b) with a gene encoding an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering;

(d) culturing host cells containing the gene operably linked in step (c); and

(e) isolating an antigen-binding molecule from the culture solution obtained in step (d).

18. The production method of claim 17, wherein the Fc region has an amino acid substitution at at least one or more positions selected from the group consisting of 233, 234, 237, 264, 265, 266, 267, 268, 269, 272, 274, 296, 326, 327, 330, 331, 332, 333, 355, 356, 358, 396, 409, and 419 as indicated by EU numbering.

19. The method of claim 18, wherein the amino acids of the Fc region include any one or more of the following amino acids indicated by EU numbering:

Asp at amino acid position 233;

Tyr at amino acid position 234;

Asp at amino acid position 237;

Ile at amino acid position 264;

Glu at amino acid position 265;

any one of Phe, Met, and Leu at amino acid position 266;

any one of Ala, Glu, Gly, and Gln at amino acid position 267;

any one of Asp, Glu, and Gln at amino acid position 268;

Asp at amino acid position 269;

any one of Asp, Phe, Ile, Met, Asn, Pro, and Gln at amino acid position 272;

Gln at amino acid position 274;

Asp or Phe at amino acid position 296;

Ala or Asp at amino acid position 326;

Gly at amino acid position 327;

Lys or Arg at amino acid position 330;

Ser at amino acid position 331;

Thr at amino acid position 332;

any one of Thr, Lys, and Arg at amino acid position 333;

Gln at amino acid position 355;

Glu at amino acid position 356;

Met at amino acid position 358;
any one of Asp, Glu, Phe, Ile, Lys, Leu, Met, Gln, Arg, and Tyr at amino acid position 396;
Arg at amino acid position 409; and
Glu at amino acid position 419.

20. A method of producing a pharmaceutical composition comprising an antigen-binding molecule, which comprises the steps of (a) to (e) below:
(a) obtaining an antigen-binding domain whose antigen-binding activity varies depending on ion concentration conditions;
(b) obtaining a gene encoding the antigen-binding domain selected in step (a);
(c) operably linking the gene obtained in step (b) with a gene encoding an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering;
(d) culturing host cells containing the gene operably linked in step (c); and
(e) isolating the antigen-binding molecule from the culture solution obtained in step (d).

21. The production method of claim 20, wherein the Fc region has an amino acid substitution at at least one or more positions selected from the group consisting of 233, 234, 237, 264, 265, 266, 267, 268, 269, 272, 274, 296, 326, 327, 330, 331, 332, 333, 355, 356, 358, 396, 409, and 419 as indicated by EU numbering.

22. The production method of claim 21, wherein the amino acids of the Fc region include any one or more of the following amino acids indicated by EU numbering:
Asp at amino acid position 233;
Tyr at amino acid position 234;
Asp at amino acid position 237;
Ile at amino acid position 264;
Glu at amino acid position 265;
any one of Phe, Met, and Leu at amino acid position 266;
any one of Ala, Glu, Gly, and Gln at amino acid position 267;
any one of Asp, Glu, and Gln at amino acid position 268;
Asp at amino acid position 269;
any one of Asp, Phe, Ile, Met, Asn, Pro, and Gln at amino acid position 272;
Gln at amino acid position 274;
Asp or Phe at amino acid position 296;
Ala or Asp at amino acid position 326;

Gly at amino acid position 327;
Lys or Arg at amino acid position 330;
Ser at amino acid position 331;
Thr at amino acid position 332;
any one of Thr, Lys, and Arg at amino acid position 333;
Gln at amino acid position 355;
Glu at amino acid position 356;
Met at amino acid position 358;
any one of Asp, Glu, Phe, Ile, Lys, Leu, Met, Gln, Arg, and Tyr at amino acid position 396;
Arg at amino acid position 409; and
Glu at amino acid position 419.

CLAIMS

1. An antigen-binding molecule, wherein the antigen-binding molecule comprises an antigen-binding domain whose antigen-binding activity varies depending on ion concentration conditions, and an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering, wherein the Fc region is an Fc region of IgG-type immunoglobulins, wherein the ion concentration conditions are calcium ion concentration conditions and/or pH conditions.

2. The antigen-binding molecule of claim 1, wherein the Fc region has an amino acid substitution at at least one or more positions selected from the group consisting of 233, 234, 237, 264, 265, 266, 267, 268, 269, 272, 274, 296, 326, 327, 330, 331, 332, 333, 355, 356, 358, 396, 409, and 419 as indicated by EU numbering.

3. The antigen-binding molecule of claim 2, wherein the amino acids of the Fc region include any one or more of the following amino acids indicated by EU numbering:
Asp at amino acid position 233;
Tyr at amino acid position 234;
Asp at amino acid position 237;
Ile at amino acid position 264;
Glu at amino acid position 265;
any one of Phe, Met, and Leu at amino acid position 266;
any one of Ala, Glu, Gly, and Gln at amino acid position 267;
any one of Asp, Glu, and Gln at amino acid position 268;
Asp at amino acid position 269;
Asp, Phe, Ile, Met, Asn, Pro, or Gln at amino acid position 272;
Gln at amino acid position 274;
Asp or Phe at amino acid position 296;
Ala or Asp at amino acid position 326;
Gly at amino acid position 327;
Lys or Arg at amino acid position 330;
Ser at amino acid position 331;
Thr at amino acid position 332;
any one of Thr, Lys, and Arg at amino acid position 333;
Gln at amino acid position 355;

Glu at amino acid position 356;
Met at amino acid position 358;
any one of Asp, Glu, Phe, Ile, Lys, Leu, Met, Gln, Arg, and Tyr at amino acid position 396;
Arg at amino acid position 409; and
Glu at amino acid position 419.

4. The antigen-binding molecule of claims 1 to 3, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity varies such that the antigen-binding activity under a low calcium ion concentration condition is lower than an antigen-binding activity under a high calcium ion concentration condition.

5. The antigen-binding molecule of claim s 1 to 4, wherein the antigen-binding domain is an antigen-binding domain whose antigen-binding activity varies such that the antigen-binding activity under an acidic pH range condition is lower than an antigen-binding activity under a neutral pH range condition.

6. The antigen-binding molecule of any one of claims 1 to 5, wherein the antigen-binding domain is an antibody variable region.

7. The antigen-binding molecule of any one of claims 1 to 6, wherein the Fc region is an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering in the Fc region included in any one of SEQ ID NOs: 14, 15, 16, or 17.

8. The antigen-binding molecule of any one of claims 1 to 7, wherein the FcRn-binding activity of the Fc region under an acidic pH range condition is enhanced compared to the FcRn-binding activity of the Fc region included in any one of SEQ ID NO: 14, 15, 16, or 17.

9. The antigen-binding molecule of claim 8, wherein the Fc region with enhanced binding is an Fc region having an amino acid substitution at at least one or more positions selected from the group consisting of 244, 245, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 260, 262, 265, 270, 272, 279, 283, 285, 286, 288, 293, 303, 305, 307, 308, 309, 311, 312, 314, 316, 317, 318, 332, 339, 340, 341, 343, 356, 360, 362, 375, 376, 377, 378, 380, 382, 385, 386, 387, 388, 389, 400, 413, 415, 423, 424, 427,

428, 430, 431, 433, 434, 435, 436, 438, 439, 440, 442, and 447, as indicated by EU numbering, in the amino acid sequence of the Fc region included in any one of SEQ ID NO: 14, 15, 16, or 17.

10. The antigen-binding molecule of claim 9, wherein the Fc region with enhanced binding comprises at least one or more amino acids selected from the group consisting of:
Leu at amino acid position 244;
Arg at amino acid position 245;
Pro at amino acid position 249;
Gln or Glu at amino acid position 250;
any one of Arg, Asp, Glu, and Leu at amino acid position 251;
any one of Phe, Ser, Thr, and Tyr at amino acid position 252;
Ser or Thr at amino acid position 254;
any one of Arg, Gly, Ile, and Leu at amino acid position 255;
any one of Ala, Arg, Asn, Asp, Gln, Glu, Pro, and Thr at amino acid position 256;
any one of Ala, Ile, Met, Asn, Ser, and Val at amino acid position 257;
Asp at amino acid position 258;
Ser at amino acid position 260;
Leu at amino acid position 262;
Lys at amino acid position 270;
Leu or Arg at amino acid position 272;
any one of Ala, Asp, Gly, His, Met, Asn, Gln, Arg, Ser, Thr, Trp, and Tyr at amino acid position 279;
any one of Ala, Asp, Phe, Gly, His, Ile, Lys, Leu, Asn, Pro, Gln, Arg, Ser, Thr, Trp, and Tyr at amino acid position 283;
Asn at amino acid position 285;
Phe at amino acid position 286;
Asn or Pro at amino acid position 288;
Val at amino acid position 293;
any one of Ala, Glu, Gln, and Met at amino acid position 307;
any one of Ile, Pro, and Thr at amino acid position 308;
Pro at amino acid position 309;
any one of Ala, Glu, Ile, Lys, Leu, Met, Ser, Val, and Trp at amino acid position 311;
any one of Ala, Asp, and Pro at amino acid position 312;
Ala or Leu at amino acid position 314;

Lys at amino acid position 316;
Pro at amino acid position 317;
Asn or Thr at amino acid position 318;
any one of Phe, His, Lys, Leu, Met, Arg, Ser, and Trp at amino acid position 332;
any one of Asn, Thr, and Trp at amino acid position 339;
Pro at amino acid position 341;
any one of Glu, His, Lys, Gln, Arg, Thr, or Tyr at amino acid position 343;
Arg at amino acid position 375;
any one of Gly, Ile, Met, Pro, Thr, and Val at amino acid position 376;
Lys at amino acid position 377;
any one of Asp, Asn, and Val at amino acid position 378;
any one of Ala, Asn, Ser, and Thr at amino acid position 380;
any one of Phe, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, Trp, and Tyr at amino acid position 382;
any one of Ala, Arg, Asp, Gly, His, Lys, Ser, and Thr at amino acid position 385;
any one of Arg, Asp, Ile, Lys, Met, Pro, Ser, and Thr at amino acid position 386;
any one of Ala, Arg, His, Pro, Ser, and Thr at amino acid position 387;
any one of Asn, Pro, and Ser at amino acid position 389;
Asn at amino acid position 423;
Asn at amino acid position 427;
any one of Leu, Met, Phe, Ser, and Thr at amino acid position 428;
any one of Ala, Phe, Gly, His, Ile, Lys, Leu, Met, Asn, Gln, Arg, Ser, Thr, Val, and Tyr at amino acid position 430;
His or Asn at amino acid position 431;
any one of Arg, Gln, His, Ile, Lys, Pro, and Ser at amino acid position 433;
any one of Ala, Gly, His, Phe, Ser, Trp, and Tyr at amino acid position 434;
any one of Arg, Asn, His, Ile, Leu, Lys, Met, and Thr at amino acid position 436;
any one of Lys, Leu, Thr, and Trp at amino acid position 438;
Lys at amino acid position 440; and
Lys at amino acid position 442
as indicated by EU numbering, in the amino acid sequence of the Fc region included in any one of SEQ ID NO: 14, 15, 16, or 17.

11. The antigen-binding molecule of any one of claims 1 to 10, wherein the antigen-binding molecule is an antibody.

12. A pharmaceutical composition comprising an antigen-binding molecule which comprises an antigen-binding domain whose antigen-binding activity varies depending on ion concentration conditions, and an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering, wherein the Fc region is an Fc region of IgG-type immunoglobulins, wherein the ion concentration conditions are calcium ion concentration conditions and/or pH conditions.

13. The pharmaceutical composition of claim 12, wherein the Fc region has an amino acid substitution at at least one or more positions selected from the group consisting of 233, 234, 237, 264, 265, 266, 267, 268, 269, 272, 274, 296, 326, 327, 330, 331, 332, 333, 355, 356, 358, 396, 409, and 419 as indicated by EU numbering.

14. The pharmaceutical composition of claim 13, wherein the amino acids of the Fc region include any one or more of the following amino acids indicated by EU numbering:
Asp at amino acid position 233;
Tyr at amino acid position 234;
Asp at amino acid position 237;
Ile at amino acid position 264;
Glu at amino acid position 265;
any one of Phe, Met, and Leu at amino acid position 266;
any one of Ala, Glu, Gly, and Gln at amino acid position 267;
any one of Asp, Glu, and Gln at amino acid position 268;
Asp at amino acid position 269;
any one of Asp, Phe, Ile, Met, Asn, Pro, and Gln at amino acid position 272;
Gln at amino acid position 274;
Asp or Phe at amino acid position 296;
Ala or Asp at amino acid position 326;
Lys or Arg at amino acid position 330;
Gly at amino acid position 327;
Ser at amino acid position 331;
Thr at amino acid position 332;
any one of Thr, Lys, and Arg at amino acid position 333;
Gln at amino acid position 355;
Glu at amino acid position 356;
Met at amino acid position 358;

any one of Asp, Glu, Phe, Ile, Lys, Leu, Met, Gln, Arg, and Tyr at amino acid position 396;
Arg at amino acid position 409; and
Glu at amino acid position 419.

15. A method of producing an antigen-binding molecule, comprising the steps of (a) to (e) below:
(a) obtaining an antigen-binding domain whose antigen-binding activity varies depending on ion concentration conditions;
(b) obtaining a gene encoding the antigen-binding domain selected in step (a);
(c) operably linking the gene obtained in step (b) with a gene encoding an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering;
(d) culturing host cells containing the gene operably linked in step (c); and
(e) isolating an antigen-binding molecule from the culture solution obtained in step (d), wherein the Fc region is an Fc region of IgG-type immunoglobulins, wherein the ion concentration conditions are calcium ion concentration conditions and/or pH conditions.

16. The production method of claim 15, wherein the Fc region has an amino acid substitution at at least one or more positions selected from the group consisting of 233, 234, 237, 264, 265, 266, 267, 268, 269, 272, 274, 296, 326, 327, 330, 331, 332, 333, 355, 356, 358, 396, 409, and 419 as indicated by EU numbering.

17. The method of claim 16, wherein the amino acids of the Fc region include any one or more of the following amino acids indicated by EU numbering:
Asp at amino acid position 233;
Tyr at amino acid position 234;
Asp at amino acid position 237;
Ile at amino acid position 264;
Glu at amino acid position 265;
any one of Phe, Met, and Leu at amino acid position 266;
any one of Ala, Glu, Gly, and Gln at amino acid position 267;
any one of Asp, Glu, and Gln at amino acid position 268;
Asp at amino acid position 269;
any one of Asp, Phe, Ile, Met, Asn, Pro, and Gln at amino acid position 272;
Gln at amino acid position 274;

Asp or Phe at amino acid position 296;
Ala or Asp at amino acid position 326;
Gly at amino acid position 327;
Lys or Arg at amino acid position 330;
Ser at amino acid position 331;
Thr at amino acid position 332;
any one of Thr, Lys, and Arg at amino acid position 333;
Gln at amino acid position 355;
Glu at amino acid position 356;
Met at amino acid position 358;
any one of Asp, Glu, Phe, Ile, Lys, Leu, Met, Gln, Arg, and Tyr at amino acid position 396;
Arg at amino acid position 409; and
Glu at amino acid position 419.

18. A method of producing a pharmaceutical composition comprising an antigen-binding molecule, which comprises the steps of (a) to (e) below:
(a) obtaining an antigen-binding domain whose antigen-binding activity varies depending on ion concentration conditions;
(b) obtaining a gene encoding the antigen-binding domain selected in step (a);
(c) operably linking the gene obtained in step (b) with a gene encoding an Fc region in which the amino acid at position 238 is Asp and the amino acid at position 271 is Gly as indicated by EU numbering;
(d) culturing host cells containing the gene operably linked in step (c); and
(e) isolating the antigen-binding molecule from the culture solution obtained in step (d) , wherein the Fc region is an Fc region of IgG-type immunoglobulins, wherein the ion concentration conditions are calcium ion concentration conditions and/or pH conditions.

19. The production method of claim 18, wherein the Fc region has an amino acid substitution at at least one or more positions selected from the group consisting of 233, 234, 237, 264, 265, 266, 267, 268, 269, 272, 274, 296, 326, 327, 330, 331, 332, 333, 355, 356, 358, 396, 409, and 419 as indicated by EU numbering.

20. The production method of claim 19, wherein the amino acids of the Fc region include any one or more of the following amino acids indicated by EU numbering:

Asp at amino acid position 233;
Tyr at amino acid position 234;
Asp at amino acid position 237;
Ile at amino acid position 264;
Glu at amino acid position 265;
any one of Phe, Met, and Leu at amino acid position 266;
any one of Ala, Glu, Gly, and Gln at amino acid position 267;
any one of Asp, Glu, and Gln at amino acid position 268;
Asp at amino acid position 269;
any one of Asp, Phe, Ile, Met, Asn, Pro, and Gln at amino acid position 272;
Gln at amino acid position 274;
Asp or Phe at amino acid position 296;
Ala or Asp at amino acid position 326;
Gly at amino acid position 327;
Lys or Arg at amino acid position 330;
Ser at amino acid position 331;
Thr at amino acid position 332;
any one of Thr, Lys, and Arg at amino acid position 333;
Gln at amino acid position 355;
Glu at amino acid position 356;
Met at amino acid position 358;
any one of Asp, Glu, Phe, Ile, Lys, Leu, Met, Gln, Arg, and Tyr at amino acid position 396;
Arg at amino acid position 409; and
Glu at amino acid position 419.