Claims

1. An Fc region variant whose amino acid at position 238 according to EU numbering is Asp, and which comprises at least one amino acid selected from the amino acid group consisting of Asp at amino acid position 268, Gly at amino acid position 271, wherein binding activity of the variant to Fcγ receptors [KD value for FcγRIIa (type R) of a polypeptide comprising an Fc region variant]/[KD value for FcγRIIb of a polypeptide comprising an Fc region variant] has a value which is 20.0 or greater.

2. The Fc region variant of claim 1, wherein the value for [KD value for FcγRIIb of a polypeptide comprising an Fc region to which an amino acid alteration(s) has not been introduced]/[KD value for FcγRIIb of a polypeptide comprising an Fc region variant] is 15.0 or more.

3. The Fc region variant of claim 1 or 2, wherein the value for [KD value for FcγRIIb of a polypeptide comprising an Fc region to which an amino acid alteration(s) has not been introduced]/[KD value for FcγRIIb of a polypeptide comprising an Fc region variant] is 50.0 or more.

4. The Fc region variant of any one of claims 1 to 3, wherein the value for [KD value for FcγRIIb of a polypeptide comprising an Fc region to which an amino acid alteration(s) has not been introduced]/[KD value for FcγRIIb of a polypeptide comprising an Fc region variant] is 100.0 or more.

5. The Fc region variant of any one of claims 1 to 4, wherein the Fc region variant comprises any one of the following set of amino acid alterations of (a) to (x):

(a) amino acid alterations at positions 238, 233, 237, 268, 271, 296, and 330 (EU numbering) of an Fc region;

(b) amino acid alterations at positions 238, 237, 268, 271, 296, and 330 (EU numbering) of an Fc region;

(c) amino acid alterations at positions 238, 233, 237, 268, 271, 296, 330, and 332 (EU numbering) of an Fc region;

(d) amino acid alterations at positions 238, 233, 237, 264, 267, 268, 271, and 330 (EU numbering) of an Fc region;

(e) amino acid alterations at positions 238, 233, 237, 267, 268, 271, 296, 330, and 332 (EU numbering) of an Fc region;

(f) amino acid alterations at positions 238, 237, 267, 268, 271, 296, 330, and 332 (EU numbering) of an Fc region;

(g) amino acid alterations at positions 238, 233, 237, 268, 271, 296, 327, and 330 (EU numbering) of an Fc region;

(h) amino acid alterations at positions 238, 233, 237, 264, 267, 268, and 271 (EU numbering) of an Fc region;

(i) amino acid alterations at positions 238, 233, 237, 264, 267, 268, 271, 296, and 330 (EU numbering) of an Fc region;

(j) amino acid alterations at positions 238, 233, 237, 264, 267, 268, 271, 296, 330, and 396 (EU numbering) of an Fc region;

(k) amino acid alterations at positions 238, 237, 264, 267, 268, 271, and 330 (EU numbering) of an Fc region;

(l) amino acid alterations at positions 238, 237, 264, 267, 268, 271, 296, and 330 (EU numbering) of an Fc region;

(m) amino acid alterations at positions 238, 264, 267, 268, and 271 (EU numbering) of an Fc region;

(n) amino acid alterations at positions 238, 264, 267, 268, 271, and 296 (EU numbering) of an Fc region;

(o) amino acid alterations at positions 238, 237, 267, 268, 271, 296, and 330 (EU numbering) of an Fc region;

(p) amino acid alterations at positions 238, 233, 237, 264, 267, 268, 271, 330, and 396 (EU numbering) of the Fc region;

(q) amino acid alterations at positions 238, 233, 237, 264, 267, 268, 271, 296, 327, 330, and 396 (EU numbering) of an Fc region;

(r) amino acid alterations at positions 238, 233, 237, 264, 267, 268, 271, 272, and 296 (EU numbering) of an Fc region;

(s) amino acid alterations at positions 238, 237, 264, 267, 268, 271, 272, and 330 (EU numbering) of an Fc region;

(t) amino acid alterations at positions 238, 237, 264, 267, 268, 271, 272, 296, and 330 (EU numbering) of an Fc region;

(u) amino acid alterations at positions 238, 233, 264, 267, 268, and 271 (EU numbering) of an Fc region;

(v) amino acid alterations at positions 238, 237, 267, 268, 271, 296, and 330 (EU numbering) of an Fc region;

(w) amino acid alterations at positions 238, 264, 267, 268, 271, 272, and 296 (EU numbering) of an Fc region; and

(x) amino acid alterations at positions 238, 233, 264, 267, 268, 271, and 296 (EU numbering) of an Fc region.

6. The Fc region variant of any one of claims 1 to 5, wherein the Fc region variant comprises any one of the following amino acid sequences of (a) to (x):

(a) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 268 is Asp, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(b) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 237 is Asp, the amino acid at position 268 is Asp or Glu, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(c) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 268 is Asp, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, the amino acid at position 330 is Arg, and the amino acid at position 332 is Thr, according to EU numbering, in an Fc region;

(d) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Gly or Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(e) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, the amino acid at position 330 is Arg, and the amino acid at position 332 is Thr, according to EU numbering, in an Fc region;

(f) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 237 is Asp, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, the amino acid at position 330 is Arg, and the amino acid at position 332 is Thr, according to EU numbering, in an Fc region;

(g) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 268 is Asp, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, the amino acid at

position 327 is Gly, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(h) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, and the amino acid at position 271 is Gly, according to EU numbering, in an Fc region;

(i) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(j) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, the amino acid at position 330 is Arg, and the amino acid at position 396 is Met or Leu, according to EU numbering, in an Fc region;

(k) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(l) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(m) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, and the amino acid at position 271 is Gly, according to EU numbering, in an Fc region;

(n) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, and the amino acid at position 296 is Asp, according to EU numbering, in an Fc region;

(o) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 237 is Asp, the amino acid at position 267 is Ala or Gly, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(p) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 330 is Arg, and the amino acid at position 396 is Met or Leu, according to EU numbering, in an Fc region;

(q) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, the amino acid at position 327 is Gly, the amino acid at position 330 is Arg, and the amino acid at position 396 is Met, according to EU numbering, in an Fc region;

(r) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 272 is Asp, and the amino acid at position 296 is Asp, according to EU numbering, in an Fc region;

(s) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 272 is Pro, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(t) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 237 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, the amino acid at position 272 is Pro, the amino acid at position 296 is Asp, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(u) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, and the amino acid at position 271 is Gly, according to EU numbering, in an Fc region;

(v) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 237 is Asp, the amino acid at position 267 is Gly, the amino acid at position 268 is Asp, the amino acid at position 271 is Gly, the amino acid at position 296 is Asp, and the amino acid at position 330 is Arg, according to EU numbering, in an Fc region;

(w) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu,

the amino acid at position 271 is Gly, the amino acid at position 272 is Asp, and the amino acid at position 296 is Asp, according to EU numbering, in an Fc region; and

(x) an amino acid sequence in which the amino acid at position 238 is Asp, the amino acid at position 233 is Asp, the amino acid at position 264 is Ile, the amino acid at position 267 is Ala, the amino acid at position 268 is Glu, the amino acid at position 271 is Gly, and the amino acid at position 296 is Asp, according to EU numbering, in an Fc region.

7. A polypeptide comprising at least two Fc region variants of any one of claims 1 to 6, wherein the two Fc region variants are associated.

8. The polypeptide of claim 7, wherein the amino acid sequences of the two associated Fc region variants in the polypeptide are the same.

9. The polypeptide of claim 7, wherein the amino acid sequences of the two associated Fc region variants in the polypeptide are different.

10. The polypeptide of claim 9, wherein the amino acid sequences of the two associated Fc region variants have different amino acid(s) at at least one amino acid position selected from positions 235, 236, 237, and 239 according to EU numbering in the Fc region variant.

11. The polypeptide of claim 10, wherein one of the amino acid sequences of the two associated Fc region variants is an amino acid sequence comprising at least one amino acid selected from Asp, Gln, Glu, or Thr at amino acid position 235, Asn at amino acid position 236, Phe or Trp at amino acid position 237, and Asp or Glu at amino acid position 239 according to EU numbering.

12. The polypeptide of any one of claims 7 to 11, wherein the polypeptide comprising the Fc region variant is an IgG antibody.

13. The polypeptide of any one of claims 7 to 11, wherein the polypeptide comprising the Fc region variant is an Fc fusion protein molecule.

14. A pharmaceutical composition comprising the polypeptide of any one of claims 7 to 13.