comparison with a parent polypeptide. As a result, the present inventors discovered that a polypeptide comprising an antibody Fc region that comprises an alteration produced by substituting Pro at position 238 (EU numbering) with Asp or Leu at position 328 (EU numbering) with Glu enhances FcγRIIb-binding activity, and decreases Fc region-mediated binding activity towards both allotypes of FcγRIIa, types H and R. Furthermore, the present inventors discovered that a polypeptide comprising an antibody Fc region that comprises an alteration of substituting Pro at position 238 (EU numbering) with Asp and several other alterations that enhance FcγRIIb-binding activity, and maintains or decreases Fc region-mediated binding activities towards both allotypes of FcγRIIa, types H and R.

In one aspect, there is provided a polypeptide variant comprising an antibody Fc region with at least one amino acid alteration, which has maintained or decreased binding activities towards FcγRIIa (type R) and FcγRIIa (type H), and enhanced FcγRIIb-binding activity in comparison with a parent polypeptide, and wherein the value of [KD value of the polypeptide variant for FcγRIIa (type H)] / [KD value of the polypeptide variant for FcγRIIb] is 4.2 or more, wherein the amino acid alteration comprises substitution of Pro at position 238 (EU numbering) with Asp.

In another aspect, there is provided a pharmaceutical composition comprising the polypeptide of the present disclosure.

In another aspect, there is provided an agent for use in suppressing activation of B cells, mast cells, dendritic cells, and/or basophils, which comprises the polypeptide of the present disclosure or the pharmaceutical composition of the present disclosure.

In yet another aspect, there is provided an agent for use in treating or preventing an immunological inflammatory disease, which comprises the polypeptide of the present disclosure or the pharmaceutical composition of the present disclosure.

In a further aspect, there is provided an agent for use in treating a disease, which comprises the polypeptide of the present disclosure or the pharmaceutical composition of the present disclosure, wherein the disease is a disease with deficiency of a biologically essential protein.

In yet a further aspect, there is provided an antiviral agent comprising the polypeptide of the present disclosure or the pharmaceutical composition of the present disclosure.

In yet a further aspect, there is provided use of a polypeptide of the present disclosure or the pharmaceutical composition of the present disclosure, in the manufacture of a medicament for treating or preventing an immunological inflammatory disease.

In yet a further aspect, there is provided use of a polypeptide of the present disclosure or the pharmaceutical composition of the present disclosure, in the manufacture of a medicament for suppressing activation of B cells, mast cells, dendritic cells, and/or basophils.

More specifically, the present disclosure provides the following:

[1] a polypeptide variant comprising an antibody Fc region with at least one amino acid

alteration, which has maintained or decreased binding activities towards FcγRIIa (type R) and FcγRIIa (type H), and enhanced FcγRIIb-binding activity in comparison with a parent polypeptide, and wherein the value of [KD value of the polypeptide variant for FcγRIIa (type R)] / [KD value of the polypeptide variant for FcγRIIb] is 1.2 or more;

[2] the polypeptide of [1], wherein the value of [KD value of the polypeptide variant for FcγRIIa (type H)] / [KD value of the polypeptide variant for FcγRIIb] is 4.2 or more;

[3] the polypeptide of [1] or [2], wherein the value of [KD value of the parent polypeptide for FcγRIIb] / [KD value of the polypeptide variant for FcγRIIb] is 1.6 or more;

[4] the polypeptide of any one of [1] to [3], wherein the value of [KD value of the stronger of the binding activities of the polypeptide variant towards FcγRIIa (type R) and FcγRIIa (type H)] / [KD value of the stronger of the binding activities of the parent polypeptide towards FcγRIIa (type R) and FcγRIIa (type H)] is 0.7 or more;

[5] the polypeptide of any one of [1] to [4], which has maintained or decreased FcγRIIIa-binding activity compared with that of a parent polypeptide;

[6] the polypeptide of any one of [1] to [5], which has maintained or decreased FcγRIa-binding activity compared with that of a parent polypeptide;

[7] the polypeptide of any one of [1] to [6], wherein an amino acid alteration is substitution of Pro at position 238 (EU numbering) with Asp or substitution of Leu at position 328 (EU numbering) with Glu;

[8] the polypeptide of any one of [1] to [7], wherein an amino acid alteration is substitution of Pro at position 238 (EU numbering) with Asp, and at least one substitution selected from the group consisting of:

substitution of Gly at position 237 (EU numbering) with Trp;

substitution of Gly at position 237 (EU numbering) with Phe;

substitution of Ser at position 267 (EU numbering) with Val;

CLAIMS

1. A polypeptide variant comprising an antibody Fc region with at least one amino acid alteration, which has maintained or decreased binding activities towards FcγRIIa (type R) and FcγRIIa (type H), and enhanced FcγRIIb-binding activity in comparison with a parent polypeptide, and wherein the value of [KD value of the polypeptide variant for FcγRIIa (type H)] / [KD value of the polypeptide variant for FcγRIIb] is 4.2 or more, wherein the amino acid alteration comprises substitution of Pro at position 238 (EU numbering) with Asp.

2. The polypeptide of claim 1, wherein the value of [KD value of the parent polypeptide for FcγRIIb] / [KD value of the polypeptide variant for FcγRIIb] is 1.6 or more.

3. The polypeptide of claim 1 or 2, wherein the value of [KD value of the stronger of the binding activities of the polypeptide variant towards FcγRIIa (type R) and FcγRIIa (type H)] / [KD value of the stronger of the binding activities of the parent polypeptide towards FcγRIIa (type R) and FcγRIIa (type H)] is 0.7 or more.

4. The polypeptide of any one of claims 1 to 3, which has maintained or decreased FcγRIIIa-binding activity compared with that of a parent polypeptide.

5. The polypeptide of any one of claims 1 to 4, which has maintained or decreased FcγRIa-binding activity compared with that of a parent polypeptide.

6. The polypeptide of any one of claims 1 to 5, wherein the polypeptide further

comprises an additional amino acid alteration selected from the group consisting of:

substitution of Gly at position 237 (EU numbering) with Trp;

substitution of Gly at position 237 (EU numbering) with Phe;

substitution of Ser at position 267 (EU numbering) with Val;

substitution of Ser at position 267 (EU numbering) with Gln;

substitution of His at position 268 (EU numbering) with Asn;

substitution of Pro at position 271 (EU numbering) with Gly;

substitution of Lys at position 326 (EU numbering) with Leu;

substitution of Lys at position 326 (EU numbering) with Gln;

substitution of Lys at position 326 (EU numbering) with Glu;

substitution of Lys at position 326 (EU numbering) with Met;

substitution of Ser at position 239 (EU numbering) with Asp;

substitution of Ser at position 267 (EU numbering) with Ala;

substitution of Leu at position 234 (EU numbering) with Trp;

substitution of Leu at position 234 (EU numbering) with Tyr;

substitution of Gly at position 237 (EU numbering) with Ala;

substitution of Gly at position 237 (EU numbering) with Asp;

substitution of Gly at position 237 (EU numbering) with Glu;

substitution of Gly at position 237 (EU numbering) with Leu;

substitution of Gly at position 237 (EU numbering) with Met;

substitution of Gly at position 237 (EU numbering) with Tyr;

substitution of Ala at position 330 (EU numbering) with Lys;

substitution of Ala at position 330 (EU numbering) with Arg;

substitution of Glu at position 233 (EU numbering) with Asp;

substitution of His at position 268 (EU numbering) with Asp;

substitution of His at position 268 (EU numbering) with Glu;
substitution of Lys at position 326 (EU numbering) with Asp;
substitution of Lys at position 326 (EU numbering) with Ser;
substitution of Lys at position 326 (EU numbering) with Thr;
substitution of Val at position 323 (EU numbering) with Ile;
substitution of Val at position 323 (EU numbering) with Leu;
substitution of Val at position 323 (EU numbering) with Met;
substitution of Tyr at position 296 (EU numbering) with Asp;
substitution of Lys at position 326 (EU numbering) with Ala;
substitution of Lys at position 326 (EU numbering) with Asn; and
substitution of Ala at position 330 (EU numbering) with Met.

7. The polypeptide of any one of claims 1 to 6, wherein the polypeptide comprising the antibody Fc region is an IgG antibody.

8. The polypeptide of any one of claims 1 to 6, wherein the polypeptide comprising the antibody Fc region is an Fc fusion protein molecule.

9. A pharmaceutical composition comprising the polypeptide of any one of claims 1 to 8.

10. An agent for use in suppressing activation of B cells, mast cells, dendritic cells, and/or basophils, which comprises the polypeptide of any one of claims 1 to 8 or the pharmaceutical composition of claim 9.

11. An agent for use in treating or preventing an immunological inflammatory disease, which comprises the polypeptide of any one of claims 1 to 8 or the pharmaceutical composition of claim 9.

12. The agent of claim 11, wherein the immunological inflammatory disease is an autoimmune disease and is a disease which may be caused by production of an antibody against an autoantigen.

13. An agent for use in treating a disease, which comprises the polypeptide of any one of claims 1 to 8 or the pharmaceutical composition of claim 9, wherein the disease is a disease with deficiency of a biologically essential protein.

14. An antiviral agent comprising the polypeptide of any one of claims 1 to 8 or the pharmaceutical composition of claim 9.

15. Use of a polypeptide according to any one of claims 1 to 8 or the pharmaceutical composition of claim 9, in the manufacture of a medicament for treating or preventing an immunological inflammatory disease.

16. Use of a polypeptide according to any one of claims 1 to 8 or the pharmaceutical composition of claim 9, in the manufacture of a medicament for suppressing activation of B cells, mast cells, dendritic cells, and/or basophils.