CLAIMS

1. A polypeptide comprising an Fc region of an IgG1 antibody, wherein the Fc region comprises a substitution of the amino acid at position 250 (EU numbering) with Val and a substitution of the amino acid at position 307 (EU numbering) with Pro, and wherein the polypeptide has improved thermal stability as compared to that of a parent polypeptide not having said amino acid modifications.

2. The polypeptide of claim 1, wherein the thermal stability is assessed or determined using melting temperature (Tm) as an index.

3. The polypeptide of claim 1 or 2, wherein at least one or more amino acid mutations have further been introduced into the Fc region at amino acid position(s) selected from the group consisting of position 234 (EU numbering), position 235 (EU numbering), position 236 (EU numbering), position 237 (EU numbering), position 238 (EU numbering), position 239 (EU numbering), position 247 (EU numbering), position 265 (EU numbering), position 266 (EU numbering), position 267 (EU numbering), position 268 (EU numbering), position 269 (EU numbering), position 270 (EU numbering), position 271 (EU numbering), position 295 (EU numbering), position 296 (EU numbering), position 298 (EU numbering), position 300 (EU numbering), position 309 (EU numbering), position 315 (EU numbering), position 324 (EU numbering), position 325 (EU numbering), position 326 (EU numbering), position 327 (EU numbering), position 329 (EU numbering), position 330 (EU numbering), position 333 (EU numbering), position 335 (EU numbering), position 337 (EU numbering), position 360 (EU numbering), position 385 (EU numbering), position 386 (EU numbering), position 387 (EU numbering), position 389 (EU numbering), position 428 (EU numbering), and position 433 (EU numbering).

4. The polypeptide of any one of claims 1 to 3, which further has FcγR-binding activity that is maintained or enhanced as compared to that of the parent polypeptide.

5. The polypeptide of any one of claims 1 to 3, which further has FcγR-binding activity that is decreased as compared to that of the parent polypeptide.

6. A polypeptide comprising an Fc region of an IgG1 antibody, wherein the Fc region comprises (a) Val at position 250 (EU numbering) and (b) Pro at position 307 (EU numbering), and wherein the polypeptide has improved thermal stability as compared to that of a parent polypeptide, and wherein the parent polypeptide comprises amino acids different from those of said (a) and said (b) at position 250 (EU numbering) and at position 307 (EU numbering).

7. The polypeptide of any one of claims 1 to 6, wherein the Fc region is a human IgG1 Fc region.

8. The polypeptide of any one of claims 1 to 7, wherein the polypeptide is an antibody.

9. A method for improving thermal stability of a polypeptide comprising an Fc region of an IgG1 antibody, said method comprising introducing into the Fc region a substitution of the amino acid at position 250 (EU numbering) with Val and a substitution of the amino acid at position 307 (EU numbering) with Pro, wherein the thermal stability of said polypeptide is improved as compared to that of a parent polypeptide not having said amino acid modifications.

10. The method of claim 9, wherein the thermal stability is assessed or determined using melting temperature (Tm) as an index.

11. A method for producing a polypeptide comprising an an Fc region of an IgG1 antibody, and has improved thermal stability as compared to that of a parent polypeptide, wherein the method comprises the steps of:
(A) introducing into an Fc region of a parent polypeptide comprising an Fc region of an IgG1 antibody a substitution of the amino acid at position 250 (EU numbering) with Val and a substitution of the amino acid at position 307 (EU numbering) with Pro;
(B) determining the thermal stability of the polypeptide modified in step (A); and
(C) selecting a polypeptide with improved thermal stability as compared to that of the parent polypeptide.

12. A method for producing a modified polypeptide comprising an an Fc region of an IgG1 antibody, and has improved thermal stability as compared to that of a parent polypeptide, wherein the method comprises the steps of:
(A) modifying a nucleic acid encoding the parent polypeptide so as to introduce into an Fc region of a parent polypeptide comprising an Fc region of an IgG1 antibody at least two amino acid modifications comprising a substitution of the amino acid at position 250 (EU numbering) with Val and a substitution of the amino acid at position 307 (EU numbering) with Pro;
(B) introducing the modified nucleic acid into a host cell and culturing the cell to induce expression of the nucleic acid; and
(C) collecting the modified polypeptide from the host cell culture.

13. The method any one of of claims 9 to 12, comprises further introducing at least one or more amino acid modification(s) at amino acid position(s) selected from the group consisting of position 234 (EU

numbering), position 235 (EU numbering), position 236 (EU numbering), position 237 (EU numbering), position 238 (EU numbering), position 239 (EU numbering), position 247 (EU numbering), position 265 (EU numbering), position 266 (EU numbering), position 267 (EU numbering), position 268 (EU numbering), position 269 (EU numbering), position 270 (EU numbering), position 271 (EU numbering), position 295 (EU numbering), position 296 (EU numbering), position 298 (EU numbering), position 300 (EU numbering), position 309 (EU numbering), position 315 (EU numbering), position 324 (EU numbering), position 325 (EU numbering), position 326 (EU numbering), position 327 (EU numbering), position 329 (EU numbering), position 330 (EU numbering), position 333 (EU numbering), position 335 (EU numbering), position 337 (EU numbering), position 360 (EU numbering), position 385 (EU numbering), position 386 (EU numbering), position 387 (EU numbering), position 389 (EU numbering), position 428 (EU numbering), and position 433 (EU numbering).

14. A method for producing a polypeptide comprising an Fc region of an IgG1 antibody, wherein the method comprises producing said polypeptide using a gene encoding said polypeptide, wherein
(A) an Fc region comprised in the produced polypeptide comprises (a) Val at position 250 (EU numbering) and (b) Pro at position 307 (EU numbering), and
(B) the produced polypeptide has improved thermal stability as compared to that of a parent polypeptide, and wherein the paretnt polypeptide comprises amino acids different from those of said (a) and said (b) at position 250 (EU numbering) and at position 307 (EU numbering).

15. The method of any one of claims 9 to 14, wherein the Fc region is a human IgG1 Fc region.

16. The method of any one of claims 9 to 15, wherein the polypeptide is an antibody.

17. A nucleic acid encoding a polypeptide comprising an Fc region of an IgG1 antibody, wherein the Fc region comprises a substitution of the amino acid at position 250 (EU numbering) with Val and a substitution of the amino acid at position 307 (EU numbering) with Pro, and has improved thermal stability as compared to that of a parent polypeptide not having said amino acid modifications.

18. A vector comprising the nucleic acid of claim 17.

19. A host cell transformed with the vector of claim 18.

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

21. Use of an agent comprising the pharmaceutical composition of claim 20 in the manufacture of a medicament for the treatment or prevention of an immune-inflammatory disease or cancer.

22. The use of claim 21, wherein the immune-inflammatory disease is rheumatoid arthritis, autoimmune hepatitis, autoimmune thyroiditis, autoimmune bullous dermatosis, autoimmune adrenocortical inflammation, autoimmune hemolytic anemia, autoimmune thrombocytopenic purpura, megalocytic anemia, autoimmune atrophic gastritis, autoimmune neutropenia, autoimmune orchitis, autoimmune encephalomyelitis, autoimmune receptor disease, autoimmune infertility, chronic active hepatitis, glomerulonephritis, interstitial pulmonary fibrosis, multiple sclerosis, Paget's disease, osteoporosis, multiple myeloma, uveitis, acute and chronic spondylitis, gouty arthritis, inflammatory bowel disease, adult respiratory distress syndrome (ARDS), psoriasis, Crohn's disease, Basedow's disease, juvenile diabetes, Addison's disease, myasthenia gravis, lenticular uveitis, systemic lupus erythematosus, allergic rhinitis, allergic dermatitis, ulcerative colitis, hypersensitivity, asthma, myodegeneration, cachexia, systemic scleroderma, localized scleroderma, Sjogren's syndrome, Behcet's disease, Reiter's syndrome, type I and type II diabetes, bone resorption disease, graft versus host reaction, ischemia reperfusion injury, atherosclerosis, brain trauma, multiple sclerosis, cerebral malaria, sepsis, septic shock, toxic shock syndrome, malgias due to fever and staining, aplastic anemia, hemolytic anemia, sudden thrombocytopenia, Goodpasture's syndrome, Guillain-Barre syndrome, Hashimoto's disease, pemphigus, IgA nephropathy, pollinosis, antiphospholipid antibody syndrome, polymyositis, Wegener's sarcoma, arteritis nodosa, mixed connective tissue disease, or fibromyalgia.

23. The use of claim 21, wherein the cancer is pancreatic cancer, prostate cancer, breast cancer, skin cancer, gastrointestinal cancer, lung cancer, hepatoma, cervical cancer, endometrial cancer, ovarian cancer, fallopian tube cancer, vaginal cancer, liver cancer, cholangioma, bladder cancer, ureteral cancer, thyroid cancer, adrenal carcinoma, renal cancer, other glandular tissue cancers, liposarcoma, leiomyosarcoma, rhabdomyosarcoma, synovial sarcoma, angiosarcoma, fibrosarcoma, malignant peripheral nerve tumor, gastrointestinal stromal tumor, desmoid tumor, Ewing's sarcoma, osteosarcoma, chondrosarcoma, leukemia, lymphoma, myeloma, or other solid organ tumors.