

WHAT IS CLAIMED IS:

1. A polypeptide comprising one or more variant Fc regions, each of the variant Fc regions comprising two CH2 domains, wherein at least one CH2 domain in at least one of the variant Fc regions is a variant CH2 domain comprising amino acid substitutions at positions 234, 235 and 265 (all positions expressed by EU numbering), wherein the amino acid residues at positions 234, 235, and 265 of the variant CH2 domain are Ala, Ala, and Gly, respectively, or Ala, Ala, and Asn, respectively, wherein each of the one or more variant Fc regions is a variant IgG1 Fc region, a variant IgG4 Fc region or a variant IgG1/IgG4 Fc region, and wherein the polypeptide has reduced binding affinity to an Fc γ RI, an Fc γ RII and an Fc γ RIII as compared to a parent polypeptide comprising a parent CH2 domain without amino acid substitutions at positions 234, 235 and 265.
2. The polypeptide according to claim 1, further comprising an amino acid substitution at position 329 of the variant CH2 domain, wherein the amino acid residue at position 329 of the variant CH2 domain is Ala.
3. The polypeptide according to claim 1 or 2, wherein the Fc γ RI, Fc γ RII and Fc γ RIII are human Fc γ RI, Fc γ RII and Fc γ RIII.
4. The polypeptide according to claim 1 or 2, wherein the Fc γ RI, Fc γ RII and Fc γ RIII are cynomolgus Fc γ RI, Fc γ RII and Fc γ RIII.
5. The polypeptide according to claim 1 or 2, wherein the polypeptide has reduced binding affinity to an Fc γ receptor (Fc γ R) by 50% or more as compared to a parent polypeptide comprising a parent CH2 domain without amino acid substitutions at positions 234, 235, and 265.
6. The polypeptide according to claim 5, wherein the Fc γ R is a human Fc γ R or a cynomolgus Fc γ R.

7. The polypeptide according to claim 5, wherein the Fc γ R is a human Fc γ R.
8. The polypeptide according to any one of claims 5 to 7, wherein the Fc γ R is Fc γ RI.
9. The polypeptide according to any one of claims 1 to 8, wherein the polypeptide comprises one or more variant IgG1 Fc regions.
10. The polypeptide according to any one of claims 1 to 8, wherein the polypeptide comprises one variant Fc region.
11. The polypeptide according to any one of claims 1 to 8, wherein the polypeptide comprises one variant IgG1 Fc region.
12. The polypeptide according to any one of claims 1 to 11, wherein the amino acid residues at positions 234, 235, and 265 of the variant CH2 domain are Ala, Ala, and Gly, respectively.
13. The polypeptide according to any one of claims 1 to 11, wherein the amino acid residues at positions 234, 235, and 265 of the variant CH2 domain are Ala, Ala, and Asn, respectively.
14. The polypeptide according to claim 12 or 13, wherein a thermal denaturation midpoint temperature (T_m) of the variant CH2 domain is within 1°C of the T_m of a parent CH2 domain without amino acid substitutions at positions 234, 235 and 265.
15. The polypeptide according to claim 12, wherein a thermal denaturation midpoint temperature (T_m) of the variant CH2 domain is higher by 1°C or more than the T_m of a parent CH2 domain without amino acid substitutions at positions 234, 235 and 265.

16. The polypeptide according to claim 15, wherein the T_m of the variant CH2 domain is higher by 3°C or more than the T_m of the parent CH2 domain.
17. The polypeptide according to any one of claims 1 to 16, wherein the polypeptide is an antibody or a functional fragment thereof.
18. The polypeptide according to claim 17, wherein the antibody or functional fragment thereof binds a tumor antigen.
19. The polypeptide according to claim 17, wherein the antibody is a bispecific or multispecific antibody.
20. A fusion protein comprising the polypeptide according to any one of claims 1 to 21 and a heterologous polypeptide.
21. A polypeptide-drug conjugate comprising the polypeptide according to any one of claims 1 to 19 conjugated to one or more drugs or modifying agents.
22. The polypeptide-drug conjugate according to claim 21, wherein the drug is a chemotherapeutic agent or a cytotoxic agent.
23. The polypeptide-drug conjugate according to claim 21, wherein the modifying agent is a non-proteinaceous polymer.
24. A nucleic acid comprising a nucleotide sequence encoding the polypeptide according to any one of claims 1 to 19 or a portion thereof.

25. A host cell comprising the nucleic acid according to claim 24.
26. A method for producing the polypeptide according to any one of claims 1 to 19 or a portion thereof, the method comprising culturing the host cell according to claim 25 in a medium under conditions suitable for expression of the polypeptide or the portion thereof, and recovering the polypeptide or the portion thereof from the medium or the host cell.
27. A pharmaceutical composition comprising the polypeptide according to any one of claims 1 to 19, the fusion protein according to claim 20, or the polypeptide-drug conjugate according to any one of claims 21 to 23, and a pharmaceutically acceptable carrier.
28. A polypeptide according to any one of claims 1 to 19, a fusion protein according to claim 20, or a polypeptide-drug conjugate according to any one of claims 21 to 23, for use in therapy.
29. Use of the polypeptide according to any one of claims 1 to 19, the fusion protein according to claim 20 or polypeptide-drug conjugate according to any one of claims 21 to 23 in the manufacture of a medicament for treatment of a cancer, an immune disease, an inflammatory disease or an infectious disease.