CLAIMS

1. A method of increasing an effector function of a parent polypeptide comprising an Fc-domain of an immunoglobulin and a binding region, which method comprises introducing a mutation to the parent polypeptide in the amino acid residue corresponding to E345K, in the Fc-region of a human IgG1 heavy chain.

2. The method according to claim 1 of increasing an effector function of a parent antibody, comprising introducing a mutation to the parent antibody in the amino acid residue corresponding to E345K in the Fc-region of a human IgG1 heavy chain,.

3. The method according to claim 2, wherein the parent antibody is a monospecific, bispecific or multispecific antibody.

4. The method according to claim 3, wherein the parent antibody is a bispecific antibody which comprises a first polypeptide comprising a first CH2-CH3 region of an immunoglobulin and a first antigen-binding region, and a second polypeptide comprising a second CH2-CH3 region of an immunoglobulin and a second antigen-binding region, wherein the first and second antigen-binding regions bind different epitopes on the same antigen or on different antigens, and wherein said first CH2-CH3 region comprises a further amino acid substitution at a position selected from those corresponding to K409, T366, L368, K370, D399, F405, and Y407 in the Fc-region of a human IgG1 heavy chain; and wherein said second CH2-CH3 region comprises a further amino acid substitution at a position selected from those corresponding to F405, T366, L368, K370, D399, Y407, and K409 in the Fc-region of a human IgG1 heavy chain, and wherein said further amino acid substitution in the first CH2-CH3 region is different from the said further amino acid substitution in the second CH2-CH3 region.

5. The method according to claim 3 or 4, wherein the parent antibody is a bispecific antibody and comprises a first polypeptide and a second polypeptide, wherein said first polypeptide comprises a first CH2-CH3 region of an immunoglobulin and a first antigen-binding region, and said second polypeptide comprises a second CH2-CH3 region of an immunoglobulin and a second antigen-binding region, wherein the first and second antigen-binding regions bind different epitopes on the same antigen or on different antigens, said method comprising introducing to each of the first and second CH2-CH3 region a mutation in the amino acid residue corresponding to E345K in the Fc-region of a human IgG1 heavy chain.

6. A method according to any one of the claims 1 to 5, said method comprises introducing further introducing a mutation

(i) in each of the amino acid residues corresponding to K439 and S440 in the Fc-region of a human IgG1 heavy chain, with the proviso that the mutation in S440 is not S440Y or S440W, (ii) in each of the amino acid residues corresponding to K447 and 448 in the Fc-region of a human IgG1 heavy chain, such as K447K/R/H and 448E/D in the Fc-region of a human IgG1 heavy chain, preferably K447K and 448E in the Fc-region of a human IgG1 heavy chain, or (iii) in each of the amino acid residues corresponding to K447, 448 and 449 in the Fc-region of a human IgG1 heavy chain, such as K447D/E, 448K/R/H and 449P in the Fc-region of a human IgG1 heavy chain, preferably K447E, 448K and 449P in the Fc-region of a human IgG1 heavy chain.

7. The method according to claim 6, said method further introducing a mutation in each of the amino acid residues corresponding to K439 and S440 in the Fc-region of a human IgG1 heavy chain, with the proviso that the mutation in S440 is not S440Y or S440W.

8. The method according to claim 7, wherein the mutation in the position corresponding to K439 in the Fc-region of human IgG1 heavy chain is K439D/E, and/or the mutation in the position corresponding to S440 in the Fc-region of human IgG1 heavy chain is S440K/H/R.

9. The method according to any one of the claims 1 to 5, comprising introducing to the parent antibody a mutation in at least one further amino acid residues selected from those corresponding to, E430, S440, Q386, P247, I253, S254, Q311, D/E356, T359, E382, Y436, and K447 in the Fc region of a human IgG1 heavy chain, with the proviso that the mutation in S440 is S440Y or S440W.

10. The method according to claim 9, comprising introducing to the parent antibody a mutation in at least one further amino acid residues selected from those corresponding to E430, Q386, and S440 in the Fc-region of a human IgG1 heavy chain, with the proviso that the mutation in S440 is S440Y or S440W, such as wherein the mutation in the at least one further amino acids are selected from the following: E430 to T, S, or G, S440 to Y or W, or Q386 to K.

11. The method according to any one of the claims 1 to 10, wherein the effector function is an Fc-mediated effector function selected from an Fc-mediated effector function selected from

C1q-binding, complement activation, complement dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxity (ADCC), FcRn-binding, Fc-receptor binding including Fc-gamma receptor-binding, Protein A-binding, Protein G-binding, antibody-dependent cellular phagocytosis (ADCP), complement-dependent cellular cytotoxicity (CDCC), complement-enhanced cytotoxicity , opsonisation, Fc-containing polypeptide internalization, target downmodulation, ADC uptake, induction of apoptosis, cell death, cell cycle arrest, and any combination thereof.

12. The method according to any one of the claims 1 to 11, wherein the effector function is increased when the antibody is bound to its antigen.

13. The method according to claim 12, wherein the antigen is on an antigen-expressing cell, cell membrane, or virion.

14. A method of inducing an effector response, against a cell, cell membrane, or virion expressing a target to which a parent polypeptide comprising an Fc-domain of an immunoglobulin and a binding region binds, comprising

(i) providing a parent polypeptide which has been mutated according to any one of the claims 1 to 11; and

(ii) contacting a preparation of the mutated parent polypeptide of step (i) with the cell, cell membrane, or virion expressing an antigen in the presence of human complement or an effector cell.

15. The method according to claim 14 of inducing an effector response, against a cell, cell membrane, or virion expressing an antigen to which a parent antibody binds, comprising

(i) providing a parent antibody which has been mutated according to any one of the claims 1 to 11; and

(ii) contacting a preparation of the mutated parent antibody of step (i) with the cell, cell membrane, or virion expressing an antigen in the presence of human complement or an effector cell.

16. The method according to claim 14 or 15, wherein the effector response is complement dependent cytotoxicity (CDC), an Fc-mediated effector response selected from an Fc-mediated effector response selected from C1q-binding, complement activation, complement dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxity (ADCC), FcRn-binding, Fc-receptor binding including Fc-gamma receptor-binding, Protein A-binding, Protein G-binding, antibody-dependent cellular phagocytosis (ADCP), complement-dependent cellular cytotoxicity

(CDCC), complement-enhanced cytotoxicity , opsonisation, Fc-containing polypeptide internalization, target downmodulation, ADC uptake, induction of apoptosis, cell death, cell cycle arrest, and any combination thereof.

17. The method according to any one of the claims 1 to 16, wherein the parent is a human IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, IgD or IgE, optionally a human full-length antibody, such as a human full-length IgG1 antibody.

18. A variant of a parent polypeptide comprising an Fc-domain of an immunoglobulin and a binding region, wherein the variant comprises a mutation in the amino acid residue corresponding to E345K, in the Fc-region of a human IgG1 heavy chain.

19. The variant according to claim 18 of a parent antibody comprising an antigen-binding region and a Fc-domain, wherein the variant comprises a mutation in the amino acid residue corresponding to E345K, in the Fc-region of a human IgG1 heavy chain.

20. A variant of a parent polypeptide comprising an Fc-domain of an immunoglobulin and a binding region, wherein the variant comprises a mutation corresponding to E345K in the Fc-region of human IgG1 heavy chain and at least one further amino acid residue selected from those corresponding to E430, S440, Q386, P247, I253, S254, Q311, D/E356, T359, E382, Y436, and K447 in the Fc-region of a human IgG1 heavy chain, with the proviso that the mutation in S440 is S440Y or S440W.

21. The variant according to claim 20, wherein the variant comprises a mutation corresponding to E345K in the Fc-region of human IgG1 heavy chain and in at least one further amino acid residue selected from those corresponding to E430X, S440W/Y, Q386K, P247G, I253V, S254L, Q311L/W, D/E356R, E382V, and Y436I in the Fc region of a human IgG1 heavy chain, wherein X is any amino acid, such as a natural occurring amino acid.

22. The variant according to claim 21, wherein the variant comprises a mutation corresponding to E345K in the Fc-region of human IgG1 heavy chain and in at least one further amino acid residue selected from the group of corresponding to those of E430X, S440W/Y, and Q386K in

the Fc-region of a human IgG1 heavy chain, wherein X is any amino acid, such as a natural occurring amino acid.

23. The variant according to claim 22, wherein the variant comprises a mutation corresponding to E345K in the Fc-region of human IgG1 heavy chain and in at least one further amino acid residue selected from those corresponding to E430T/S/G/A/C/D/F/H/I/L/K/M/N/P/Q/R/V/W/Y, S440W/Y, and Q386K in the Fc region of a human IgG1 heavy chain.

24. The variant according to claim 23, wherein the mutation corresponding to E345K in the Fc-region og human IgG1 heavy chain and in at least one further amino acid residue selected from those corresponding to E430T/S/G, S440Y/W, and Q386K in the Fc-region of a human IgG1 heavy chain.

25. The variant according to any one of the claims 18 to 24, wherein the at least one further mutation is in position(s) other than S440 and K447, and wherein the variant further comprises a mutation
(i) in at least one amino acid residue corresponding to K439 or S440 in the Fc-region of a human IgG1 heavy chain, with the proviso that the mutation in S440 is not S440W or S440Y;

(ii) in at least one amino acid residue corresponding to K447D/E or corresponding to K447K/R/H and 448P in the Fc region of a human IgG1 heavy chain; or
(iii) in at least one amino acid residue corresponding to K447D/E or corresponding to K447K/R/H and 448K/R/H and 449P in the Fc region of a human IgG1 heavy chain.

26. The variant according to claim 25, wherein the at least one further mutation is in position(s) other than S440, and wherein the variant further comprises a mutation in at least one amino acid residue corresponding to K439 or S440 in the Fc-region of a human IgG1 heavy chain, with the proviso that the mutation in S440 is not S440W or S440Y.

27. The variant according to any one of the claims 25 to 26, wherein the mutation in the position corresponding to K439 in the Fc-region of human IgG1 heavy chain is K439D/E, and/or the mutation in the position corresponding to S440 in the Fc-region of human IgG1 heavy chain is S440K/H/R.

28. The variant according to any one of the claims 18 to 27, wherein said variant is conjugated to a drug, toxin or radiolabel, such as wherein the variant is conjugated to a toxin via a linker.

29. The variant according to any one of the claims 18 to 27, wherein said variant is part of a fusion protein.

30. The variant according to any one of the claims 18 to 29, wherein the variant is a human IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, IgD or IgE antibody, optionally a human full-length antibody, such as a human full-length IgG1 antibody.

31. A composition comprising the variant according to any one of the claims 18 to 30 and a pharmaceutically acceptable carrier.

32. A kit-of-parts comprising a first variant and a second variant as defined in any one of the claims 18 to 30 for simultaneous, separate or sequential use in therapy.

33. The variant, composition or kit-of-parts according to any one of the claims 18 to 32 for use in the treatment of a disease, such as cancer.

34. The use of the variant, the composition or the kit-of-parts according to any one of the claims 18 to 32 in the manufacture of a medicament for the treatment of a human.

35. The use of the variant, the composition or the kit-of-parts according to any one of the claims 18 to 32 in the manufacture of a medicament for the treatment of cancer in a human.

What is claimed is:

1. An invention not claimed in any divisional application.