

WHAT IS CLAIMED IS:

1. A polypeptide complex comprising:
a first polypeptide comprising a first CH3 domain,
a second polypeptide comprising a second CH3 domain,
5 wherein a third polypeptide is fused to the first CH3 domain at a region from position 344 to position 382 of the first CH3 domain according to EU numbering.
2. The polypeptide complex of claim 1, wherein the third polypeptide is linked to a first amino acid residue and a second amino acid residue of the first CH3 domain, wherein the first and
10 the second amino acid residues are selected from the group consisting of amino acid residues at positions 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, and 383 of the first CH3 domain according to EU numbering.
- 15 3. The polypeptide complex of claim 1, wherein the third polypeptide is fused to the first CH3 domain at a region from position 351 to position 362 of the first CH3 domain according to EU numbering.
- 20 4. The polypeptide complex of claim 3, wherein the third polypeptide is linked to a first amino acid residue and a second amino acid residue of the first CH3 domain, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, and 363 of the first CH3 domain according to EU numbering.
- 25 5. The polypeptide complex of claim 1, wherein the third polypeptide is fused to the first CH3 domain at a region from position 358 to position 362 of the first CH3 domain according to EU numbering.
- 30 6. The polypeptide complex of claim 5, wherein the third polypeptide is linked to a first amino acid residue and a second amino acid residue of the first CH3 domain, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues

at positions 357, 358, 359, 360, 361, 362, and 363 of the first CH3 domain according to EU numbering.

- 5 7. The polypeptide complex of claim 2, 4 or 6, wherein one or more amino acid residues in a wildtype CH3 domain between the first and the second amino acid residues in the first CH3 domain are deleted.
8. The polypeptide complex of any one of claims 1-7, wherein the first polypeptide further comprises a CH2 domain.
- 10 9. The polypeptide complex of any one of claims 1-8, wherein the second polypeptide further comprises a CH2 domain.
10. The polypeptide complex of any one of claims 1-9, wherein the first polypeptide further comprises a heavy chain variable domain and/or a heavy chain CH1 domain.
- 15 11. The polypeptide complex of any one of claims 1-10, wherein the second polypeptide further comprises a heavy chain variable domain and/or a heavy chain CH1 domain.
12. The polypeptide complex of any one of claims 1-11, wherein the polypeptide complex comprises two light chain polypeptides.
- 20 13. The polypeptide complex of any one of claims 1-12, wherein the polypeptide complex is an IgG-like antibody.
- 25 14. The polypeptide complex of any one of claims 1-13, wherein the third polypeptide is linked to the first polypeptide through a linker sequence.
15. The polypeptide complex of claim 14, wherein the linker sequence comprises 5-20 amino acid residues.
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16. The polypeptide complex of claim 14 or 15, wherein the linker sequence comprises at least four glycine residues.
17. The polypeptide complex of any one of claims 14-16, wherein the linker sequence comprises a sequence that is at least 80% identical to GGGGSGGGGS (SEQ ID NO: 30).
18. The polypeptide complex of any one of claims 1-17, wherein the third polypeptide has more than 6 amino acid residues.
19. The polypeptide complex of any one of claims 1-18, wherein the third polypeptide has about 6 to 500 amino acid residues.
20. The polypeptide complex of any one of claims 1-19, wherein the third polypeptide is a soluble polypeptide.
21. The polypeptide complex of claim 20, wherein the soluble protein is a cytokine (e.g., IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, IL-19, IL-20, IL-21, IL-22, IL-23, IL-24, IL-25, IL-26, IL-27, IL-28, IL-29, IL-30, IL-31, IL-32, IL-33, IL-35, or IL-36).
22. The polypeptide complex of claim 21, wherein the third polypeptide is IL3, IL4, IL5, IL6, IL-7, IL8, IL9, IL13, IL15, or IL21.
23. The polypeptide complex of any one of claims 1-19, wherein the third polypeptide comprises a single chain antigen-binding polypeptide (e.g., a single chain variable fragment (scFv), or a single-domain antibody (nanobody)).
24. The polypeptide complex of claim 23, wherein the single chain antigen-binding polypeptide specifically binds to a cell antigen (e.g., an effector cell antigen).

25. The polypeptide complex of any one of claims 1-19, wherein the third polypeptide comprises a soluble portion (e.g., an extracellular region) of a transmembrane protein (e.g., transforming growth factor beta receptor 2 (TGFbR2)) or a secretory protein.
- 5 26. The polypeptide complex of any one of claims 1-19, wherein the third polypeptide is a ligand (e.g., ATOR1015-CD86).
27. The polypeptide complex of any one of claims 1-19, wherein the third polypeptide is a nanobody (e.g., KN035) or a VHH.
- 10 28. The polypeptide complex of any one of claims 1-27, wherein the third polypeptide in the polypeptide complex has about the same or a higher level of biological activity as compared to an isolated third polypeptide.
- 15 29. The polypeptide complex of any one of claims 1-28, wherein the polypeptide complex has about the same or a higher level of binding affinity to a target as compared to a parent polypeptide complex.
- 20 30. The polypeptide complex of any one of claims 1-29, wherein the polypeptide complex specifically binds to two antigens, and the polypeptide complex has about the same or a higher expression level as compared to that of a bispecific antibody that specifically binds to the same two antigens.
- 25 31. The polypeptide complex of any one of claims 1-30, wherein the polypeptide complex does not form aggregates in a purified form.
32. The polypeptide complex of any one of claims 1-31, wherein the polypeptide complex in an isolated form can bind to an Fc receptor.

33. The polypeptide complex of any one of claims 1-32, wherein the third polypeptide comprises a scFv, and wherein the scFv has about the same or a higher level of binding affinity as compared to that of an isolated scFv.
- 5 34. The polypeptide complex in any one of claims 1-33, further comprising:
a fourth polypeptide, wherein the fourth polypeptide is fused to the second CH3 domain at a region from position 344 to position 382 of the second CH3 domain according to EU numbering.
- 10 35. The polypeptide complex of claim 34, wherein the fourth polypeptide is linked to a first amino acid residue and a second amino acid residue of the second CH3 domain, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 15 376, 377, 378, 379, 380, 381, 382, and 383 of the second CH3 domain according to EU numbering.
- 20 36. The polypeptide complex of claim 34, wherein the fourth polypeptide is fused to the second CH3 domain at a region from position 351 to position 362 of the second CH3 domain according to EU numbering.
- 25 37. The polypeptide complex of claim 36, wherein the fourth polypeptide is linked to a first amino acid residue and a second amino acid residue of the second CH3 domain, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, and 363 of the second CH3 domain according to EU numbering.
- 30 38. The polypeptide complex of claim 34, wherein the fourth polypeptide is fused to the second CH3 domain at a region from position 358 to position 362 of the second CH3 domain according to EU numbering.

39. The polypeptide complex of claim 38, wherein the fourth polypeptide is linked to a first amino acid residue and a second amino acid residue of the second CH3 domain, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 357, 358, 359, 360, 361, 362, and 363 of the second CH3 domain according to EU numbering.
40. The polypeptide complex of any one of claims 1-39, further comprising:
a fifth polypeptide, wherein the fifth polypeptide is fused to the C-terminus of the first polypeptide.
41. The polypeptide complex of claim 40, wherein the fifth polypeptide is fused to the C-terminus of the first polypeptide through a linker sequence.
42. The polypeptide complex of claim 41, wherein the linker sequence comprises 10-40 amino acid residues.
43. The polypeptide complex of claim 42, wherein the linker sequence comprises a sequence that is at least 80% identical to GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 9).
44. The polypeptide complex of any one of claims 40-43, wherein the fifth polypeptide has more than 10 amino acid residues.
45. The polypeptide complex of any one of claims 40-44, wherein the fifth polypeptide has about 10 to 500 amino acid residues.
46. The polypeptide complex of any one of claims 40-45, wherein the fifth polypeptide is a cytokine.
47. The polypeptide complex of claim 46, wherein the cytokine is IFN α 4.
48. The polypeptide complex of any one of claims 1-47, further comprising:

a sixth polypeptide, wherein the sixth polypeptide is fused to the C-terminus of the second polypeptide.

- 5 49. The polypeptide complex of any one of claims 1-48, wherein the first polypeptide and the second polypeptide form a heterodimer through knobs-in-holes (KIH) technique.
- 10 50. The polypeptide complex of any one of claims 1-49, wherein the first polypeptide interacts with a light chain polypeptide, forming an antigen-binding site, wherein the second polypeptide does not interact with the light chain polypeptide.
- 15 51. The polypeptide complex of any one of claims 1-50, wherein the first polypeptide interacts with a first light chain polypeptide, forming a first antigen-binding site, wherein the second polypeptide interacts with a second light chain polypeptide, forming a second antigen-binding site, wherein the first antigen-binding site and the second antigen-binding site specifically bind to a same antigen or different antigens.
- 20 52. The polypeptide complex of any one of claim 1-51, wherein the polypeptide complex can bind to an Fc receptor when the third polypeptide in the polypeptide complex does not interact with a binding partner for the third polypeptide.
- 25 53. A protein comprising a variant Fc, wherein a polypeptide is fused to the variant Fc at a region from position 344 to position 382 of the variant Fc according to EU numbering.
- 30 54. The protein of claim 53, wherein the polypeptide is linked to a first amino acid residue and a second amino acid residue of the variant Fc, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, and 383 of the variant Fc according to EU numbering.

55. The protein of claim 54, wherein the polypeptide is fused to the variant Fc at a region from position 351 to position 362 of the variant Fc according to EU numbering.
56. The protein of claim 55, wherein the polypeptide is linked to a first amino acid residue and a second amino acid residue of the variant Fc, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, and 363 of the variant Fc according to EU numbering.
57. The protein of claim 53, wherein the polypeptide is fused to the variant Fc at a region from position 358 to position 362 of the variant Fc according to EU numbering.
58. The protein of claim 57, wherein the polypeptide is linked to a first amino acid residue and a second amino acid residue of the variant Fc, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 357, 358, 359, 360, 361, 362, and 363 of the variant Fc according to EU numbering.
59. A protein comprising a variant Fc, wherein a polypeptide is fused to the variant Fc at a region from position 383 to position 391 of the variant Fc according to EU numbering.
60. The protein of claim 59, wherein the polypeptide is linked to a first amino acid residue and a second amino acid residue of the variant Fc, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, and 392 of the variant Fc according to EU numbering.
61. A protein comprising a variant Fc, wherein a polypeptide is fused to the variant Fc at a region from position 383 to position 385 of the variant Fc according to EU numbering.
62. The protein of claim 61, wherein the polypeptide is linked to a first amino acid residue and a second amino acid residue of the variant Fc, wherein the first and the second amino acid

residues are selected from the group consisting of amino acid residues at positions 382, 383, 384, 385, and 386 of the variant Fc according to EU numbering.

- 5 63. A protein comprising a variant Fc, wherein a polypeptide is fused to the variant Fc at a region from position 413 to position 422 of the variant Fc according to EU numbering.
- 10 64. The protein of claim 63, wherein the polypeptide is linked to a first amino acid residue and a second amino acid residue of the variant Fc, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423 of the variant Fc according to EU numbering.
- 15 65. The protein of any one of claims 53-64, wherein the Fc is an IgG Fc.
66. The protein of any one of claims 53-64, wherein the Fc is an IgG1, IgG2, or IgG4 Fc.
67. The protein of any one of claims 53-64, wherein the protein is an IgG-like antibody or an immunoglobulin (e.g., IgM, IgD, IgE, IgA, or IgG).
- 20 68. The protein of any one of claims 53-67, wherein the protein is a multispecific antibody (e.g., a bispecific antibody).
69. A polypeptide complex comprising:
a first polypeptide comprising a first CH3 domain,
25 a second polypeptide comprising a second CH3 domain,
wherein a third polypeptide is fused to the first CH3 domain at a region from position 383 to position 391 of the first CH3 domain according to EU numbering.
- 30 70. The polypeptide complex of claim 69, wherein the third polypeptide is linked to a first amino acid residue and a second amino acid residue of the first CH3 domain, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues

at positions 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, and 392 of the first CH3 domain according to EU numbering.

71. A polypeptide complex comprising:
- 5 a first polypeptide comprising a first CH3 domain,
 a second polypeptide comprising a second CH3 domain,
 wherein a third polypeptide is fused to the first CH3 domain at a region from position 383 to position 385 of the first CH3 domain according to EU numbering.
- 10 72. The polypeptide complex of claim 71, wherein the third polypeptide is linked to a first amino acid residue and a second amino acid residue of the first CH3 domain, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 382, 383, 384, 385, and 386 of the first CH3 domain according to EU numbering.
- 15 73. A polypeptide complex comprising:
- a first polypeptide comprising a first CH3 domain,
 a second polypeptide comprising a second CH3 domain,
 wherein a third polypeptide is fused to the first CH3 domain at a region from position 413 to position 422 of the first CH3 domain according to EU numbering.
- 20 74. The polypeptide complex of claim 73, wherein the third polypeptide is linked to a first amino acid residue and a second amino acid residue of the first CH3 domain, wherein the first and the second amino acid residues are selected from the group consisting of amino acid residues at positions 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423 of the first CH3 domain according to EU numbering.
- 25 75. A modified antibody, comprising:
- a first heavy chain polypeptide comprising a first non-native polypeptide sequence;
 a second heavy chain polypeptide;
30 a first light chain polypeptide; and
 a second light chain polypeptide;

wherein the first heavy chain polypeptide and the first light chain polypeptide associate with each other, forming a first antigen binding region,
wherein the second heavy chain polypeptide and the second light chain polypeptide associate with each other, forming a second antigen binding region,
5 wherein the first non-native polypeptide sequence is fused to the first heavy chain polypeptide at a region from position 344 to position 382 of the first heavy chain polypeptide according to EU numbering.

10 76. The modified antibody of claim 75, wherein the second heavy chain polypeptide comprises a second non-native polypeptide sequence, wherein the second non-native polypeptide sequence is fused to the second heavy chain polypeptide at a region from position 344 to position 382 of the second heavy chain polypeptide according to EU numbering.

15 77. The modified antibody of claim 75 or 76, wherein the first antigen binding region and the second antigen binding region specifically bind to a same antigen.

78. The modified antibody of claim 75 or 76, wherein the first antigen binding region and the second antigen binding region specifically bind to different antigens.

20 79. The modified antibody of claim 75 or 76, wherein the first antigen binding region and/or the second antigen binding region specifically bind to a tumor associated antigen.

25 80. The modified antibody of claim 75 or 76, wherein the first non-native polypeptide sequence and/or the second non-native polypeptide sequence (e.g., a scFV or a nanobody) comprising an antigen-binding site that specifically binds to a cell antigen (e.g., an effector cell antigen).

81. The modified antibody of any one of claims 75-80, wherein a functional polypeptide is linked to the C-terminus of the first heavy chain polypeptide.

30 82. The modified antibody of any one of claims 75-81, wherein a functional polypeptide is linked to the C-terminus of the second heavy chain polypeptide.

83. A fusion polypeptide, comprising
a first region comprising CH2, and a first portion of CH3;
a second region comprising a non-native polypeptide sequence;
5 a third region comprising a second portion of CH3,
wherein the first portion of CH3 comprises amino acid residues 341-343 of a CH3 domain according to EU numbering, and the second portion of CH3 comprises amino acid residues 383-447 of a CH3 domain according to EU numbering.
- 10 84. The fusion polypeptide of claim 83, wherein the first portion of CH3 comprises amino acid residues 341-350 of a CH3 domain according to EU numbering, and the second portion of CH3 comprises amino acid residues 363-447 of a CH3 domain according to EU numbering.
- 15 85. The fusion polypeptide of claim 83, wherein the first portion of CH3 comprises amino acid residues 341-357 of a CH3 domain according to EU numbering, and the second portion of CH3 comprises amino acid residues 363-447 of a CH3 domain according to EU numbering.
- 20 86. The fusion polypeptide of any one of claims 83-85, wherein the first region further comprises VH and/or CH1.
87. A modified antibody comprising
two light chain polypeptides; and
two of the fusion heavy chain polypeptides of any one of claims 83-86.
- 25 88. A multispecific antibody comprising
a first antigen binding site that specifically binds a first antigen,
a second antigen binding site that specifically binds to a second antigen,
wherein when the second antigen binding site specifically binds to the second antigen,
effector function of the multispecific antibody is inhibited or reduced.

89. The multispecific antibody of claim 88, wherein the multispecific antibody comprises a heavy chain CH3 domain and the polypeptide is fused to the heavy chain CH3 domain at a region from position 344 to position 382 of the heavy chain CH3 domain according to EU numbering.
90. The multispecific antibody of claim 88, wherein the multispecific antibody comprises a heavy chain CH3 domain and the polypeptide is fused to the heavy chain CH3 domain at a region from position 351 to position 362 of the heavy chain CH3 domain according to EU numbering.
91. The multispecific antibody of claim 88, wherein the multispecific antibody comprises a heavy chain CH3 domain and the polypeptide is fused to the heavy chain CH3 domain at a region from position 358 to position 362 of the heavy chain CH3 domain according to EU numbering.
92. The multispecific antibody of any one of claims 88-91, wherein the first antigen is from a tumor cell and the second antigen is from an effector cell.
93. The multispecific antibody of claim 92, wherein the effector cell is a NK cell, a T cell, a B cell, a monocyte, a microphage, a dendritic cell, or a neutrophil.
94. The multispecific antibody of any one of claims 88-93, wherein when the first antigen binding site specifically binds a first antigen and the second antigen binding site does not bind to the second antigen, the multispecific antibody induces the effector function.
95. The multispecific antibody of any one of claims 88-94, wherein the effector function is ADCC or ADCP.
96. The multispecific antibody of any one of claims 88-95, wherein the second antigen binding site is located within the polypeptide comprising a single chain antigen-binding polypeptide (e.g., a scFv or a nanobody).

97. The multispecific antibody of any one of claims 88-96, wherein the second antigen binding site is located within a scFv or a nanobody that is fused at a CH3 domain of the multispecific antibody.
98. The multispecific antibody of any one of claims 88-97, wherein the first antigen binding site is a scFv or a nanobody that is linked to N terminal of a CH1 domain or a CH2 domain.
99. The multispecific antibody of any one of claims 88-98, wherein the first antigen binding site is formed by a VH and a VL.
100. The multispecific antibody of any one of claims 88-99, wherein the multispecific antibody is a bispecific antibody.
101. A modified antibody comprising
an antigen binding site that specifically binds an antigen,
a binding polypeptide that specifically interacts with its binding partner,
wherein the receptor binding site is located within a polypeptide fused to the modified antibody, wherein when the receptor binding site specifically binds to the receptor, effector function of the modified antibody is inhibited or reduced.
102. The modified antibody of claim 101, wherein
(1) the binding polypeptide is a ligand and the binding partner is a receptor for the ligand, or
(2) the binding polypeptide is a soluble portion of a receptor and the binding partner is a ligand that specifically interacts with the receptor.
103. The modified antibody of claim 101 or 102, wherein the modified antibody comprises a heavy chain CH3 domain and the polypeptide is fused to the heavy chain CH3 domain at a region from position 344 to position 382 of the heavy chain CH3 domain according to EU numbering.

104. The modified antibody of claim 101 or 102, wherein the modified antibody comprises a heavy chain CH3 domain and the polypeptide is fused to the heavy chain CH3 domain at a region from position 351 to position 362 of the heavy chain CH3 domain according to EU numbering.
105. The modified antibody of claim 101 or 102, wherein the modified antibody comprises a heavy chain CH3 domain and the polypeptide is fused to the heavy chain CH3 domain at a region from position 358 to position 362 of the heavy chain CH3 domain according to EU numbering.
106. A pharmaceutical composition comprising the polypeptide, the polypeptide complex, or the antibody of any one of claims 1-105.
- 5 107. A nucleic acid encoding the polypeptide, the polypeptide complex, or the antibody of any one of claims 1-105.
108. A vector comprising the nucleic acid of claim 107.
- 10 109. A host cell comprising the nucleic acid of claim 107.
110. A method for producing a polypeptide, a polypeptide complex, or an antibody, the method comprising culturing the host cell of claim 109 under conditions suitable to produce the polypeptide, the polypeptide complex, or the antibody.

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