

**CLAIMS**

What is claimed is:

1. An antibody or a recombinant antibody comprising a heavy chain variable region (V<sub>H</sub>) having at least 80% identity to amino acid sequence SEQ ID NO: 8 and a light chain variable region (V<sub>L</sub>) having at least 80% identity to amino acid sequence SEQ ID NO: 7.
2. The antibody or the recombinant antibody of claim 1 comprising the light chain variable region (V<sub>L</sub>) having at least 85% identity to amino acid sequence SEQ ID NO: 7.
3. The antibody or the recombinant antibody of claim 1 comprising the light chain variable region (V<sub>L</sub>) having at least 90% identity to amino acid sequence SEQ ID NO: 7.
4. The antibody or the recombinant antibody of claim 1 comprising the light chain variable region (V<sub>L</sub>) having at least 95% identity to amino acid sequence SEQ ID NO: 7.
5. The antibody or the recombinant antibody of claim 1 comprising the light chain variable region (V<sub>L</sub>) having at least 99% identity to amino acid sequence SEQ ID NO: 7.
6. The antibody or the recombinant antibody of claim 1 comprising the light chain variable region (V<sub>L</sub>) having at least 100% identity to amino acid sequence SEQ ID NO: 7.
7. The antibody or the recombinant antibody of any one of claims 1-6 comprising the heavy chain variable region (V<sub>H</sub>) having at least 85% identity to amino acid sequence SEQ ID NO: 8.
8. The antibody or the recombinant antibody of any one of claims 1-6 comprising the heavy chain variable region (V<sub>H</sub>) having at least 90% identity to amino acid sequence SEQ ID NO: 8.
9. The antibody or the recombinant antibody of any one of claims 1-6 comprising the heavy chain variable region (V<sub>H</sub>) having at least 95% identity to amino acid sequence SEQ ID NO: 8.
10. The antibody or the recombinant antibody of any one of claims 1-6 comprising the heavy chain variable region (V<sub>H</sub>) having at least 99% identity to amino acid sequence SEQ ID NO: 8.
11. The antibody or the recombinant antibody of any one of claims 1-6 comprising the heavy

chain variable region (V<sub>H</sub>) having at least 100% identity to amino acid sequence SEQ ID NO: 8.

12. An antibody or a recombinant antibody, comprising a heavy chain sequence comprising a complementarity determining region (CDR) H1 having at least 80% identity to amino acid sequence SEQ ID NO: 4, a CDR H2 having at least 80% identity to amino acid sequence SEQ ID NO: 5, and a CDR H3 having at least 80% identity to amino acid sequence SEQ ID NO: 6, and a light chain sequence comprising a CDR L1 having at least 80% identity to amino acid sequence SEQ ID NO: 1, a CDR L2 having at least 80% identity to amino acid sequence SEQ ID NO: 2, and a CDR L3 having at least 80% identity to amino acid sequence SEQ ID NO: 3.
13. The antibody or the recombinant antibody of claim 12 in which the CDR L1 has at least 85% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 85% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 85% identity to amino acid sequence SEQ ID NO: 3.
14. The antibody or the recombinant antibody of claim 12 in which the CDR L1 has at least 90% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 90% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 90% identity to amino acid sequence SEQ ID NO: 3.
15. The antibody or the recombinant antibody of claim 12 in which the CDR L1 has at least 95% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 95% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 95% identity to amino acid sequence SEQ ID NO: 3.
16. The antibody or the recombinant antibody of claim 12 in which the CDR L1 has at least 99% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 99% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 99% identity to amino acid sequence SEQ ID NO: 3.
17. The antibody or the recombinant antibody of claim 12 in which the CDR L1 has at least 100% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 100% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 100% identity to amino acid sequence SEQ ID NO: 3.

18. The antibody or the recombinant antibody of any one of claims 12-17 in which the CDR H1 has at least 85% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 85% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 85% identity to amino acid sequence SEQ ID NO: 6.
19. The antibody or the recombinant antibody of any one of claims 12-17 in which the CDR H1 has at least 90% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 90% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 90% identity to amino acid sequence SEQ ID NO: 6.
20. The antibody or the recombinant antibody of any one of claims 12-17 in which the CDR H1 has at least 95% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 95% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 95% identity to amino acid sequence SEQ ID NO: 6.
21. The antibody or the recombinant antibody of any one of claims 12-17 in which the CDR H1 has at least 99% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 99% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 99% identity to amino acid sequence SEQ ID NO: 6.
22. The antibody or the recombinant antibody of any one of claims 12-17 in which the CDR H1 has at least 100% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 100% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 100% identity to amino acid sequence SEQ ID NO: 6.
23. An antibody or a recombinant antibody comprising a heavy chain variable region ( $V_H$ ) having at least 80% identity to amino acid sequence SEQ ID NO: 8.
24. The antibody or the recombinant antibody of claim 23, wherein the heavy chain variable region ( $V_H$ ) is at least 90% identity to amino acid sequence SEQ ID NO: 8.
25. The antibody or the recombinant antibody of claim 23, wherein the heavy chain variable region ( $V_H$ ) is at least 95% identity to amino acid sequence SEQ ID NO: 8.
26. The antibody or the recombinant antibody of claim 23, wherein the heavy chain variable region ( $V_H$ ) is at least 99% identity to amino acid sequence SEQ ID NO: 8.
27. The antibody or the recombinant antibody of claim 23, wherein the heavy chain variable

region (V<sub>H</sub>) is at least 100% identity to amino acid sequence SEQ ID NO: 8.

28. The antibody or the recombinant antibody according to any one of claims 23-27, further comprising a light chain variable region (V<sub>L</sub>) having at least 80% identity to amino acid sequence SEQ ID NO: 7.
29. The antibody or the recombinant antibody according to any one of claims 23-27, further comprising a light chain variable region (V<sub>L</sub>) having at least 90% identity to amino acid sequence SEQ ID NO: 7.
30. The antibody or the recombinant antibody according to any one of claims 23-27, further comprising a light chain variable region (V<sub>L</sub>) having at least 95% identity to amino acid sequence SEQ ID NO: 7.
31. The antibody or the recombinant antibody according to any one of claims 23-27, further comprising a light chain variable region (V<sub>L</sub>) having at least 99% identity to amino acid sequence SEQ ID NO: 7.
32. The antibody or the recombinant antibody according to any one of claims 23-27, further comprising a light chain variable region (V<sub>L</sub>) having at least 100% identity to amino acid sequence SEQ ID NO: 7.
33. An antibody or a recombinant antibody comprising a light chain variable region (V<sub>L</sub>) having at least 99% identity to amino acid sequence SEQ ID NO: 7.
34. The antibody or the recombinant antibody of claim 33, wherein the light chain variable region (V<sub>L</sub>) is at least 100% identity to amino acid sequence SEQ ID NO: 7.
35. The antibody or the recombinant antibody according to any one of claims 33-34, further comprising a heavy chain variable region (V<sub>H</sub>) having at least 80% identity to amino acid sequence SEQ ID NO: 8.
36. The antibody or the recombinant antibody according to any one of claims 33-34, further comprising a heavy chain variable region (V<sub>H</sub>) having at least 90% identity to amino acid sequence SEQ ID NO: 8.
37. The antibody or the recombinant antibody according to any one of claims 33-34, further comprising a heavy chain variable region (V<sub>H</sub>) having at least 95% identity to amino acid

sequence SEQ ID NO: 8.

38. The antibody or the recombinant antibody according to any one of claims 33-34, further comprising a heavy chain variable region ( $V_H$ ) having at least 99% identity to amino acid sequence SEQ ID NO: 8.
39. The antibody or the recombinant antibody according to any one of claims 33-34, further comprising a heavy chain variable region ( $V_H$ ) having at least 100% identity to amino acid sequence SEQ ID NO: 8.
40. An antibody or a recombinant antibody, comprising a complementarity determining region (CDR) H1 having at least 80% identity to amino acid sequence SEQ ID NO: 4, a CDR H2 having at least 80% identity to amino acid sequence SEQ ID NO: 5, and a CDR H3 having at least 80% identity to amino acid sequence SEQ ID NO: 6.
41. The antibody or the recombinant antibody of claim 40, comprising a complementarity determining region (CDR) H1 having at least 90% identity to amino acid sequence SEQ ID NO: 4, a CDR H2 having at least 90% identity to amino acid sequence SEQ ID NO: 5, and a CDR H3 having at least 90% identity to amino acid sequence SEQ ID NO: 6.
42. The antibody or the recombinant antibody of claim 40, comprising a complementarity determining region (CDR) H1 having at least 95% identity to amino acid sequence SEQ ID NO: 4, a CDR H2 having at least 95% identity to amino acid sequence SEQ ID NO: 5, and a CDR H3 having at least 95% identity to amino acid sequence SEQ ID NO: 6.
43. The antibody or the recombinant antibody of claim 40, comprising a complementarity determining region (CDR) H1 having at least 99% identity to amino acid sequence SEQ ID NO: 4, a CDR H2 having at least 99% identity to amino acid sequence SEQ ID NO: 5, and a CDR H3 having at least 99% identity to amino acid sequence SEQ ID NO: 6.
44. The antibody or the recombinant antibody of claim 40, comprising a complementarity determining region (CDR) H1 having at least 100% identity to amino acid sequence SEQ ID NO: 4, a CDR H2 having at least 100% identity to amino acid sequence SEQ ID NO: 5, and a CDR H3 having at least 100% identity to amino acid sequence SEQ ID NO: 6.
45. The antibody or the recombinant antibody of any one of claims 40-44, further comprising a light chain sequence comprising at least one complementarity determining region (CDR) L1 having at least 80% identity to amino acid sequence SEQ ID NO: 1, a CDR L2 having at

least 80% identity to amino acid sequence SEQ ID NO: 2, and a CDR L3 having at least 80% identity to amino acid sequence SEQ ID NO: 3.

46. The antibody or the recombinant antibody of claim 45, in which the CDR L1 has at least 90% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 90% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 90% identity to amino acid sequence SEQ ID NO: 3.
47. The antibody or the recombinant antibody of claim 45, in which the CDR L1 has at least 95% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 95% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 95% identity to amino acid sequence SEQ ID NO: 3.
48. The antibody or the recombinant antibody of claim 45, in which the CDR L1 has at least 99% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 99% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 99% identity to amino acid sequence SEQ ID NO: 3.
49. The antibody or the recombinant antibody of claim 45, in which the CDR L1 has at least 100% identity to amino acid sequence SEQ ID NO: 1, the CDR L2 has at least 100% identity to amino acid sequence SEQ ID NO: 2, and the CDR L3 has at least 100% identity to amino acid sequence SEQ ID NO: 3.
50. The antibody or the recombinant antibody of any one of claims 40-44, further comprising a light chain variable region (V<sub>L</sub>) has at least 80% identity to amino acid sequence SEQ ID NO: 7.
51. The antibody or the recombinant antibody of any one of claims 45-49, wherein the light chain variable region (V<sub>L</sub>) having at least 80% identity to amino acid sequence SEQ ID NO: 7.
52. The antibody or the recombinant antibody according to any one of claims 40-51, comprising a heavy chain variable region (V<sub>H</sub>) having at least 80% identity to amino acid sequence SEQ ID NO: 8.
53. An antibody or a recombinant antibody, comprising a light chain sequence comprising a complementarity determining region (CDR) CDR L1 having at least 99% identity to amino acid sequence SEQ ID NO: 1, a CDR L2 having at least 99% identity to amino acid

sequence SEQ ID NO: 2, and a CDR L3 having at least 99% identity to amino acid sequence SEQ ID NO: 3.

54. An antibody or a recombinant antibody, comprising a light chain sequence comprising complementarity determining region (CDR) CDR L1 having at least 100% identity to amino acid sequence SEQ ID NO: 1, a CDR L2 having at least 100% identity to amino acid sequence SEQ ID NO: 2, and a CDR L3 having at least 100% identity to amino acid sequence SEQ ID NO: 3.
55. The antibody or the recombinant antibody of any one of claims 53-54, further comprising a heavy chain sequence comprising at least one complementarity determining region (CDR) H1 having at least 80% identity to amino acid sequence SEQ ID NO: 4, a CDR H2 having at least 80% identity to amino acid sequence SEQ ID NO: 5, and a CDR H3 having at least 80% identity to amino acid sequence SEQ ID NO: 6.
56. The antibody or the recombinant antibody of claim 55, in which the CDR H1 has at least 90% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 90% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 90% identity to amino acid sequence SEQ ID NO: 6.
57. The antibody or the recombinant antibody of claim 55, in which the CDR H1 has at least 95% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 95% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 95% identity to amino acid sequence SEQ ID NO: 6.
58. The antibody or the recombinant antibody of claim 55, in which the CDR H1 has at least 99% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 99% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 99% identity to amino acid sequence SEQ ID NO: 6.
59. The antibody or the recombinant antibody of claim 55, in which the CDR H1 has at least 100% identity to amino acid sequence SEQ ID NO: 4, the CDR H2 has at least 100% identity to amino acid sequence SEQ ID NO: 5, and the CDR H3 has at least 100% identity to amino acid sequence SEQ ID NO: 6.
60. The antibody or the recombinant antibody according to any one of claims 53-54, further comprising a heavy chain variable region (V<sub>H</sub>) having at least 80% identity to amino acid

sequence SEQ ID NO: 8.

61. The antibody or the recombinant antibody of any one of claims 55-59, wherein the heavy chain variable region (V<sub>H</sub>) has at least 80% identity to amino acid sequence SEQ ID NO: 8.
62. The antibody or the recombinant antibody of any one of claims 53-59, in which the light chain sequence comprises light chain variable region (V<sub>L</sub>) having at least 80% identity to amino acid sequence SEQ ID NO: 7.
63. The antibody or the recombinant antibody according to any one of claims 1-62, further comprising a human heavy chain constant region or a human light chain constant region.
64. The antibody or the recombinant antibody of claim 63, wherein the human heavy chain constant region is IgG1 or IgG4 or a fragment thereof.
65. The antibody or the recombinant antibody of any one of claims 1-64, wherein the heavy chain has at least 80% identity to the amino acid sequence of SEQ ID NO: 10.
66. The antibody or the recombinant antibody of any one of claims 1-65, wherein the light chain has at least 80% identity to the amino acid sequence of SEQ ID NO: 9.
67. The antibody or the recombinant antibody of any one of claims 1-64 or 66, wherein the heavy chain has at least 80% identity to the amino acid sequence of SEQ ID NO: 12.
68. The antibody or the recombinant antibody of any one of claims 1-65 or 66, wherein the heavy chain has at least 80% identity to the amino acid sequence of SEQ ID NO: 11.
69. The antibody or the recombinant antibody of any one of claims 1-64, wherein the heavy chain has at least 80% identity to the amino acid sequence of SEQ ID NO: 13.
70. The antibody or the recombinant antibody of any one of claims 1-69, comprising human a human variable framework region and a murine constant region.
71. The antibody or the recombinant antibody according to claim 70, further comprising a murine heavy chain constant region or a murine light chain constant region.
72. The antibody or the recombinant antibody of claim 71, wherein the murine heavy chain constant region is IgG2A.
73. The antibody or the recombinant antibody of claim 72, wherein the heavy chain has at least

80% identity to the amino acid sequence of SEQ ID NO: 15.

74. The antibody or the recombinant antibody of claim 72, wherein the heavy chain has at least 80% identity to the amino acid sequence of SEQ ID NO: 16.
75. The antibody or the recombinant antibody of claim 72, wherein the light chain has at least 80% identity to the amino acid sequence of SEQ ID NO: 14.
76. The antibody or the recombinant antibody according to any one of claims 1-75, wherein the antibody or the recombinant antibody is an antibody fragment comprising a single heavy chain, a single light chain, Fab, Fab', F(ab)', F(ab')<sub>2</sub>, Fd, scFv, a variable heavy domain, a variable light domain, a variable NAR domain, bi-specific scFv, a bi-specific Fab<sub>2</sub>, a tri-specific Fab<sub>3</sub>, a single chain binding polypeptide, a dAb fragment, or a diabody.
77. The antibody or the recombinant antibody according to any one of claims 1-76 that specifically binds to a CD163 protein expressed on an immunosuppressive human myeloid cell, wherein binding of the antibody or the recombinant antibody to the myeloid cell promotes an immune cell function as measured by one or both of the following parameters:
  - (i) activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof;
  - and
  - (ii) proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof.
78. The antibody or the recombinant antibody according to claim 77, wherein the activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof is measured as an enhanced level of IFN- $\gamma$ , TNF- $\alpha$ , or perforin, or any combination thereof.
79. The antibody or the recombinant antibody according to claim 77, wherein the immunosuppressive human myeloid cell is a macrophage or a myeloid-derived suppressor cell.
80. The antibody or the recombinant antibody according to claim 77, wherein the immune cell function is in a tumor microenvironment.
81. The antibody or the recombinant antibody according to any one of claims 77-80, wherein the immune cell function is *in vivo*.
82. The antibody or the recombinant antibody according to any one of claims 1-76 that specifically binds to a CD163 protein expressed on a human macrophage, wherein binding

of the antibody or the recombinant antibody to the macrophage increases an immunostimulatory activity in a tumor microenvironment.

83. The antibody or the recombinant antibody according to claim 82, wherein the tumor microenvironment is *in vivo*.
84. The antibody or the recombinant antibody according to any one of claims 79-83, wherein binding of the antibody or the recombinant antibody to the macrophage reduces an immunosuppression activity of the macrophage.
85. The antibody or the recombinant antibody according to any one of claims 79-84, wherein binding of the antibody or the recombinant antibody to the macrophage reduces a tumor promoting activity of the macrophage.
86. The antibody or the recombinant antibody according to any one of claims 79-85, wherein the macrophage is a tumor-associated macrophage.
87. The antibody or the recombinant antibody according to any one of claims 79-85, wherein the antibody or the recombinant antibody alters expression of at least one marker on the macrophage.
88. The antibody or the recombinant antibody according to any one of claims 77-86, wherein the CD163 protein is a glycoform of CD163.
89. The antibody or the recombinant antibody according to any one of claims 77-87, wherein the CD163 protein is a 150 kDa glycoform of CD163.
90. The antibody or the recombinant antibody according to any one of claims 79-89, wherein the antibody or recombinant antibody does not specifically bind to a 130 kDa glycoform of CD163 expressed by the human macrophage.
91. The antibody or the recombinant antibody according to any one of claims 1-90, having a constant domain that enables binding to an Fc receptor.
92. The antibody or the recombinant antibody according to claim 91, wherein the Fc receptor is expressed on the macrophage.
93. The antibody or the recombinant antibody according to any one of claims 1-92, having an antibody fragment comprising a single heavy chain, a single light chain, Fab, Fab', F(ab)',

F(ab')<sub>2</sub>, Fd, scFv, a variable heavy domain, a variable light domain, a variable NAR domain, bi-specific scFv, a bi-specific Fab<sub>2</sub>, a tri-specific Fab<sub>3</sub>, a single chain binding polypeptide, a dAb fragment, or a diabody.

94. The antibody or the recombinant antibody according to any one of claims 79-93, wherein at least one marker on the human macrophage is CD16, CD64, TLR2, or Siglec-15.
95. The antibody or the recombinant antibody according to any one of claims 79-93, wherein the human macrophage is an M2 macrophage or a M2-like macrophage.
96. The antibody or the recombinant antibody according to any one of claims 79-93, wherein the human macrophage is an M2a, M2b, M2c, or M2d macrophage.
97. The antibody or the recombinant antibody according to any one of claims 79-96, wherein the CD163 protein is a component of a cell surface complex comprising at least one other protein expressed by the macrophage.
98. The antibody or the recombinant antibody according to claim 97, wherein the at least one other protein is a galectin-1 protein, a LILRB2 protein, a casein kinase II protein, or any combination thereof.
99. The antibody or the recombinant antibody according to any one of claims 79-98, wherein upon binding with the CD163 protein, the antibody or recombinant antibody is internalized by the human macrophage.
100. The antibody or the recombinant antibody according to any one of claims 79-99, wherein binding to the CD163 protein is not cytotoxic to the macrophage.
101. The antibody or the recombinant antibody according to any one of claims 79-100, wherein binding to the CD163 protein promotes CD4<sup>+</sup> T cell activation, CD4<sup>+</sup> T cell proliferation, or both CD4<sup>+</sup> T cell activation and proliferation.
102. The antibody or the recombinant antibody according to any one of claims 77-101, wherein binding to the CD163 protein promotes expression of CD69, ICOS, OX40, PD1, LAG3, CTLA4, or any combination thereof by CD4<sup>+</sup> T cells.
103. The antibody or the recombinant antibody according to any one of claims 77-102, wherein binding to the CD163 protein promotes CD8<sup>+</sup> T cell activation, CD8<sup>+</sup> T cell proliferation, or

both CD8<sup>+</sup> T cell activation and proliferation.

104. The antibody or the recombinant antibody according to any one of claims 77-103, wherein binding to the CD163 protein promotes expression of ICOS, OX40, PD1, LAG3, CTLA4, or any combination thereof by CD8<sup>+</sup> T cells.
105. The antibody or the recombinant antibody according to any one of claims 77-104, wherein binding to the CD163 protein reduces immunosuppression in a tumor microenvironment.
106. The antibody or the recombinant antibody according to any one of claims 77-105, wherein binding to the CD163 protein promotes tumor cell killing in a tumor microenvironment.
107. The antibody or the recombinant antibody according to any one of claims 77-106, wherein binding to the CD163 protein promotes cytotoxic lymphocyte-mediated killing of cancer cells.
108. The antibody or the recombinant antibody according to any one of claims 77-107, wherein binding to the CD163 protein promotes NK cell-mediated tumor cell killing.
109. The antibody or the recombinant antibody according to any one of claims 77-108, wherein binding to the CD163 protein promotes expression of IL-2 by T cells.
110. The antibody or the recombinant antibody according to any one of claims 77-109, wherein binding to the CD163 protein increases CD4<sup>+</sup> T cells, CD196<sup>+</sup> T cells, CXCR3<sup>+</sup> T cells, CCR4<sup>+</sup> T cells, or any combination thereof.
111. The antibody or the recombinant antibody according to any one of claims 77-110, wherein binding to CD163 reduces immunosuppression in a tumor microenvironment caused by a macrophage.
112. The antibody or the recombinant antibody according to any one of claims 1-111 that specifically binds to a CD163 protein expressed on a human macrophage, wherein binding results in at least one of the following effects:
  - (a) reduced expression of at least one marker by the macrophage, wherein the at least one marker is CD16, CD64, TLR2, or Siglec-15;
  - (b) internalization of the antibody by the macrophage;
  - (c) secretion of IFN- $\gamma$ , TNF- $\alpha$  and perforin;
  - (d) activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof;

- (e) proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof;  
and
- (f) promotion of tumor cell killing in a tumor microenvironment.
113. The antibody or the recombinant antibody of claim 112, wherein the binding results in: two or more of (a) through (e); three or more of (a) through (e); four or more of (a) through (e); or all of (a) through (e).
114. The antibody or the recombinant antibody according to any one of claims 1-113 that specifically binds to a CD163<sup>+</sup> immunosuppressive myeloid cell in a tumor microenvironment, wherein the binding reduces suppression of cytotoxic T cell-mediated killing of tumor cells in the tumor microenvironment.
115. The antibody or the recombinant antibody according to any one of claims 1-114 that specifically binds to a CD163 protein expressed on a human tumor-associated macrophage and reduces expression of CD16, CD64, TLR2, Siglec-15, or a combination thereof by the macrophage, for use in a method of treating cancer.
116. The antibody or the recombinant antibody according to claims 79-115, wherein binding of the antibody or the recombinant antibody to the macrophage modulates an immune function of a cell in a tumor microenvironment.
117. The antibody or the recombinant antibody according to claims 79-115, wherein binding of the antibody or the recombinant antibody to the macrophage promotes an anti-tumor immune function.
118. The antibody or the recombinant antibody according to any one of claims 1-117, wherein the antibody or the recombinant antibody specifically binds to a CD163 epitope comprising amino acid sequence SEQ ID NO: 18.
119. The antibody or the recombinant antibody according to any one of claims 1-117, wherein the antibody or the recombinant antibody specifically binds to a CD163 epitope comprising amino acid sequence SEQ ID NO: 19.
120. The antibody or the recombinant antibody according to any one of claims 1-117, wherein the antibody or the recombinant antibody specifically binds to a CD163 epitope comprising amino acid sequence SEQ ID NO: 20.

121. The antibody or the recombinant antibody according to any one of claims 1-117, wherein the antibody or the recombinant antibody specifically binds to a CD163 epitope comprising each of amino acid sequence SEQ ID NO: 18, SEQ ID NO: 19, and SEQ ID NO: 20.
122. The antibody or the recombinant antibody according to any one of claims 1-121, wherein the antibody or the recombinant antibody specifically binds to CD163 with a  $K_D$  from 1nM to 100nM.
123. The antibody or the recombinant antibody of claim 122, wherein the antibody or the recombinant antibody specifically binds to CD163 with a  $K_D$  from 1nM to 50nM.
124. The antibody or the recombinant antibody of claim 123, wherein the antibody or the recombinant antibody specifically binds to CD163 with a  $K_D$  from 1nM to 10nM.
125. The antibody or the recombinant antibody according to any one of claims 1-121, wherein the antibody or the recombinant antibody specifically binds to human M2c macrophages with a  $K_D$  from 1nM to 100nM.
126. The antibody or the recombinant antibody of claim 125, wherein the antibody or the recombinant antibody specifically binds to human M2c macrophages with a  $K_D$  from 1nM to 50nM.
127. The antibody or the recombinant antibody of claim 126, wherein the antibody or the recombinant antibody specifically binds to human M2c macrophages with a  $K_D$  from 1nM to 10nM.
128. A composition comprising an antibody or a recombinant antibody according to any one of claims 1-127, and an excipient.
129. A pharmaceutical composition, comprising an antibody or a recombinant antibody according to any one of claims 1-127 and a pharmaceutically acceptable excipient.
130. Use of an antibody or a recombinant antibody according to any one of claims 1-127, for the manufacture of a medicament for treating cancer in a human subject.
131. Use of an antibody or a recombinant antibody according to any one of claims 1-127, for the manufacture of a medicament that reduces immunosuppression by a tumor-associated macrophage in a human subject having a cancer.

132. Use of an antibody or a recombinant antibody according to any one of claims 1-127, for the manufacture of a medicament that promotes T cell-mediated tumor cell killing in a human subject having a cancer.
133. A method of promoting an immune cell function in a subject in need thereof, the method comprising: administering an antibody or a recombinant antibody according to any one of claims 1-132 to an individual in need thereof; wherein  
promoting an immune cell function as measured by one or both of the following parameters:
  - (i) activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof;and
  - (ii) proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof.
134. The method of claim 133, wherein the activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof is measured as an increased level of IFN- $\gamma$ , TNF- $\alpha$ , or perforin, or any combination thereof.
135. The method of claim 133, wherein the immunosuppressive human myeloid cell is a macrophage.
136. The method of claim 135, wherein the immunosuppressive human myeloid cell is a myeloid-derived suppressor cell.
137. The method of claim 136, wherein the antibody is an antibody or a recombinant antibody according to any one of claims 76-127.
138. A method of treating cancer in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of an antibody or a recombinant antibody according to any one of claims 1-127, thereby treating the cancer in the individual.
139. A method of treating cancer in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of an antibody or a recombinant antibody according to any one of claims 1-127, whereby immunosuppression by a tumor-associated macrophage in the individual is reduced.
140. A method of treating cancer in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of an antibody or a

recombinant antibody according to any one of claims 1-127, whereby T cell-mediated tumor cell killing in the individual is increased.

141. A method of reducing a tumor promoting activity of a tumor-associated macrophage in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of an antibody or a recombinant antibody according to any one of claims 1-127 that is effective to modulate a CD4<sup>+</sup> T cell activation, CD4<sup>+</sup> T cell proliferation, CD8<sup>+</sup> T cell activation, CD8<sup>+</sup> T cell proliferation, or any combination.
142. A method of promoting lymphocyte-mediated tumor cell killing in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of an antibody or a recombinant antibody according to any one of claims 1-127.
143. The method according to any one of claims 138-142, wherein the cancer is a lung cancer or sarcoma.
144. The method according to claim 143, wherein the lung cancer is a lung carcinoma or lung adenocarcinoma.
145. The method according to any one of claims 138-142, wherein the antibody or the recombinant antibody binds to a macrophage in a tumor microenvironment.
146. The method according to any one of claims 138-142, further comprising administering to the individual an additional anticancer therapy.
147. The method according to claim 146, wherein the additional anticancer therapy is surgical therapy, chemotherapy, radiation therapy, cryotherapy, hormonal therapy, immunotherapy, and cytokine therapy, and combinations thereof
148. The method according to claim 147, wherein the additional anticancer therapy is an immunotherapy.
149. The method according to claim 148, wherein the immunotherapy is a composition comprising a checkpoint inhibitor.
150. A method of modulating an activity of a tumor-associated macrophage in a tumor microenvironment, the method comprising contacting the tumor-associated macrophage with an antibody or a recombinant antibody according to any one of claims 1-127 that binds

to a CD163-expressing human macrophage and comprises at least one of the following effects:

- (a) the binding of the antibody reduces expression of at least one marker on the macrophage, wherein the at least one marker is CD16, CD64, TLR2, or Siglec-15;
- (b) upon binding of the antibody with the CD163 protein, the antibody is internalized by the human macrophage;
- (c) the binding of the antibody is not cytotoxic to the macrophage;
- (d) the binding of the antibody increases the levels of IFN- $\gamma$ , TNF- $\alpha$  and perforin;
- (e) the binding of the antibody promotes an activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof;
- (f) the binding of the antibody promotes a proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof; and
- (g) the binding of the antibody promotes tumor cell killing in the tumor microenvironment.

151. The method according to claim 150, wherein the binding results in: two or more of (a) through (g); three or more of (a) through (g); four or more of (a) through (g); five or more of (a) through (g); six or more of (a) through (g); or all of (a) through (g).
152. An antibody that specifically binds to a CD163 protein expressed on an immunosuppressive human myeloid cell, wherein binding of the antibody to the myeloid cell promotes an immune cell function as measured by one or both of the following parameters:
  - (i) activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof; and
  - (ii) proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof.
153. The antibody according to claim 152, wherein the immunosuppressive human myeloid cell is a macrophage or a myeloid-derived suppressor cell.
154. An antibody that specifically binds to a CD163 protein expressed on a human macrophage, wherein binding of the antibody to the macrophage promotes an immune cell function as measured by one or both of the following parameters:
  - (i) activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof; and
  - (ii) proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof.
155. The antibody according to any one of claims 152-154, wherein the immune cell function is in a tumor microenvironment.
156. The antibody according to any one of claims 152-155, wherein the immune cell function is *in vivo*.

157. An antibody that specifically binds to a CD163 protein expressed on a human macrophage, wherein binding of the antibody to the macrophage increases an immunostimulatory activity in a tumor microenvironment.
158. The antibody according to claim 157, wherein the tumor microenvironment is *in vivo*.
159. The antibody according to any one of claims 153-158, wherein binding of the antibody to the macrophage reduces an immunosuppression activity of the macrophage.
160. The antibody according to any one of claims 153-159, wherein binding of the antibody to the macrophage reduces a tumor promoting activity of the macrophage.
161. The antibody according to any one of claims 153-160, wherein the macrophage is a tumor-associated macrophage.
162. The antibody according to any one of claims 153-161, wherein the antibody alters expression of at least one marker on the macrophage.
163. The antibody according to any one of claims 152-162, wherein the CD163 protein is a glycoform of CD163.
164. The antibody according to any one of claims 152-163, wherein the CD163 protein is a 150 kDa glycoform of CD163.
165. The antibody according to any one of claims 153-164, wherein the antibody does not specifically bind to a 130 kDa glycoform of CD163 expressed by the human macrophage.
166. The antibody according to any one of claims 152-165, having a constant domain that enables binding to an Fc receptor.
167. The antibody according to claim 166, wherein the Fc receptor is expressed on the macrophage.
168. The antibody according to any one of claims 152-167, having an antibody fragment comprising a single heavy chain, a single light chain, Fab, Fab', F(ab)', F(ab')<sub>2</sub>, Fd, scFv, a variable heavy domain, a variable light domain, a variable NAR domain, bi-specific scFv, a bi-specific Fab<sub>2</sub>, a tri-specific Fab<sub>3</sub>, a single chain binding polypeptide, a dAb fragment, or a diabody.
169. An antibody according to any one of claims 153-168, wherein at least one marker on the human macrophage is CD16, CD64, TLR2, or Siglec-15.
170. The antibody according to any one of claims 153-169, wherein the human macrophage is an M2 macrophage or a M2-like macrophage.
171. The antibody according to claim 170, wherein the human macrophage is an M2a, M2b, M2c, or M2d macrophage.
172. The antibody according to any one of claims 153-171, wherein the CD163 protein is a

component of a cell surface complex comprising at least one other protein expressed by the macrophage.

173. The antibody according to claim 172, wherein the at least one other protein is a galectin-1 protein, a LILRB2 protein, a casein kinase II protein, or any combination thereof.
174. The antibody according to any one of claims 153-173, wherein upon binding with the CD163 protein, the antibody is internalized by the human macrophage.
175. The antibody according to any one of claims 153-174, wherein binding to the CD163 protein is not cytotoxic to the macrophage.
176. The antibody according to any one of claims 152-175, wherein binding to the CD163 protein promotes CD4<sup>+</sup> T cell activation, CD4<sup>+</sup> T cell proliferation, or both CD4<sup>+</sup> T cell activation and proliferation.
177. The antibody according to any one of claims 152-176, wherein binding to the CD163 protein promotes expression of CD69, ICOS, OX40, PD1, LAG3, CTLA4, or any combination thereof by CD4<sup>+</sup> T cells.
178. The antibody according to any one of claims 152-177, wherein binding to the CD163 protein promotes CD8<sup>+</sup> T cell activation, CD8<sup>+</sup> T cell proliferation, or both CD8<sup>+</sup> T cell activation and proliferation.
179. The antibody according to any one of claims 152-178, wherein binding to the CD163 protein promotes expression of ICOS, OX40, PD1, LAG3, CTLA4, or any combination thereof by CD8<sup>+</sup> T cells.
180. The antibody according to any one of claims 152-179, wherein binding to the CD163 protein reduces immunosuppression in a tumor microenvironment.
181. The antibody according to any one of claims 152-180, wherein binding to the CD163 protein promotes tumor cell killing in a tumor microenvironment.
182. The antibody according to any one of claims 152-181, wherein binding to the CD163 protein promotes cytotoxic lymphocyte-mediated killing of cancer cells.
183. The antibody according to any one of claims 152-182, wherein binding to the CD163 protein promotes NK cell-mediated tumor cell killing.
184. The antibody according to any one of claims 152-183, wherein binding to the CD163 protein promotes expression of IL-2 by T cells.
185. The antibody according to any one of claims 152-184, wherein binding to the CD163 protein increases CD4<sup>+</sup> T cells, CD196<sup>-</sup> T cells, CXCR3<sup>+</sup> T cells, CCR4<sup>-</sup> T cells, or any combination thereof.
186. The antibody according to claims 152-185, wherein binding to CD163 reduces

- immunosuppression in a tumor microenvironment caused by a macrophage.
187. An antibody that specifically binds to a CD163 protein expressed on a human macrophage, wherein binding results in at least one of the following effects:
- (a) reduced expression of at least one marker by the macrophage, wherein the at least one marker is CD16, CD64, TLR2, or Siglec-15;
  - (b) internalization of the antibody by the macrophage;
  - (c) activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof;
  - (d) proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof; and
  - (e) promotion of tumor cell killing in a tumor microenvironment.
188. The antibody of claim 187, wherein the binding results in: two or more of (a) through (e); three or more of (a) through (e); four or more of (a) through (e); or all of (a) through (e).
189. An antibody that specifically binds to a CD163<sup>+</sup> immunosuppressive myeloid cell in a tumor microenvironment, wherein the binding reduces suppression of cytotoxic T cell-mediated killing of tumor cells in the tumor microenvironment.
190. An antibody that specifically binds to a CD163 protein expressed on a human tumor-associated macrophage and reduces expression of CD16, CD64, TLR2, Siglec-15, or a combination thereof by the macrophage, for use in a method of treating cancer.
191. The antibody according to claims 153-190, wherein binding of the antibody to the macrophage modulates an immune function of a cell in a tumor microenvironment.
192. The antibody according to claims 153-191, wherein binding of the antibody to the macrophage promotes an anti-tumor immune function.
193. A composition comprising an antibody according to any one of claims 152-192, and an excipient.
194. A pharmaceutical composition, comprising an antibody according to any one of claims 152-192 and a pharmaceutically acceptable carrier.
195. Use of an antibody according to any one of claims 152-192, for the manufacture of a medicament for treating cancer in a human subject.
196. Use of an antibody according to any one of claims 152-192, for the manufacture of a medicament that reduces immunosuppression by a tumor-associated macrophage in a human subject having a cancer.
197. Use of an antibody according to any one of claims 152-192, for the manufacture of a medicament that promotes T cell-mediated tumor cell killing in a human subject having a cancer.
198. A method of promoting an immune cell function, the method comprising:

- specifically binding an antibody to a CD163 protein expressed on an immunosuppressive human myeloid cell; and
- promoting an immune cell function as measured by one or both of the following parameters:
- (i) activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof; and
  - (ii) proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof.
199. The method of claim 198, wherein the immunosuppressive human myeloid cell is a macrophage.
200. The method of claim 198, wherein the immunosuppressive human myeloid cell is a myeloid-derived suppressor cell.
201. The method of claim 198, wherein the antibody is an antibody according to any one of claims 152-192.
202. A method of treating cancer in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of an antibody according to any one of claims 152-192, thereby treating the cancer in the individual.
203. A method of treating cancer in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of an antibody according to any one of claims 152-192, whereby immunosuppression by a tumor-associated macrophage in the individual is reduced.
204. A method of treating cancer in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of an antibody according to any one of claims 152-192, whereby T cell-mediated tumor cell killing in the individual is increased.
205. The method according to any one of claims 198-204, wherein the cancer is a lung cancer or sarcoma.
206. The method according to claim 205, in wherein the lung cancer is a lung carcinoma or lung adenocarcinoma.
207. A method of reducing a tumor promoting activity of a tumor-associated macrophage in an individual in need thereof, the method comprising administering to the individual an amount of a pharmaceutical composition according to claim 194 that is effective to modulate a CD4<sup>+</sup> T cell activation, CD4<sup>+</sup> T cell proliferation, CD8<sup>+</sup> T cell activation, CD8<sup>+</sup> T cell proliferation, or any combination thereof in the tumor microenvironment.
208. The method according to claim 207, further comprising promoting tumor cell killing in the tumor microenvironment.
209. A method of promoting lymphocyte-mediated tumor cell killing in an individual in need

thereof, the method comprising administering to the individual an effective amount of a pharmaceutical composition according to claim 194.

210. A method of modulating an activity of a tumor-associated macrophage in a tumor microenvironment, the method comprising contacting the tumor-associated macrophage with an antibody that binds to a CD163-expressing human macrophage and comprises at least one of the following effects:
- (a) the binding of the antibody reduces expression of at least one marker on the macrophage, wherein the at least one marker is CD16, CD64, TLR2, or Siglec-15;
  - (b) upon binding of the antibody with the CD163 protein, the antibody is internalized by the human macrophage;
  - (c) the binding of the antibody is not cytotoxic to the macrophage;
  - (d) the binding of the antibody promotes an activation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof;
  - (e) the binding of the antibody promotes a proliferation of a CD4<sup>+</sup> T cell, CD8<sup>+</sup> T cell, NK cell, or any combination thereof; and
  - (f) the binding of the antibody promotes tumor cell killing in the tumor microenvironment.
211. The method according to claim 210, wherein the binding results in: two or more of (a) through (f); three or more of (a) through (f); four or more of (a) through (f); five or more of (a) through (f); or all of (a) through (f).
212. The method according to any one of claims 198-211, wherein the method occurs in a tumor microenvironment.
213. The method according to any one of claims 198-212, wherein the method occurs *in vivo*.
214. The method according to any one of claims 198-213, wherein binding of the antibody to the macrophage modulates an immune function of a cell in a tumor microenvironment.
215. The method according to any one of claims 198-214, wherein binding of the antibody to the macrophage promotes an anti-tumor immune function.
216. The method according to any one of claims 198-215, wherein the antibody comprises a constant domain and the constant domain binds to an Fc receptor.
217. The method according to claim 216, wherein the Fc receptor is expressed on the macrophage.
218. The method according to any one of claims 198-217, further comprising internalizing the antibody by the human macrophage upon binding with the CD163 protein.
219. The method according to any one of claims 198-218, wherein binding to the CD163 protein is not cytotoxic to the human macrophage.

- 220. The method according to any one of claims 198-219, further comprising promoting expression of CD69, ICOS, OX40, PD1, LAG3, CTLA4, or any combination thereof by CD4<sup>+</sup> T cells.
- 221. The method according to any one of claims 198-220, further comprising promoting expression of ICOS, OX40, PD1, LAG3, CTLA4, or any combination thereof by CD8<sup>+</sup> T cells.
- 222. The method according to any one of claims 198-221, comprising reducing immunosuppression in a tumor microenvironment.
- 223. The method according to any one of claims 198-222, comprising promoting cytotoxic lymphocyte-mediated killing of cancer cells.
- 224. The method according to any one of claims 198-223, comprising promoting NK cell-mediated tumor cell killing.
- 225. The method according to any one of claims 198-224, comprising promoting expression of IL-2 by T cells.
- 226. The method according to any one of claims 198-225, comprising increasing CD4<sup>+</sup> T cells, CD196<sup>-</sup> T cells, CXCR3<sup>+</sup> T cells, CCR4<sup>-</sup> T cells, or any combination thereof.