Claims

1. A composition comprising

   i) a compound selected from the group consisting of: an anti-PD-1 antibody, an anti-CTLA4 antibody and a fusion protein comprising first and second peptide portions wherein said first peptide portion consists of an amino acid sequence selected from: wild type B7-DC, an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO:1 and which competes *in vitro* with wild-type B7-DC for binding to PD-1, a fragment of B7-DC which competes *in vitro* with wild-type B7-DC for binding to PD-1, and an extracellular domain of B7-DC and said second peptide portion comprises a portion of an immunoglobulin (Ig) and

   ii) a potentiating agent selected from the group of: cyclophosphamide and an analog of cyclophosphamide,

for use in the treatment of cancer or infection.

2. A composition comprising

   i) a compound, wherein said compound is a fusion protein comprising first and second peptide portions wherein said first peptide portion consists of an amino acid sequence selected from: wild type B7-DC, an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO:1 and which competes *in vitro* with wild-type B7-DC for binding to PD-1, a fragment of B7-DC which competes *in vitro* with wild-type B7-DC for binding to PD-1, and an extracellular domain of B7-DC and said second peptide portion comprises a portion of an immunoglobulin (Ig) and

   ii) a potentiating agent selected from the group of: cyclophosphamide and an analog of cyclophosphamide,

for use in the treatment of cancer or infection.

3. Use of a composition comprising

   i) a compound selected from the group consisting of: an anti-PD-1 antibody, an anti-CTLA4 antibody and a fusion protein comprising first and second peptide portions wherein said first peptide portion consists of an amino acid sequence selected from: wild type B7-DC, an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO:1 and which competes *in vitro* with wild-type B7-DC for binding to PD-1, a fragment of B7-DC which competes *in vitro* with wild-type B7-DC for binding to PD-1, and an extracellular domain of B7-DC and said second peptide portion comprises a portion of an immunoglobulin (Ig) and

   ii) a potentiating agent selected from the group of: cyclophosphamide and an analog of cyclophosphamide,

   for the manufacture of a medicament for treating cancer.

4. Use of a composition comprising

   i) a compound, wherein said compound is a fusion protein comprising first and second peptide portions wherein said first peptide portion consists of an amino acid sequence selected from: wild type B7-DC, an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO:1 and which competes *in vitro* with wild-type B7-DC for binding to PD-1, a fragment of B7-DC which competes *in vitro* with wild-type B7-DC for binding to PD-1, and an extracellular domain of B7-DC and said second peptide portion comprises a portion of an immunoglobulin (Ig) and

   ii) a potentiating agent selected from the group of: cyclophosphamide and an analog of cyclophosphamide,

   for the manufacture of a medicament for treating cancer.

5. Use of a composition comprising cyclophosphamide and a fusion protein comprising a first and second peptide portions wherein said first peptide portion consists of amino acids 20-221 of SEQ ID NO: 1, and said second peptide portion comprises a portion of an immunoglobulin (Ig) for the manufacture of a medicament for treating cancer.

6. The composition according to claim 1 or claim 2, or use of the composition according to claim 3 or claim 4, wherein said potentiating agent is to be administered before said compound and said compound is to be administered without said potentiating agent following the administration of said potentiating agent.

7. The composition according to claim 1, 2 or 6, or use of the composition according to claim 3, 4 or 6, wherein said first peptide portion consists of a wild type B7-DC polypeptide.

8. The composition or use of the composition according to claim 7, wherein said B7-DC is a human B7-DC.

9. The composition according to claim 1, 2 or 6, or use of the composition according to claim 3, 4 or 6, wherein said first peptide portion consists of a fragment of B7-DC which does not comprise any portion of the trans-membrane portion of said B7-DC polypeptide.

10. The composition or use of the composition according to claim 9, wherein said first peptide portion consists of the soluble portion of said B7-DC polypeptide and said second peptide portion comprises the Fc region of an antibody but does not comprise any of the variable region of said antibody.

11. The composition or use of the composition according to claim 9 or claim 10, wherein said first peptide portion consists of the amino acid sequence of

SEQ ID NO: 3 and said second polypeptide portion comprises the Fc region of an antibody but does not comprise any of the variable region of said antibody.

12. The composition according to claim 1, 2 or 6, or use of the composition according to claim 3, 4 or 6, wherein said first peptide portion consists of an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO: 1.

13. The composition or use of the composition according to claim 12, wherein said first peptide portion consists of the amino acid sequence of amino acids 20-221 or 20-121 of SEQ ID NO: 1.

14. The composition according to claim 1, 2 or 6, or use of the composition according to claim 3, 4 or 6, wherein said fusion protein comprises an amino acid sequence having at least 95% identity to the sequence of SEQ ID NO: 9, 10, 12 or 13.

15. The composition or use of the composition according to claim 14, wherein said fusion protein comprises the amino acid sequence of SEQ ID NO: 9, 10, 12, or 13.

16. The composition according to any one of claims 1, 2 and 6-15, or use of the composition according to any one of claims 3, 4 and 6-15, wherein said fusion protein is a monomer.

17. The composition according to any one of claims 1, 2 and 6-14, or use of the composition according to any one of claims 3, 4 and 6-14, wherein said fusion protein is a dimer.

18. The composition or use of the composition according to claim 17, wherein

said fusion protein is a homodimer.

19. The composition or use of the composition according to claim 17, wherein said fusion protein is a heterodimer.

20. The composition according to any one of claims 1, 2 and 6-19, or use of the composition according to any one of claims 3, 4 and 6-19, wherein said potentiating agent is cyclophosphamide.

21. The composition according to any one of claims 6-20, or use of the composition according to any one of claims 6-20, wherein said potentiating agent is to be administered at least X hours before the administration of the compound, wherein X is selected from 1, 2, 3, 5, 10, 15, 20, 24 and 30.

22. The composition according to any one of claims 1, 2 and 6-21, or use of the composition according to any one of claims 3, 4 and 6-21, wherein said fusion protein comprises a fragment of wild-type B7-DC which competes *in vitro* with wild-type B7-DC for binding to PD-1.

23. The composition or use of the composition according to claim 22, wherein said fragment of wild-type B7-DC does not comprise any portion of the transmembrane portion of such polypeptide.

24. The composition or use of the composition according to claim 23, wherein said B7-DC polypeptide is human B7-DC polypeptide.

25. The composition according to claim 1, 2 or 6, or use of the composition according to claim 3, 4 or 6, wherein said first peptide portion consists of the extracellular domain of B7-DC or a polypeptide differing therefrom by only conservative amino acid substitutions.

26. The composition according to any one of claims 1, 2 and 6-25, or use of the composition according to any one of claims 3, 4 and 6-25, wherein said fusion protein is present in an amount sufficient to treat cancer or infection by an increased T cell-mediated immune response.

27. The composition according to claim 1, 2 or 3, for use in the treatment of cancer.

28. The composition according to claim 1, 2 or 3, for use in the treatment of an infectious disease.

29. The composition according to claim 27, or use of the composition according to claim 3 or claim 4, wherein said cancer is bladder cancer, brain cancer, breast cancer, cervical cancer, colo-rectal cancer, esophageal cancer, kidney cancer, liver cancer, lung cancer, nasopharangeal cancer, pancreatic cancer, prostate cancer, skin cancer, stomach cancer, uterine cancer, ovarian cancer, testicular cancer, or hematologic cancer.

30. The composition according to claim 6, or use of the composition according to claim 3 or claim 4, further comprising at least one additional agent selected from the group consisting of an anti-PD-1 antibody, an anti-CTLA4 antibody, a mitosis inhibitor, an aromatase inhibitor, an A2AR antagonist, and an angiogenesis inhibitor with said fusion protein which is also to be administered.

31. A composition comprising cyclophosphamide and a fusion protein comprising a first and second peptide portions wherein said first peptide portion consists of amino acids 20-221 of SEQ ID NO: 1, and said second peptide portion comprises a portion of an immunoglobulin (Ig) for use in treating cancer.

32. The composition according to claim 31, or use of the composition according to claim 5, wherein said cyclophosphamide is to be administered before said

fusion protein and said fusion protein is to be administered without cyclophosphamide following the administration of cyclophosphamide.

33. The composition according to claim 31 or claim 32, or use of the composition according to claim 5 or claim 32, wherein said second peptide portion comprises amino acids 245-476 of human IgG1.

34. The composition or use of the composition according to claim 32, wherein said cyclophosphamide is to be administered to said patient at least 24 hours prior to the administration of the fusion protein.

35. A medical kit for increasing immune response, said kit comprising:
(a) a dosage supply of a compound according to the composition of any one of claims 1, 2 and 6-33;
(b) a supply of a potentiating agent selected from cyclophosphamide or an analog of cyclophosphamide;
(c) a supply of pharmaceutically acceptable carrier; and
(d) printed instructions for administering the compound and potentiating agent in a use according to the composition of claim 21 or a use of the use of the composition according to any one of claims 5-34.

36. The kit according to claim 35, wherein said first peptide portion consists of consists of the amino acid sequence of amino acids 20-221 or 20-121 of SEQ ID NO: 1 and said second peptide portion consists of the hinge, C_H2 and C_H3 regions of a human immunoglobulin Cγ1.

37. The kit according to claim 35 or claim 36, wherein said potentiating agent is cyclophosphamide.

Claims

1. A composition comprising

    i) a compound selected from the group consisting of: an anti-PD-1 antibody and a fusion protein comprising first and second peptide portions wherein said first peptide portion consists of an amino acid sequence selected from: wild type B7-DC, an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO:1 and which binds to PD-1, a fragment of B7-DC which binds to PD-1, and an extracellular domain of B7-DC and said second peptide portion comprises a portion of an immunoglobulin (Ig) and

    ii) an agent selected from the group of: cyclophosphamide and an analog of cyclophosphamide,

for use in the treatment of cancer or infection, wherein the dose of the agent is not effective to have direct anti-tumor activity; and wherein the T cell response achieved by the combination of the compound and the agent is greater than the T cell response achieved by administering either the compound alone or the agent alone.

2. A composition comprising

    i) a compound, wherein said compound is a fusion protein comprising first and second peptide portions wherein said first peptide portion consists of an amino acid sequence selected from: wild type B7-DC, an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO:1 and which binds to PD-1, a fragment of B7-DC which binds to PD-1, and an extracellular domain of B7-DC and said second peptide portion comprises a portion of an immunoglobulin (Ig) and

    ii) an agent selected from the group of: cyclophosphamide and an analog of cyclophosphamide,

for use in the treatment of cancer or infection, wherein the dose of the agent is not effective to have direct anti-tumor activity; and wherein the T cell response achieved by the combination of the compound and the agent is greater than the T cell response achieved by administering either the compound alone or the agent alone.

3. Use of a composition comprising
    i) a compound selected from the group consisting of: an anti-PD-1 antibody and a fusion protein comprising first and second peptide portions wherein said first peptide portion consists of an amino acid sequence selected from: wild type B7-DC, an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO:1 and which binds to PD-1, a fragment of B7-DC which binds to PD-1, and an extracellular domain of B7-DC and said second peptide portion comprises a portion of an immunoglobulin (Ig) and
    ii) an agent selected from the group of: cyclophosphamide and an analog of cyclophosphamide,

    for the manufacture of a medicament for treating cancer, wherein the dose of the agent is not effective to have direct anti-tumor activity; and wherein the T cell response achieved by the combination of the compound and the agent is greater than the T cell response achieved by administering either the compound alone or the agent alone.

4. Use of a composition comprising
    i) a compound, wherein said compound is a fusion protein comprising first and second peptide portions wherein said first peptide portion consists of an amino acid sequence selected from: wild type B7-DC, an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO:1 and which binds to PD-1, a fragment of B7-DC which binds to PD-1,

and an extracellular domain of B7-DC and said second peptide portion comprises a portion of an immunoglobulin (Ig) and

ii) an agent selected from the group of: cyclophosphamide and an analog of cyclophosphamide,

for the manufacture of a medicament for treating cancer, wherein the dose of the agent is not effective to have direct anti-tumor activity; and wherein the T cell response achieved by the combination of the compound and the agent is greater than the T cell response achieved by administering either the compound alone or the agent alone.

5. Use of a composition comprising cyclophosphamide and a fusion protein comprising a first and second peptide portions wherein said first peptide portion consists of amino acids 20-221 of SEQ ID NO: 1, and said second peptide portion comprises a portion of an immunoglobulin (Ig) for the manufacture of a medicament for treating cancer, wherein the dose of the agent is not effective to have direct anti-tumor activity; and wherein the T cell response achieved by the combination of the compound and the agent is greater than the T cell response achieved by administering either the compound alone or the agent alone.

6. The composition according to claim 1 or 2, or use of the composition according to claim 3 or 4, wherein said first peptide portion consists of a wild type B7-DC polypeptide.

7. The composition or use of the composition according to claim 6, wherein said B7-DC is a human B7-DC.

8. The composition according to claim 1 or 2, or use of the composition according to claim 3 or 4, wherein said first peptide portion consists of a fragment of B7-DC which does not comprise any portion of the trans-membrane portion of said B7-DC polypeptide.

9. The composition or use of the composition according to claim 8, wherein said first peptide portion consists of the soluble portion of said B7-DC polypeptide and said second peptide portion comprises the Fc region of an antibody but does not comprise any of the variable region of said antibody.

10. The composition or use of the composition according to claim 8 or claim 9, wherein said first peptide portion consists of the amino acid sequence of SEQ ID NO: 3 and said second polypeptide portion comprises the Fc region of an antibody but does not comprise any of the variable region of said antibody.

11. The composition according to claim 1 or 2, or use of the composition according to claim 3 or 4, wherein said first peptide portion consists of an amino acid sequence having at least 98% identity to amino acids 20-221 or 20-121 of SEQ ID NO: 1.

12. The composition or use of the composition according to claim 11, wherein said first peptide portion consists of the amino acid sequence of amino acids 20-221 or 20-121 of SEQ ID NO: 1.

13. The composition according to claim 1 or 2, or use of the composition according to claim 3 or 4, wherein said fusion protein comprises an amino acid sequence having at least 95% identity to the sequence of SEQ ID NO: 9, 10, 12 or 13.

14. The composition or use of the composition according to claim 13, wherein said fusion protein comprises the amino acid sequence of SEQ ID NO: 9, 10, 12, or 13.

15. The composition according to any one of claims 1, 2 and 6-14, or use of the composition according to any one of claims 3, 4 and 6-14, wherein said fusion protein is a monomer.

16. The composition according to any one of claims 1, 2 and 6-14, or use of the composition according to any one of claims 3, 4 and 6-14, wherein said fusion protein is a dimer.

17. The composition or use of the composition according to claim 16, wherein said fusion protein is a homodimer.

18. The composition or use of the composition according to claim 16, wherein said fusion protein is a heterodimer.

19. The composition according to any one of claims 1, 2 and 6-18, or use of the composition according to any one of claims 3, 4 and 6-18, wherein said agent is cyclophosphamide.

20. The composition according to any one of claims 1, 2 and 6-19, or use of the composition according to any one of claims 3, 4 and 6-19, wherein said fusion protein comprises a fragment of wild-type B7-DC which binds to PD-1.

21. The composition or use of the composition according to claim 20, wherein said fragment of wild-type B7-DC does not comprise any portion of the transmembrane portion of such polypeptide.

22. The composition or use of the composition according to claim 21, wherein said B7-DC polypeptide is human B7-DC polypeptide.

23. The composition according to claim 1 or 2, or use of the composition according to claim 3 or 4, wherein said first peptide portion consists of the extracellular domain of B7-DC or a polypeptide differing therefrom by only conservative amino acid substitutions.

24. The composition according to any one of claims 1, 2 and 6-23, or use of the composition according to any one of claims 3, 4 and 6-23, wherein said fusion protein is present in an amount sufficient to treat cancer or infection by an increased T cell-mediated immune response.

25. The composition according to claim 1 or 2, for use in the treatment of cancer.

26. The composition according to claim 1 or 2, for use in the treatment of an infectious disease.

27. The composition according to claim 25, or use of the composition according to claim 3 or claim 4, wherein said cancer is bladder cancer, brain cancer, breast cancer, cervical cancer, colo-rectal cancer, esophageal cancer, kidney cancer, liver cancer, lung cancer, nasopharangeal cancer, pancreatic cancer, prostate cancer, skin cancer, stomach cancer, uterine cancer, ovarian cancer, testicular cancer, or hematologic cancer.

28. The composition according to claims 1 or 2, or use of the composition according to claim 3 or claim 4, further comprising at least one additional agent selected from the group consisting of an anti-PD-1 antibody, an anti-CTLA4 antibody, a mitosis inhibitor, an aromatase inhibitor, an A2AR antagonist, and an angiogenesis inhibitor with said fusion protein which is also to be administered.

29. A composition comprising cyclophosphamide and a fusion protein comprising a first and second peptide portions wherein said first peptide portion consists of amino acids 20-221 of SEQ ID NO: 1, and said second peptide portion

comprises a portion of an immunoglobulin (Ig) for use in treating cancer, wherein the dose of the agent is not effective to have direct anti-tumor activity; and wherein the T cell response achieved by the combination of the compound and the agent is greater than the T cell response achieved by administering either the compound alone or the agent alone.

30. The composition according to claim 29 or use of the composition according to claim 5, wherein said second peptide portion comprises amino acids 245-476 of human IgG1.

31. A medical kit for increasing immune response, said kit comprising:
(a) a dosage supply of a compound according to the composition of any one of claims 1, 2 and 6-30;
(b) a supply of an agent selected from cyclophosphamide or an analog of cyclophosphamide;
(c) a supply of pharmaceutically acceptable carrier; and
(d) printed instructions for administering the compound and agent in a use of the use of the composition according to any one of claims 5-30.

32. The kit according to claim 31, wherein said first peptide portion consists of the amino acid sequence of amino acids 20-221 or 20-121 of SEQ ID NO: 1 and said second peptide portion consists of the hinge, C_H2 and C_H3 regions of a human immunoglobulin Cγ1.

33. The kit according to claim 31 or 32, wherein said agent is cyclophosphamide.