In certain aspects, the present invention provides for use of a substance for manufacture of a medicament for the treatment or prevention of a disease associated with modulation of activity of human IL-10 . The substance comprises a heterodimeric protein comprised of a first polypeptide containing amino acid sequence of SEQ ID NO. 1 and a second polypeptide containing amino acid sequence of SEQ ID NO. 2. The disease associated with modulation of activity of human IL-10 may be an arthritis, a gout, a rheumatoid arthritis, a Cryopyrin-Associated Periodic Syndromes (CAPS), a scleroderma, a diabetes, a atherosclerosis, a dry eye disease, an ocular allergy, or an uveitis.

In certain aspects, the present invention provides for a method of treating or preventing a disease or condition associated with modulation of activity of human IL-10. The method comprising administering to a patient in need for treating or preventing a disease associated with modulation of activity of human IL-10 a therapeutically effective amount of a pharmaceutical composition. The pharmaceutical composition comprising a heterodimeric protein comprised of a first polypeptide containing amino acid sequence of SEQ ID NO. 1 and a second polypeptide containing amino acid sequence of SEQ ID NO. 2. The disease associated with modulation of activity of human IL-10 may be an arthritis, a gout, a rheumatoid arthritis, a Cryopyrin-Associated Periodic Syndromes (CAPS), a scleroderma, a diabetes, a atherosclerosis, a dry eye disease, an ocular allergy, or an uveitis.

In one aspect, the present disclosure provides a use of a pharmaceutical composition in the manufacture of a medicament for treating or preventing a disease or condition associated with modulation of activity of human IL- 1 β, the pharmaceutical composition comprising a heterodimeric protein comprising a first polypeptide comprising amino acid sequence of SEQ ID NO. 1 and a second polypeptide comprising amino acid sequence of SEQ ID NO. 2.

In certain aspects the present invention provides for a heterodimeric protein composition capable of binding human IL-10. The protein composition is capable of inhibiting human IL-6 production in human lung fibroblasts in response to treating the fibroblasts with human IL-lp. The inhibiting is characterized by an IC50 value of about 2.3 pM.

In one aspect, the present disclosure provides a heterodimeric protein composition capable of binding human IL-1 β, said protein composition being capable of inhibiting human IL-6 production in human lung fibroblasts in response to treating the fibroblasts with human IL-1 β, said inhibiting having an IC50 value of about 2.3 pM, wherein the composition comprises a

heterodimeric protein comprising a first polypeptide comprising amino acid sequence of SEQ ID NO. 1 and a second polypeptide comprising amino acid sequence of SEQ ID NO. 2.

BRIEF DESCRIPTION OF THE DRAWINGS

The following drawings and descriptions are provided to aid in the understanding of the invention:

Figure 1 illustratively shows a heterodimeric protein assembly of the present teachings comprising an extracellular portion of IL1-R1 fused with an IgG-Fc domain (Fc-II) via a flexible

What is claimed is:

1. A heterodimeric protein composition capable of binding human IL-1 β, said protein composition comprising:

a first polypeptide comprising

a first amino acid sequence comprising amino acids 18 through 333 of human IL1-R1 (GenBank: AAM88423.1), and

a second amino acid sequence comprising a first mutant of a Fc portion of human immunoglobulin gamma-1 Fc;

a second polypeptide comprising

another first amino acid sequence comprising amino acids 21 through 358 of human ILl-RAcP (GenBank: BAA2542 1.1), and

another second amino acid sequence comprising a second mutant of the Fc portion of human immunoglobulin gamma-1 Fc; and

wherein said first and second mutants are selected as to favor heterodimeric assembly between said first and second mutants over any homodimeric assembly; and

wherein said first polypeptide comprises amino acid sequence of SEQ ID NO.l and said second polypeptide comprises amino acid sequence of SEQ ID NO.2.

2. The protein composition of claim 1, wherein said protein composition exhibits human IL-1 β binding activity in an ELISA assay with an EC50 of about 50 ng/ml.

3. A therapeutic composition, the composition comprising a heterodimeric protein composition capable of binding human IL-1 β, said heterodimeric protein composition comprising:

a first polypeptide comprising

a first amino acid sequence comprising amino acids 18 through 333 of human IL1-R1, and

a second amino acid sequence comprising a first mutant of a Fc portion of human immunoglobulin gamma-1 Fc;

a second polypeptide comprising

another first amino acid sequence comprising amino acids 21 through 358 of human ILl-RAcP, and

another second amino acid sequence comprising a second mutant of the Fc portion of human immunoglobulin gamma-1 Fc; and

wherein said first and second mutants are selected as to favor heterodimeric assembly between said first and second mutants over any homodimeric assembly; and

wherein said first polypeptide comprises amino acid sequence of SEQ ID NO.l and said second polypeptide comprises amino acid sequence of SEQ ID NO.2.

4. The therapeutic composition of claim 3, wherein half-life of said heterodimeric protein composition in systemic circulation in mice after a subcutaneous administration at a dose of 5 mg/kg is at least about 88 hours, as assayed by human Fc ELISA.

5. An isolated nucleic acid encoding a polypeptide comprising amino acid sequence of SEQ ID NO. 3.

6. An isolated nucleic acid encoding a polypeptide comprising amino acid sequence of SEQ ID NO. 5.

7. The nucleic acid of claim 5 or claim 6, wherein the codon usage is optimized for high expression of said polypeptide in a mammalian cell.

8. The nucleic acid of claim 5, wherein the nucleic acid sequence comprises the sequence of SEQ ID NO. 4.

9. The nucleic acid of claim 6, wherein the nucleic acid sequence comprises the sequence of SEQ ID NO. 6.

10. The nucleic acid of claim 8 or claim 9, wherein said nucleic acid comprises an expression vector.

11. An isolated nucleic acid of SEQ ID NO. 7.

12. An in vitro heterologous expression system, the expression system harboring an expression vector comprising a nucleic acid sequence encoding a first polypeptide comprising amino acid sequence of SEQ ID NO. 3 and another nucleic acid sequence encoding a second polypeptide comprising amino acid sequence of SEQ ID NO. 5.

13. The expression system of claim 12, wherein said expression vector is harbored in a mammalian cell.

14. The expression system of claim 13, wherein said mammalian cell is a CHO cell.

15. The expression system of claim 13, wherein said expression system is capable of expressing a heterodimeric protein comprising a first polypeptide comprising amino acid sequence of SEQ ID NO. 1 and a second polypeptide comprising amino acid sequence of SEQ ID NO. 2, and wherein the level of expression of said heterodimeric protein is at least 300 mg per liter of cell culture.

16. Use of a substance for manufacture of a medicament for the treatment or prevention of a disease associated with modulation of activity of human IL-1 β, the substance comprising a heterodimeric protein comprising a first polypeptide comprising amino acid sequence of SEQ ID NO. 1 and a second polypeptide comprising amino acid sequence of SEQ ID NO. 2.

17. Use of a pharmaceutical composition in the manufacture of a medicament for treating or preventing a disease or condition associated with modulation of activity of human IL- 1 β, the pharmaceutical composition comprising a heterodimeric protein comprising a first polypeptide comprising amino acid sequence of SEQ ID NO. 1 and a second polypeptide comprising amino acid sequence of SEQ ID NO. 2.

18. The use according to claim 16 or claim 17, wherein said disease is an arthritis.

19. The use according to claim 16 or claim 17, wherein said disease is a gout.

20. The use according to claim 16 or claim 17, wherein said disease is a rheumatoid arthritis.

21. The use according to claim 16 or claim 17, wherein said disease is a Cryopyrin-Associated Periodic Syndromes (CAPS).

22. The use according to claim 16 or claim 17, wherein said disease is a scleroderma.

23. The use according to claim 16 or claim 17, wherein said disease is a diabetes.

24. The use according to claim 16 or claim 17, wherein said disease is atherosclerosis.

25. The use according to claim 16 or claim 17, wherein said disease is a dry eye disease.

26. The use according to claim 16 or claim 17, wherein said disease is an ocular allergy.

27. The use according to claim 16 or claim 17, wherein said disease is an uveitis.

28. A heterodimeric protein composition capable of binding human IL-1 β, said protein composition being capable of inhibiting human IL-6 production in human lung fibroblasts in response to treating the fibroblasts with human IL-1 β, said inhibiting having an IC50 value of about 2.3 pM, wherein the composition comprises a heterodimeric protein comprising a first polypeptide comprising amino acid sequence of SEQ ID NO. 1 and a second polypeptide comprising amino acid sequence of SEQ ID NO. 2.