

CLAIMS

1. A fusion protein comprising linked extracellular domains of:
 - (a) human SIRP α ,
 - (b) human CD40 ligand, and
 - (c) a linker positioned between and adjoining (a) and (b), the linker being a polypeptide comprising a flexible amino acid sequence.
2. The fusion protein of claim 1, wherein the fusion protein is capable of:
 - (a) reducing or eliminating an immune inhibitory signal, and
 - (b) increasing or activating an immune stimulatory signal.
3. The fusion protein of claim 1, wherein the fusion protein is capable of:
inhibiting the ability of a macrophage to phagocytose a target cell;
causing activation of antigen presenting cells;
shifting the balance of immune cells in favor of immune attack of a tumor;
increasing a ratio of effector T cells to regulatory T cells;
causing an increase of one or more of T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, dendritic cells, monocytes, and macrophages into a tumor or the tumor microenvironment;
and/or
enhancing one or more of IL-2, IL-4, IL-5, IL-10, IL-13, IL-17A, IL-22, TNF α or IFN γ in the serum of a subject receiving the heterodimeric protein.
4. The fusion protein of claim 1, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 95% identical to SEQ ID NO: 33.
5. The fusion protein of claim 4, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 97% identical to SEQ ID NO: 33.
6. The fusion protein of claim 1, wherein the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 95% identical to SEQ ID NO: 60.
7. The fusion protein of claim 6, wherein the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 97% identical to SEQ ID NO: 60.

8. The fusion protein of claim 1, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 95% identical to SEQ ID NO: 33, and the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 95% identical to SEQ ID NO: 60.
9. The fusion protein of claim 1, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 97% identical to SEQ ID NO: 33, and the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 97% identical to SEQ ID NO: 60.
10. The fusion protein of claim 1, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 98% identical to SEQ ID NO: 33, and the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 98% identical to SEQ ID NO: 60.
11. The fusion protein of claim 1, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 99% identical to SEQ ID NO: 33, and the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 99% identical to SEQ ID NO: 60.
12. The fusion protein of claim 1, wherein the chimeric protein is expressed by a mammalian host cell as a secretable and functional single polypeptide chain.
13. A fusion protein comprising linked extracellular domains of:
 - (a) a human SIRP α , comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 33,
 - (b) a human CD40 ligand, comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 60, and
 - (c) a linker positioned between and adjoining (a) and (b), the linker being a polypeptide comprising a flexible amino acid sequence.
14. The fusion protein of claim 13, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 97% identical to SEQ ID NO: 33.
15. The fusion protein of claim 13, wherein the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 97% identical to SEQ ID NO: 60.

16. The fusion protein of claim 13, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 97% identical to SEQ ID NO: 33, and the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 97% identical to SEQ ID NO: 60.
17. A nucleic acid encoding a polypeptide comprising linked extracellular domains of human SIRP α , human CD40 ligand and a linker positioned between and adjoining the extracellular domains, the linker being a polypeptide comprising a flexible amino acid sequence.
18. A host cell, comprising an expression vector comprising the nucleic acid of claim 17.
19. A pharmaceutical composition, comprising the fusion protein of claim 1.
20. The nucleic acid of claim 17, wherein the extracellular domain of human SIRP α comprises an amino acid sequence that is at least 95% identical to SEQ ID NO: 33, and the extracellular domain of human CD40 ligand comprises an amino acid sequence that is at least 95% identical to SEQ ID NO: 60.