

WHAT IS CLAIMED IS:

1. A heterodimer comprising two polypeptides selected from the group consisting of SIRP α , PD1, TIGIT, LILRB2 and SIGLEC10, wherein each of said two polypeptides is capable of binding a natural binding pair thereof, and wherein said heterodimer does not comprise an amino acid sequence of a type II membrane protein capable of binding a natural binding pair thereof.

2. The heterodimer of claim 1, wherein said heterodimer comprises a dimerizing moiety attached to said two polypeptides.

3. The heterodimer of claim 2, wherein said dimerizing moiety is an Fc domain of an antibody or a fragment thereof.

4. The heterodimer of claim 3, wherein said Fc domain is modified to alter its binding to an Fc receptor, reduce an immune activating function thereof and/or improve half-life of said fusion.

5. ~~The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said SIRP α polypeptide and said PD1 polypeptide.~~

6. The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said TIGIT polypeptide and said PD1 polypeptide, or
wherein said heterodimer comprises said SIRP α polypeptide and said LILRB2 polypeptide.

7. ~~The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said SIRP α polypeptide and said SIGLEC10 polypeptide.~~

8. ~~The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said SIRP α polypeptide and said TIGIT polypeptide.~~

9. — The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said ~~TIGIT polypeptide and said PD1 polypeptide.~~

10. — The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said ~~TIGIT polypeptide and said LILRB2 polypeptide.~~

11. — The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said ~~TIGIT polypeptide and said SIGLEC10 polypeptide.~~

12. — The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said ~~PD1 polypeptide and said SIGLEC10 polypeptide.~~

13. — The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said ~~LILRB2 polypeptide and said SIGLEC10 polypeptide.~~

14. — The heterodimer of any one of claims 1-3, wherein said heterodimer comprises said ~~PD1 polypeptide and said LILRB2 polypeptide.~~

145. The heterodimer of any one of claims 1-144, wherein each of said polypeptides is a monomer in said heterodimer.

146. The heterodimer of any one of claims 1-144, wherein said two polypeptides are comprised in a monomer of said heterodimer.

147. A composition comprising the heterodimer of any one of claims 1-146, wherein said heterodimer is the predominant form of said two polypeptides in said composition.

148. A nucleic acid construct or system comprising at least one polynucleotide encoding the heterodimer of any one of claims 1-146, and a regulatory element for directing expression of said polynucleotide in a host cell.

1910. A host cell comprising the heterodimer of any one of claims ~~1-16~~7 or the nucleic acid construct or system of claim ~~18~~9.

2011. A method of producing a heterodimer, the method comprising introducing the nucleic acid construct or system of claim ~~18-9~~ to a host cell or culturing the cells of claim ~~19~~10.

~~21. The method of claim 20, comprising isolating the heterodimer.~~

~~22. A method of treating a disease that can benefit from treatment with said heterodimer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the heterodimer of any one of claims 1-16, the composition of claim 17, the nucleic acid construct or system of claim 18 or the cell of claim 19, thereby treating the disease in the subject.~~

2312. The heterodimer of any one of claims ~~1-16~~7, the composition of claim ~~17~~8, the nucleic acid construct or system of claim ~~18~~9 or the cell of claim ~~19~~10, for use in treating a disease that can benefit from treatment with said heterodimer in a subject in need thereof.

~~24. The method of claim 22 or the heterodimer, the composition, the nucleic acid construct or system or the cell for use of claim 23, wherein said disease can benefit from activating immune cells.~~

2513. The ~~method or the~~ heterodimer, the composition, the nucleic acid construct or system or the cell for use of ~~any one of claims 22-24~~claim 12, wherein cells associated with said disease express said natural binding pair.

2614. The ~~method or the~~ heterodimer, the composition, the nucleic acid construct or system or the cell for use of any one of claims ~~22-25~~12-13, wherein said disease is cancer.

~~27. The method or the heterodimer, the composition, the nucleic acid construct or system or the cell for use of claim 26, wherein said cancer is selected from the group consisting of~~

~~lymphoma, leukemia, colon carcinoma, ovarian carcinoma, lung carcinoma, head and neck carcinoma and hepatocellular carcinoma.~~

~~28. The method or the heterodimer, the composition, the nucleic acid construct or system or the cell for use of claim 26, wherein said cancer is non-small cell lung cancer (NSCLC) or mesothelioma.~~

2915. A method of activating immune cells, the method comprising in-vitro activating immune cells in the presence of the heterodimer of any one of claims 1-746, the composition of claim 478, the nucleic acid construct or system of claim 489 or the cell of claim 4910.

~~30. The method of claim 29, wherein said activating is in the presence of cells expressing said natural binding pair.~~