

WHAT IS CLAIMED IS:

1. A modified $\alpha 1$ - $\alpha 2$ domain of a natural NKG2D ligand molecule, wherein said modified $\alpha 1$ - $\alpha 2$ domain comprises an amino acid sequence comprising at least 90% identity to SEQ ID NO: 4, wherein in said amino acid sequence comprising at least 90% identity to SEQ ID NO: 4, the positions corresponding to positions 8, 80, 154, 155, 156, 157, 158, and 159 of SEQ ID NO: 4 are substituted as compared to SEQ ID NO: 4, and wherein said amino acid sequence having at least 90% identity to SEQ ID NO: 4 has all of the following features:

the amino acid at the position corresponding to position 80 of SEQ ID NO: 4 is W;

the amino acid at the position corresponding to position 154 of SEQ ID NO: 4 is T;

the amino acid at the position corresponding to position 155 of SEQ ID NO: 4 is I, L, or M;

the amino acid at the position corresponding to position 157 of SEQ ID NO: 4 is W;

the amino acid at the position corresponding to position 158 of SEQ ID NO: 4 is Q, G, or S;

and

the amino acid at the position corresponding to position 159 of SEQ ID NO: 4 is T or W.

2. The modified $\alpha 1$ - $\alpha 2$ domain of claim 1, wherein in said amino acid sequence having at least 90% identity to SEQ ID NO: 4, one or more of the positions corresponding to positions 8 and 156 of SEQ ID NO: 4 is substituted as compared to SEQ ID NO: 4.

3. The modified $\alpha 1$ - $\alpha 2$ domain of claim 1, which comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 111, 113, 115 and 117.

4. The modified $\alpha 1$ - $\alpha 2$ domain of claim 3, wherein in said amino acid sequence having at least 90% identity to SEQ ID NO: 4, the amino acid at the position corresponding to position 8 of SEQ ID NO: 4 is S.

5. The modified $\alpha 1$ - $\alpha 2$ domain of claim 2, wherein in said amino acid sequence having at least 90% identity to SEQ ID NO: 4, the amino acid at the position corresponding to position 156 of SEQ ID NO: 4 is L or M.
6. The modified $\alpha 1$ - $\alpha 2$ domain of claim 1, further comprising an attached atom or an attached heterologous molecule.
7. The modified $\alpha 1$ - $\alpha 2$ domain of claim 6, wherein the heterologous molecule is a peptide or a polypeptide.
8. The modified $\alpha 1$ - $\alpha 2$ domain of claim 7, wherein the polypeptide is an antibody, antibody fragment, cytokine, lymphokine, or hormone.
9. The modified $\alpha 1$ - $\alpha 2$ domain of claim 6, wherein the heterologous molecule is an oligosaccharide, dendrimer, knottin, hormone, nucleic acid, or lipid.
10. The modified $\alpha 1$ - $\alpha 2$ domain of claim 1, further comprising an attached mammalian cell.
11. The modified $\alpha 1$ - $\alpha 2$ domain of claim 10, wherein the mammalian cell is a lymphocyte or a macrophage.
12. The modified $\alpha 1$ - $\alpha 2$ domain of claim 11, wherein the mammalian cell is a human lymphocyte or a human macrophage.
13. The modified $\alpha 1$ - $\alpha 2$ domain of claim 6, wherein when said modified $\alpha 1$ - $\alpha 2$ domain is contacted with a mammalian cell having a non-natural NKG2D receptor ectodomain attached thereto, said atom or heterologous molecule is delivered to said mammalian cell.

14. The modified $\alpha 1$ - $\alpha 2$ domain of claim 13, which exhibits an enhanced activation of a cell expressing the non-natural NKG2D ectodomain resulting in the cell exhibiting greater target cell killing potency than does a natural NKG2D ligand or a bispecific molecule with a natural or native $\alpha 1$ - $\alpha 2$ domain delivered to the cell.

15. The modified $\alpha 1$ - $\alpha 2$ domain of claim 13, which exhibits greater activation of a cell expressing the non-natural NKG2D ectodomain than activation of a cell expressing a natural NKG2D ectodomain resulting in the cell expressing the non-natural NKG2D ectodomain exhibiting greater target cell killing potency than does a cell expressing the natural NKG2D ectodomain.