CLAIMS

WHAT IS CLAIMED IS:

1. A complex comprising: a segment comprising a peptide, one or more linkers, and a segment comprising a human HLA class 1 heavy chain sequence, wherein said human HLA class 1 heavy chain sequence comprises HLA-C, and wherein said one or more linkers comprises a conformation configured to not block one or more killer-cell immunoglobulin-like receptor binding sites on said human HLA class 1 heavy chain sequence; and wherein said human HLA class 1 heavy chain sequence comprises one or more mutations as compared to an endogenous HLA of the same type, wherein said mutations occur at one or more of amino acid residues 115, 122, 128, 194, 197, 198, 212, 214, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 243, 245, 248, 262, or any combination thereof.

2. The complex of claim 1, wherein said peptide is coupled to one or more HLA binding groove domain residues of said human HLA class 1 heavy chain sequence.

3. The complex of claim 1 or 2, wherein said peptide modulates a conformation of said human HLA class 1 heavy chain sequence.

4. The complex of any one of claims 1 to 3, wherein said HLA-C is synthetic.

5. The complex of any one of claims 1 to 4, wherein a linker of said one or more linkers are disposed between said peptide and said human HLA class 1 heavy chain sequence, and wherein said one or more linkers are configured to resist proteolytic cleavage.

6. The complex of claim 5, wherein said human HLA class 1 heavy chain sequence is inhibited from eliciting a T-cell response when said complex is interrogated by one or more T cells.

7. The complex of any one of claims 1 to 6, wherein said peptide is coupled to said complex by a disulfide bond.

8. The complex of any one of claims 1 to 7, wherein said complex further comprises one or more immune checkpoint agonists.

9. The complex of claim 8, wherein said one or more immune checkpoint agonists comprise CD47, PD-L1, A2AR, B7-H3, B7-H4, BTLA, CTLA-4, IDO, KIR, LAG3, NOX2, PD-1, TIM-3, VISTA, SIGLEC7, or a combination thereof.

10. The complex of any one of claims 1 to 9, wherein a linker of said one or more linkers is disposed between said peptide and a human β2-microglobulin sequence, between a human β2-microglobulin sequence and said human HLA class 1 heavy chain sequence, or both.

11. The complex of any one of claims 1 to 10, wherein a linker of said one or more linkers comprises a sequence at least about 70%, 80%, 90%, or 99% identical to any one of SEQ ID NOs: 48-54.

12. The complex of any one of claims 1 to 11, wherein said human HLA class 1 heavy chain sequence is engineered to inhibit a T-cell response when said complex is interrogated by one or more CD8 cells.

13. The complex of any one of claims 1 to 12, wherein said complex further comprises a synthetic HLA-E or fragment thereof.

14. The complex of claim 13, wherein said synthetic HLA-E or fragment thereof comprises one or more mutations as compared to an endogenous HLA-E or equivalent fragment thereof.

15. The complex of any one of claims 1 to 14, wherein said peptide comprises an amino acid sequence comprising nine amino acid residues, and wherein said peptide comprises, in N-terminus to C-terminus order:

a. an amino acid residue selected from E, P, L, Q, A, R, H, S, T, V, M, D, and K at a second position of said amino acid sequence; and

b. an amino acid residue selected from V, I, F, W, Y, L, R, and K at a ninth position of said amino acid sequence.

16. A nucleic acid molecule encoding the complex of any one of claims 1-15.

17. An engineered vector comprising the nucleic acid molecule of claim 16.

18. The engineered vector of claim 18, wherein said vector is a plasmid, adenovirus, adeno-associated virus (AAV), lentivirus, retrovirus, or transposon.

19. An isolated cell comprising said nucleic acid molecule of claim 16, or said vector of claim 17 or 18.

20. The isolated cell of claim 19, wherein said isolated cell is a stem cell.

21. The isolated cell of claim 20, wherein said stem cell is an embryonic stem cell, a hematopoietic stem cell, a mesenchymal stem cell, or an induced pluripotent stem cell.

22. A method of generating an immune incompetent cell, comprising administering said complex of any one of claims 1-15, or said nucleic acid molecule of claim 16, or said vector of claim 17 or 18 to a cell.

23. The method of claim 22, wherein said cell is a stem cell.

24. The method of claim 23, wherein said stem cell is an embryonic stem cell, a hematopoietic stem cell, a mesenchymal stem cell, or an induced pluripotent stem cell.

25. A therapeutically effective amount of said nucleic acid molecule of claim 16 or said isolated cell of any one of claims 19-21, for use in treating a disease or disorder in a subject in need thereof.