WHAT IS CLAIMED IS:

1. A genetically-modified non-human animal expressing a fusion protein comprising β2 microglobulin (B2M) and a human or humanized major histocompatibility complex (MHC) α chain;

wherein:

the fusion protein comprises a human B2M protein and a chimeric MHC α chain comprising human HLA-A α1 and α2 domains and a mouse H2-D1 α3 domain; or the fusion protein comprises a human B2M protein and a human HLA-A protein;

the human HLA-A is human HLA-A2.1;

the animal does not express endogenous B2M;

a sequence encoding a region of endogenous B2M is replaced with a sequence encoding the fusion protein, and the sequence encoding the region of endogenous B2M comprises exon 1, exon 2, and exon 3 of endogenous B2M gene;

the fusion protein further comprises a signal peptide of human HLA-A2.1; and

the animal is a mouse.

2. The animal of claim 1, wherein genome of the animal comprises at least one chromosome comprising a sequence encoding the fusion protein.

3. The animal of any one of claim 2, wherein the sequence encoding the fusion protein is operably linked to an endogenous regulatory element at the endogenous β2 microglobulin (B2M) gene locus in the at least one chromosome.

4. The animal of claim 1, wherein the human B2M and the human HLA-A are linked via a linker peptide sequence.

5. The animal of claim 1, wherein the human B2M comprises or consists of an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 4 or amino acids 21-119 of SEQ ID NO: 4.

6. The animal of claim 1, wherein the human HLA-A comprises or consists of an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 8, amino acids 25-365 of SEQ ID NO: 8, SEQ ID NO: 59, or amino acids 22-362 of SEQ ID NO: 59.

7. The animal of claim 1, wherein the fusion protein comprises or consists of an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 62.

8. The animal of claim 1, wherein the human B2M and the chimeric MHC α chain are linked via a linker peptide sequence.

9. The animal of claim 1, wherein the chimeric MHC α chain comprises a α3 domain, a connecting peptide, a transmembrane region, and a cytoplasmic region of an endogenous MHC; and

the animal is a mouse, and the chimeric MHC α chain comprises a α3 domain, a connecting peptide, a transmembrane region, and a cytoplasmic region of mouse H2-D1.

10. The animal of claim 1, wherein the chimeric MHC α chain comprises an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 99%, or 100% identical to amino acids 207-362 of SEQ ID NO: 6.

11. The animal of claim 1, wherein the chimeric MHC α chain comprises an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 99%, or 100% identical to SEQ ID NO: 61 or SEQ ID NO: 63.

12. The animal of claim 1, wherein the animal is heterozygous with respect to the sequence encoding the fusion protein.

13. The animal of claim 1, wherein the animal is homozygous with respect to the sequence encoding the fusion protein.

14. The animal of claim 1, wherein the animal does not express endogenous MHC α chain.

15. The animal of any one of claims 1-14, wherein B2M and the MHC α chain can associate with each other, forming a functional MHC protein complex, wherein the protein complex can present a non-self antigen to the surface of one or more cells.

16. The animal of any one of claims 1-14, wherein the animal is a mouse with a C57BL/6 background.

17. The animal of any one of claims 1-14, wherein the animal is an immunodeficient mouse.

18. The animal of any one of claims 1-14, wherein the genome of the animal comprises a disruption in the animal's endogenous CD132 gene.

19. A method for making a genetically-modified, non-human animal, comprising:

replacing in at least one cell of the animal, at an endogenous B2M gene locus, a sequence encoding a region of endogenous B2M with a sequence encoding a human B2M or a sequence encoding a fusion protein comprising a human B2M and a human or humanized MHC α chain;

wherein,

the sequence encoding the fusion protein comprises the following elements:

(a) exon 1, exon 2, and exon 3 of human B2M;

(b) an optional sequence encoding a linker peptide sequence; and

(c) exon 2 and exon 3 of human HLA-A2.1, or a sequence encoding human HLA-A2.1;

the sequence encoding the region of endogenous B2M comprises all of exon 1, exon 2, and exon 3 of endogenous B2M gene;

the fusion protein further comprises a signal peptide of human HLA-A2.1; and

the animal is a mouse.

20. A method of determining effectiveness of an agent or a combination of agents for the treatment of cancer, comprising:

engrafting tumor cells to the animal of any one of claims 1-18, thereby forming one or more tumors in the animal;

administering the agent or the combination of agents to the animal; and

determining the inhibitory effects on the tumors;

wherein the tumor cells are from cancer cell lines, or from a tumor sample obtained from a human patient.

21. A method of producing an animal comprising a human hemato-lymphoid system, the method comprising:

engrafting a population of cells comprising human hematopoietic cells or human peripheral blood cells into the animal of any one of claims 1-18.