Marked-up Claims:

1. A ~~non-human animal~~rodent comprising at an endogenous Major Histocompatibility Complex I (MHC I) locus a nucleotide sequence encoding a chimeric human/non-human MHC I polypeptide,

wherein a human portion of the chimeric polypeptide comprises α1, α2, and α3 domains of a human MHC I polypeptide, and

wherein the ~~non-human animal~~rodent expresses the chimeric human/non-human MHC I polypeptide, and

wherein the rodent is a rat or a mouse.

~~2. The non-human animal of claim 1, wherein the animal is a rodent, wherein the rodent comprises at an endogenous Major Histocompatibility Complex I (MHC I) locus a nucleotide sequence encoding a chimeric human/rodent MHC I polypeptide,~~

~~wherein a human portion of the chimeric polypeptide comprises α1, α2, and α3 domains of a human MHC I polypeptide, and~~

~~wherein the rodent expresses the chimeric human/rodent MHC I polypeptide.~~

~~3~~2. The rodent of claim ~~2~~1, wherein the rodent does not express α1, α2, and α3 domains of an endogenous rodent MHC I polypeptide from an endogenous rodent MHC I locus.

~~4~~3. The rodent of claim ~~2~~1, wherein the nucleotide sequence is operably linked to endogenous rodent regulatory elements.

~~5~~4. The rodent of claim ~~2~~1, wherein the rodent is a mouse.

~~6~~5. The mouse of claim ~~5~~4, wherein the endogenous locus is a mouse H-2K locus.

~~7~~6. The rodent of claim ~~2~~1, wherein a rodent portion of the chimeric polypeptide comprises transmembrane and cytoplasmic domains of an endogenous rodent MHC I polypeptide.

~~8~~7. The rodent of claim ~~7~~6, wherein the rodent is a mouse, the endogenous rodent MHC I locus is an H-2K locus, and the endogenous rodent MHC I polypeptide is H-2K.

~~9~~8. The rodent of claim ~~2~~1, wherein the human MHC I polypeptide is selected from the group

consisting of HLA-A, HLA-B, and HLA-C.

~~10~~9. The mouse of claim ~~5~~ 4 comprising at an endogenous H-2K locus a nucleotide sequence encoding a chimeric human/mouse MHC I polypeptide,

wherein a human portion of the chimeric polypeptide comprises α1, α2, and α3 domains of a human HLA-A2 polypeptide and a mouse portion comprises transmembrane and cytoplasmic domains of a mouse H-2K polypeptide, and

wherein the mouse expresses the chimeric HLA-A2/H-2K polypeptide.

~~11~~10. The mouse of claim ~~10~~9, wherein the mouse does not express α1, α2, and α3 domains of the mouse H-2K polypeptide from an endogenous H-2K locus.

~~12~~11. The rodent of claim ~~2~~ 1 or the mouse of claim ~~10~~9, wherein the human portion of the chimeric polypeptide comprises a human leader sequence.

~~13~~12. The mouse of claim ~~10~~9, wherein the nucleotide sequence is operably ~~liked~~ linked to endogenous mouse regulatory elements.

~~14~~13. The mouse of claim ~~10~~9, wherein the human HLA-A2 polypeptide is an HLA-A2.1 polypeptide.

~~15~~14. The mouse of claim ~~11~~10, wherein the mouse H-2K locus is an H-2Kb locus.

~~16~~15. A method of modifying an MHC I locus of a mouse to express a chimeric human/mouse MHC I polypeptide, wherein the method comprises replacing at the endogenous MHC I locus a nucleotide sequence encoding α1, α2, and α3 domains of a mouse MHC I polypeptide with a nucleotide sequence encoding α1, α2, and α3 domains of a human MHC I polypeptide.

~~17~~16. The method of claim ~~16~~15, wherein the mouse does not express the α1, α2, and α3 domains of the mouse MHC I polypeptide from an endogenous mouse MHC I locus.

~~18~~17. The method of claim ~~17~~16, wherein the mouse MHC I locus is an H-2K locus, and the mouse MHC I polypeptide is an H-2K polypeptide.

~~19~~18. The rodent of claim ~~9~~ 8 or the method of claim ~~17~~16, wherein the human MHC I polypeptide is an HLA-A polypeptide.

~~20~~19. The method of claim ~~17~~16, wherein the mouse expresses transmembrane and cytoplasmic domains of the mouse MHC I polypeptide.

~~21~~20. A ~~non-human animal,~~ rodent or mouse according to any one of claims 1-~~15~~ 14 further comprising at an endogenous non-human β2 microglobulin locus a nucleotide sequence encoding a polypeptide comprising a human β2 microglobulin amino acid sequence, wherein the non-human animal expresses a human or humanized β2 microglobulin polypeptide.

~~22~~21. The ~~non-human animal~~rodent of claim ~~21~~20, ~~wherein the animal is a rodent,~~ wherein the rodent comprises at an endogenous rodent β2 microglobulin locus a nucleotide sequence encoding a polypeptide comprising a human β2 microglobulin amino acid sequence, and wherein the rodent expresses a human or humanized β2 microglobulin polypeptide.

~~23~~22. The rodent of claim ~~22~~21, wherein the rodent does not express a functional endogenous rodent β2 microglobulin polypeptide from an endogenous rodent β2 microglobulin locus.

~~24~~23. The rodent of claim ~~22~~21, wherein the nucleotide sequence is operably linked to endogenous rodent β2 microglobulin regulatory elements.

~~25~~24. The rodent of claim ~~22~~21, wherein the nucleotide sequence comprises a nucleotide sequence set forth in exon 2 to exon 4 of a human β2 microglobulin gene.

~~26~~25. The rodent of claim ~~22~~21, wherein the nucleotide sequence comprises nucleotide sequences set forth in exons 2, 3, and 4 of a human β2 microglobulin gene.

~~27~~26. The rodent of claim ~~26~~25, wherein the nucleotide sequence further comprises a nucleotide sequence set forth in exon 1 of a rodent β2 microglobulin gene.

~~28~~27. The rodent of any one of claims ~~22~~21-~~27~~26, wherein the rodent is a mouse.

~~29~~28. The method of any one of claims ~~16~~15-~~20~~19, further comprising modifying a β2

microglobulin locus of a mouse to express a human or humanized β2 microglobulin polypeptide, wherein the method comprises replacing at the endogenous mouse β2 microglobulin locus a nucleotide sequence encoding a mouse β2 microglobulin polypeptide with a nucleotide sequence encoding a human or humanized β2 microglobulin polypeptide.

~~30~~29. The method of claim ~~29~~28, wherein the mouse does not express a functional mouse β2 microglobulin polypeptide from an endogenous β2 microglobulin locus.

~~31~~30. The method of claim ~~29~~28, wherein the nucleotide sequence encoding the human or humanized β2 microglobulin polypeptide comprises a nucleotide sequence set forth in exon 2 to exon 4 of a human β2 microglobulin gene.

~~32~~31. The method of claim ~~29~~28, wherein the nucleotide sequence encoding the human or humanized β2 microglobulin polypeptide comprises nucleotide sequences set forth in exons 2, 3, and 4 of a human β2 microglobulin gene.

~~33~~32. The method of claim ~~29~~28, wherein the modified locus retains a nucleotide sequence of exon 1 of a mouse β2 microglobulin gene.

~~34~~33. The method of any one of claims ~~16~~ 15 – ~~20~~ 19 or ~~29~~28, wherein the replacement is made in a single ES cell, and the single ES cell is introduced into a mouse embryo to make a mouse.

~~35~~34. The mouse of claim ~~28~~27, wherein the expression of the human or humanized β2 microglobulin polypeptide increases the expression of the chimeric human/mouse MHC I polypeptide as compared to the expression of the chimeric human/mouse MHC I polypeptide in the absence of expression of human or humanized β2 microglobulin polypeptide.

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CLAIMS

1. A non-human animal comprising at an endogenous Major Histocompatibility Complex I (MHC I) locus a nucleotide sequence encoding a chimeric human/non-human MHC I polypeptide,

wherein a human portion of the chimeric polypeptide comprises α1, α2, and α3 domains of a human MHC I polypeptide, and

wherein the non-human animal expresses the chimeric human/non-human MHC I polypeptide.

2. The non-human animal of claim 1, wherein the animal is a rodent, wherein the rodent comprises at an endogenous Major Histocompatibility Complex I (MHC I) locus a nucleotide sequence encoding a chimeric human/rodent MHC I polypeptide,

wherein a human portion of the chimeric polypeptide comprises α1, α2, and α3 domains of a human MHC I polypeptide, and

wherein the rodent expresses the chimeric human/rodent MHC I polypeptide.

3. The rodent of claim 2, wherein the rodent does not express α1, α2, and α3 domains of an endogenous rodent MHC I polypeptide from an endogenous rodent MHC I locus.

4. The rodent of claim 2, wherein the nucleotide sequence is operably linked to endogenous rodent regulatory elements.

5. The rodent of claim 2, wherein the rodent is a mouse.

6. The mouse of claim 5, wherein the endogenous locus is a mouse H-2K locus.

7. The rodent of claim 2, wherein a rodent portion of the chimeric polypeptide comprises transmembrane and cytoplasmic domains of an endogenous rodent MHC I polypeptide.

8. The rodent of claim 7, wherein the rodent is a mouse, the endogenous rodent MHC I locus is an H-2K locus, and the endogenous rodent MHC I polypeptide is H-2K.

9. The rodent of claim 2, wherein the human MHC I polypeptide is selected from the group consisting of HLA-A, HLA-B, and HLA-C.

10. The mouse of claim 5 comprising at an endogenous H-2K locus a nucleotide sequence encoding a chimeric human/mouse MHC I polypeptide,

wherein a human portion of the chimeric polypeptide comprises α1, α2, and α3 domains of a human HLA-A2 polypeptide and a mouse portion comprises transmembrane and cytoplasmic domains of a mouse H-2K polypeptide, and

wherein the mouse expresses the chimeric HLA-A2/H-2K polypeptide.

11. The mouse of claim 10, wherein the mouse does not express α1, α2, and α3 domains of the mouse H-2K polypeptide from an endogenous H-2K locus.

12. The rodent of claim 2 or the mouse of claim 10, wherein the human portion of the chimeric polypeptide comprises a human leader sequence.

13. The mouse of claim 10, wherein the nucleotide sequence is operably liked to endogenous mouse regulatory elements.

14. The mouse of claim 10, wherein the human HLA-A2 polypeptide is an HLA-A2.1 polypeptide.

15. The mouse of claim 11, wherein the mouse H-2K locus is an H-2Kb locus.

16. A method of modifying an MHC I locus of a mouse to express a chimeric human/mouse MHC I polypeptide, wherein the method comprises replacing at the endogenous MHC I locus a nucleotide sequence encoding α1, α2, and α3 domains of a mouse MHC I polypeptide with a nucleotide sequence encoding α1, α2, and α3 domains of a human MHC I polypeptide.

17. The method of claim 16, wherein the mouse does not express the α1, α2, and α3 domains of the mouse MHC I polypeptide from an endogenous mouse MHC I locus.

18. The method of claim 17, wherein the mouse MHC I locus is an H-2K locus, and the mouse MHC I polypeptide is an H-2K polypeptide.

19. The rodent of claim 9 or the method of claim 17, wherein the human MHC I polypeptide is an HLA-A polypeptide.

20. The method of claim 17, wherein the mouse expresses transmembrane and cytoplasmic domains of the mouse MHC I polypeptide.

21. A non-human animal, rodent or mouse according to any one of claims 1-15 further comprising at an endogenous non-human β2 microglobulin locus a nucleotide sequence encoding a polypeptide comprising a human β2 microglobulin amino acid sequence, wherein the non-human animal expresses a human or humanized β2 microglobulin polypeptide.

22. The non-human animal of claim 21, wherein the animal is a rodent, wherein the rodent comprises at an endogenous rodent β2 microglobulin locus a nucleotide sequence encoding a polypeptide comprising a human β2 microglobulin amino acid sequence, and wherein the rodent expresses a human or humanized β2 microglobulin polypeptide.

23. The rodent of claim 22, wherein the rodent does not express a functional endogenous rodent β2 microglobulin polypeptide from an endogenous rodent β2 microglobulin locus.

24. The rodent of claim 22, wherein the nucleotide sequence is operably linked to endogenous rodent β2 microglobulin regulatory elements.

25. The rodent of claim 22, wherein the nucleotide sequence comprises a nucleotide sequence set forth in exon 2 to exon 4 of a human β2 microglobulin gene.

26. The rodent of claim 22, wherein the nucleotide sequence comprises nucleotide sequences set forth in exons 2, 3, and 4 of a human β2 microglobulin gene.

27. The rodent of claim 26, wherein the nucleotide sequence further comprises a nucleotide sequence set forth in exon 1 of a rodent β2 microglobulin gene.

28. The rodent of any one of claims 22-27, wherein the rodent is a mouse.

29. The method of any one of claims 16-20, further comprising modifying a β2 microglobulin locus of a mouse to express a human or humanized β2 microglobulin polypeptide, wherein the method comprises replacing at the endogenous mouse β2 microglobulin locus a nucleotide

sequence encoding a mouse β2 microglobulin polypeptide with a nucleotide sequence encoding a human or humanized β2 microglobulin polypeptide.

30. The method of claim 29, wherein the mouse does not express a functional mouse β2 microglobulin polypeptide from an endogenous β2 microglobulin locus.

31. The method of claim 29, wherein the nucleotide sequence encoding the human or humanized β2 microglobulin polypeptide comprises a nucleotide sequence set forth in exon 2 to exon 4 of a human β2 microglobulin gene.

32. The method of claim 29, wherein the nucleotide sequence encoding the human or humanized β2 microglobulin polypeptide comprises nucleotide sequences set forth in exons 2, 3, and 4 of a human β2 microglobulin gene.

33. The method of claim 29, wherein the modified locus retains a nucleotide sequence of exon 1 of a mouse β2 microglobulin gene.

34. The method of any one of claims 16 – 20 or 29, wherein the replacement is made in a single ES cell, and the single ES cell is introduced into a mouse embryo to make a mouse.

35. The mouse of claim 28, wherein the expression of the human or humanized β2 microglobulin polypeptide increases the expression of the chimeric human/mouse MHC I polypeptide as compared to the expression of the chimeric human/mouse MHC I polypeptide in the absence of expression of human or humanized β2 microglobulin polypeptide.

CLAIMS:

1. A rodent comprising at an endogenous Major Histocompatibility Complex I (MHC I) locus a nucleotide sequence encoding a chimeric human/rodent MHC I polypeptide,

wherein a human portion of the chimeric polypeptide comprises α1, α2, and α3 domains of a human MHC I polypeptide, and

wherein the rodent expresses the chimeric human/non-human MHC I polypeptide, and

wherein the rodent is a rat or a mouse.

2. The rodent of claim 1, wherein the rodent does not express α1, α2, and α3 domains of an endogenous rodent MHC I polypeptide from an endogenous rodent MHC I locus.

3. The rodent of claim 1, wherein the nucleotide sequence is operably linked to endogenous rodent regulatory elements.

4. The rodent of claim 1, wherein the rodent is a mouse.

5. The mouse of claim 4, wherein the endogenous locus is a mouse H-2K locus.

6. The rodent of claim 1, wherein a rodent portion of the chimeric polypeptide comprises transmembrane and cytoplasmic domains of an endogenous rodent MHC I polypeptide.

7. The rodent of claim 6, wherein the rodent is a mouse, the endogenous rodent MHC I locus is an H-2K locus, and the endogenous rodent MHC I polypeptide is H-2K.

8. The rodent of claim 1, wherein the human MHC I polypeptide is selected from the group consisting of HLA-A, HLA-B, and HLA-C.

9. The mouse of claim 4, comprising at an endogenous H-2K locus a nucleotide sequence encoding a chimeric human/mouse MHC I polypeptide,

wherein a human portion of the chimeric polypeptide comprises α1, α2, and α3 domains of a human HLA-A2 polypeptide and a mouse portion comprises transmembrane and cytoplasmic domains of a mouse H-2K polypeptide, and

wherein the mouse expresses the chimeric HLA-A2/H-2K polypeptide.

10. The mouse of claim 9, wherein the mouse does not express α1, α2, and α3 domains of

the mouse H-2K polypeptide from an endogenous H-2K locus.

11. The rodent of claim 1 or the mouse of claim 9, wherein the human portion of the chimeric polypeptide comprises a human leader sequence.

12. The mouse of claim 9, wherein the nucleotide sequence is operably linked to endogenous mouse regulatory elements.

13. The mouse of claim 9, wherein the human HLA-A2 polypeptide is an HLA-A2.1 polypeptide.

14. The mouse of claim 10, wherein the mouse H-2K locus is an H-2Kb locus.

15. A method of modifying an MHC I locus of a mouse to express a chimeric human/mouse MHC I polypeptide, wherein the method comprises replacing at the endogenous MHC I locus a nucleotide sequence encoding α1, α2, and α3 domains of a mouse MHC I polypeptide with a nucleotide sequence encoding α1, α2, and α3 domains of a human MHC I polypeptide.

16. The method of claim 15, wherein the mouse does not express the α1, α2, and α3 domains of the mouse MHC I polypeptide from an endogenous mouse MHC I locus.

17. The method of claim 16, wherein the mouse MHC I locus is an H-2K locus, and the mouse MHC I polypeptide is an H-2K polypeptide.

18. The rodent of claim 8 or the method of claim 16, wherein the human MHC I polypeptide is an HLA-A polypeptide.

19. The method of claim 16, wherein the mouse expresses transmembrane and cytoplasmic domains of the mouse MHC I polypeptide.

20. A rodent or mouse according to any one of claims 1-14 further comprising at an endogenous non-human β2 microglobulin locus a nucleotide sequence encoding a polypeptide comprising a human β2 microglobulin amino acid sequence, wherein the rodent expresses a human or humanized β2 microglobulin polypeptide.

21. The rodent of claim 20, wherein the rodent comprises at an endogenous rodent β2 microglobulin locus a nucleotide sequence encoding a polypeptide comprising a human β2

microglobulin amino acid sequence, and wherein the rodent expresses a human or humanized β2 microglobulin polypeptide.

22. The rodent of claim 21, wherein the rodent does not express a functional endogenous rodent β2 microglobulin polypeptide from an endogenous rodent β2 microglobulin locus.

23. The rodent of claim 21, wherein the nucleotide sequence is operably linked to endogenous rodent β2 microglobulin regulatory elements.

24. The rodent of claim 21, wherein the nucleotide sequence comprises a nucleotide sequence set forth in exon 2 to exon 4 of a human β2 microglobulin gene.

25. The rodent of claim 21, wherein the nucleotide sequence comprises nucleotide sequences set forth in exons 2, 3, and 4 of a human β2 microglobulin gene.

26. The rodent of claim 25, wherein the nucleotide sequence further comprises a nucleotide sequence set forth in exon 1 of a rodent β2 microglobulin gene.

27. The rodent of any one of claims 21-26, wherein the rodent is a mouse.

28. The method of any one of claims 15-19, further comprising modifying a β2 microglobulin locus of a mouse to express a human or humanized β2 microglobulin polypeptide, wherein the method comprises replacing at the endogenous mouse β2 microglobulin locus a nucleotide sequence encoding a mouse β2 microglobulin polypeptide with a nucleotide sequence encoding a human or humanized β2 microglobulin polypeptide.

29. The method of claim 28, wherein the mouse does not express a functional mouse β2 microglobulin polypeptide from an endogenous β2 microglobulin locus.

30. The method of claim 28, wherein the nucleotide sequence encoding the human or humanized β2 microglobulin polypeptide comprises a nucleotide sequence set forth in exon 2 to exon 4 of a human β2 microglobulin gene.

31. The method of claim 28, wherein the nucleotide sequence encoding the human or humanized β2 microglobulin polypeptide comprises nucleotide sequences set forth in exons 2, 3, and 4 of a human β2 microglobulin gene.

32. The method of claim 29, wherein the modified locus retains a nucleotide sequence of exon 1 of a mouse β2 microglobulin gene.

33. The method of any one of claims 15-19 or 28, wherein the replacement is made in a single ES cell, and the single ES cell is introduced into a mouse embryo to make a mouse.

34. The mouse of claim 27, wherein the expression of the human or humanized β2 microglobulin polypeptide increases the expression of the chimeric human/mouse MHC I polypeptide as compared to the expression of the chimeric human/mouse MHC I polypeptide in the absence of expression of human or humanized β2 microglobulin polypeptide.