

What is claimed is:

1. A genetically modified mouse, whose genome comprises a replacement at an endogenous mouse IL-15 locus, of a mouse genomic fragment comprising mouse IL-15 exon sequences coding for a mature mouse IL-15 polypeptide, with a human genomic segment comprising human IL-15 exons 3-6 and coding for a mature human IL-15 polypeptide, to form a humanized IL-15 gene, wherein the humanized IL-15 gene is under control of endogenous mouse IL-15 upstream regulatory elements at the endogenous mouse IL-15 locus.
2. The genetically modified mouse of claim 1, wherein the human IL-15 exons in said human genomic segment consist of human IL-15 exons 3, 4, 5 and 6.
3. The genetically modified mouse of claim 1, wherein the humanized IL-15-encoding gene encodes a protein which comprises the amino acid sequence of SEQ ID NO: 4.
4. The genetically modified mouse of claim 1, wherein the human genomic segment further comprises a human nucleic acid present downstream of the human IL-15 3'-UTR at a human IL-15 locus.
5. A method of making a genetically modified mouse, comprising modifying the genome of a mouse by replacing a mouse genomic fragment comprising mouse IL-15 exon sequences coding for a mature mouse IL-15 polypeptide at the endogenous mouse IL-15 locus with a human genomic segment comprising human IL-15 exons 3-6 and coding for a mature human IL-15 polypeptide to form a humanized IL-15 gene, wherein the humanized IL-15 gene is under control of endogenous mouse IL-15 upstream regulatory elements at the endogenous mouse IL-15 locus.
6. The method of claim 5, wherein the human IL-15 exons in the human genomic segment consist of human IL-15 exons 3, 4, 5 and 6.
7. The method of claim 5, wherein the human genomic segment further comprises a human nucleic acid present downstream of the human IL-15 3'-UTR at a human IL-15 locus.

8. The method of claim 5, wherein the humanized IL-15-encoding gene encodes a protein which comprises the amino acid sequence of SEQ ID NO: 4.
9. A genetically modified mouse, whose genome comprises a humanized IL-15 gene, wherein said humanized IL-15 gene comprises mouse IL-15 exons 1-2 and a human genomic segment comprising human IL-15 exons 3-6, wherein the humanized IL-15 gene is under control of mouse IL-15 upstream regulatory elements from an endogenous mouse IL-15 locus, and said humanized IL-15 gene encodes a protein comprising a mature human IL-15 polypeptide sequence.
10. The genetically modified mouse of claim 9, wherein the human IL-15 exons in said human genomic segment consist of human IL-15 exons 3, 4, 5 and 6.
11. The genetically modified mouse of claim 9, wherein the humanized IL-15-encoding gene encodes a protein which comprises the amino acid sequence of SEQ ID NO: 4.
12. The genetically modified mouse of claim 9, wherein the human genomic segment further comprises a human nucleic acid present downstream of the human IL-15 3'-UTR at a human IL-15 locus.
13. The genetically modified mouse of claim 9, wherein the humanized IL-15 gene is at a position in the genome of the mouse that is other than an endogenous IL-15 locus.
14. A method of making a genetically modified mouse, comprising introducing into the genome of a mouse a humanized IL-15 gene which comprises a mouse genomic segment comprising mouse IL-15 exons 1-2, and a human genomic segment comprising human IL-15 exons 3-6, wherein the humanized IL-15 gene is under control of mouse IL-15 upstream regulatory elements from an endogenous mouse IL-15 locus, and said humanized IL-15 gene encodes a protein comprising a mature human IL-15 polypeptide sequence.
15. The method of claim 14, wherein the humanized IL-15 gene is integrated into the genome at a position that is other than an endogenous IL-15 locus.

What is claimed is:

1. A genetically modified mouse whose genome comprises a replacement at an endogenous mouse IL-15 locus of a mouse genomic segment comprising sequences of mouse exons 3, 4, 5 and 6 coding for a mature mouse IL-15 polypeptide with a human genomic segment comprising human IL-15 exons coding for a mature human IL-15 polypeptide to form a humanized IL-15 gene, wherein the human IL-15 exons in said human genomic segment consist of human exons 3, 4, 5 and 6, wherein the humanized IL-15 gene is under control of endogenous mouse IL-15 upstream regulatory elements at the endogenous mouse IL-15 locus, and wherein the genetically modified mouse comprises a human IL-15 polypeptide in serum following treatment of said mouse with Poly I:C.
2. The genetically modified mouse of claim 1, wherein the humanized IL-15-encoding gene encodes a protein which comprises the amino acid sequence of SEQ ID NO: 5.
3. A method of making a genetically modified mouse, comprising modifying the genome of a mouse by replacing at an endogenous mouse IL-15 locus of a mouse genomic segment comprising sequences of mouse exons 3, 4, 5 and 6 coding for a mature mouse IL-15 polypeptide with a human genomic segment comprising human IL-15 exons coding for a mature human IL-15 polypeptide to form a humanized IL-15 gene, wherein the human IL-15 exons in said human genomic segment consist of human exons 3, 4, 5 and 6, wherein the humanized IL-15 gene is under control of endogenous mouse IL-15 upstream regulatory elements at the endogenous mouse IL-15 locus, and wherein the genetically modified mouse comprises a human IL-15 polypeptide in serum following treatment of said genetically modified mouse with Poly I:C.
4. The method of claim 3, wherein the humanized IL-15-encoding gene encodes a protein which comprises the amino acid sequence of SEQ ID NO: 5.