## AMENDED CLAIMS
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1. A genetically modified mouse comprising a replacement at an endogenous mouse IL-6 locus of a mouse gene encoding IL-6 with a human gene encoding human IL-6, wherein the human gene encoding human IL-6 is under control of endogenous mouse regulatory elements at the endogenous mouse IL-6 locus.

2. The genetically modified mouse of claim 1, wherein the human gene encoding human IL-6 comprises exons 1 through 5 of the human IL-6 gene of the CTD-2369M23 bacterial artificial chromosome.

3. The genetically modified mouse of claim 1, wherein the mouse expresses a mouse IL-6Rα.

4. The genetically modified mouse of claim 1, wherein the mouse expresses a humanized IL-6Rα from an endogenous mouse IL-6Rα locus comprising a replacement of a mouse IL-6Rα immunoglobulin superfamily domain-encoding sequence with a human IL-6Rα immunoglobulin superfamily domain-encoding sequence.

5. The genetically modified mouse of claim 1, wherein the mouse does not exhibit a feature selected from plasmocytosis, glomerulosclerosis, glomerulonephritis, kidney failure, hypergammaglobulinemia, elevated megakaryocytes in spleen, elevated megakaryocytes in bone marrow, splenomegaly, lymph node enlargement, compacted abnormal plasma cells, and a combination thereof.

6. The genetically modified mouse of claim 4, wherein the humanized IL-6Rα comprises a human immunoglobulin superfamily domain of a human IL-6Rα.

7. The genetically modified mouse of claim 6, wherein the humanized IL-6Rα comprises a mouse transmembrane domain and a mouse cytoplasmic domain.

8. A genetically modified mouse, comprising a humanization of an endogenous mouse IL-6Rα gene, wherein the humanization comprises a replacement of a mouse IL-6Rα immunoglobulin superfamily domain-encoding sequence with a

human IL-6Rα immunoglobulin superfamily domain-encoding sequence at the endogenous mouse IL-6Rα locus, and wherein the humanized IL-6Rα gene is under control of endogenous mouse regulatory elements.

9. The genetically modified mouse of claim 8, wherein a contiguous mouse sequence comprising mouse exons 1 through 8 is replaced with a contiguous genomic fragment of human IL-6Rα sequence encoding a human IL-6Rα immunoglobulin superfamily domain.

10. The genetically modified mouse of claim 9, wherein the contiguous genomic fragment of human IL-6Rα sequence encoding the immunoglobulin superfamily domain is from the CTD-2192J23 bacterial artificial chromosome.

11. The genetically modified mouse of claim 8, further comprising a humanized IL-6 gene comprising a replacement at an endogenous mouse IL-6 locus of a mouse gene encoding IL-6 with a human gene encoding human IL-6.

12. The genetically modified mouse of claim 11, wherein the mouse comprises a replacement at an endogenous mouse IL-6 locus of a mouse IL-6 gene with a human IL-6 gene.

13. The genetically modified mouse of claim 11, wherein the humanized IL-6 gene is under control of endogenous mouse regulatory elements.

14. A method for making a humanized mouse, comprising replacing a mouse gene sequence encoding mouse IL-6 with a human gene encoding human IL-6 so that the human IL-6 gene is under control of endogenous mouse regulatory elements.

15. The method of claim 14, wherein the replacement is at an endogenous mouse IL-6 locus, and the human gene encoding human IL-6 is operably linked to endogenous mouse regulatory sequences.

16. A method for making a humanized mouse, comprising replacing all mouse exons encoding the immunoglobulin superfamily domain of mouse IL-6Rα with a human genomic fragment encoding the immunoglobulin superfamily domain of

human IL-6Rα to form a humanized IL-6Rα gene, wherein the humanized IL-6Rα gene is under control of endogenous mouse regulatory elements.

17. The method of claim 16, wherein the replacement is at an endogenous mouse IL-6Rα locus, and the humanized IL-6Rα gene is operably linked to endogenous mouse regulatory sequences.

18. A genetically modified mouse comprising a humanized IL-6Rα gene comprising a replacement of mouse immunoglobulin superfamily domain-encoding sequence with human immunoglobulin superfamily domain-encoding sequence, wherein the humanized IL-6Rα gene comprises a mouse transmembrane sequence and a mouse cytoplasmic sequence; wherein the mouse further comprises a gene encoding a human IL-6, wherein the genes encoding human IL-6 and humanized IL-6Rα are under control of endogenous mouse regulatory elements.

19. The genetically modified mouse of claim 19, wherein the mouse does not express a mouse IL-6Rα and does not express a mouse IL-6.

CLAIMS

1. A genetically modified mouse comprising a replacement at an endogenous mouse IL-6 locus of a mouse gene encoding IL-6 with a human gene encoding human IL-6, wherein the human gene encoding human IL-6 is under control of endogenous mouse regulatory elements at the endogenous mouse IL-6 locus.

2. The genetically modified mouse of claim 1, wherein the human gene encoding human IL-6 comprises exons 1 through 5 of the human IL-6 gene found in the CTD-2369M23 bacterial artificial chromosome.

3. The genetically modified mouse of claim 1, wherein the mouse expresses a mouse IL-6Rα.

4. The genetically modified mouse of claim 1, wherein the mouse expresses a humanized IL-6Rα wherein the endogenous mouse IL-6Rα gene has been replaced with a human sequence comprising a sequence that encodes an ectodomain of a human IL-6Rα.

5. The genetically modified mouse of claim 1, wherein the mouse does not exhibit a feature selected from plasmocytosis, glomerulosclerosis, glomerulonephritis, kidney failure, hypergammaglobulinemia, elevated megakaryocytes in spleen, elevated megakaryocytes in bone marrow, splenomegaly, lymph node enlargement, compacted abnormal plasma cells, and a combination thereof.

6. The genetically modified mouse of claim 4, wherein the humanized IL-6Rα comprises a human ectodomain.

7. The genetically modified mouse of claim 6, wherein the humanized IL-6Rα comprises a mouse transmembrane domain and a mouse cytoplasmic domain.

8. The genetically modified mouse of claim 1, wherein the mouse comprises a cell that expresses an IL-6Rα that comprises a human ectodomain on the surface of the cell.

9. A genetically modified mouse, comprising a humanization of an endogenous mouse IL-6Rα gene, wherein the humanization comprises a replacement of mouse IL-6Rα ectodomain-encoding sequence with human IL-6Rα ectodomain-encoding sequence at the endogenous mouse IL-6Rα locus, and wherein the humanized IL-6Rα gene is under control of endogenous mouse regulatory elements.

10. The genetically modified mouse of claim 9, wherein a contiguous mouse sequence comprising mouse exons 1 through 8 is replaced with a contiguous genomic fragment of human IL-6Rα sequence encoding a human IL-6Rα ectodomain.

11. The genetically modified mouse of claim 10, wherein the contiguous genomic fragment of human IL-6Rα sequence encoding the ectodomain is found in the CTD-2192J23 bacterial artificial chromosome.

12. The genetically modified mouse of claim 9, further comprising a humanized IL-6 gene comprising a replacement at an endogenous mouse IL-6 locus of a mouse gene encoding IL-6 with a human gene encoding human IL-6.

13. The genetically modified mouse of claim 12, wherein the humanized IL-6 gene is under control of endogenous mouse regulatory elements.

14. A method for making a humanized mouse, comprising replacing a mouse gene sequence encoding mouse IL-6 with a human gene encoding human IL-6 so that the human IL-6 gene is under control of endogenous mouse regulatory elements.

15. A method for making a humanized mouse, comprising replacing all mouse exons encoding ectodomain sequences of mouse IL-6Rα with a human genomic fragment encoding human IL-6Rα ectodomain to form a humanized IL- 6Rα gene, wherein the humanized IL-6Rα gene is under control of endogenous mouse regulatory elements.

16. A genetically modified mouse comprising a humanized IL-6Rα gene comprising a replacement of mouse ectodomainencoding sequence with human ectodomain sequence, wherein the humanized IL-6Rα gene comprises a mouse transmembrane sequence and a mouse cytoplasmic sequence; wherein the mouse further comprises a gene encoding a human IL-6, wherein the genes encoding human IL-6 and humanized IL-6Rα are under control of endogenous mouse regulatory elements.

17. The genetically modified mouse of claim 16, wherein the mouse does not express a mouse IL-6Rα and does not express a mouse IL-6.