

Claims

1. A genetically modified murine animal comprising a replacement at an endogenous murine IL-6 locus of a murine 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 murine regulatory elements at the endogenous murine IL-6 locus.
2. The genetically modified murine animal 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 murine animal of claim 1, wherein the murine animal expresses a murine IL-6R α .
4. The genetically modified murine animal of claim 1, wherein the murine animal expresses a humanized IL-6R α wherein the endogenous murine IL-6R α gene has been replaced with a human sequence comprising a sequence that encodes an ectodomain of a human IL-6R α .
5. The genetically modified murine animal of claim 1, wherein the murine animal 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 murine animal of claim 4, wherein the humanized IL-6R α comprises a mouse transmembrane domain and a murine cytoplasmic domain.
7. The genetically modified murine animal of claim 1, wherein the murine animal comprises a cell that expresses an IL-6R α that comprises a human ectodomain on the surface of the cell.
8. A genetically modified murine animal, comprising a humanization of an endogenous murine IL-6R α gene, wherein the humanization comprises a replacement of murine IL-6R α ectodomain-encoding sequence with human IL-6R α ectodomain-encoding sequence at the endogenous murine IL-6R α locus, and

wherein the humanized IL-6R α gene is under control of endogenous murine regulatory elements.

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

10. The genetically modified murine animal of claim 9, wherein the contiguous genomic fragment of human IL-6R α sequence encoding the ectodomain is found in the CTD-2192J23 bacterial artificial chromosome.

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

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

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

14. A genetically modified murine animal comprising a humanized IL-6R α gene comprising a replacement of murine ectodomain-encoding sequence with human ectodomain sequence, wherein the humanized IL-6R α gene comprises a murine transmembrane sequence and a mouse cytoplasmic sequence, wherein the murine animal further comprises a gene encoding a human IL-6, and wherein the genes encoding human IL-6 and humanized IL-6R α are under control of endogenous murine regulatory elements.

15. The genetically modified murine animal of claim 14, wherein the murine animal does not express a murine animal IL-6R α and does not express a murine IL-6.

CLAIMS

1. A genetically modified rat comprising a replacement at an endogenous rat IL-6 locus of a rat 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 rat regulatory elements at the endogenous rat IL-6 locus.