CLAIMS

That which is claimed is:

1. A genetically modified rodent, comprising:

a nucleic acid sequence that encodes a human erythropoietin protein (hEPO), wherein the nucleic acid is operably linked to an endogenous erythropoietin *(EPO)* gene promoter at the rodent *EPO* gene locus, wherein the operable linkage results in a null mutation in the rodent *EPO* gene at the rodent *EPO* gene locus, and wherein the rodent expresses additional human proteins selected from the group consisting of:

a hM-CSF protein encoded by a nucleic acid under the control of an *M-csf* promoter wherein the *M-csf* promoter is an endogenous rodent *M-csf* promoter at the rodent *M-csf* gene locus and wherein the rodent is heterozygous null or homozygous null for the rodent *M-csf* gene,

a hIL3 protein encoded by a nucleic acid under the control of an *Il-3* promoter wherein the *Il-3* promoter is an endogenous rodent *Il-3* promoter at the rodent *Il-3* gene locus and wherein the rodent is heterozygous null or homozygous null for the rodent *Il-3* gene,

a hGM-CSF protein encoded by a nucleic acid under the control of a *Gm-csf* promoter wherein the *Gm-csf* promoter is an endogenous rodent *Gm-csf* promoter at the rodent *Gm-csf* gene locus and wherein the rodent is heterozygous null or homozygous null for the rodent *Gm-csf* gene,

a hTPO protein encoded by a nucleic acid under the control of a *TPO* promoter wherein the *TPO* promoter is an endogenous rodent *TPO* promoter at the rodent *TPO* gene locus and wherein the rodent is heterozygous null or homozygous null for the rodent *TPO* gene, and

a hSirpa protein encoded by a nucleic acid under the control of a *Sirpa* promoter wherein the *Sirpa* promoter is an endogenous rodent *Sirpa* promoter at the rodent *Sirpa* gene locus and wherein the rodent is heterozygous null or homozygous null for the rodent *Sirpa* gene,

wherein the human proteins include at least hTPO, hIL3, hGM-CSF, and hSirpa, and

wherein the rodent is immunodeficient and the immunodeficiency is caused by a deficiency for both of Rag2 and Il2rg.

2. The rodent according to claim 1, wherein the rodent is heterozygous for the allele comprising the nucleic acid sequence that encodes the hEPO.

3. The rodent according to claim 1, wherein the rodent is homozygous for the allele comprising the nucleic acid sequence that encodes the hEPO.

4. The rodent according to any one of claims 1-3, wherein the nucleic acid sequence that encodes the hEPO comprises human *EPO* genomic coding and non-coding sequence.

5. The rodent according to any one of claims 1-3, wherein the nucleic acid sequence that encodes the hEPO comprises human *EPO* cDNA sequence.

6. The rodent according to any one of claims 1-5, wherein the rodent is a mouse.

7. The rodent according to any one of claims 1-6, wherein the rodent further comprises an engraftment of human hematopoietic cells.

8. The rodent according to claim 7, wherein the human hematopoietic cells comprise one or more cells selected from the group consisting of a human CD34-positive cell, a human hematopoietic stem cell, a human myeloid precursor cell, a human erythroid precursor cell, a human myeloid cell, a human dendritic cell, a human monocyte, a human granulocyte, a human erythrocyte, a human neutrophil, a human mast cell, a human thymocyte, and a human B lymphocyte.

9. The rodent according to claim 8, wherein the rodent comprises clodronate.

10. The rodent according to claim 9, wherein the rodent further comprises an infection with a pathogen that targets human cells of the erythroid lineage.

11. The rodent according to claim 10, wherein the pathogen is selected from a *Plasmodium* sp., *Babesia* sp., and a *Theileri* sp.