CLAIMS

1. A genetically modified rodent that comprises:

a nucleic acid encoding human IL-6 operably linked to an IL-6 promoter, wherein the rodent expresses a human IL-6 polypeptide and does not express a functional native IL-6 polypeptide, and at least one additional nucleic acid selected from the group consisting of:

i) a nucleic acid encoding human SIRPa operably linked to a SIRPa promoter, wherein the rodent expresses a human SIRPa polypeptide;

ii) a nucleic acid encoding human M-CSF operably linked to a M-CSF promoter, wherein the rodent expresses a human M-CSF polypeptide;

iii) a nucleic acid encoding human IL-3 operably linked to an IL-3 promoter, wherein the rodent expresses a human IL-3 polypeptide;

iv) a nucleic acid encoding human GM-CSF operably linked to a GM-CSF promoter, wherein the rodent expresses a human GM-CSF polypeptide; and

v) a nucleic acid encoding human TPO operably linked to a TPO promoter, wherein the rodent expresses a human TPO polypeptide.

2. The genetically modified rodent of claim 1, wherein the IL-6 promoter is the rodent IL-6 promoter, and the nucleic acid encoding human IL-6 is operably linked to the rodent IL-6 promoter at the rodent IL-6 locus.

3. The genetically modified rodent of claim 1, wherein the nucleic acid encoding human M-CSF is at the rodent M-CSF locus, the nucleic acid encoding human IL-3 is at the rodent IL-3 locus, the nucleic acid encoding human GM-CSF is at the rodent GM-CSF locus, and the nucleic acid encoding human TPO is at the rodent TPO locus.

4. The genetically modified rodent of claim 1 or claim 3, wherein the rodent is immunodeficient.

5. The genetically modified rodent of claim 4, wherein the rodent does not express a recombination activating gene (RAG), IL2 receptor gamma chain (IL2rg), or both a RAG and IL2rg.

6. The genetically modified rodent of claim l, further comprising an engraftment of human hematopoietic cells.

7. The genetically modified rodent of claim 6, wherein the human hematopoietic cells are CD34+ cells.

8. The genetically modified rodent of claim 6, wherein the human hematopoietic cells are multiple myeloma cells.

9. The genetically modified rodent of any one of claims 1-8, wherein the rodent is a mouse.

10. A method of generating a rodent model of human B cell development and function, the method comprising:

transplanting a population of human hematopoietic cells into a genetically modified rodent that is immunodeficient and comprises a nucleic acid encoding human IL-6 operably linked to an IL-6 promoter, wherein the rodent expresses a human IL-6 polypeptide and does not express a functional native IL-6 polypeptide.

11. The method of claim 10, wherein the IL-6 promoter is the rodent IL-6 promoter and the nucleic acid encoding human IL-6 is operably linked to the rodent IL-6 promoter at the rodent IL-6 locus.

12. The method of claim 10, wherein the transplanted population of hematopoietic cells comprises CD34+ cells.

13. The method of claim 10, wherein the transplanted population of hematopoietic cells comprises multiple myeloma cells.

14. The method of claim 10, wherein the transplanting comprises intrafemoral and/or intratibial injection.

15. The method of claim 10, wherein the rodent further comprises a nucleic acid encoding human SIRPa operably linked to a SIRPa promoter, wherein the rodent expresses a human SIRPa polypeptide.

16. The method of claim 15, wherein the immunodeficient, genetically modified rodent expresses at least one additional human nucleic acid selected from the group consisting of:

i) a nucleic acid encoding human M-CSF operably linked to a M-CSF promoter, wherein the rodent expresses a human M-CSF polypeptide;

ii) a nucleic acid encoding human IL-3 operably linked to an IL-3 promoter, wherein the rodent expresses a human IL-3 polypeptide;

iii) a nucleic acid encoding human GM-CSF operably linked to a GM-CSF promoter, wherein the rodent expresses a human GM-CSF polypeptide; and

iv) a nucleic acid encoding human TPO operably linked to a TPO promoter, wherein the rodent expresses a human TPO polypeptide.

17. The method of any one of claims 10-16, wherein the rodent is a mouse.

18. A method of screening a candidate agent for the ability to treat a hematopoietic cancer, the method comprising, contacting a genetically modified rodent of any one of claims 10-17 that has been engrafted with human hematopoietic cancer cells with a candidate agent, and comparing the viability and/or proliferative rate of human hematopoietic cancer cells in the contacted rodent to the viability and/or proliferative rate of human hematopoietic cancer cells in a genetically modified rodent of any one of claims 10-17 that is engrafted with human hematopoietic cancer cells but not contacted with candidate agent, wherein a decrease in the viability and/or rate of proliferation of the human hematopoietic cancer cells in the contacted rodent indicates that the candidate agent will treat the hematopoietic cancer.

19. The method of claim 18, wherein the hematopoietic cancer is multiple myeloma.

20. A genetically modified rodent that comprises:

a nucleic acid encoding human IL-6 operably linked to an IL-6 promoter,

wherein the rodent is immunodeficient for an endogenous immune system,

wherein the rodent expresses human IL-6 polypeptide, and

wherein the rodent does not express a functional native IL-6 polypeptide.