

CLAIMS

1. A genetically modified non-human animal comprising a genome comprising at least one nucleic acid encoding at least one of the group consisting of human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO, wherein the at least one nucleic acid is operably linked to a promoter, and wherein the animal expresses at least one polypeptide selected from the group consisting of human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO.
2. The genetically modified non-human animal of claim 1, comprising a genome comprising a nucleic acid encoding human M-CSF, a nucleic acid encoding human IL-3, a nucleic acid encoding human GM-CSF, a nucleic acid encoding human SIRPA and a nucleic acid encoding human TPO, wherein each of the nucleic acids encoding human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO is operably linked to a promoter, and wherein the animal expresses human M-CSF polypeptide, human IL-3 polypeptide, human GM-CSF polypeptide, human SIRPA polypeptide and human TPO polypeptide.
3. The genetically modified non-human animal of claim 1, wherein the animal is immunodeficient.
4. The genetically modified immunodeficient non-human animal of claim 3 wherein the animal does not express recombination activating gene 2 (Rag-2^{-/-}).
5. The genetically modified immunodeficient non-human animal of claim 3 wherein the animal does not express IL2 receptor gamma chain (gamma chain^{-/-}).
6. The genetically modified immunodeficient non-human animal of claim 3 wherein the animal does not express Rag-2 and wherein the animal does not express IL2 receptor gamma chain (Rag-2^{-/-} gamma chain^{-/-}).

7. The genetically modified non-human animal of claim 1, wherein the animal is a rodent.
8. The genetically modified non-human animal of claim 1, wherein the animal is a mouse.
9. The genetically modified animal of claim 1, further comprising human hematopoietic cells.
10. The genetically modified animal of claim 1, further comprising a human cancer cell.
11. The genetically modified animal of claim 10, wherein the human cancer cell is a leukemia cell or a melanoma cell.
12. A method of hematopoietic stem and progenitor cell (HSPC) engraftment in a genetically modified non-human animal, wherein the animal expresses at least one of the group consisting of human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO, the method comprising the step of: administering at least one HSPC to the genetically modified animal expressing at least one of the group consisting of human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO.
13. The method of claim 12, wherein the genetically modified non-human animal is a rodent.
14. The method of claim 12, wherein the genetically modified non-human animal is a mouse.
15. The method of claim 12, wherein the genetically modified non-human animal is immunodeficient.

16. The method of claim 15, wherein the genetically modified immunodeficient non-human animal does not express recombination activating gene 2 ($\text{Rag-2}^{-/-}$).

17. The method of claim 15, wherein the genetically modified immunodeficient non-human animal does not express endogenous IL2 receptor ($\text{gamma chain}^{-/-}$).

18. The method of claim 15, wherein the genetically modified immunodeficient non-human animal does not express endogenous Rag-2 and does not express endogenous gamma chain ($\text{Rag-2}^{-/-}$ $\text{gamma chain}^{-/-}$).

19. The method of claim 12, wherein the genetically modified animal comprises a human cancer cell.

20. The method of claim 19, wherein the human cancer cell is a leukemia cell or a melanoma cell.

21. A genetically modified $\text{Rag-2}^{-/-}$, $\text{gamma chain}^{-/-}$ mouse having a genome comprising at least one nucleic acid encoding at least one of the group consisting of human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO, wherein the at least one nucleic acid is operably linked to at least one promoter, wherein the mouse expresses at least one polypeptide selected from the group consisting of human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO.

22. The genetically modified non-human animal of claim 21, comprising a genome comprising a nucleic acid encoding human M-CSF, a nucleic acid encoding human IL-3, a nucleic acid encoding human GM-CSF, a nucleic acid encoding human SIRPA and a nucleic acid encoding human TPO, wherein each of the nucleic acids encoding human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO is operably linked to a promoter, and wherein the animal expresses human M-CSF polypeptide, human IL-3 polypeptide, human GM-CSF polypeptide,

human SIRPA polypeptide and human TPO polypeptide.

23. The genetically modified non-human animal of claim 21, wherein the animal is a rodent.

24. The genetically modified non-human animal of claim 21, wherein the animal is a mouse.

25. The genetically modified animal of claim 21, further comprising human hematopoietic cells.

26. The genetically modified animal of claim 21, further comprising a human cancer cell.

27. The genetically modified animal of claim 26, wherein the human cancer cell is a leukemia cell or a melanoma cell.

CLAIMS

1. A genetically modified non-human animal comprising in its genome a nucleic acid encoding human M-CSF, a nucleic acid encoding human IL-3, a nucleic acid encoding human GM-CSF, a nucleic acid encoding human SIRPA and a nucleic acid encoding human TPO, wherein each of the nucleic acids encoding human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO is operably linked to a promoter, and wherein the animal expresses human M-CSF polypeptide, human IL-3 polypeptide, human GM-CSF polypeptide, human SIRPA polypeptide and human TPO polypeptide.

2. The genetically modified non-human animal of claim 1, wherein the animal is immunodeficient.

3. The genetically modified immunodeficient non-human animal of claim 2 wherein the animal comprises a recombination activating gene 2(Rag2) gene knock-out.

4. The genetically modified immunodeficient non-human animal of claim [[3]]2 or 3 wherein the animal comprises an IL2 receptor gamma chain (IL2rg) gene knock-out.

5. The genetically modified non-human animal of any one of the preceding claims, wherein the animal is a rodent.

6. The genetically modified non-human animal of claim 5, wherein the animal is a mouse.

7. The genetically modified animal of any one of the preceding claims, further comprising human hematopoietic cells.

8. The genetically modified animal of any one of the preceding claims, further comprising a human cancer cell.

9. The genetically modified animal of claim 8, wherein the human cancer cell is a leukemia cell or a melanoma cell.

10. A method of hematopoietic stem and progenitor cell (HSPC) engraftment comprising the step of administering at least one HSPC to a genetically modified non-human animal,

wherein the animal expresses human M-CSF, human IL-3, human GM-CSF, human SIRPA and human TPO.

11. The method of claim 10, wherein the genetically modified non-human animal is a rodent.

12. The method of claim 11, wherein the genetically modified non-human animal is a mouse.

13. The method of any one of claims 10-12, wherein the genetically modified non-human animal is immunodeficient.

14. The method of claim 13, wherein the genetically modified immunodeficient non-human animal comprises a recombination activating gene 2(Rag2) gene knock-out.

15. The method of claim 13 or 14, wherein the genetically modified immunodeficient non-human animal comprises an IL2 receptor gamma chain (IL2rg) gene knock-out.

16. The method of any one of claims 10-15, wherein the genetically modified animal comprises a human cancer cell.

17. The method of claim 16, wherein the human cancer cell is a leukemia cell or a melanoma cell.