What is claimed is:

1. A genetically engineered hematopoietic stem or progenitor cell, which comprises a genetic mutation in the exon 3 of an endogenous CD33 gene, wherein the genetic mutation is at a site targeted by a gRNA, which comprises the nucleotide sequence of CCUCACUAGACUUGACCCAC (SEQ ID NO: 70), and wherein the genetic mutation causes a reduced expression level of CD33 as compared with a wild-type counterpart cell.

2. The genetically engineered hematopoietic stem or progenitor cell of claim 1, which expresses less than 20% of the CD33 expressed by the wild-type counterpart.

3. The genetically engineered hematopoietic stem or progenitor cell of claim 2, which does not express CD33.

4. The genetically engineered hematopoietic stem or progenitor cell of any one of claims 1-3, which is CD34+.

5. The genetically engineered hematopoietic stem or progenitor cell of any one of claims 1-4, which is from bone marrow cells or peripheral blood mononuclear cells of a subject.

6. The genetically engineered hematopoietic stem or progenitor cell of claim 5, wherein the subject is a human patient having a hematopoietic malignancy.

7. The genetically engineered hematopoietic stem or progenitor cell of claim 5, wherein the subject is a healthy human donor.

8. The genetically engineered hematopoietic stem or progenitor cell of any of claims 1- 7, which does not comprise a mutation at any of SEQ ID NOs: 99-112 ~~in any predicted off-target site, e.g., in any site listed in Figure 30~~.

9. A cell population, comprising a plurality of the genetically engineered hematopoietic stem or progenitor cell of any one of claims 1-8.

10. A method of producing a genetically engineered hematopoietic stem or progenitor cell, comprising:

(i) providing a hematopoietic stem or progenitor cell, and

(ii) introducing into the cell (a) a guide RNA (gRNA) that comprises a nucleotide sequence at least 90% identical to SEQ ID NO: 70; and (b) a Cas ~~Cas9~~ endonuclease, thereby producing a genetically engineered hematopoietic stem or progenitor cell.

11. The method of claim 10, wherein the genetically engineered hematopoietic stem or progenitor cell expresses less than 20% of the CD33 expressed by the wild-type counterpart.

12. The method of claim 11, wherein the genetically engineered hematopoietic stem or progenitor cell does not express CD33.

13. The method of any of claims 10-12, wherein (a) and (b) are encoded on one vector, which is introduced into the cell.

14. The method of claim 13, wherein the vector is a viral vector.

15. The method of any of claims 10-12, wherein (a) and (b) are introduced into the cell as a pre-formed ribonucleoprotein complex.

16. The method of claim 15, wherein the ribonucleoprotein complex is introduced into the cell via electroporation.

17. The method of any of claims 10-12, wherein the ~~Cas9~~ Cas endonuclease is introduced into the cell by delivering into the cell a mRNA molecule coding for the ~~Cas9~~ Cas endonuclease.

18. The method of any one of claims 10-17, wherein the Cas endonuclease is a Cas9 endonuclease.

19. ~~18.~~ The method of any one of claims 10-18 ~~17~~, wherein the gRNA is a single-molecule guide RNA (sgRNA).

20. ~~19.~~ The method of claim 19 ~~18~~, wherein the gRNA is a chemically modified sgRNA.

21. ~~20.~~ The method of any one of claims 10-20 ~~19~~, wherein the hematopoietic stem or progenitor cell is CD34+.

22. ~~21.~~ The method of any one of claims 10-21 ~~20~~, wherein the hematopoietic stem or progenitor cell is from bone marrow cells or peripheral blood mononuclear cells (PBMCs) of a subject.

23. ~~22.~~ The method of claim 22 ~~21~~, wherein the subject has a hematopoietic disorder.

24. ~~23.~~ A genetically engineered hematopoietic stem or progenitor cell, which is produced by a method of any one of claims 10-23 ~~12-22~~.

25. ~~24.~~ A genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use in a method of treating a hematopoietic disorder, comprising administering to a subject in need thereof an effective amount of the genetically engineered hematopoietic stem or progenitor cell of any one of claims 1-8 and 24 ~~23~~, or the cell population of claim 9.

26. ~~25.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of claim 25 ~~24~~, wherein the hematopoietic disorder is a hematopoietic malignancy.

27. ~~26.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of claim 25 ~~24~~ or claim 26 ~~25~~, further comprising administering to the subject an effective amount of an agent that targets CD33, and wherein the agent comprises an antigen-binding fragment that binds CD33.

28. ~~27.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of claim 27 ~~26~~, wherein the agent that targets CD33 is an immune cell expressing a chimeric antigen receptor (CAR), which comprises the antigen-binding fragment that binds CD33.

29. ~~28.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of claim 28 ~~27~~, wherein the immune cell is a T cell.

30. ~~29.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of any one of claims 25-29 ~~24-28~~, wherein the immune cells, the genetically engineered hematopoietic stem or progenitor cell, or both, are allogeneic.

31. ~~30.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of any one of claims 25-30 ~~24-29~~, wherein the immune cells, the genetically engineered hematopoietic stem or progenitor cell, or both, are autologous.

32. ~~31.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of any one of claims 28-31 ~~27-30~~, wherein the antigen-binding fragment in the chimeric receptor is a single-chain antibody fragment (scFv) that specifically binds human CD33.

33. ~~32.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of any one of claims 25-32 ~~24-31~~, wherein the subject is a human patient having Hodgkin's lymphoma, non-Hodgkin's lymphoma, leukemia, or multiple myeloma.

34. ~~33.~~ The genetically engineered hematopoietic stem or progenitor cell, or cell population thereof, for use ~~method~~ of claim 33 ~~32~~, wherein the subject is a human patient having leukemia, which is acute myeloid leukemia, chronic myelogenous leukemia, acute lymphoblastic leukemia, or chronic lymphoblastic leukemia.

35. ~~34.~~ A guide ribonucleic acid (gRNA) comprising a spacer sequence that is at least 90% identical to SEQ ID NO:70 and wherein the gRNA is chemically modified.

36. ~~35.~~ The gRNA of claim 35 ~~34~~, wherein the gRNA is a single-molecule gRNA (sgRNA).

~~36. The gRNA of claim 34 or claim 35, wherein the gRNA is chemically modified.~~

37. The gRNA of claim 35 or 36 ~~any one of claims 34-36~~, wherein the spacer sequence is SEQ ID NO:70.

38. The gRNA of any one of claims 35-37 ~~34-37~~, which does not direct genetic editing at any of SEQ ID NOs: 99-112 ~~to any predicted off-target site in a target cell, e.g., does not direct genetic editing to any site listed in Figure 30 in a target cell.~~

~~39. A genetically engineered hematopoietic stem or progenitor cell, which comprises a genetic mutation in the exon 3 of an endogenous CD33 gene, wherein the genetic mutation is at a site targeted by a gRNA which comprises the nucleotide sequence of AUCCCUGGCACUCUAGAACC (SEQ ID NO: 67).~~

~~40. A guide ribonucleic acid (gRNA) comprising a spacer sequence that is at least 90% identical to SEQ ID NO: 67.~~