CLAIMS:

1. ____A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of ~~SEQ ID NO: 21~~ any one of SEQ ID NOs: 21-30 or 48-51.

~~2. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 22.~~

~~3. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 23.~~

~~4. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 24.~~

~~5. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 25.~~

~~6. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 26.~~

~~7. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 27.~~

~~8. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 28.~~

~~9. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 29.~~

~~10. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 30.~~

~~11. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 48.~~

~~12. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 49.~~

~~13. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 50.~~

~~14. A gRNA comprising a targeting domain, wherein the targeting domain comprises a sequence of SEQ ID NO: 51.~~

~~15. A gRNA comprising a targeting domain which binds a target domain of Table 1, 2, 6, or 8.~~

~~16. A gRNA comprising a targeting domain capable of directing cleavage or editing of a target domain of Table 1, 2, 6, or 8.~~

~~17. The gRNA of any of claim 1-16, which comprises a first complementarity domain, a linking domain, a second complementarity domain which is complementary to the first complementarity domain, and a proximal domain.~~

~~18. The gRNA of any of claims 1-17, which is a single guide RNA (sgRNA).~~

~~19. The gRNA of any of claims 1-18, which comprises one or more 2'O-methyl nucleotide.~~

~~20. The gRNA of any of claims 1-19, which comprises one or more phosphorothioate or thioPACE linkage.~~

~~21. A method of producing a genetically engineered cell, comprising:~~

~~(i) providing a cell (e.g., a hematopoietic stem or progenitor cell, e.g., a wild-type hematopoietic stem or progenitor cell), and~~

(ii) introducing into the cell (a) a gRNA of any of claims 1-20; and (b) a Cas9 molecule that binds the gRNA,

thereby producing the genetically engineered cell.

22. The method of claim 21, wherein the Cas molecule comprises a SpCas9 endonuclease, a SaCas9 endonuclease, or a Cpf1 endonuclease.

23. The method of claim 21 or 22, wherein (i) and (ii) are introduced into the cell as a pre-formed ribonucleoprotein complex.

24. The method of claim 21, wherein the ribonucleoprotein complex is introduced into the cell via electroporation.

25. A genetically engineered hematopoietic stem or progenitor cell, which is produced by a method of claim 21.

26. A cell population, comprising a plurality of the genetically engineered hematopoietic stem or progenitor cells of claim 25.

27. The cell population of claim 26, which further comprises one or more cells that comprise one or more non-engineered CD123 genes.

28. The cell population of claim 26 or 27, which expresses less than 20% of the CD123 expressed by a wild-type counterpart cell population.

29. The cell population of any of claims 26-28, which comprises both of hematopoietic stem cells and hematopoietic progenitor cells.

30. The cell population of any of claims 26-29, which further comprises a second mutation at a gene encoding a lineage-specific cell surface antigen other than CD123.

31. The cell population of claim 28, wherein the gene encoding a lineage-specific cell surface antigen other than CD123 is CD33 or CLL1.

~~32. A method, comprising administering to a subject in need thereof a cell population of any of claims 26-31.~~

~~33. The method of claim 28, wherein the subject has a hematopoietic malignancy.~~

~~34. The method of claim 28 or 33, which further comprises administering to the subject an effective amount of an agent that targets CD123, wherein the agent comprises an antigen-binding fragment that binds CD123.~~

2. A gRNA comprising a targeting domain which binds a target domain of Table 1, 2, 6, or 8.

3. A gRNA comprising a targeting domain capable of directing cleavage or editing of a target domain of Table 1, 2, 6, or 8.

4. The gRNA of any one of claims 1 to 3, wherein the gRNA comprises a first complementarity domain, a linking domain, a second complementarity domain which is complementary to the first complementarity domain, and a proximal domain.

5. The gRNA of any one of claims 1 to 4, wherein the gRNA is a single guide RNA (sgRNA).

6. The gRNA of any one of claims 1 to 5, wherein the gRNA comprises one or more 2'O-methyl nucleotide.

7. The gRNA of any one of claims 1 to 6, wherein the gRNA comprises one or more phosphorothioate or thioPACE linkage.

8. A method of producing a genetically engineered cell, wherein the method comprises:

(i) providing a cell (e.g., a hematopoietic stem or progenitor cell, e.g., a wild-type hematopoietic stem or progenitor cell), and

(ii) introducing into the cell (a) the gRNA of any of claims 1 to 7; and (b) a Cas9 molecule that binds the gRNA,

thereby producing the genetically engineered cell.

9. The method of claim 8, wherein the Cas9 molecule comprises a SpCas9 endonuclease, a SaCas9 endonuclease, or a Cpf1 endonuclease.

10. The method of claim 8 or 9, wherein the gRNA of (a) and the Cas9 molecule of (b) are introduced into the cell as a pre-formed ribonucleoprotein complex.

11. The method of claim 10, wherein the ribonucleoprotein complex is introduced into the cell via electroporation.

12. A genetically engineered hematopoietic stem or progenitor cell, wherein the genetically engineered hematopoietic stem or progenitor cell is produced by the method of any one of claims 8 to 11.

13. A cell population comprising a plurality of the genetically engineered hematopoietic stem or progenitor cells of claim 12.

14. The cell population of claim 13, further comprising one or more cells comprising one or more non-engineered CD123 genes.

15. The cell population of claim 13 or 14, wherein the cell population expresses less than 20% of the CD123 expressed by a wild-type counterpart cell population.

16. The cell population of any one of claims 13 to 15, wherein the cells of the population comprise both hematopoietic stem cells and hematopoietic progenitor cells.

17. The cell population of any one of claims 13 to16, wherein the cells of the population further comprise a second mutation at a gene encoding the lineage-specific cell surface antigen other than CD123.

18. The cell population of claim 17, wherein the gene encoding a lineage-specific cell surface antigen other than CD123 is CD33 or CLL1.

19. Use of the cell population of any one of claims 13 to 17 in the manufacture of a medicament for treating a hematopoietic malignancy in a subject.

20. The use of claim 19, wherein the medicament is to be administered to the subject in combination with an effective amount of an agent that targets CD123, wherein the agent comprises an antigen-binding fragment that binds CD123.