What is claimed is:

1. A method for generating a population of modified human hematopoietic stem and progenitor cells (HSPCs) that are resistant to a CD33 CAR-T therapy, comprising:

introducing into the HSPCs a CRISPR system comprising a guide nucleic acid, wherein the CRISPR system produces an insertion and/or deletion in an endogenous CD33 coding sequence comprising the nucleic acid sequence set forth in SEQ ID NO: 4, and wherein the insertion and/or deletion is capable of downregulating gene expression of CD33,

thereby generating the population of modified human HSPCs.

2. The method of claim 1, wherein the CRISPR system further comprises a homology-directed repair (HDR) template comprising a single-stranded oligonucleotide donor (ssODN) sequence.

3. The method of claim 2, wherein the ssODN sequence comprises (i) the nucleotide sequence set forth in SEQ ID NO: 4 with an extra adenine inserted or (ii) the nucleotide sequence set forth in SEQ ID NO: 5.

4. The method of claim 1, wherein the HSPCs are human cells obtained from a source selected from the group consisting of peripheral blood mononuclear cells, cord blood cells, bone marrow, lymph node, and spleen.

5. The method of claim 1, wherein the HSPCs are CD34+ HSPCs.

6. A method for generating a population of modified human hematopoietic stem and progenitor cells (HSPCs) that are resistant to a CD33 CAR-T therapy, comprising introducing into the HSPCs a CRISPR system comprising:

a guide nucleic acid; and

a single-stranded oligonucleotide donor (ssODN) sequence, wherein the ssODN sequence comprises the nucleotide sequence set forth in SEQ ID NO:5,

wherein the CRISPR system produces an insertion and/or deletion in an endogenous CD33 coding sequence comprising the nucleic acid sequence set forth in SEQ ID NO: 4, and wherein the insertion and/or deletion is capable of downregulating gene expression of CD33,

thereby generating the population of modified human HSPCs.

7. The HSPCs of claim 6, wherein the HSPCs are human cells obtained from a source selected from the group consisting of peripheral blood mononuclear cells, cord blood cells, bone marrow, lymph node, and spleen.

8. The HSPCs of claim 6, wherein the HSPCs are CD34+ HSPCs.

9. A population of modified human hematopoietic stem and progenitor cells (HSPCs) that are resistant to a CD33 CAR-T therapy, wherein the HSPCs comprise an insertion and/or deletion in an endogenous CD33 coding sequence comprising the nucleic acid sequence set forth in SEQ ID NO: 4, wherein the insertion and/or deletion is mediated by a CRISPR system comprising a guide nucleic acid, and wherein the insertion and/or deletion is capable of downregulating gene expression of CD33.

10. The HSPCs of claim 9, wherein the CRISPR system further comprises a homology-directed repair (HDR) template comprising a single-stranded oligonucleotide donor (ssODN) sequence.

11. The HSPCs of claim 10, wherein the ssODN sequence comprises (i) the nucleotide sequence set forth in SEQ ID NO:4 with an extra adenine inserted or (ii) the nucleotide sequence set forth in SEQ ID NO:5.

12. The HSPCs of claim 9, wherein the HSPCs are autologous human cells obtained from a source selected from the group consisting of peripheral blood mononuclear cells, cord blood cells, bone marrow, lymph node, and spleen.

13. The HSPCs of claim 9, wherein the HSPCs are CD34+ HSPCs.