

CLAIMS

1. A composition comprising:
a retrovirus comprising one or more nucleic acids, a viral envelope protein comprising at least one mutation that diminishes its native function, and a non-viral membrane-bound protein comprising an extracellular targeting domain that binds to a protein on the surface of a hematopoietic stem cell (HSC).
2. The composition of claim 1, wherein the extracellular targeting domain is stem cell factor (SCF), FMS-like tyrosine kinase 3 ligand (FLT3L), or thrombopoietin (TPO).
3. The composition of claim 1 or 2, wherein the protein on the surface of the HSC is CD34, CD90, CD133, CD49f, CD201, c-Kit, FMS-like tyrosine kinase 3 (FLT3), or thrombopoietin receptor.
4. The composition of any one of claims 1-3, wherein the extracellular targeting domain comprises an amino acid sequence set forth in any one of SEQ ID NOs. 54-59.
5. The composition of any one of claims 1-4, wherein at least one of the one or more nucleic acids encodes a gene of interest, optionally wherein the gene of interest encodes a protein of interest.
6. The composition of claim 5, wherein the protein of interest is a gene editing protein.
7. The composition of claim 6, wherein the gene editing protein is a Cas endonuclease, a zinc finger nuclease, a transcription activator-like effector nuclease (TALEN), or a meganuclease, optionally wherein the Cas endonuclease is a Cas9 endonuclease.
8. The composition of any one of claims 1-5, wherein at least one of the one or more nucleic acids is a guide RNA.
9. The composition of any one of claims 1-8, wherein the retrovirus is a lentivirus.

10. The composition of any one of claims 1-9, wherein the viral envelope protein is a VSV-G envelope protein, a measles virus envelope protein, a nipah virus envelope protein, or a cocal virus G protein.
11. The composition of claim 10, where the at least one mutation of a VSV-G envelope protein is a mutation selected from the group consisting of H8, I41, K47, Y209, and R354.
12. The composition of claim 10, where the viral envelope protein comprises a VSV-G envelope protein comprising the amino acid sequence set forth in SEQ ID NO: 16 or SEQ ID NO: 17.
13. The composition of claim 10, where the at least one mutation of the measles virus envelope protein is a mutation selected from the group consisting of Y481, R533, S548, and F549.
14. The composition of claim 10, where the viral envelope protein comprises a measles virus envelope protein comprising the amino acid sequence set forth in SEQ ID NO: 21.
15. The composition of claim 10, where the at least one mutation of the nipah virus envelope protein is a mutation selected from the group consisting of E501, W504, Q530, and E533.
16. The composition of claim 10, where the viral envelope protein comprises a nipah virus envelope protein comprising the amino acid sequence set forth in SEQ ID NO: 23.
17. The composition of claim 10, where the at least one mutation of the cocal virus G protein is a mutation selected from the group consisting of K64 and R371.
18. The composition of claim 10, where the viral envelope protein comprises a cocal virus G protein comprising the amino acid sequence set forth in SEQ ID NO: 26.
19. The composition of any one of claims 1-18, wherein a linker is positioned between the membrane-bound domain and the extracellular targeting domain.

20. The composition of claim 19, wherein the linker is a rigid linker, optionally comprising a PDGFR stalk or a CD8 α stalk.
21. The composition of claim 19, wherein the linker is a flexible linker, optionally comprising an amino acid sequence comprising GAPGAS (SEQ ID NO: 5) or GGGGS (SEQ ID NO: 7).
22. The composition of claim 19, wherein the linker is an oligomerized linker, optionally comprising an IgG4 hinge or an amino acid sequence that can form a tetrameric coiled coil.
23. The composition of any one of claims 1-22, wherein the one or more nucleic acids encode a chimeric antigen receptor.
24. A composition comprising:
a retrovirus comprising one or more nucleic acids encoding a gene editing composition, a viral envelope protein comprising at least one mutation that diminishes its native function, and a non-viral membrane-bound protein comprising an extracellular targeting domain that binds to a protein on the surface of a hematopoietic stem cell (HSC), wherein the gene editing composition specifically targets a section of the chromosomal DNA of the HSC.
25. The composition of claim 24, wherein the extracellular targeting domain is stem cell factor (SCF), FMS-like tyrosine kinase 3 ligand (FLT3L), or thrombopoietin (TPO).
26. The composition of claim 24 or 25, wherein the protein on the surface of the HSC is CD34, CD90, CD133, CD49f, CD201, c-Kit, FMS-like tyrosine kinase 3 (FLT3), or thrombopoietin receptor.
27. The composition of any one of claims 24-26, wherein the extracellular targeting domain comprises an amino acid sequence set forth in any one of SEQ ID NOs. 54-59.

28. The composition of any one of claims 24-27, wherein the gene editing composition comprises one of the one or more nucleic acids, wherein the one or more nucleic acids encode a gene editing protein and/or a guide RNA.
29. The composition of claim 28, wherein the gene editing protein is a Cas endonuclease, a zinc finger nuclease, a transcription activator-like effector nuclease (TALEN), or a meganuclease, optionally wherein the Cas endonuclease is a Cas9 endonuclease.
30. The composition of any one of claims 24-29, wherein the retrovirus is a lentivirus.
31. The composition of any one of claims 24-30, wherein the viral envelope protein is a VSV-G envelope protein, a measles virus envelope protein, a nipah virus envelope protein, or a coxsa virus G protein.
32. The composition of claim 31, where the at least one mutation of a VSV-G envelope protein is a mutation selected from the group consisting of H8, I41, K47, Y209, and R354.
33. The composition of claim 31, where the viral envelope protein comprises a VSV-G envelope protein comprising the amino acid sequence set forth in SEQ ID NO: 16 or SEQ ID NO: 17.
34. The composition of claim 31, where the at least one mutation of the measles virus envelope protein is a mutation selected from the group consisting of Y481, R533, S548, and F549.
35. The composition of claim 31, where the viral envelope protein comprises a measles virus envelope protein comprising the amino acid sequence set forth in SEQ ID NO: 21.
36. The composition of claim 31, where the at least one mutation of the nipah virus envelope protein is a mutation selected from the group consisting of E501, W504, Q530, and E533.

37. The composition of claim 31, where the viral envelope protein comprises a nipah virus envelope protein comprising the amino acid sequence set forth in SEQ ID NO: 23.
38. The composition of claim 31, where the at least one mutation of the cocal virus G protein is a mutation selected from the group consisting of K64 and R371.
39. The composition of claim 31, where the viral envelope protein comprises a cocal virus G protein comprising the amino acid sequence set forth in SEQ ID NO: 26.
40. The composition of any one of claims 24-39, wherein a linker is positioned between the membrane-bound domain and the extracellular targeting domain.
41. The composition of claim 40, wherein the linker is a rigid linker, optionally comprising a PDGFR stalk or a CD8 α stalk.
42. The composition of claim 40, wherein the linker is a flexible linker, optionally comprising an amino acid sequence comprising GAPGAS (SEQ ID NO: 5) or GGGGS (SEQ ID NO: 7).
43. The composition of claim 40, wherein the linker is an oligomerized linker, optionally comprising an IgG4 hinge or an amino acid sequence that can form a tetrameric coiled coil.
44. The composition according to any one of claims 1 to 43 for use as a medicament.
45. Use of the composition according to any one of claims 1 to 43 in the manufacture of a medicament for the treatment of a genetic disease/disorder.
46. The use according to claim 45, wherein the genetic disease/disorder is related to HSC dysfunction.
47. The use according to claim 45 or 46, wherein the genetic disease/disorder is sickle cell anemia, severe combined immunodeficiency (SCID) or blood cancer such as leukemia and lymphoma.

48. The use according to any one of claims 45-47, wherein the composition is to be administered in cell or gene therapy.

49. The use according to any one of claims 45-48, wherein the composition is to be administered to deliver one or more nucleic acids to a hematopoietic stem cell (HSC).