CLAIMS

What is claimed is:

1. A replication-defective adeno-associated virus (AAV) comprising a correction genome enclosed in a capsid,

the capsid being an AAV Clade F capsid; and

the correction genome comprising (a) an editing element selected from an internucleotide bond or a nucleotide sequence for integration into a target locus of a mammalian chromosome, (b) a 5' homologous arm nucleotide sequence 5' of the editing element, having homology to a 5' region of the mammalian chromosome relative to the target locus, and (c) a 3' homologous arm nucleotide sequence 3' of the editing element, having homology to a 3' region of the mammalian chromosome relative to the target locus.

2. A replication-defective adeno-associated virus (AAV) comprising a correction genome enclosed in a capsid,

the capsid being an AAV Clade F capsid; and

the correction genome comprising an editing element nucleotide sequence for integration into a target locus of a mammalian chromosome, the correction genome having an essential absence of a promoter operatively linked to the editing element nucleotide sequence.

3. A replication-defective adeno-associated virus (AAV) comprising a correction genome enclosed in a capsid, wherein

the capsid being an AAV Clade F capsid;

the correction genome comprising an editing element selected from an internucleotide bond or a nucleotide sequence for integration into a target locus of a mammalian chromosome in a cell; and

the AAV having a chromosomal integration efficiency of at least about 1% for integrating the editing element into the target locus of the mammalian chromosome in the cell.

4. The AAV of claim 3, wherein the AAV has a chromosomal integration efficiency of at least about 1% in the absence of an exogenous nuclease for integrating the editing element into the target locus of the mammalian chromosome in the cell.

5. The AAV of any one of claims 1-4, wherein the correction genome comprises a 5' inverted terminal repeat (5' ITR) nucleotide sequence 5' of the 5' homologous arm nucleotide sequence, and a 3' inverted terminal repeat (3' ITR) nucleotide sequence 3' of the 3' homologous arm nucleotide sequence.

6. The AAV of claim 5, wherein the 5' ITR nucleotide sequence and the 3' ITR nucleotide sequence are substantially identical to an AAV2 virus 5'ITR and an AAV2 virus 3' ITR, respectively.

7. The AAV of any one of claims 5 or 6, wherein the 5' ITR nucleotide sequence and the 3' ITR nucleotide sequence are substantially mirror images of each other.

8. The AAV of any one of claims 5-7, wherein the 5' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:36, and the 3' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:37.

9. The AAV of claim 4, wherein the 5' ITR nucleotide sequence and the 3' ITR nucleotide sequence are substantially identical to an AAV5 virus 5'ITR and an AAV5 virus 3' ITR, respectively.

10. The AAV of claim 9, wherein the 5' ITR nucleotide sequence and the 3' ITR nucleotide sequence are substantially mirror images of each other.

11. The AAV of any one of claims 5, 9 or 10, wherein the 5' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:38, and the 3' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:39.

12. The AAV of any one of claims 1 or 3-11, wherein the correction genome has an essential absence of a promoter operatively linked to the editing element nucleotide sequence.

13. The AAV of any one of claims 1 or 3-11, wherein the correction genome further comprises an exogenous promoter operatively linked to the editing element.

14. The AAV of any one of the preceding claims, wherein the replication-defective AAV genome comprises an essential absence of an AAV *rep* gene and an AAV *cap* gene.

15. The AAV of any one of the preceding claims, wherein each of the 5' and 3' homologous arm nucleotide sequences independently has a nucleotide length of between about 500 to 1000 nucleotides or between about 600 to 1000 nucleotides.

16. The AAV of any one of the preceding claims, wherein the 5' and 3' homologous arm nucleotide sequences have substantially equal nucleotide lengths.

17. The AAV of any one of the preceding claims, wherein the 5' and 3' homologous arm nucleotide sequences have asymmetrical nucleotide lengths.

18. The AAV of any one of the preceding claims, wherein the 5' homologous arm nucleotide sequence has at least about 95% nucleotide sequence identity to the 5' region of the mammalian chromosome relative to the target locus.

19. The AAV of any one of the preceding claims, wherein the 3' homologous arm nucleotide sequence has at least about 95% nucleotide sequence identity to the 3' region of the mammalian chromosome relative to the target locus.

20. The AAV of any one of claims 1 to 19, wherein the 5' homologous arm nucleotide sequence has 100% sequence identity to the 5' region of the mammalian chromosome relative to the target locus and the 3' homologous arm nucleotide sequence has 100% sequence identity to the 3' region of the mammalian chromosome relative to the target locus.

21. The AAV of any one of the preceding claims, wherein the editing element consists of one nucleotide.

22. The AAV of claim 21, wherein the target locus is a nucleotide sequence consisting of one nucleotide, and the target locus represents a point mutation of the mammalian chromosome.

23. The AAV of any one of claims 1-20, wherein the editing element comprises at least 1, 2, 10, 100, 200, 500, 1000, 1500, 2000, 3000, 4000, or 5000 nucleotides.

24. The AAV of any one of claims 1-20, wherein the editing element comprises 1 to 5500, 1 to 5000, 1 to 4500, 1 to 4000, 1 to 3000, 1 to 2000, 1 to 1000, 1 to 500, 1 to 200, or 1 to 100 nucleotides, or 2 to 5500, 2 to 5000, 2 to 4500, 2 to 4000, 2 to 3000, 2 to 2000, 2 to 1000, 2 to 500, 2 to 200, or 2 to 100 nucleotides, or 10 to 5500, 10 to 5000, 10 to 4500, 10 to 4000, 10 to 3000, 10 to 2000, 10 to 1000, 10 to 500, 10 to 200, or 10 to 100 nucleotides.

25. The AAV of any one of claims 1-24, wherein the editing element comprises an exon, an intron, a 5' untranslated region (UTR), a 3' UTR, a promoter, a splice donor, a splice acceptor, a sequence encoding or non-coding RNA, an insulator, a gene, or a combination thereof.

26. The AAV of claim 25, wherein the editing element is a fragment of a coding sequence of a gene within or spanning the target locus.

27. The AAV of any one of the preceding claims, wherein

the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to one;

the editing element comprises m nucleotides where m is an integer equal to n; and

the editing element represents a substitution for the target locus of the mammalian chromosome.

28. The AAV of any one of the preceding claims, wherein

the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to one;

the editing element comprises m nucleotides where m is an integer greater than n; and

the editing element represents a substitutive addition for the target locus of the mammalian chromosome.

29. The AAV of any of the preceding claims, wherein

the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to two;

the editing element comprises m nucleotides where m is an integer less than n; and

the editing element represents a substitutive deletion for the target locus of the mammalian chromosome.

30. The AAV of any of the preceding claims, wherein

the target locus is an internucleotide bond;

the editing element comprises m nucleotides where m is an integer greater than or equal to one; and

the editing element represents an addition for the target locus of the mammalian chromosome.

31. The AAV of any one of claims 1 or 3-26, wherein the editing element is an internucleotide bond.

32. The AAV of claim 31, wherein the target locus is a nucleotide sequence comprising one or more nucleotides, and the editing element comprises a deletion for the target locus of the mammalian chromosome.

33. The AAV of any one of the preceding claims, wherein the target locus of the mammalian chromosome is a mutant target locus comprising one or more mutant nucleotides, relative to a corresponding wild type mammalian chromosome.

34. The AAV of claim 33, wherein the mutant target locus comprises a point mutation, a missense mutation, a nonsense mutation, an insertion of one or more nucleotides, a deletion of one or more nucleotides, or combinations thereof.

35. The AAV of claim 33 or 34, wherein the mutant target locus comprises an amorphic mutation, a neomorphic mutation, or an antimorphic mutation.

36. The AAV of any one of claims 33 to 35, wherein the mutant target locus comprises an autosomal dominant mutation, an autosomal recessive mutation, a heterozygous mutation, a homozygous mutation, or combinations thereof.

37. The AAV of claims 33 or 34, wherein the mutant target locus is selected from a promoter, an enhancer, a signal sequence, an intron, an exon, a splice donor site, a splice acceptor site, an internal ribosome entry site, an inverted exon, an insulator, a gene, a chromosomal inversion, and a chromosomal translocation within the mammalian chromosome.

38. The AAV of any one of the preceding claims, wherein the AAV Clade F capsid comprises at least one protein selected from Clade F VP1, Clade F VP2 and Clade F VP3.

39. The AAV of any one of the preceding claims, wherein the AAV Clade F capsid comprises at least two proteins selected from Clade F VP1, Clade F VP2 and Clade F VP3.

40. The AAV of any of the preceding claims, wherein the AAV Clade F capsid comprises Clade F VP1, Clade F VP2 and Clade F VP3 proteins.

41. The AAV of any one of the preceding claims, wherein the AAV Clade F capsid comprises a VP1, VP2, or VP3 protein that has at least 90% amino acid sequence identity to amino acids 1 to 736, amino acids 138 to 736 or amino acids 203 to 736 of SEQ ID NO:1, respectively, which correspond to the amino acid sequences of AAV9 capsid proteins VP1, VP2 and VP3, respectively.

42. The AAV of any one of the preceding claims, wherein the AAV Clade F capsid comprises:

VP1 and VP2 proteins that have at least 90% amino acid sequence identity to amino acids 1 to 736 and amino acids 138 to 736 of SEQ ID NO:1, respectively, which correspond to the amino acid sequences of AAV9 capsid proteins VP1 and VP2, respectively;

VP1 and VP3 proteins that have at least 90% amino acid sequence identity to amino acids 1 to 736 and amino acids 203 to 736 of SEQ ID NO:1, respectively, which correspond to the amino acid sequences of AAV9 capsid proteins VP1 and VP3, respectively; or

VP2 and VP3 proteins that have at least 90% amino acid sequence identity to amino acids 138 to 736 and amino acids 203 to 736 of SEQ ID NO:1, respectively, which correspond to the amino acid sequences of AAV9 capsid proteins VP2 and VP3, respectively.

43. The AAV of any one of the preceding claims, wherein the AAV Clade F capsid comprises VP1, VP2, and VP3 proteins that have at least 90% amino acid sequence identity to amino acids 1 to 736, amino acids 138 to 736 and amino acids 203 to 736 of SEQ ID NO:1, respectively, which correspond to the amino acid sequences of AAV9 capsid proteins VP1, VP2 and VP3, respectively.

44. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises a VP1, VP2, or VP3 protein that has at least 90% amino acid sequence identity to amino acids 1 to 736, amino acids 138 to 736 or amino acids 203 to 736 of any one of SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively, which correspond to the amino acid sequences of AAVF1 through AAVF9 and AAVF11 through AAVF17 capsid proteins VP1, VP2 and VP3, respectively.

45. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises:

VP1 and VP2 proteins that have at least 90% amino acid sequence identity to amino acids 1 to 736 and amino acids 138 to 736 of any one of SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively, which correspond to the amino acid sequences of AAVF1 through AAVF9 and AAVF11 through AAVF17 capsid proteins VP1 and VP2, respectively;

VP1 and VP3 proteins that have at least 90% amino acid sequence identity to amino acids 1 to 736 and amino acids 203 to 736 of any one of SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively, which correspond to the amino acid sequences of AAVF1 through AAVF9 and AAVF11 through AAVF17 capsid proteins VP1 and VP3, respectively; or

VP2 and VP3 proteins that have at least 90% amino acid sequence identity to amino acids 138 to 736 and amino acids 203 to 736 of any one of SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively, which correspond to the amino acid sequences of AAVF1 through AAVF9 and AAVF11 through AAVF17 capsid proteins VP2 and VP3, respectively.

46. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises VP1, VP2, and VP3 proteins that have at least 90% amino acid sequence identity to amino acids 1 to 736, amino acids 138 to 736 and amino acids 203 to 736 of any one of SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively, which correspond to

the amino acid sequences of AAVF1 through AAVF9 and AAVF11 through AAVF17 capsid proteins VP1, VP2 and VP3, respectively.

47. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises a VP1, VP2, or VP3 protein that is encoded by a nucleotide sequence comprising at least 90% nucleotide sequence identity to SEQ ID NO:18, respectively, which corresponds to a nucleotide sequence encoding AAV9 capsid proteins VP1, VP2 and VP3, respectively.

48. The AAV of any one of claims 1-37, wherein the AAV Clade F capsid comprises:

VP1 and VP2 proteins that are encoded by nucleotide sequences comprising at least 90% nucleotide sequence identity to SEQ ID NOs:18;

VP1 and VP3 proteins that are encoded by a nucleotide sequence comprising at least 90% nucleotide sequence identity to SEQ ID NOs:18; or

VP2 and VP3 proteins that are encoded by a nucleotide sequence comprising at least 90% nucleotide sequence identity to SEQ ID NOs:18.

49. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises VP1, VP2, and VP3 proteins that are encoded by a nucleotide sequence comprising at least 90% nucleotide sequence identity to SEQ ID NO:18, which corresponds to a nucleotide sequence encoding AAV9 capsid proteins VP1, VP2 and VP3.

50. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises a VP1, VP2, or VP3 protein that is encoded by a nucleotide sequence comprising at least 90% nucleotide sequence identity to any one of SEQ ID NOs: 20, 21, 22, 23, 25, 24, 27, 28, 29, 26, 30, 31, 32, 33, 34 or 35, respectively, which correspond to nucleotide sequences encoding AAVF1 through AAVF9 and AAVF11 through AAVF17 capsid proteins VP1, VP2 and VP3, respectively.

51. The AAV of any one of claims 1-37, wherein the AAV Clade F capsid comprises:

VP1 and VP2 proteins that are encoded by nucleotide sequences comprising at least 90% nucleotide sequence identity to any one of SEQ ID NOs:20-35;

VP1 and VP3 proteins that are encoded by a nucleotide sequence comprising at least 90% nucleotide sequence identity to any one of SEQ ID NOs:20-35; or

VP2 and VP3 proteins that are encoded by a nucleotide sequence comprising at least 90% nucleotide sequence identity to any one of SEQ ID NOs:20-35.

52. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises VP1, VP2, and VP3 proteins that are encoded by a nucleotide sequence comprising at least 90% nucleotide sequence identity to any one of SEQ ID NOs: 20, 21, 22, 23, 25, 24, 27, 28, 29, 26, 30, 31, 32, 33, 34 or 35, which correspond to nucleotide sequences encoding AAVF1 through AAVF9 and AAVF11 through AAVF17 capsid proteins VP1, VP2 and VP3, respectively.

53. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises AAV9 VP1, VP2, or VP3 capsid proteins, which correspond to amino acids 1 to 736, amino acids 138 to 736 and amino acids 203 to 736 as set forth in SEQ ID NO:1, respectively.

54. The AAV of any one of claims 1-40, wherein the AAV Clade F capsid comprises:

AAV9 VP1 and VP2 capsid proteins, which correspond to amino acids 1 to 736 and amino acids 138 to 736 as set forth in SEQ ID NO:1, respectively;

AAV9 VP1 and VP3 capsid proteins, which correspond to amino acids 1 to 736 and amino acids 203 to 736 as set forth in SEQ ID NO:1, respectively; or

AAV9 VP2 and VP3 capsid proteins, which correspond to amino acids 138 to 736 and amino acids 203 to 736 as set forth in SEQ ID NO:1, respectively.

55. The AAV of any one of the preceding claims, wherein the AAV Clade F capsid comprises AAV9 capsid proteins VP1, VP2 and VP3, which correspond to amino acids 1 to 736, amino acids 138 to 736 and amino acids 203 to 736 as set forth in SEQ ID NO:1, respectively.

56. The AAV of any one of claims 1-52, wherein the AAV Clade F capsid comprises a VP1 capsid protein selected from a VP1 capsid protein of any one of AAVF1 through AAVF9 and AAVF11 through AAVF17, which corresponds to amino acids 1 to 736 as set forth in SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively.

57. The AAV of any one of claims 1-52, wherein the AAV Clade F capsid comprises a VP1 and a VP2 capsid protein independently selected from a VP1 and VP2 capsid protein of

any one of AAVF1 through AAVF9 and AAVF11 through AAVF17, which correspond to amino acids 1 to 736 and amino acids 138 to 736 as set forth in SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively.

58. The AAV of any one of claims 1-52, wherein the AAV Clade F capsid comprises a VP1, a VP2 and a VP3 capsid protein independently selected from a VP1, VP2 and VP3 capsid protein of any one of AAVF1 through AAVF9 and AAVF11 through AAVF17, which correspond to amino acids 1 to 736, amino acids 138 to 736 and amino acids 203 to 736 as set forth in SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively.

59. The AAV of any one of claims 1-52, wherein the AAV Clade F capsid comprises each of the VP1, VP2 and VP3 capsid proteins of any one of AAVF1 through AAVF9 and AAVF11 through AAVF17, which correspond to amino acids 1 to 736, amino acids 138 to 736 and amino acids 203 to 736 as set forth in SEQ ID NOs: 2, 3, 5, 6, 11, 7, 8, 9, 10, 4, 12, 14, 15, 16, 17 or 13, respectively.

60. The AAV of any one of claims 1-4, wherein the mammalian chromosome is selected from human chromosome 1, 2, 3, 4, 5, 6, 7, 8, 9, 10,11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, X and Y.

61. The AAV of any one of claims 1-4, wherein the mammalian chromosome is selected from mouse chromosome 1, 2, 3, 4, 5, 6, 7, 8, 9, 10,11, 12, 13, 14, 15, 16, 17, 18, 19, X and Y.

62. The AAV of any one of claims 1-4, wherein the mammalian chromosome is not human chromosome 19.

63. The AAV of any one of claims 60 to 62, wherein the mammalian chromosome is a somatic cell chromosome.

64. The AAV of claim 63, wherein the somatic cell is from a tissue selected from the group consisting of connective tissue (including blood), muscle tissue, nervous tissue, endothelial tissue and epithelial tissue.

65. The AAV of claim 63, wherein the somatic cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage.

66. The AAV of any one of claims 63 to 65, wherein the somatic cell is a CD34+ cell.

67. The AAV any one of claims 60 to 62, wherein the cell is a stem cell.

68. The AAV of claim 67, wherein the stem cell is a hematopoietic stem cell, a cord blood stem cell, a bone marrow stem cell, a fetal liver stem cell, or a peripheral blood stem cell.

69. The AAV of any one of claims 60 to 62, wherein the cell is selected from the group consisting of a CD34+ Hematopoietic stem cell line (HSC), a K562 CD34+ leukemia cell line, a HepG2 human liver cell line, a peripheral blood stem cell, a cord blood stem cell, a CD34+ peripheral blood stem cell, a WI-38 human diploid fibroblast cell line, a MCF7 human breast cancer cell line, a Y79 human retinoblastoma cell line, a SCID-X1 LBL human EBV-immortalized B cell line, a primary human hepatocyte, a primary hepatic sinusoidal endothelial cell, and a primary skeletal muscle myoblast.

70. The AAV of any one of the preceding claims, wherein the AAV has a chromosomal integration efficiency of at least about 5% for integrating the editing element into the target locus of the mammalian chromosome in the cell.

71. The AAV of any one of the preceding claims, wherein the AAV has a chromosomal integration efficiency of at least about 10% for integrating the editing element into the target locus of the mammalian chromosome in the cell.

72. A composition comprising an adeno-associated virus (AAV) of any one of the preceding claims, wherein the composition is in a pharmaceutically acceptable formulation.

73. The composition of claim 72, wherein the formulation is constituted for administration to a mammal.

74. The composition of claim 73, wherein the formulation is constituted for administration to a mammal via intravenous injection, subcutaneous injection, intramuscular injection, autologous cell transfer, or allogeneic cell transfer.

75. The composition of claim 72, wherein the pharmaceutically acceptable formulation comprises an excipient.

76. The composition of claim 75, wherein the excipient is selected from a carrier, an adjuvant and a vehicle, or combinations thereof.

77. A packaging system for recombinant preparation of an adeno-associated virus (AAV), wherein the packaging system comprises

a Rep nucleotide sequence encoding one or more AAV Rep proteins;

a Cap nucleotide sequence encoding one or more AAV Cap proteins of an AAV Clade F capsid; and

a correction genome as defined in any one of claims 1 to 71;

wherein the packaging system is operative in a cell for enclosing the correction genome in the capsid to form the adeno-associated virus.

78. The packaging system of claim 77, wherein the packaging system comprises a first vector comprising the Rep nucleotide sequence and the Cap nucleotide sequence, and a second vector comprising the correction genome.

79. The packaging system of claim 77 or 78, wherein the AAV Clade F capsid comprises at least one protein selected from Clade F VP1, Clade F VP2 and Clade F VP3.

80. The packaging system of claim 77 or 78, wherein the AAV Clade F capsid comprises at least two proteins selected from Clade F VP1, Clade F VP2 and Clade F VP3.

81. The packaging system of claim 77 or 78, wherein the AAV Clade F capsid comprises Clade F VP1, Clade F VP2 and Clade F VP3 proteins.

82. The packaging system of claim 77 or 78, wherein the AAV Clade F capsid is the AAV Clade F capsid as defined in any one of claims 38-59.

83. The packaging system of any one of claims 77-82, wherein the Rep nucleotide sequence encodes an AAV2 Rep protein.

84. The packaging system of claim 83, wherein the AAV2 Rep protein encoded is at least one of Rep 78/68 or Rep 68/52.

85. The packaging system of claim 83 or 84, wherein the nucleotide sequence encoding the AAV2 Rep protein comprises a nucleotide sequence having a minimum percent sequence identity to the AAV2 Rep nucleotide sequence of SEQ ID NO:40, wherein the minimum percent sequence identity is at least 70% across the length of the nucleotide sequence encoding the AAV2 Rep protein.

86. The packaging system of any one of claims 77-85, further comprising a third vector, wherein the third vector is a helper virus vector.

87. The packaging system of claim 86, wherein the helper virus vector is an independent third vector.

88. The packaging system of claim 86, wherein the helper virus vector is integral with the first vector.

89. The packaging system of claim 86, wherein the helper virus vector is integral with the second vector.

90. The packaging system of any one of claims 86-89, wherein the third vector comprises genes encoding helper virus proteins.

91. The packaging system of any one of claims 89-90, wherein the helper virus is selected from the group consisting of adenovirus, herpes virus (including herpes simplex virus (HSV)), vaccinia virus, and cytomegalovirus (CMV).

92. The packaging system of claim 91, wherein the helper virus is adenovirus.

93. The packaging system of claim 92, wherein the adenovirus genome comprises one or more adenovirus RNA genes selected from the group consisting of E1, E2, E4 and VA.

94. The packaging system of claim 91, wherein the helper virus is HSV.

95. The packaging system of claim 94, wherein the HSV genome comprises one or more of HSV genes selected from the group consisting of UL5/8/52, ICPO, ICP4, ICP22 and UL30/UL42.

96. The packaging system of any one of claims 86-95, wherein the first vector and the third vector are contained within a first transfecting plasmid.

97. The packaging system of any one of claims 86-95, wherein the nucleotides of the second vector and the third vector are contained within a second transfecting plasmid.

98. The packaging system of any one of claims 86-95, wherein the nucleotides of the first vector and the third vector are cloned into a recombinant helper virus.

99. The packaging system of any one of claims 86-95, wherein the nucleotides of the second vector and the third vector are cloned into a recombinant helper virus.

100. The packaging system of any one of claims 77-99, wherein the AAV capsid is the capsid of a Clade F AAV selected from the group consisting of AAV9, AAVF1, AAVF2, AAVF3, AAVF4, AAVF5, AAVF6, AAVF7, AAVF8, AAVF9, AAVF11, AAVF12, AAVF13, AAVF14, AAVF15, AAVF16, AAVF17, AAVHU31, and AAVHU32.

101. A gene editing vector comprising a replication-defective adeno-associated virus (AAV) comprising a correction genome enclosed in an AAV capsid, the correction genome comprising

an editing element selected from an internucleotide bond or a nucleotide sequence for integration into a target locus of a mammalian cell chromosome;

a 5' homologous arm nucleotide sequence 5' of the editing element having homology to a 5' region of the chromosome relative to the target locus;

a 3' homologous arm nucleotide sequence 3' of the editing element having homology to a 3' region of the chromosome relative to the target locus; and

wherein the AAV has a chromosomal integration efficiency of at least 10% for integrating the editing element into the target locus of the mammalian cell chromosome in the absence of an exogenous nuclease.

102. The gene editing vector of claim 101, wherein the correction genome is as defined in any one of claims 5 to 71.

103. A method for recombinant preparation of an adeno-associated virus (AAV), wherein the method comprises transfecting a cell with a packaging system of any one of claims 77-97 under conditions operative for enclosing the correction genome in the capsid to form the AAV.

104. A method for recombinant preparation of an adeno-associated virus (AAV), wherein the method comprises transducing a cell with a packaging system of any one of claims 77-96, 98 or 99 under conditions operative for enclosing the correction genome in the capsid to form the AAV.

105. A method for editing a target locus of a mammalian genome, wherein the method comprises transducing a cell comprising the mammalian genome with an adeno-associated virus (AAV) of any one of claims 1-71.

106. The method of claim 105, wherein the cell is a mammalian cell.

107. The method of claim 106, wherein the mammalian cell is from a tissue selected from the group consisting of connective tissue (including blood), muscle tissue, nervous tissue, endothelial tissue, and epithelial tissue.

108. The method of claim 106 or 107, wherein the mammalian cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage.

109. The method of claim 106 or 107, wherein the mammalian cell is a stem cell.

110. The method of claim 109, wherein the stem cell is a hematopoietic stem cell, a cord blood stem cell or peripheral blood stem cell.

111. The method of claim 106, wherein the mammalian cell is a myoblast, an endothelial cell, a liver cell, a fibroblast, a breast cell, a lymphocyte, or a retinal cell.

112. A method for editing a target locus of a mammalian genome, wherein the method comprises:

(a) obtaining mammalian cells from a mammal;

(b) culturing the mammalian cells ex-vivo to form an ex-vivo culture;

(c) transducing the mammalian cells with an adeno-associated virus (AAV) of any one of claims 1-71 in the ex-vivo culture to form transduced mammalian cells; and

(d) administering the transduced mammalian cells to the mammal.

113. A method for editing a target locus of a mammalian genome, wherein the method comprises:

(a) obtaining mammalian cells from a first mammal;

(b) culturing the mammalian cells ex-vivo to form an ex-vivo culture;

(c) transducing the mammalian cells with an adeno-associated virus (AAV) of any one of claims 1-71 in the ex-vivo culture to form transduced mammalian cells; and

(d) administering the transduced mammalian cells to a second mammal.

114. The method of claim 113, wherein the first mammal and the second mammal are the same species.

115. The method of claim 113 or 114, wherein the mammalian cells are from a tissue selected from the group consisting of connective tissue (including blood), muscle tissue, nervous tissue, endothelial tissue, and epithelial tissue.

116. The method of claim 113 or 114, wherein the mammalian cells are from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage.

117. The method of claim 113 or 114, wherein the mammalian cells are stem cells.

118. The method of claim 117, wherein the stem cells are hematopoietic stem cells, cord blood stem cells, or peripheral blood stem cells.

119. The method of any one of claims 113 to 118, wherein the mammalian cells are a CD34+ cells.

120. The method of any one of claims 113 to 119, wherein the mammalian cells are myoblasts, endothelial cells, liver cells, fibroblasts, breast cells, lymphocytes, or retinal cells.

121. A method for editing a target locus of a mammalian genome, wherein the method comprises:

administering an adeno-associated virus (AAV) of any one of claims 1-71 or a composition of any one of claims 72-76 to a mammal in an amount effective to transduce cells of the mammal with the adeno-associated virus (AAV) in-vivo.

122. The method of any one of claims 105-121 wherein the AAV is transduced or administered without co-transducing or co-administering an exogenous nuclease or a nucleotide sequence that encodes an exogenous nuclease.

123. The method of any one of claims 105-122, wherein the AAV has a chromosomal integration efficiency of at least about 1% for integrating the editing element into the target locus of the mammalian chromosome.

124. The method of any one of claims 105-122, wherein the chromosomal integration efficiency of the AAV is at least about 2%, 3%, 4% or 5% for integrating the editing element into the target locus of the mammalian chromosome.

125. The method of any one of claims 105-122, wherein the editing element of the correction genome is integrated into the target locus of the mammalian chromosome with a chromosomal integration efficiency of at least 10%, 20%, 40%, or 50% of the mammalian cells.

126. The method of any one of claims 105-122, wherein the editing element of the correction genome is integrated into the target locus of the mammalian chromosome with a chromosomal integration efficiency ranging from 10% to 70%, 20% to 70%, 40% to 70%, or 50% to 70% of the mammalian cells.

127. The method of any one of claims 105-122, wherein the AAV has a chromosomal integration efficiency further characterized by an allele frequency in a population of cells of at least about 10% for the allele comprising the editing element integrated into the target locus of the mammalian chromosome.

128. The method of any one of claims 105-122, wherein the AAV has a chromosomal integration efficiency further characterized by an allele frequency in a population of cells of at least about 50% for the allele comprising the editing element integrated into the target locus of the mammalian chromosome.

129. The method of any one of claims 105-122, wherein the AAV has a chromosomal integration efficiency further characterized by an allele frequency in a population of cells of at least about 75% for the allele comprising the editing element integrated into the target locus of the mammalian chromosome.

130. The method of any one of claims 127 to 129, wherein the allele frequency in a population of cells is an allele frequency in a population of cells in vitro.

131. A method for generating a transgenic non-human animal, the method comprising:

administering an adeno-associated virus (AAV) of any one of claims 1-71 or a composition of any one of claims 72-76 to a non-human animal; or

transducing a non-human animal cell with the AAV of any one of claims 1-71 or the composition of any one of claims 72-76 and implanting the cell into a host non-human animal under conditions sufficient to generate a transgenic non-human animal from the host non-human animal.

132. The method of claim 131, wherein the non-human animal cell is derived from a zygote or an embryo of a non-human animal.

133. The method of claim 131 or 132, wherein the non-human animal is a mouse, rat, rabbit, pig, bovine, sheep, goat, chicken, cat, dog, ferret, or primate.

134. A transgenic non-human animal obtainable by the method of any one of claims 131 to 133.

135. A tissue derived from the transgenic non-human animal of claim 134.

136. The tissue of claim 135, wherein the tissue is selected from the group consisting of connective tissue (including blood), muscle tissue, nervous tissue, endothelial tissue and epithelial tissue.

137. The tissue of claim 135, wherein the tissue is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage.

138. A cell derived from the transgenic non-human animal of claim 134.

139. The cell of claim 138, wherein the cell is a primary cell.

140. The cell of claim 138, wherein the cell is a CD34+ cell, a hepatocyte, a myoblast, an endothelial cell, a liver cell, a fibroblast, a breast cell, a lymphocyte, or a retinal cell.

141. The cell of claim 138, wherein the cell is an inducible pluripotent stem (iPS) cell.

142. The cell of claim 138, wherein the cell is from a tissue selected from the group consisting of connective tissue (including blood), muscle tissue, nervous tissue, endothelial tissue, and epithelial tissue.

143. The cell of claim 138, wherein the cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage.

144. The cell of claim 138, wherein the cell is a stem cell.

145. The cell of claim 144, wherein the stem cell is a hematopoietic stem cell, a cord blood stem cell, or peripheral blood stem cell.

146. A cell obtainable by a method of any one of claims 105-111.

CLAIMS

1. A replication-defective adeno-associated virus (AAV) comprising a correction genome enclosed in a capsid, wherein the capsid comprises an AAV Clade F capsid; and wherein the correction genome comprises:

(a) an editing element comprising an internucleotide bond or a nucleotide sequence for integration into a target locus of a mammalian chromosome;

(b) a 5' homologous arm nucleotide sequence 5' of the editing element, having homology to a 5' region of the mammalian chromosome relative to the target locus; and

(c) a 3' homologous arm nucleotide sequence 3' of the editing element, having homology to a 3' region of the mammalian chromosome relative to the target locus,

wherein the AAV Clade F capsid comprises an AAV capsid protein comprising:

(d) an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 203-736 of SEQ ID NO: 2, 3, 4, 6, 7, 10, 11, 12, 13, 15, 16, or 17, wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H;

the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A;

the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N;

the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S; the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y;

the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K;

the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; or

the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; and/or

(ii) the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or

the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; and/or

(e) an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 138-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, or 17, wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 151 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 160 of SEQ ID NO: 2 is D;

the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H;

the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A;

the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N;

the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S;

the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y;

the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K;

the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; or

the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; and/or

(ii) the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or

the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; and/or

(f) an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 1-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, or 17, wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 2 of SEQ ID NO: 2 is T;

the amino acid in the capsid protein corresponding to amino acid 65 of SEQ ID NO: 2 is I;

the amino acid in the capsid protein corresponding to amino acid 68 of SEQ ID NO: 2 is V;

the amino acid in the capsid protein corresponding to amino acid 77 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 119 of SEQ ID NO: 2 is L;

the amino acid in the capsid protein corresponding to amino acid 151 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 160 of SEQ ID NO: 2 is D;

the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C;

the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H;

the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q;

the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A;

the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N;

the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S;

the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I;

the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y;

the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;

the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;

the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K;

the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; or

the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; and/or

(ii) the amino acid in the capsid protein corresponding to amino acid 2 of SEQ ID NO: 2 is T, and the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q;
the amino acid in the capsid protein corresponding to amino acid 65 of SEQ ID NO: 2 is I, and the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is Y;
the amino acid in the capsid protein corresponding to amino acid 77 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K;
the amino acid in the capsid protein corresponding to amino acid 119 of SEQ ID NO: 2 is L, and the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S;
the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;
the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M;
the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R;
the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or
the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C.

2. The AAV of claim 1, wherein the correction genome comprises a 5’ inverted terminal repeat (5’ ITR) nucleotide sequence 5’ of the 5’ homologous arm nucleotide sequence, and a 3’ inverted

terminal repeat (3' ITR) nucleotide sequence 3' of the 3' homologous arm nucleotide sequence, wherein:

(a) the 5' ITR nucleotide sequence and the 3' ITR nucleotide sequence are substantially identical to an AAV2 virus 5'ITR and an AAV2 virus 3' ITR, respectively;

(b) the 5' ITR nucleotide sequence and the 3' ITR nucleotide sequence are substantially mirror images of each other;

(c) the 5' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:36, and the 3' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:37; and/or

(d) the 5' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:38, and the 3' ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO:39.

3. The AAV of claim 1 or claim 2, wherein the correction genome has an essential absence of a promoter operatively linked to the editing element nucleotide sequence, or the correction genome further comprises an exogenous promoter operatively linked to the editing element.

4. The AAV of any one of claims 1 to 3, wherein the replication-defective AAV genome comprises an essential absence of an AAV *rep* gene and an AAV *cap* gene.

5. The AAV of any one of claims 1 to 4, wherein:

(a) each of the 5' and 3' homologous arm nucleotide sequences independently has a nucleotide length of between about 500 to 1000 nucleotides or between about 600 to 1000 nucleotides;

(b) the 5' and 3' homologous arm nucleotide sequences have substantially equal nucleotide lengths;

(c) the 5' and 3' homologous arm nucleotide sequences have asymmetrical nucleotide lengths;

(d) the 5' homologous arm nucleotide sequence has at least about 95% nucleotide sequence identity to the 5' region of the mammalian chromosome relative to the target locus;

(e) the 3' homologous arm nucleotide sequence has at least about 95% nucleotide sequence identity to the 3' region of the mammalian chromosome relative to the target locus; and/or

(f) the 5’ homologous arm nucleotide sequence has 100% sequence identity to the 5’ region of the mammalian chromosome relative to the target locus and the 3’ homologous arm nucleotide sequence has 100% sequence identity to the 3’ region of the mammalian chromosome relative to the target locus.

6. The AAV of any one of claims 1 to 5, wherein:

(a) the editing element consists of one nucleotide, wherein the target locus is selected from a nucleotide sequence consisting of one nucleotide, and the target locus represents a point mutation of the mammalian chromosome;

(b) the editing element comprises at least 1, 2, 10, 100, 200, 500, 1000, 1500, 2000, 3000, 4000, or 5000 nucleotides;

(c) the editing element comprises 1 to 5500, 1 to 5000, 1 to 4500, 1 to 4000, 1 to 3000, 1 to 2000, 1 to 1000, 1 to 500, 1 to 200, or 1 to 100 nucleotides, or 2 to 5500, 2 to 5000, 2 to 4500, 2 to 4000, 2 to 3000, 2 to 2000, 2 to 1000, 2 to 500, 2 to 200, or 2 to 100 nucleotides, or 10 to 5500, 10 to 5000, 10 to 4500, 10 to 4000, 10 to 3000, 10 to 2000, 10 to 1000, 10 to 500, 10 to 200, or 10 to 100 nucleotides;

(d) the editing element comprises an exon, an intron, a 5’ untranslated region (UTR), a 3’ UTR, a promoter, a splice donor, a splice acceptor, a sequence encoding or non-coding RNA, an insulator, a gene, or a combination thereof, wherein the editing element is a fragment of a coding sequence of a gene selected from a fragment within the target locus and a fragment spanning the target locus;

(e) the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to one, the editing element comprises m nucleotides where m is an integer equal to n, and the editing element represents a substitution for the target locus of the mammalian chromosome;

(f) the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to one, the editing element comprises m nucleotides where m is an integer greater than n, and the editing element represents a substitutive addition for the target locus of the mammalian chromosome;

(g) the target locus is a nucleotide sequence comprising n nucleotides where n is an integer greater than or equal to two, the editing element comprises m nucleotides where m is an integer less than n, and the editing element represents a substitutive deletion for the target locus of the mammalian chromosome;

(h) the target locus is an internucleotide bond, the editing element comprises m nucleotides where m is an integer greater than or equal to one, and the editing element represents an addition for the target locus of the mammalian chromosome;

(i) the editing element is an internucleotide bond, wherein the target locus comprises a nucleotide sequence comprising one or more nucleotides, and the editing element comprises a deletion for the target locus of the mammalian chromosome; and/or

(j) the target locus of the mammalian chromosome is a mutant target locus comprising one or more mutant nucleotides, relative to a corresponding wild type mammalian chromosome, wherein:

(i) the mutant target locus comprises a point mutation, a missense mutation, a nonsense mutation, an insertion of one or more nucleotides, a deletion of one or more nucleotides, or combinations thereof;

(ii) the mutant target locus comprises an amorphic mutation, a neomorphic mutation, or an antimorphic mutation;

(iii) the mutant target locus comprises an autosomal dominant mutation, an autosomal recessive mutation, a heterozygous mutation, a homozygous mutation, or combinations thereof; and/or

(iv) the mutant target locus is selected from a promoter, an enhancer, a signal sequence, an intron, an exon, a splice donor site, a splice acceptor site, an internal ribosome entry site, an inverted exon, an insulator, a gene, a chromosomal inversion, and a chromosomal translocation within the mammalian chromosome.

7. The AAV of any one of claims 1 to 6, wherein:

(a) the AAV capsid protein comprises the amino acid sequence of amino acids 203-736 of SEQ ID NO: 2, 3, 4, 6, 7, 10, 11, 12, 13, 15, 16, or 17;

(b) the AAV capsid protein comprises the amino acid sequence of amino acids 138-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, or 17;

(i) (c) the AAV capsid protein comprises an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 1-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, or 17.

8. The AAV of any one of claims 1 to 7, wherein:

(a) the mammalian chromosome is selected from human chromosome 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, X and Y;

(b) the mammalian chromosome is selected from mouse chromosome 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, X and Y;

(c) the mammalian chromosome is not human chromosome 19;

(d) the mammalian chromosome is a somatic cell chromosome, wherein:

(i) the somatic cell is from a tissue selected from the group consisting of connective tissue (including blood), muscle tissue, nervous tissue, endothelial tissue and epithelial tissue;

(ii) the somatic cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage; and/or

(iii) the somatic cell is a CD34+ cell;

(e) the mammalian chromosome is a stem cell chromosome, wherein the stem cell is selected from a hematopoietic stem cell, a cord blood stem cell, a bone marrow stem cell, a fetal liver stem cell, and a peripheral blood stem cell; and/or

(f) the mammalian chromosome is a chromosome of a cell selected from the group consisting of a CD34+ Hematopoietic stem cell line (HSC), a K562 CD34+ leukemia cell line, a HepG2 human liver cell line, a peripheral blood stem cell, a cord blood stem cell, a CD34+ peripheral blood stem cell, a WI-38 human diploid fibroblast cell line, a MCF7 human breast cancer cell line, a Y79 human retinoblastoma cell line, a SCID-X1 LBL human EBV-immortalized B cell line, a primary human hepatocyte, a primary hepatic sinusoidal endothelial cell, and a primary skeletal muscle myoblast.

9. The AAV of any one of claims 1 to 8, wherein the AAV has a chromosomal integration efficiency of at least about 5% or at least about 10% for integrating the editing element into the target locus of the mammalian chromosome in the cell.

10. A composition comprising an adeno-associated virus (AAV) of any one of claims 1 to 9, wherein the composition is in a pharmaceutically acceptable formulation, wherein:

(a) the formulation is constituted for administration to a mammal;

(b) the formulation is constituted for administration to a mammal via intravenous injection, subcutaneous injection, intramuscular injection, autologous cell transfer, or allogeneic cell transfer; and/or

(c) the formulation comprises an excipient, wherein the excipient is selected from a carrier, an adjuvant, a vehicle, and combinations thereof.

11. A packaging system for recombinant preparation of an adeno-associated virus (AAV), wherein the packaging system comprises:

(a) a Rep nucleotide sequence encoding one or more AAV Rep proteins;

(b) a Cap nucleotide sequence encoding one or more AAV capsid proteins as set forth in any one of claims 1 to 9; and

(c) a correction genome as set forth in any one of claims 1 to 9;

wherein the packaging system is operative in a cell for enclosing the correction genome in the capsid to form the AAV.

12. The packaging system of claim 11, wherein:

(a) the packaging system comprises a first vector comprising the Rep nucleotide sequence and the Cap nucleotide sequence, and a second vector comprising the correction genome; and/or

(b) the Rep nucleotide sequence encodes an AAV2 Rep protein, wherein the AAV2 Rep protein comprises one or both of Rep 78/68 and Rep 68/52; and/or the AAV2 Rep protein comprises an amino acid sequence having a minimum percent sequence identity to the AAV2 Rep amino acid sequence of SEQ ID NO: 40, wherein the minimum percent sequence identity is at least 70% across the length of the amino acid sequence encoding the AAV2 Rep protein.

13. The packaging system of claim 11 or claim 12, further comprising a third vector, wherein the third vector is a helper virus vector, wherein:

(a) the helper virus vector is an independent third vector;

(b) the helper virus vector is integral with the first vector;

(c) the helper virus vector is integral with the second vector;

(d) the third vector comprises genes encoding helper virus proteins; and/or

(e) the helper virus is selected from the group consisting of adenovirus, herpes virus, vaccinia virus, and cytomegalovirus (CMV); wherein

(i) the adenovirus genome comprises one or more adenovirus RNA genes selected from the group consisting of E1, E2, E4 and VA; or

(f) the helper virus is herpes simplex virus (HSV), wherein the HSV genome comprises one or more HSV genes selected from the group consisting of UL5/8/52, ICPO, ICP4, ICP22 and UL30/UL42.

14. The packaging system of any one of claims 11 to 13, wherein:

(a) the first vector and the third vector are contained within a first transfecting plasmid;

(b) the nucleotides of the second vector and the third vector are contained within a second transfecting plasmid;

(c) the nucleotides of the first vector and the third vector are cloned into a recombinant helper virus; or

(d) the nucleotides of the second vector and the third vector are cloned into a recombinant helper virus.

15. A method for recombinant preparation of an adeno-associated virus (AAV), wherein the method comprises introducing the packaging system of any one of claims 11 to 14 into a cell under conditions operative for enclosing the correction genome in the capsid to form the AAV.

16. An *ex vivo* method for editing a target locus of a mammalian genome, wherein the method comprises transducing a mammalian cell comprising the mammalian genome with an adeno-associated virus (AAV) of any one of claims 1 to 9, wherein:

(a) the mammalian cell is from a tissue selected from the group consisting of connective tissue comprising blood, muscle tissue, nervous tissue, endothelial tissue, and epithelial tissue;

(b) the mammalian cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage;

(c) the mammalian cell is a stem cell, wherein the stem cell comprises one or more stem cells selected from the group consisting of a hematopoietic stem cell, a cord blood stem cell and a peripheral blood stem cell; or

(d) the mammalian cell is one or more of the group consisting of a myoblast, an endothelial cell, a liver cell, a fibroblast, a breast cell, a lymphocyte, and a retinal cell.

17. The method of claim 16, wherein:

(a) the AAV is transduced without co-transducing an exogenous nuclease or a nucleotide sequence that encodes an exogenous nuclease;

(b) the AAV has a chromosomal integration efficiency of at least about 1%, 2%, 3%, 4% or 5% for integrating the editing element into the target locus of the mammalian chromosome;

(c) the editing element of the correction genome is integrated into the target locus of the mammalian chromosome with a chromosomal integration efficiency of at least 10%, 20%, 40%, or 50% of the mammalian cells;

(d) the editing element of the correction genome is integrated into the target locus of the mammalian chromosome with a chromosomal integration efficiency ranging from 10% to 70%, 20% to 70%, 40% to 70%, or 50% to 70% of the mammalian cells;

(e) the AAV has a chromosomal integration efficiency further characterized by an allele frequency in a population of cells of at least about 10%, at least about 50%, or at least about 75% for the allele comprising the editing element integrated into the target locus of the mammalian chromosome; and/or

(f) the allele frequency in a population of cells is an allele frequency in a population of cells in vitro.

18. A method for generating a transgenic non-human animal, the method comprising:

transducing a non-human animal cell with the AAV of any one of claims 1 to 9 or the composition of claim 10 and implanting the cell into a host non-human animal under conditions sufficient to generate a transgenic non-human animal from the host non-human animal, wherein:

(i) the non-human animal cell is derived from a zygote or an embryo of a non-human animal; and/or

(ii) the non-human animal cell is derived from a zygote or an embryo of a non-human animal.

19. A transgenic non-human animal obtained by the method of claim 18.

20. A tissue derived from the transgenic non-human animal of claim 19.

21. The tissue of claim 20, wherein:

(a) the tissue is selected from the group consisting of connective tissue comprising blood, muscle tissue, nervous tissue, endothelial tissue and epithelial tissue; or

(b) the tissue is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage.

22. A cell derived from the transgenic non-human animal of claim 19.

23. The cell of claim 22, wherein:

(a) the cell is a primary cell;

(b) the cell is a CD34+ cell, a hepatocyte, a myoblast, an endothelial cell, a liver cell, a fibroblast, a breast cell, a lymphocyte, or a retinal cell;

(c) the cell is an inducible pluripotent stem (iPS) cell;

(d) the cell is from a tissue selected from the group consisting of connective tissue comprising blood, muscle tissue, nervous tissue, endothelial tissue, and epithelial tissue;

(e) the cell is from an organ selected from the group consisting of lung, heart, liver, kidney, muscle, brain, eye, breast, bone, and cartilage; and/or

(f) the cell is a stem cell, wherein the stem cell is selected from the group consisting of a hematopoietic stem cell, a cord blood stem cell, and a peripheral blood stem cell.

24. A cell obtained by the method of claim 16.

25. The AAV of any one of claims 1 to 9, or the composition of claim 10, for use as a medicament.