What is claimed is:

1. (A) A non-naturally occurring or engineered composition comprising a vector system comprising one or more vectors comprising

I. a first regulatory element operably linked to a CRISPR-Cas system chimeric RNA (chiRNA) polynucleotide sequence, wherein the polynucleotide sequence comprises

(a) a guide sequence capable of hybridizing to a target sequence in a eukaryotic cell,

(b) a tracr mate sequence, and

(c) a tracr sequence, and

II. a second regulatory element operably linked to an enzyme-coding sequence encoding a CRISPR enzyme comprising at least one or more nuclear localization sequences,

wherein (a), (b) and (c) are arranged in a 5' to 3' orientation,

wherein components I and II are located on the same or different vectors of the system,

wherein when transcribed, the tracr mate sequence hybridizes to the tracr sequence and the guide sequence directs sequence-specific binding of a CRISPR complex to the target sequence, and

wherein the CRISPR complex comprises the CRISPR enzyme complexed with (1) the guide sequence that is hybridized to the target sequence, and (2) the tracr mate sequence that is hybridized to the tracr sequence,

or

(B) a non-naturally occurring or engineered composition comprising a vector system comprising one or more vectors comprising

I. a first regulatory element operably linked to

(a) a guide sequence capable of hybridizing to a target sequence in a eukaryotic cell, and

(b) at least one or more tracr mate sequences,

II. a second regulatory element operably linked to an enzyme-coding sequence encoding a CRISPR enzyme, and

III. a third regulatory element operably linked to a tracr sequence,

wherein components I, II and III are located on the same or different vectors of the system,

wherein when transcribed, the tracr mate sequence hybridizes to the tracr sequence and the guide sequence directs sequence-specific binding of a CRISPR complex to the target sequence,

wherein the CRISPR complex comprises the CRISPR enzyme complexed with (1) the guide sequence that is hybridized to the target sequence, and (2) the tracr mate sequence that is hybridized to the tracr sequence, and

wherein, in (A) or (B), the CRISPR enzyme is a Cas9 ortholog of a genus belonging to the group consisting of *Corynebacter, Sutterella, Legionella, Treponema, Filifactor, Eubacterium, Streptococcus, Lactobacillus, Mycoplasma, Bacteroides, Flaviivola, Flavobacterium, Sphaerochaeta, Azospirillum, Gluconacetobacter, Neisseria, Roseburia, Parvibaculum, Staphylococcus, Nitratifractor, Mycoplasma* and *Campylobacter*.

2. A modified CRISPR enzyme wherein the enzyme is a Cas9 ortholog of a genus belonging to the group consisting of *Corynebacter, Sutterella, Legionella, Treponema, Filifactor, Eubacterium, Streptococcus, Lactobacillus, Mycoplasma, Bacteroides, Flaviivola, Flavobacterium, Sphaerochaeta, Azospirillum, Gluconacetobacter, Neisseria, Roseburia, Parvibaculum, Staphylococcus, Nitratifractor, Mycoplasma* and *Campylobacter* and wherein differences from the corresponding wild type CRISPR enzyme comprise:

the modified CRISPR enzyme is truncated in comparison to a wild type CRISPR enzyme, or

the CRISPR enzyme has a length of at least 500 amino acids, at least 800-899 amino acids, at least 900-999 amino acids, at least 1000-1099 amino acids, at least 1100-1199 amino acids, at least 1200-1299 amino acids, at least 1300-1399 amino acids, at least 1400-1499 amino acids, at least 1500-1599 amino acids, at least 1600-1699 amino acids or at least 2000 amino acids, and/or

the CRISPR enzyme is a nuclease directing cleavage of both strands at the location of the target sequence, or the CRISPR enzyme is a nickase directing cleavage of one strand at the location of the target sequence, and/or

the CRISPR enzyme is codon-optimized or codon-optimized for expression in a eukaryotic cell, and/or

the CRISPR enzyme comprises one or more mutations, and/or

the CRISPR enzyme comprises a chimeric CRISPR enzyme.

3. The composition according to claim 1, or the enzyme according to claim 2, wherein the CRISPR enzyme has one or more mutations in any domain of the enzyme.

4. The composition or enzyme according to any preceding claim, wherein the CRISPR enzyme has one or more mutations in a catalytic domain.

5. The composition or enzyme according to claim 3 or 4, wherein the one or more mutations is in a RuvC I, RuvC II, RuvC III or HNH domain of the CRISPR enzyme.

6. The composition or enzyme according to claim 4 or 5, wherein the CRISPR enzyme comprises one or more mutations corresponding to the position numbering of SpCas9 at positions D10A, E762A, H840A, N854A, N863A or D986A.

7. The composition or enzyme according to any preceding claim , wherein the enzyme further comprises a functional domain.

8. The composition or enzyme according to claim 7, wherein the functional domain is a transcriptional activator domain.

9. The composition or enzyme according to claim 8, wherein the transcriptional activator domain is VP64.

10. The composition or enzyme according to claim 7 to 9, wherein the functional domain is a transcriptional repressor domain.

11. The composition or enzyme according to claim 10, wherein the transcriptional repressor domain is KRAB, SID or SID4X.

12. A method of modifying an organism or a non-human organism by manipulation of a target sequence in a genomic locus of interest comprising

delivering a non-naturally occurring or engineered composition comprising a vector system operably encoding a composition of any preceding claim for expression thereof.

13. The method according to claim 12 wherein delivery is via one or more viral vectors.

14. A non-naturally occurring or engineered composition comprising a vector system comprising one or more vectors comprising

I. a first regulatory element operably linked to a first CRISPR-Cas system chimeric RNA (chiRNA) polynucleotide sequence, wherein the first polynucleotide sequence comprises

(i) a first guide sequence capable of hybridizing to a first target sequence at a first genomic locus in a cell of the organism,

(ii) a first tracr mate sequence, and

(iii) a first tracr sequence, and

II. a second regulatory element operably linked to a second CRISPR-Cas system chimeric RNA (chiRNA) polynucleotide sequence, wherein the second polynucleotide sequence comprises

(i) a second guide sequence capable of hybridizing to a second target sequence at a second genomic locus in the cell of the organism,

(ii) a second tracr mate sequence, and

(iii) a second tracr sequence, and

III. a third regulatory element operably linked to an enzyme-coding sequence encoding a first CRISPR enzyme comprising at least one or more nuclear localization sequences and operably linked to a first functional domain,

IV. a fourth regulatory element operably linked to an enzyme-coding sequence encoding a second CRISPR enzyme comprising at least one or more nuclear localization sequences and operably linked to a second functional domain,

wherein (i), (ii) and (iii) in I and II are arranged in a 5' to 3' orientation,

wherein components I, II, III and IV are located on the same or different vectors of the system,

wherein when transcribed, each tracr mate sequences hybridizes to its corresponding tracr sequence and the first and second guide sequences direct sequence-specific binding of the first and second CRISPR complex to the first and second target sequence,

wherein the CRISPR complex comprises the CRISPR enzyme complexed with (1) the guide sequence that is hybridized to the target sequence, and (2) the tracr mate sequence that is hybridized to the tracr sequence and wherein expression of the CRISPR enzyme provides manipulation of the target sequence,

wherein the first and second CRISPR enzyme each comprise two or more mutations, and

wherein the first and second CRISPR enzyme is a Cas9 ortholog of a genus belonging to the group consisting of *Corynebacter, Sutterella, Legionella, Treponema, Filifactor, Eubacterium, Streptococcus, Lactobacillus, Mycoplasma, Bacteroides, Flaviivola, Flavobacterium, Sphaerochaeta, Azospirillum, Gluconacetobacter, Neisseria, Roseburia, Parvibaculum, Staphylococcus, Nitratifractor, Mycoplasma* and *Campylobacter*.

15. A method of modulating the expression of two or more genomic loci of interest in an organism comprising

delivering a non-naturally occurring or engineered composition comprising a vector system comprising one or more vectors comprising

I. a first regulatory element operably linked to a first CRISPR-Cas system chimeric RNA (chiRNA) polynucleotide sequence, wherein the first polynucleotide sequence comprises

(i) a first guide sequence capable of hybridizing to a first target sequence at a first genomic locus in a cell of the organism,

(ii) a first tracr mate sequence, and

(iii) a first tracr sequence, and

II. a second regulatory element operably linked to a second CRISPR-Cas system chimeric RNA (chiRNA) polynucleotide sequence, wherein the second polynucleotide sequence comprises

(i) a second guide sequence capable of hybridizing to a second target sequence at a second genomic locus in the cell of the organism,

(ii) a second tracr mate sequence, and

(iii) a second tracr sequence, and

III. a third regulatory element operably linked to an enzyme-coding sequence encoding a first CRISPR enzyme comprising at least one or more nuclear localization sequences and operably linked to a first functional domain,

IV. a fourth regulatory element operably linked to an enzyme-coding sequence encoding a second CRISPR enzyme comprising at least one or more nuclear localization sequences and operably linked to a second functional domain,

wherein (i), (ii) and (iii) in I and II are arranged in a 5' to 3' orientation,

wherein components I, II, III and IV are located on the same or different vectors of the system,

wherein, when transcribed, each tracr mate sequences hybridizes to its corresponding tracr sequence and the first and second guide sequences direct sequence-specific binding of the first and second CRISPR complex to the first and second target sequence,

wherein the CRISPR complex comprises the CRISPR enzyme complexed with (1) the guide sequence that is hybridized to the target sequence, and (2) the tracr mate sequence that is

hybridized to the tracr sequence and wherein expression of the CRISPR enzyme provides manipulation of the target sequence,

wherein the first and second CRISPR enzyme each comprise two or more mutations,

wherein the first and second CRISPR enzyme is a Cas9 ortholog of a genus belonging to the group consisting of *Corynebacter, Sutterella, Legionella, Treponema, Filifactor, Eubacterium, Streptococcus, Lactobacillus, Mycoplasma, Bacteroides, Flaviivola, Flavobacterium, Sphaerochaeta, Azospirillum, Gluconacetobacter, Neisseria, Roseburia, Parvibaculum, Staphylococcus, Nitratifractor, Mycoplasma* and *Campylobacter*, and

wherein the first genomic locus is modulated by the activity of the first functional domain and the second genomic locus is modulated by the activity of the second functional domain.

16. The composition according to claim 14, or the method according to claim 15, wherein the first functional domain is selected from the group consisting of a transcriptional activator, transcriptional repressor, a recombinase, a transposase, a histone remodeler, a DNA methyltransferase, a cryptochrome and a light inducible/controllable domain or a chemically inducible/controllable domain.

17. The composition according to claim 14 or 16, or the method according to claim 15 or 16, wherein the second functional domain is selected from the group consisting of a transcriptional activator, transcriptional repressor, a recombinase, a transposase, a histone remodeler, a DNA methyltransferase, a cryptochrome and a light inducible/controllable domain or a chemically inducible/controllable domain.

18. The composition or method according to claim 16 or 17, , wherein the first or second functional domain is a transcriptional activator domain.

19. The composition or method according to claim 47, wherein the transcriptional activator domain is VP64.

20. The composition or method according to claim 16 or 17, wherein the first or second functional domain is a transcriptional repressor domain.

21. The composition or method according to claim 20, wherein the transcriptional repressor domain is KRAB, SID or SID4X.

22. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Sutterella wadsworthensis Cas9.

23. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Filifactor alocis Cas9.

24. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Lactobacillus johnsonii Cas9.

25. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Campylobacter lari Cas9.

26. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Corynebacter diptheriae Cas9.

27. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Parvibaculum lavamentivorans Cas9.

28. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Mycoplasma gallisepticum Cas9.

29. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Staphylococcus aureus subsubspecies Aureus Cas9.

30. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Legionella pneumophila Paris Cas9.

31. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Treponema denticola Cas9.

32. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Staphylococcus pseudintermedius Cas9.

33. The composition or method according to any of claims 14 to 21wherein the first or second CRISPR enzyme is a Neisseria cinerea Cas9.

34. A method of treating or inhibiting a condition caused by a defect in a target sequence in a genomic locus of interest in a subject or a non-human subject in need thereof comprising modifying the subject or a non-human subject by manipulation of the target sequence and wherein the condition is susceptible to treatment or inhibition by manipulation of the target sequence comprising providing treatment comprising:

delivering a non-naturally occurring or engineered composition comprising an AAV vector system comprising one or more AAV vectors comprising operably encoding a composition of any of claims 1 or 3 to 11 for expression thereof, wherein the target sequence is manipulated by the composition when expressed.

35. A method of claim 34 including inducing expression.

36. The method of claim 34 or 35 wherein the organism or subject is a eukaryote or a non-human eukaryote.

37. The method of any of claims 34 to 36 wherein the organism or subject is a plant.

38. The method of any of claims 34 to 36 wherein the organism or subject is a mammal or a non-human mammal.

39. The method any of claims 34 to 37 wherein the organism or subject is algae.

40. The method of any of claims 34 to 39 wherein the viral vector is an AAV.

41. A composition or enzyme according to any of claims 1-11, 14, or 16-33for use in medicine or for use in therapy.

42. A composition or enzyme according to any of claims 1-11, 14, or 16-33for use in a method according to any of claims 12, 13, or 15-40.

43. Use of a composition or enzyme according to any of claims 1-11, 14, or 16-33in *ex vivo* gene or genome editing.

44. Use of a composition or enzyme according to any of claims 1-11, 14, or 16-33in the manufacture of a medicament for *ex vivo* gene or genome editing or for use in a method according to any of claims 12, 13, or 15-40.

45. A composition or enzyme according to any of claims 1-11, 14, or 16-33, wherein the target sequence is flanked at its 3' end by 5'-NRG (where N is any Nucleotide), especially where the Cas9 is (or is derived from) *S. pyogenes* or *S. aureus* Cas9.

46. A method of preparing an AAV for delivery of the composition or enzyme according to any of claims 1-11, 14, or 16-33comprising transfecting plasmid(s) containing or consisting essentially of nucleic acid molecule(s) coding for the AAV into AAV-infected cells, and supplying AAV rep and/or cap obligatory for replication and packaging of the AAV.

47. The method of claim 46, wherein the AAV rep and/or cap obligatory for replication and packaging of the AAV are supplied by transfecting the cells with helper plasmid(s) or helper virus(es).

48. The method of claim 47, wherein the helper virus is a poxvirus, adenovirus, herpesvirus or baculovirus.

49. The method of claim 48, wherein the poxvirus is a vaccinia virus.

50. The method of any of claims 46 to 49, wherein:

- the cells are mammalian cells; or

- the cells are insect cells and the helper virus is baculovirus.

51. A method of delivering the CRISPR enzyme of any of claims 2-11 comprising delivering to a cell mRNA encoding the CRISPR enzyme.

52. A chimeric Cas enzyme wherein the enzyme comprises one or more fragments from a first Cas ortholog and one or more fragments from a second Cas ortholog.

53. The enzyme according to claim 52 wherein the one or more fragments of the first or second Cas ortholog are from the C- or N-terminal of the first or second Cas ortholog.

54. The enzyme according to claim 52 or 53 wherein the first or second Cas ortholog is selected from a genus belonging to the group consisting of *Corynebacter, Sutterella, Legionella, Treponema, Filifactor, Eubacterium, Streptococcus, Lactobacillus, Mycoplasma, Bacteroides, Flaviivola, Flavobacterium, Sphaerochaeta, Azospirillum, Gluconacetobacter, Neisseria, Roseburia, Parvibaculum, Staphylococcus, Nitratifractor, Mycoplasma* and *Campylobacter*.

55. Use of the composition or enzyme according to any of claims 1-11, 14, 16-33, or 52-54in the preparation of a medicament for modification of a target sequence.

56. The composition according to any of claims 1 to 11, wherein the CRISPR enzyme is truncated in comparison to a wild type CRISPR enzyme or the CRISPR enzyme is comprised of 500-2000 amino acids.

57. The composition according to any of claims 1 to 11 or 56, wherein the CRISPR enzyme is a nuclease directing cleavage of both strands at the location of the target sequence, or the CRISPR enzyme is a nickase directing cleavage of one strand at the location of the target sequence.

58. The composition according to any of claims 1 to 11 or 56-57, wherein the guide sequence comprises at least fifteen nucleotides.

59. The composition according to any of claims 1 to 11 or 56-58, wherein the CRISPR enzyme is codon-optimized or codon-optimized for expression in a eukaryotic cell.

60. The composition according to any of claims 1 to 11 or 56-59, wherein the CRISPR enzyme comprises one or more mutations.

61. The composition according to any of claims 1 to 11 or 56-60, wherein the CRISPR enzyme comprises a chimeric CRISPR enzyme.

62. A non-naturally occurring or engineered composition comprising :

A) - I. a CRISPR-Cas system chimeric RNA (chiRNA) polynucleotide sequence, wherein the polynucleotide sequence comprises:

(a) a guide sequence capable of hybridizing to a target sequence in a eukaryotic cell,

(b) a tracr mate sequence, and

(c) a tracr sequence, and

II. a polynucleotide sequence encoding a CRISPR enzyme comprising at least one or more nuclear localization sequences,

wherein (a), (b) and (c) are arranged in a 5' to 3' orientation,

wherein when transcribed, the tracr mate sequence hybridizes to the tracr sequence and the guide sequence directs sequence-specific binding of a CRISPR complex to the target sequence, and

wherein the CRISPR complex comprises the CRISPR enzyme complexed with (1) the guide sequence that is hybridized to the target sequence, and (2) the tracr mate sequence that is hybridized to the tracr sequence and the polynucleotide sequence encoding a CRISPR enzyme is DNA or RNA,

or

(B) I. polynucleotides comprising:

(a) a guide sequence capable of hybridizing to a target sequence in a prokaryotic cell, and

(b) at least one or more tracr mate sequences,

II. a polynucleotide sequence encoding a CRISPR enzyme, and

III. a polynucleotide sequence comprising a tracr sequence,

wherein when transcribed, the tracr mate sequence hybridizes to the tracr sequence and the guide sequence directs sequence-specific binding of a CRISPR complex to the target sequence, and

wherein the CRISPR complex comprises the CRISPR enzyme complexed with (1) the guide sequence that is hybridized to the target sequence, and (2) the tracr mate sequence that is hybridized to the tracr sequence, and the polynucleotide sequence encoding a CRISPR enzyme is DNA or RNA, and

wherein the CRISPR enzyme is a Cas9 ortholog of a genus belonging to the group consisting of *Corynebacter, Sutterella, Legionella, Treponema, Filifactor, Eubacterium, Streptococcus, Lactobacillus, Mycoplasma, Bacteroides, Flaviivola, Flavobacterium,*

Sphaerochaeta, Azospirillum, Gluconacetobacter, Neisseria, Roseburia, Parvibaculum, Staphylococcus, Nitratifractor, Mycoplasma and *Campylobacter*.

63. A method of modifying an organism or a non-human organism by manipulation of a target sequence in a genomic locus of interest comprising delivering a non-naturally occurring or engineered composition comprising :

A) - I. a CRISPR-Cas system chimeric RNA (chiRNA) polynucleotide sequence, wherein the polynucleotide sequence comprises:

(a) a guide sequence capable of hybridizing to a target sequence in a eukaryotic cell,

(b) a tracr mate sequence, and

(c) a tracr sequence, and

II. a polynucleotide sequence encoding a CRISPR enzyme comprising at least one or more nuclear localization sequences,

wherein (a), (b) and (c) are arranged in a 5' to 3' orientation,

wherein when transcribed, the tracr mate sequence hybridizes to the tracr sequence and the guide sequence directs sequence-specific binding of a CRISPR complex to the target sequence, and

wherein the CRISPR complex comprises the CRISPR enzyme complexed with (1) the guide sequence that is hybridized to the target sequence, and (2) the tracr mate sequence that is hybridized to the tracr sequence and the polynucleotide sequence encoding a CRISPR enzyme is DNA or RNA,

or

(B) I. polynucleotides comprising:

(a) a guide sequence capable of hybridizing to a target sequence in a prokaryotic cell, and

(b) at least one or more tracr mate sequences,

II. a polynucleotide sequence encoding a CRISPR enzyme, and

III. a polynucleotide sequence comprising a tracr sequence,

wherein when transcribed, the tracr mate sequence hybridizes to the tracr sequence and the guide sequence directs sequence-specific binding of a CRISPR complex to the target sequence, and

wherein the CRISPR complex comprises the CRISPR enzyme complexed with (1) the guide sequence that is hybridized to the target sequence, and (2) the tracr mate sequence that is

hybridized to the tracr sequence, and the polynucleotide sequence encoding a CRISPR enzyme is DNA or RNA, and

wherein the CRISPR enzyme is a Cas9 ortholog of a genus belonging to the group consisting of *Corynebacter, Sutterella, Legionella, Treponema, Filifactor, Eubacterium, Streptococcus, Lactobacillus, Mycoplasma, Bacteroides, Flaviivola, Flavobacterium, Sphaerochaeta, Azospirillum, Gluconacetobacter, Neisseria, Roseburia, Parvibaculum, Staphylococcus, Nitratifractor, Mycoplasma* and *Campylobacter*.

64. The composition according to claim 62, or method according to claim 63, wherein the CRISPR enzyme is truncated in comparison to a wild type CRISPR enzyme or the CRISPR enzyme is comprised of 500-2000 amino acids.

65. The composition or method according to claim 62-64, wherein the CRISPR enzyme is a nuclease directing cleavage of both strands at the location of the target sequence, or the CRISPR enzyme is a nickase directing cleavage of one strand at the location of the target sequence.

66. The composition or method according to claim 62-65, wherein the guide sequence comprises at least fifteen nucleotides.

67. The composition or method according to claim 62-66, wherein the CRISPR enzyme is codon-optimized or codon-optimized for expression in a eukaryotic cell.

68. The composition or method according to claim 62-67, wherein the CRISPR enzyme comprises one or more mutations.

69. The composition or method according to claim 62-68, wherein the CRISPR enzyme comprises a chimeric CRISPR enzyme.

CLAIMS

1. A CRISPR-Cas system chimeric RNA (chiRNA) comprising: (a) a guide sequence capable of hybridizing to a target sequence, (b) a tracr mate sequence capable of hybridizing to a tracr sequence and (c) a tracr sequence, in which the chiRNA is capable of forming a CRISPR-Cas complex with a *Staphylococcus aureus* Cas9 (SaCas9) protein and directing sequence-specific binding of the CRISPR-Cas complex to a target sequence adjacent to a protospacer adjacent motif (PAM) in a eukaryotic cell.

2. A CRISPR-Cas system chiRNA according to Claim 1, in which the PAM comprises NNGRR.

3. A CRISPR-Cas system chiRNA according to Claim 1 or 2, in which the tracr sequence is at least 30 nucleotides in length.

4. A CRISPR-Cas system chiRNA according to Claim 1, 2 or 3, in which the tracr sequence is at least 40 nucleotides in length.

5. A CRISPR-Cas system chiRNA according to any preceding claim, in which the tracr sequence is at least 50 nucleotides in length.

6. A CRISPR-Cas system chiRNA according to any preceding claim, in which the guide sequence is 10-30 nucleotides in length.

7. A CRISPR-Cas system chiRNA according to any preceding claim, in which the guide sequence is at least 20 nucleotides in length.

8. A CRISPR-Cas system chiRNA according to any preceding claim, in which the guide sequence is 20, 21, 22, 23 or 24 nucleotides in length.

9. A CRISPR-Cas system chiRNA according to Claim 1, in which the chiRNA comprises the following sequence:
NNNNNNNNNNNNNNNNNNNGUUUUAGUACUCUGGAAACAGAAUCUACUAAA
ACAAGGCAAAAUGCCGUGUUUAUCUCGUCAACUUGUUGGCGAGAUUUUUUU.

10. A vector comprising a polynucleotide sequence encoding a CRISPR-Cas system chiRNA according to any preceding claim.

11. A vector according to Claim 10, in which the vector encodes two or more CRISPR-Cas system chiRNAs.

12. A vector according to Claim 10 or 11, further comprising a polynucleotide sequence encoding a SaCas9 protein which is codon-optimized for expression in a eukaryotic cell.

13. A vector according to Claim 10, 11 or 12, which is a viral vector.

14. A vector according to Claim 13, which is an adeno-associated virus (AAV) vector.

15. A composition comprising the CRISPR-Cas system chiRNA according to any of Claims 1 to 9 and a SaCas9 protein.

16. A composition comprising A CRISPR-Cas system chiRNA according to any of Claims 1 to 9 and an mRNA encoding a SaCas9 protein.

17. A composition according to Claim 15 or 16, in which the CRISPR-Cas system chiRNA and the SaCas9 protein or mRNA is comprised in a nanoparticle, liposome, exosome or microvesicle.

18. A eukaryotic cell comprising a CRISPR-Cas system chiRNA according to any of Claims 1 to 9, a vector according to any of Claims 10 to 14 or a composition according to Claim 15, 16 or 17.