CLAIMS:

1. A method of altering a eukaryotic germline cell of a non-human organism comprising

introducing into the germline cell a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the one or more guide RNAs are complementary to one or more target locations on genomic DNA of a first chromosome and a second chromosome of a chromosome pair of the germline cell,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the one or more guide RNAs are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the first chromosome or the second chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the first chromosome or the second chromosome of the genomic DNA,

expressing the first foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the one or more guide RNAs wherein the RNA guided DNA binding protein nuclease and an associated guide RNA co-localize to an associated target location on the first chromosome of the genomic DNA and the second chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the first chromosome of the genomic DNA at the target location in a cleavage site specific manner and cleaves the second chromosome of the genomic DNA at the target location in a cleavage site specific manner,

inserting the first foreign nucleic acid sequence into the first chromosome of the chromosome pair of the genomic DNA at the cleavage site, and inserting the first foreign nucleic acid sequence into the second chromosome of the chromosome pair of the genomic DNA at the cleavage site to render the germline cell homozygous for the foreign nucleic acid sequence.

2. The method of claim 1 wherein the RNA guided DNA binding protein nuclease is Cas9 and creates a double stranded break, or wherein the RNA guide DNA binding protein is Cas9 nickase and creates a single stranded break.

3. The method of claim 1 or 2, wherein:

(i) at least one target location is within an essential gene and the foreign nucleic acid sequence is inserted adjacent to and replacing part of the essential gene;

(ii) the first foreign nucleic acid is inserted by homologous recombination;

(iii) the germline cell is a fungal cell, a plant cell, an insect cell or a mammalian cell; and/or

(iv) the RNA includes between about 10 to about 250, or between about 20 to about 100 nucleotides.

4. The method of any one of claims 1-3 wherein the RNA guided DNA binding protein nuclease co-localizes with an associated guide RNA at a plurality of associated target locations to cleave either the first chromosome or the second chromosome at a plurality of cleavage sites.

5. The method of claim 4 wherein cleaving at the plurality of cleavage sites removes a DNA sequence which is replaced with the first foreign nucleic acid sequence by homologous recombination.

6. The method of any one of claims 1-5, further including the step of growing the germline cell into the organism.

7. The method of claim 6 further including the step of mating the organism with a wild-type organism of the same species to produce an offspring germline cell including a first chromosome of a chromosome pair with the first foreign nucleic acid sequence.

8. The method of claim 7, wherein the first foreign nucleic acid sequence is expressed by the offspring germline cell to produce the RNA guided DNA binding protein nuclease and the one or more RNAs wherein the RNA guided DNA binding protein nuclease and an associated guide RNA co-localize to an associated target location on a second chromosome of the chromosome pair and the RNA guided DNA binding protein nuclease cleaves the second chromosome at the target location in a cleavage site specific manner and,

inserting the first foreign nucleic acid sequence into the second chromosome of the chromosome pair at the cleavage site to render the offspring germline cell homozygous for the foreign nucleic acid sequence.

9. The method of claim 8 wherein the steps of growing the germline cell into the organism and mating the organism with a wild type organism of the same species is repeated to produce a population of organisms of the same species that are homozygous for the first foreign nucleic acid sequence.

10. The method of any one of claims 1-9, wherein the first foreign nucleic acid sequence includes one or more selected gene sequences.

11. The method of claim 9, wherein:

(i) the first foreign nucleic acid sequence includes one or more selected gene sequences and the one or more selected gene sequences is within the genome of the organisms within the population of organisms;

(ii) an altered organism is introduced into the population of organisms and that includes within its genome a second foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the one or more guide RNAs are complementary to one or more target locations on the first foreign nucleic acid sequence and wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the first foreign nucleic acid sequence and wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the first foreign nucleic acid sequence,

wherein the altered organism mates with a member of the population of organisms to produce an offspring germline cell including the second foreign nucleic acid sequence and the first foreign nucleic acid sequence,

wherein the offspring germline cell expresses the second foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the one or more RNAs wherein the RNA guided DNA binding protein nuclease and an associated guide RNA co-localize to an associated target location on the first foreign nucleic acid sequence, the RNA guided DNA binding protein nuclease cleaves the first foreign nucleic acid sequence at the target location in a cleavage site specific manner and,

wherein the second foreign nucleic acid sequence is inserted into the genome of the germline cell at the cleavage site to render the offspring germline cell homozygous for the second foreign nucleic acid sequence.

(iii) altered wild type organisms are introduced into the population that have the one or more target locations on genomic DNA altered such that the one or more guide RNAs are noncomplementary to the one or more target locations and are prevented from binding to the one or more target locations such that the first foreign nucleic acid sequence does not enter the genome of the altered wild type organisms.

12. The method of claim 11, wherein in (iii) the altered wild type organisms are altered by expression of a second foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs which co-localize to the first foreign nucleic acid sequence to cleave the first foreign nucleic acid sequence in a cleavage site specific manner resulting in a recoded allele.

13. The method of any one of claims 1-10, further comprising introducing into the germline cell a second foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the one or more guide RNAs are complementary to the one or more target locations that were altered by the first foreign nucleic acid sequence,

expressing the second foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the one or more RNAs wherein the RNA guided DNA binding protein nuclease and an associated guide RNA co-localize to an associated target location on the

chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the chromosome of the genomic DNA at the target location in a cleavage site specific manner to remove the first foreign nucleic acid sequence, and

inserting the second foreign nucleic acid sequence into the chromosome of the genomic DNA at the cleavage site.

14. The method of any one of claims 1-13 wherein at least one target location is within an essential protein-coding gene and the foreign nucleic acid sequence is inserted into the essential gene such that the amino acid sequence of the essential protein is preserved but the nucleotide sequence of the gene is altered such that the one or more guide RNAs are noncomplementary to the one or more target locations

15. A method of rendering two populations of a non-human species unable to produce viable progeny comprising

altering a first population of the species to include a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more first guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence, wherein the one or more first guide RNAs are complementary to one or more target locations on an essential gene, and the nucleotide sequence of the essential gene has been altered such that the one or more guide RNAs are noncomplementary to the one or more target locations but the amino acid sequence of the encoded essential protein is preserved,

altering a second population of the species to include a second foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more second guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence, wherein the one or more second guide RNAs are complementary to one or more target locations on the essential gene that are different from the target locations of the one or more first guide RNAs, and the nucleotide sequence of the essential gene has been altered such that the one or more second guide RNAs are noncomplementary to the one or more target locations, but the amino acid sequence of the encoded essential protein is preserved,

mating the first population with the second population to produce germline cells where the first foreign nucleic acid sequence is expressed to cleave the essential gene contributed by second parent and the second foreign nucleic acid sequence are expressed to cleave the essential gene contributed by the first parent.

16. A method of replacing an allele in a eukaryotic non-human germline cell having a mutation in a target nucleic acid sequence comprising

introducing into the germline cell a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and a plurality of guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the plurality of guide RNAs are complementary to a plurality of target locations on genomic DNA of a chromosome that are adjacent to a mutation on an allele wherein the mutation prevents binding of a corresponding guide RNA to the genomic DNA,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the plurality of guide RNAs are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the chromosome of the genomic DNA,

expressing the first foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the plurality of RNAs wherein the RNA guided DNA binding protein nuclease and associated guide RNAs co-localize to a plurality of associated target locations on the chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the first chromosome of the genomic DNA at the plurality of target locations in a cleavage site specific manner so as to remove a portion of the genomic DNA including the mutation, and

inserting the first foreign nucleic acid sequence into the chromosome of the genomic DNA at the cleavage site.

17. The method of claim 16 wherein at least one of the target locations are within a gene important to the fitness of the organism such as an essential gene, such that a deletion event that removes all target locations is highly deleterious and will be removed from the population by natural selection.

18. A method of altering a eukaryotic germline cell of a non-human organism at a plurality of genes comprising

introducing into the germline cell a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and a plurality of guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence, along with one or more additional foreign nucleic acid sequences corresponding to the plurality of genes,

wherein the plurality of guide RNAs include one or more gene specific guide RNAs that are complementary to one or more target locations on a plurality of genes in the genomic DNA of a chromosome of the germline cell,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the plurality of guide RNAs are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of one of the target locations on the chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the same target location on the chromosome of the genomic DNA,

wherein each of the one or more nucleic acid sequences contain a first flanking sequence and a second flanking sequence corresponding to a first portion and a second portion of the remaining target locations,

expressing the first foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the plurality of RNAs wherein the RNA guided DNA binding protein nuclease and associated guide RNAs co-localize to a plurality of associated target locations on the chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the first chromosome of the genomic DNA at a plurality of genes in a cleavage site specific manner, and

inserting the first foreign nucleic acid sequence into the chromosome of the genomic DNA at the cleavage site.

19. The method of any one of claims 1-10 and 18, further comprising introducing into the germline cell a second foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and a plurality of guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the plurality of guide RNAs are complementary to the plurality of target locations that were altered by the first foreign nucleic acid sequence,

expressing the second foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the plurality of guide RNAs wherein the RNA guided DNA binding protein nuclease and associated guide RNAs co-localize to associated target locations on the chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the chromosome of the genomic DNA at the associated target locations in a cleavage site specific manner to remove the first foreign nucleic acid sequence, and

inserting the second foreign nucleic acid sequence into the chromosome of the genomic DNA at the cleavage site.

20. The method of claim 13 or 19 wherein the second foreign nucleic acid sequence includes genetic modifications different from the first foreign nucleic acid sequence or wherein the second foreign nucleic acid sequence includes the wild type sequence of the chromosome that was modified by the first foreign nucleic acid sequence.

21. A method of rendering two non-human populations unable to produce offspring with one another comprising

introducing into a first germline cell a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and a first set of guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the first set of guide RNAs are complementary to a first set of target locations on genomic DNA of a chromosome,

wherein the first set of target locations are within an essential protein-coding gene and the first foreign nucleic acid sequence is inserted into the essential gene such that the amino acid sequence of the essential protein is preserved but the nucleotide sequence of the gene is altered such that the first set of guide RNAs are noncomplementary to the one or more target locations

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the first set of guide RNAs and the first foreign nucleic acid sequence preserving the amino acid sequence of the essential protein are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the chromosome of the genomic DNA,

expressing the first foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the first set of guide RNAs wherein the RNA guided DNA binding protein nuclease and associated guide RNAs co-localize to a first set of associated target locations on the chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the first chromosome of the genomic DNA at the first set of target locations in a cleavage site specific manner so as to remove a portion of the genomic DNA within the essential gene, and

inserting the first foreign nucleic acid sequence into the chromosome of the genomic DNA at the cleavage site, and

introducing into a second germline cell a second foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and a second set of guide RNAs and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the second set of guide RNAs are complementary to a second set of target locations on genomic DNA of a chromosome,

wherein the second set of target locations are within the same essential protein-coding gene as the first set of target locations but are not identical to any of the first set of target locations and the second foreign nucleic acid sequence is inserted into the essential gene such that the amino acid sequence of the essential protein is preserved but the nucleotide sequence of the gene is altered such that the second set of guide RNAs are noncomplementary to the second set of target locations,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the second set of guide RNAs and the second foreign nucleic acid sequence preserving the amino acid sequence of the essential protein are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the chromosome of the genomic DNA,

expressing the second foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the second set of guide RNAs wherein the RNA guided DNA binding protein nuclease and associated second set of guide RNAs co-localize to a second set of associated target locations on the chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the first chromosome of the genomic DNA at the second set of target locations in a cleavage site specific manner so as to remove a portion of the genomic DNA within the essential, and

inserting the second foreign nucleic acid sequence into the chromosome of the genomic DNA at the cleavage site,

wherein any mutual progeny of organisms arising from the first germline cell and the second germline cell are not viable where the first set of guide RNAs causes the RNA guided DNA binding protein nuclease to cleave the first set of target locations within the second foreign nucleic acid sequence and the second set of guide RNAs causes the RNA guided DNA binding protein nuclease to cleave the second set of target locations within the first foreign nucleic acid sequence.

22. A method of producing only Y chromosome sperm from a spermatocyte comprising

introducing into the spermatocyte a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the one or more guide RNAs are complementary to one or more target locations on an X chromosome of the spermatocyte and one or more target locations on a Y chromosome of the spermatocyte,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the one or more guide RNAs are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the Y chromosome,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the Y chromosome,

expressing the first foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the one or more RNAs complementary to one or more target locations on the X chromosome of the spermatocyte and one or more target locations on the Y chromosome of the spermatocyte wherein the RNA guided DNA binding protein nuclease and an associated

guide RNA complementary to a target locations on the Y chromosome co-localize to an associated target location on the Y chromosome and the RNA guided DNA binding protein nuclease cleaves the Y chromosome at the target location in a cleavage site specific manner,

inserting the first foreign nucleic acid sequence into the Y chromosome at the cleavage site, and

wherein the RNA guided DNA binding protein nuclease and an associated guide RNA complementary to a target location on the X chromosome co-localize to an associated target location on the X chromosome and the RNA guided DNA binding protein nuclease cleaves the X chromosome at the target location in a cleavage site specific manner so as to render the X chromosome inoperable.

23. A method of producing only Y chromosome sperm from a spermatocyte comprising

expressing an RNA guided DNA binding protein nuclease and one or more guide RNAs, from sequences located on the Y chromosome using corresponding promoter sequences,

wherein the one or more guide RNAs are complementary to one or more target locations on an X chromosome of the spermatocyte,

wherein the RNA guided DNA binding protein nuclease and an associated guide RNA complementary to one or more target locations on the X chromosome co-localize to the one or more associated target locations on the X chromosome and the RNA guided DNA binding protein nuclease cleaves the X chromosome at the one or more target locations in a cleavage site specific manner so as to render the X chromosome inoperable.

24. A method of producing only X chromosome sperm from a spermatocyte comprising

expressing an RNA guided DNA binding protein nuclease and one or more guide RNAs, from sequences located on the X chromosome using corresponding promoter sequences,

wherein the one or more guide RNAs are complementary to one or more target locations on an Y chromosome of the spermatocyte,

wherein the RNA guided DNA binding protein nuclease and an associated guide RNA complementary to one or more target locations on the Y chromosome co-localize to the one or more associated target locations on the Y chromosome and the RNA guided DNA binding protein nuclease cleaves the Y chromosome at the one or more target locations in a cleavage site specific manner so as to render the Y chromosome inoperable.

25. A method of producing only Y chromosome-containing sperm from a spermatocyte comprising

modifying a Y chromosome to encode a first foreign nucleic acid sequence and a second foreign nucleic acid sequence,

wherein the first foreign nucleic acid sequence encodes a first RNA guided DNA binding protein nuclease and a first set of guide RNAs and corresponding promoter sequences,

wherein the second foreign nucleic acid sequence encodes an RNA guided DNA binding protein nuclease and a second set of guide RNAs and corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the second nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the second set of guide RNAs are between the first flanking sequence and the second flanking sequence,

wherein the first RNA guided DNA binding protein nuclease cannot recognize the second set of guide RNAs and the second RNA guided DNA binding protein nuclease cannot recognize the first set of guide RNAs,

wherein the first set of guide RNAs are complementary to a plurality of target locations on genomic DNA of a chromosome that is not a sex chromosome,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the chromosome of the genomic DNA,

wherein the first foreign nucleic acid sequence is expressed in the germline before meiosis to produce the first RNA guided DNA binding protein nuclease and the first set of RNAs wherein the RNA guided DNA binding protein nuclease and associated guide RNAs co-localize to a first set of associated target locations on the chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the chromosome of the genomic DNA at the first set of target locations in a cleavage site specific manner such that cellular repair mechanisms copy the second foreign nucleic acid sequence from the Y chromosome onto the chromosome of the genomic DNA,

wherein the copy of the second foreign nucleic acid sequence located on the chromosome of the genomic DNA is expressed prior to or during meiosis to produce the second RNA-guided DNA binding protein and the second set of guide RNAs,

wherein the second RNA guided DNA binding protein nuclease and the second set of guide RNAs complementary to one or more target locations on the X chromosome co-localize to the one or more associated target locations on the X chromosome and the RNA guided DNA binding protein nuclease cleaves the X chromosome at the one or more target locations in a cleavage site specific manner so as to render the X chromosome inoperable.

26. A method of producing only X chromosome-containing sperm from a spermatocyte comprising

modifying an X chromosome to encode a first foreign nucleic acid sequence and a second foreign nucleic acid sequence,

wherein the first foreign nucleic acid sequence encodes a first RNA guided DNA binding

protein nuclease and a first set of guide RNAs and corresponding promoter sequences,

wherein the second foreign nucleic acid sequence encodes an RNA guided DNA binding protein nuclease and a second set of guide RNAs and corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the second nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the second set of guide RNAs are between the first flanking sequence and the second flanking sequence,

wherein the first RNA guided DNA binding protein nuclease cannot recognize the second set of guide RNAs and the second RNA guided DNA binding protein nuclease cannot recognize the first set of guide RNAs,

wherein the first set of guide RNAs are complementary to a plurality of target locations on genomic DNA of a chromosome that is not a sex chromosome,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the chromosome of the genomic DNA,

wherein the first foreign nucleic acid sequence is expressed in the germline before meiosis to produce the first RNA guided DNA binding protein nuclease and the first set of RNAs wherein the RNA guided DNA binding protein nuclease and associated guide RNAs co-localize to a first set of associated target locations on the chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the chromosome of the genomic DNA at the first set of target locations in a cleavage site specific manner such that cellular repair mechanisms copy the second foreign nucleic acid sequence from the X chromosome onto the chromosome of the genomic DNA,

wherein the copy of the second foreign nucleic acid sequence located on the chromosome of the genomic DNA is expressed prior to or during meiosis to produce the second RNA-guided DNA binding protein and the second set of guide RNAs,

wherein the second RNA guided DNA binding protein nuclease and the second set of guide RNAs complementary to one or more target locations on the Y chromosome co-localize to the one or more associated target locations on the Y chromosome and the RNA guided DNA binding protein nuclease cleaves the Y chromosome at the one or more target locations in a cleavage site specific manner so as to render the Y chromosome inoperable.

27. A method of producing non-human female progeny to the exclusion of non-human male progeny with a modified X chromosome having a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs complementary to one or more target nucleic acid sequences on the Y chromosome of a sperm and one or more guide RNAs

complementary to one or more target nucleic acid sequences on the X chromosome of a sperm and a first flanking sequence and a second flanking sequence, expressing the first foreign nucleic acid sequence in the oocyte to produce an RNA guided DNA binding protein nuclease and one or more guide RNAs complementary to one or more target nucleic acid sequences on the Y chromosome and one or more target nucleic acid sequences on the X chromosome, wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the one or more guide RNAs are between the first flanking sequence and the second flanking sequence, wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the X chromosome of the genomic DNA, wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the X chromosome of the genomic DNA, expressing the first foreign nucleic acid sequence to produce an RNA guided DNA binding protein nuclease and one or more guide RNAs complementary to the one or more target nucleic acid sequences on the Y chromosome and the one or more target nucleic acid sequences on the X chromosome, wherein combining a wild type sperm having a Y chromosome with an oocyte containing the modified X chromosome results in colocalizing the RNA guided DNA binding protein nuclease and the one or more guide RNAs targeting the Y chromosome to the one or more target nucleic acid sequences on the Y chromosome and the RNA guided DNA binding protein nuclease cuts the Y chromosome rendering subsequent development of the oocyte into a male organism inoperable, and

combining a wild type sperm having a X chromosome with an oocyte containing the modified X chromosome results in colocalizing the RNA guided DNA binding protein nuclease and the one or more guide RNAs to the one or more target nucleic acid sequences on the X chromosome where the RNA guided DNA binding protein nuclease cuts the X chromosome and the first foreign nucleic acid sequence is inserted into the X chromosome.

28. A method of producing non-human male progeny to the exclusion of non-human female progeny with a modified Y chromosome having a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs complementary to one or more target nucleic acid sequences on the X chromosome located within a gene that is essential for development, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence, wherein the first flanking sequence includes a first sequence identical to a first portion of the essential gene on the X chromosome, wherein the second flanking sequence includes a second sequence identical to a second portion of the essential gene on the X chromosome, and the modified Y chromosome further includes a second nucleic acid sequence encoding the essential gene on the X chromosome that is altered such that the one or more target locations recognized by the one or more guide RNAs are noncomplementary to the sequences recognized by one or more the guide RNAs, such that when an oocyte having a wild-type X

chromosome is combined with a sperm having the modified Y chromosome results in expressing the first foreign nucleic acid sequence produce an RNA guided DNA binding protein nuclease and one or more guide RNAs complementary to one or more target nucleic acid sequences on the X chromosome, colocalizing the RNA guided DNA binding protein nuclease and the one or more guide RNAs to the one or more target nucleic acid sequences on the X chromosome where the RNA guided DNA binding protein nuclease cuts the X chromosome to remove the essential gene and to insert the first nucleic acid sequence therein, creating a modified X chromosome that remains viable due to the additional copy of the essential gene on the Y chromosome, and

combining an oocyte having a wild-type X chromosome with a sperm having the modified X chromosome results in expressing the first foreign nucleic acid sequence to produce an RNA guided DNA binding protein nuclease and one or more guide RNAs complementary to one or more target nucleic acid sequences on the X chromosome, colocalizing the RNA guided DNA binding protein nuclease and the one or more guide RNAs to the one or more target nucleic acid sequences on the X chromosome where the RNA guided DNA binding protein nuclease cuts the X chromosome to remove the essential gene and to insert the first foreign nucleic acid sequence into the X chromosome, wherein the zygote consequently lacks the essential X chromosome gene.

29. A method for generating fertile non-human males and infertile non-human females, wherein the method of claim 28 is modified in that the essential gene on the X chromosome is only essential for fertility, such that organisms lacking that gene are infertile.

30. The method of claim 28 or 29, wherein the first nucleic acid sequence additionally contains a third flanking sequence and a fourth flanking sequence, wherein the third flanking sequence includes a third sequence identical to a first portion of a gene essential for fertility, wherein the fourth flanking sequence includes a fourth sequence identical to a second portion of a gene essential for fertility, wherein the RNA-guided DNA-binding protein nuclease is located between the third flanking sequence and the fourth flanking sequence, and the first nucleic acid sequence additionally contains a second set of guide RNAs complementary to one or more target sequences located within the gene essential for fertility, expressing the RNA-guided DNA binding protein nuclease and second set of guide RNAs, colocalizing the RNA guided DNA binding protein nuclease and the one or more guide RNAs to the one or more target nucleic acid sequences within the gene essential for fertility, wherein the RNA guided DNA binding protein nuclease cuts the gene essential for fertility and inserts the first nucleic acid sequence therein.

31. A method for controlled non-human population suppression wherein the Y chromosome as defined in claim 30 is released into the population to be suppressed and the RNA guided gene drive as defined in claim 18 that alters the one or more target sequences located within the gene essential for fertility that is targeted by the Y chromosome as defined in claim 31 such that they are noncomplementary to the guide RNAs employed by the Y chromosome as defined in claim 31 but

the protein encoded by the gene retains the same amino acid sequence is released in a population to be protected such that the Y chromosome produces only sons in the population to be suppressed and produces fertile sons and sterile daughters upon mating with females that have been modified by the RNA guided gene drive released in the population to be protected.

32. A method for targeted population suppression or extinction comprising releasing the Y chromosome as defined in claim 31 into a population to be suppressed or eradicated.

33. A method of blocking gene flow from an engineered non-human organism to a wild type organism of the same species comprising first modifying the genome of the wild-type organism such that sequences corresponding to those from the middle of a gene that must be present as two functional copies for the organism to be viable that is hereafter termed the essential gene are inserted into another chromosomal region distal to the wild-type copy of the gene, and subsequently

introducing into the germline of the engineered organism a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence and a third flanking sequence and a fourth flanking sequence and a sequence encoding the same protein as the essential gene but does not utilize the same nucleic acid sequence and is hereafter termed the recoded essential gene,

wherein the one or more guide RNAs are complementary to the one or more target locations inserted into the distal region of the chromosome and also to the sequences within the essential gene,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the one or more guide RNAs and the third flanking sequence and the fourth flanking sequence and the recoded essential gene are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location in the distal region of the chromosome,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location in the distal region of the chromosome,

wherein the third flanking sequence includes a third sequence identical to a third portion of the essential gene,

wherein the fourth flanking sequence includes a fourth sequence identical to a fourth portion of the essential gene,

expressing the first foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the one or more RNAs complementary to one or more target locations in the distal region of the chromosome and to the one or more target sequences within the essential

gene, wherein the RNA guided DNA binding protein nuclease and an associated guide RNA complementary to a target location co-localize to an associated target location in the distal region of the chromosome, and the RNA guided DNA binding protein nuclease cleaves the target sequence in the distal region of the chromosome in a cleavage site specific manner,

inserting the first foreign nucleic acid sequence into the distal region of the chromosome,

wherein the RNA guided DNA binding protein nuclease and an associated guide RNA complementary to a target location co-localize to an associated target location in the wild-type essential gene, and the RNA guided DNA binding protein nuclease cleaves the wild-type essential gene in a cleavage site specific manner,

inserting the sequence between the third flanking region and the fourth flanking region into the wild-type copy of the essential gene thereby disrupting its function, such that

the engineered organism has two recoded copies of the essential gene in a distal region of the chromosome and no functional copies of the wild-type essential gene and crossing an engineered organism with a wild-type organism causes the disruption of the wild-type copy of the essential gene without inserting an additional copy of the recoded essential gene into the distal region of the chromosome.

34. The method of claim 33, where the essential gene is located on the X chromosome and does require two copies for viability, and the distal region is also on the X chromosome, and the first modification of the organism also modifies the Y chromosome such that a gene required for male fertility or viability hereafter termed the male essential gene is recoded in its nucleic acid sequence in a manner that preserves the amino acid sequence of the encoded male essential protein, and an additional copy of the male essential gene that is nonfunctional is inserted next to the recoded copy of the male essential gene, and the first nucleic acid sequence also includes a fifth flanking sequence that includes a fifth sequence identical to a fifth portion of the male essential gene, and the first nucleic acid sequence also includes a sixth flanking sequence that includes a sixth sequence identical to a sixth portion of the male essential gene, and the first nucleic acid sequence also includes a second set of guide RNAs corresponding to sequences within the wild-type male essential gene that were recoded to render the gene nonfunctional, and the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the guide RNAs and the third flanking sequence and the fourth flanking sequence and the recoded essential gene are between the fifth flanking sequence and the sixth flanking sequence which are between the first flanking sequence and the second flanking sequence, a female with two modified X chromosomes mated with a male with a modified Y chromosome yields viable male offspring because the RNA-guided DNA-binding protein nuclease does not cut the recoded or the nonfunctional male essential gene and the modified Y chromosome does not cut the essential gene on the modified X chromosome, and an oocyte from a female with two modified X chromosomes

that is fertilized by a sperm with a wild-type Y chromosome results in the RNA-guided DNA-binding protein nuclease cutting the wild-type male essential gene and copying the sequence between the fifth flanking sequence and the sixth flanking sequence in its place and resulting in a sterile or nonviable male, and an oocyte from a wild-type female that is fertilized by a sperm with a modified Y chromosome results in the RNA-guided DNA-binding protein nuclease cutting the essential gene and resulting in nonviable male progeny, and the combination of a sperm and an egg that together include a modified and a wild-type X chromosome result in the RNA-guided DNA-binding protein nuclease cutting the wild-type essential gene without copying the recoded essential gene, resulting in hybrid female progeny with one modified X chromosome and one disrupted X chromosome, and these hybrid females mated with wild-type males produce nonviable or sterile males or hybrid females, and half the male progeny of hybrid females and males bearing a modified Y chromosome are viable.

35. A method of blocking gene flow from a non-human subpopulation bearing a unique genetic polymorphism to the remainder of the wild-type population of the same species comprising releasing the RNA guided gene drive as defined in claim 18 that can spread only through populations bearing a unique polymorphism in the target location between the first flanking sequence and the second flanking sequence which additionally inserts the target sites into a distal region of the chromosome wherein the RNA guided gene drive encodes for the first and second flanking sequences for insertion of the RNA guided gene drive into the unique polymorphism region and which encodes third and fourth flanking sequences for inserting the target sites into the distal region, and subsequently

releasing an organism that has been secondarily modified by introducing into the germline of an organism so first modified a second foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and a second set of guide RNAs and a third set of guide RNAs, and including corresponding promoter sequences and a fifth flanking sequence and a sixth flanking sequence and a seventh flanking sequence and an eighth flanking sequence and a ninth flanking sequence and a tenth flanking sequence and a sequence encoding the same protein as the essential gene but that does not utilize the same nucleic acid sequence and is hereafter termed the recoded essential gene,

wherein the second set of guide RNAs are complementary to the first set of target locations inserted into the distal region of the chromosome and also to the sequences within the essential gene,

wherein the third set of guide RNAs are complementary to a set of target sequences that are uniquely found within the first nucleic acid sequence,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the one or more guide RNAs and the seventh

flanking sequence and the eighth flanking sequence and the ninth flanking sequence and the tenth flanking sequence and the recoded essential gene are between the fifth flanking sequence and the sixth flanking sequence,

wherein the fifth flanking sequence includes a fifth sequence identical to a fifth portion of the target location in the distal region of the chromosome,

wherein the sixth flanking sequence includes a sixth sequence identical to a sixth portion of the target location in the distal region of the chromosome,

wherein the seventh flanking sequence includes a seventh sequence identical to a seventh portion of the essential gene,

wherein the eighth flanking sequence includes a eighth sequence identical to a eighth portion of the essential gene,

wherein the ninth flanking sequence includes a ninth sequence identical to an ninth portion of the first flanking sequence,

wherein the tenth flanking sequence includes a tenth sequence identical to a tenth portion of the second flanking sequence,

expressing the second foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the second set RNAs complementary to the second set of target locations in the distal region of the chromosome and to the second set target sequences within the essential gene, wherein the RNA guided DNA binding protein nuclease and an associated guide RNA complementary to a target location co-localize to an associated target location in the distal region of the chromosome, and the RNA guided DNA binding protein nuclease cleaves the target sequence in the distal region of the chromosome in a cleavage site specific manner,

inserting the first foreign nucleic acid sequence into the distal region of the chromosome,

wherein the RNA guided DNA binding protein nuclease and an associated guide RNA complementary to a target location co-localize to an associated target location in the wild-type essential gene, and the RNA guided DNA binding protein nuclease cleaves the wild-type essential gene in a cleavage site specific manner,

inserting the sequence between the seventh flanking region and the eighth flanking region into the wild-type copy of the essential gene thereby disrupting its function,

expressing the third set of guide RNAs complementary to sequences uniquely located within the first nucleic acid sequence,

wherein the RNA guided DNA binding protein nuclease and an associated guide RNA complementary to a sequence within the first nucleic acid sequence co-localize to a target sequence within the first nucleic acid sequence, and the RNA guided DNA binding protein nuclease cleaves the target sequence within the first nucleic acid sequence in a cleavage site specific manner,

replacing the first nucleic acid sequence with the sequence between the ninth flanking

region and the tenth flanking region, such that

the engineered organism has no copies of the first nucleic acid sequence and two recoded copies of the essential gene in a distal region of the chromosome and no functional copies of the wild-type essential gene and crossing an engineered organism with a wild-type organism causes the disruption of the wild-type copy of the essential gene without inserting an additional copy of the recoded essential gene into the distal region of the chromosome.

36. A non-human germline cell comprising

a foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence,

wherein the one or more guide RNAs are complementary to one or more target locations on genomic DNA of a first chromosome and a second chromosome of a chromosome pair of the germline cell,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the one or more guide RNAs are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the first chromosome or the second chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the first chromosome or the second chromosome of the genomic DNA.

37. A method of altering a eukaryotic non-human germline cell of an organism comprising

introducing into the germline cell a first foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence, and including a sensitizing nucleic acid the expression of which is harmful to the organism when the organism is exposed to a chemical, compound or condition,

wherein the one or more guide RNAs are complementary to one or more target locations on genomic DNA of a first chromosome and a second chromosome of a chromosome pair of the germline cell,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the one or more guide RNAs and the sensitizing nucleic acid are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the first chromosome or the second chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second

portion of the target location on the first chromosome or the second chromosome of the genomic DNA,

expressing the first foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the one or more RNAs wherein the RNA guided DNA binding protein nuclease and an associated guide RNA co-localize to an associated target location on the first chromosome of the genomic DNA and the second chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the first chromosome of the genomic DNA at the target location in a cleavage site specific manner and cleaves the second chromosome of the genomic DNA at the target location in a cleavage site specific manner,

inserting the first foreign nucleic acid sequence into the first chromosome of the chromosome pair of the genomic DNA at the cleavage site, and inserting the first foreign nucleic acid sequence into the second chromosome of the chromosome pair of the genomic DNA at the cleavage site to render the germline cell homozygous for the foreign nucleic acid sequence, and

expressing the sensitizing nucleic acid rendering the resulting organism sensitive to the chemical, compound or condition such that the resulting organism perishes or is rendered sterile when exposed to the chemical, compound or condition.

38. The method of claim 37 wherein:

(1) expression of the sensitizing nucleic acid increases toxicity of the chemical, compound or condition to the organism;

(2) the germline cell is grown into an organism wherein the sensitizing nucleic acid increases toxicity of the chemical, compound or condition to the organism;

(3) the organism is a weed or pest;

(4) the sensitizing nucleic acid is a sensitizing gene which replaces an existing gene, wherein optionally:

(a) the sensitizing gene is the exact or codon-altered ancestral version of an existing mutant gene in wild populations, such that the current mutated version is replaced with the ancestral form;

(b) the existing gene has acquired a mutation contributing to resistance to a pesticide, herbicide, or fungicide; or

(c) the sensitizing gene replaces an existing gene whose function is required for the organism to survive or reproduce;

(5) the chemical or compound is a pesticide, herbicide or fungicide, wherein optionally the pesticide, herbicide, or fungicide is one of: a Bt toxin produced by Cry1A.105, CryIAb, CryIF, Cry2Ab, Cry3Bb1, Cry34Ab1, Cry35Ab1, mCry3A, or VIP, 2,4-D or glyphosate; or

(6) the chemical is a prodrug and the sensitizing gene encodes a corresponding prodrug-converting enzyme, wherein optionally the enzyme/chemical pairing is cytosine deaminase/5-fluorocytosine, or nitroreductase/CB1954.

39. A method of altering a eukaryotic non-human germline cell of an organism including a first sensitizing gene drive comprising

introducing into the germline cell a second foreign nucleic acid sequence encoding an RNA guided DNA binding protein nuclease and one or more guide RNAs, and including corresponding promoter sequences and a first flanking sequence and a second flanking sequence, and including a second sensitizing nucleic acid sequence the expression of which is harmful to the organism when the organism is exposed to a chemical, compound or condition,

wherein the one or more guide RNAs are complementary to one or more target locations on genomic DNA of a first chromosome including the first sensitizing gene drive and a second chromosome of a chromosome pair of the germline cell including the first sensitizing gene drive,

wherein the nucleic acid sequence encoding the RNA guided DNA binding protein nuclease and the nucleic acid sequence encoding the one or more guide RNAs of the second foreign nucleic acid sequence and the second sensitizing nucleic acid sequence are between the first flanking sequence and the second flanking sequence,

wherein the first flanking sequence includes a first sequence identical to a first portion of the target location on the first chromosome or the second chromosome of the genomic DNA,

wherein the second flanking sequence includes a second sequence identical to a second portion of the target location on the first chromosome or the second chromosome of the genomic DNA,

expressing the second foreign nucleic acid sequence to produce the RNA guided DNA binding protein nuclease and the one or more RNAs wherein the RNA guided DNA binding protein nuclease and an associated guide RNA co-localize to an associated target location on the first chromosome of the genomic DNA and the second chromosome of the genomic DNA and the RNA guided DNA binding protein nuclease cleaves the first chromosome of the genomic DNA at the target location in a cleavage site specific manner and cleaves the second chromosome of the genomic DNA at the target location in a cleavage site specific manner,

inserting the second foreign nucleic acid sequence into the first chromosome of the chromosome pair of the genomic DNA at the cleavage site, and inserting the second foreign nucleic acid sequence into the second chromosome of the chromosome pair of the genomic DNA at the cleavage site to render the germline cell homozygous for the second foreign nucleic acid sequence, and

expressing the second sensitizing nucleic acid sequence rendering the resulting organism sensitive to the chemical, compound or condition such that the resulting organism perishes or is rendered sterile when exposed to the chemical, compound or condition.

40. The method of claim 39 wherein the organism is a weed or pest.