

WHAT IS CLAIMED IS:

1. An engineered retron comprising:
 - a) a pre-msr sequence;
 - b) an *msr* gene encoding multicopy single-stranded RNA (msRNA);
 - c) an *msd* gene encoding multicopy single-stranded DNA (msDNA);
 - d) a post-msd sequence comprising a self-complementary region having sequence complementarity to the pre-msr sequence, wherein the self-complementary region has a length 1 to 50 nucleotides longer than a wild-type complementary region such that the engineered retron is capable of enhanced production of the msDNA; and
 - e) a *ret* gene encoding a reverse transcriptase.
2. The engineered retron of claim 1, further comprising a heterologous sequence of interest.
3. The engineered retron of claim 2, wherein the heterologous sequence is inserted into the *msr* gene or the *msd* gene.
4. The engineered retron of claim 1, wherein the single-stranded DNA (msDNA) encoded by the *msd* gene comprises a msd stem loop, and where the loop comprises a heterologous sequence of interest.
5. The engineered retron of claim 2, wherein the heterologous sequence encodes a donor polynucleotide comprising a 5' homology arm that hybridizes to a 5' target sequence and a 3' homology arm that hybridizes to a 3' target sequence flanking a nucleotide sequence comprising an intended edit to be integrated at a target locus by homology directed repair (HDR) or recombineering.
6. The engineered retron of claim 2, wherein the heterologous sequence comprises a CRISPR protospacer DNA sequence.
7. The engineered retron of claim 6, wherein the CRISPR protospacer DNA sequence comprises a modified AAG protospacer adjacent motif (PAM).

8. The engineered retron of claim 1, further comprising a barcode sequence.
9. The engineered retron of claim 8, wherein the barcode sequence is located in a hairpin loop of the msDNA.
10. The engineered retron of claim 4, wherein the msd stem is at least 14 nucleotides (base pairs) in length.
11. The engineered retron of claim 4, wherein the msd stem can comprise one or more mismatched nucleotides.
12. The engineered retron of claim 4, wherein the msd stem has less than five or six contiguous mismatched nucleotides.
13. The engineered retron of claim 4, wherein the msd stem does not have any mismatches or insertions in sequences flanking the msd stem base.
14. The engineered retron of claim 4, wherein any msd stem mismatches or sequence alterations relative to the wild type msd sequence are within the middle of the msd stem.
15. The engineered retron of claim 1, wherein the *msr* gene and the *msd* gene are provided in a trans arrangement or a cis arrangement.
16. The engineered retron of claim 1, wherein the *ret* gene is provided in a trans arrangement with respect to the *msr* gene and the *msd* gene.
17. The engineered retron of claim 1, wherein the *msr* gene, *msd* gene, and *ret* gene are a modified bacterial retron *msr* gene, *msd* gene, and *ret* gene.

18. The engineered retron of claim 1, wherein the *msr* gene, *msd* gene, and *ret* gene are independently a modified myxobacteria retron, a modified *Escherichia coli* retron, a modified *Salmonella enterica* retron, or a modified *Vibrio cholerae* retron.

19. The engineered retron of claim 18, wherein the modified *Escherichia coli* retron is a modified EC83 or a modified EC86.

20. A vector system comprising one or more vectors comprising the engineered retron of claim 1.

21. The vector system of claim 20, wherein the *msr* gene and the *msd* gene are provided by the same vector or different vectors.

22. The vector system of claim 20, wherein the *msr* gene, the *msd* gene, and the *ret* gene are provided by the same vector.

23. The vector system of claim 22, wherein the same vector comprises a promoter operably linked to the *msr* gene and the *msd* gene.

24. The vector system of claim 23, wherein the promoter is further operably linked to the *ret* gene.

25. The vector system of claim 23, further comprising a second promoter operably linked to the *ret* gene.

26. The vector system of claim 20, wherein the *msr* gene, the *msd* gene, and the *ret* gene are provided by different vectors.

27. The vector system of claim 20, wherein the one or more vectors are viral vectors or nonviral vectors.

28. The vector system of claim 27, wherein the nonviral vectors are plasmids.
29. The vector system of claim 20, wherein the engineered retron comprises a donor polynucleotide comprising a 5' homology arm that hybridizes to a 5' target sequence and a 3' homology arm that hybridizes to a 3' target sequence flanking a nucleotide sequence comprising an intended edit to be integrated at a target locus by homology directed repair (HDR) or recombineering.
30. The vector system of claim 29, further comprising a vector encoding an RNA-guided nuclease.
31. The vector system of claim 30, wherein the RNA-guided nuclease is a Cas nuclease or an engineered RNA-guided FokI-nuclease.
32. The vector system of claim 31, wherein the Cas nuclease is Cas9 or Cpf1.
33. The vector system of claim 20, wherein the engineered retron comprises a CRISPR protospacer DNA sequence.
34. The vector system of claim 33, further comprising a vector encoding a Cas1 and/or Cas2 protein.
35. The vector system of claim 34, further comprising a vector comprising a CRISPR array sequence.
36. The vector system of claim 20, further comprising a vector encoding bacteriophage homologous recombination proteins.
37. The vector system of claim 36, wherein the vector encoding the bacteriophage homologous recombination proteins is a replication defective λ prophage comprising the *exo*, *bet*, and *gam* genes.

38. An isolated host cell comprising the engineered retron of claim 1 or the vector system of any of claim 20.

39. The host cell of claim 38, wherein the host cell is a prokaryotic, archeon, or eukaryotic host cell.

40. The host cell of claim 39, wherein the eukaryotic host cell is a mammalian host cell.

41. The host cell of claim 40, wherein the mammalian host cell is a human host cell.

42. The host cell of claim 38, wherein the host cell is an artificial cell or genetically modified cell.

43. A kit comprising the engineered retron of claim 1, the vector system of claim 20, or the host cell of claim 38.

44. The kit of claim 43, further comprising instructions for genetically modifying a cell with the engineered retron.

45. A method of genetically modifying a cell comprising:

- a) transfecting a cell with the engineered retron of claim 5;
- b) introducing an RNA-guided nuclease and guide RNA into the cell, wherein the RNA-guided nuclease forms a complex with the guide RNA, said guide RNAs directing the complex to the genomic target locus, wherein the RNA-guided nuclease creates a double-stranded break in the genomic DNA at the genomic target locus, and the donor polynucleotide generated by the engineered retron is integrated at the genomic target locus recognized by its 5' homology arm and 3' homology arm by homology directed repair (HDR) to produce a genetically modified cell.

46. The method of claim 45, wherein the RNA-guided nuclease is a Cas nuclease or an engineered RNA-guided FokI-nuclease.
47. The method of claim 45, wherein the Cas nuclease is Cas9 or Cpf1.
48. The method of claim 45, wherein the RNA-guided nuclease is provided by a vector or a recombinant polynucleotide integrated into the genome of the cell.
49. The method of claim 45, wherein the engineered retron is provided by a vector.
50. The method of claim 45, wherein the donor polynucleotide is used to create a gene replacement, gene knockout, deletion, insertion, inversion, or point mutation.
51. A method of genetically modifying a cell by recombineering, the method comprising:
- a) transfecting the cell with the engineered retron of claim 5; and
 - b) introducing bacteriophage recombination proteins into the cell, wherein the bacteriophage recombination proteins mediate homologous recombination at a target locus such that the donor polynucleotide generated by the engineered retron is integrated at the target locus recognized by its 5' homology arm and 3' homology arm to produce a genetically modified cell.
52. The method of claim 51, wherein the donor polynucleotide is used to modify a plasmid, bacterial artificial chromosome (BAC), or a bacterial chromosome in the bacterial cell by recombineering.
53. The method of claim 51, wherein the donor polynucleotide can create a gene replacement, gene knockout, deletion, insertion, inversion, or point mutation.

54. The method of claim 51, wherein said introducing bacteriophage recombination proteins into the cell comprises insertion of a replication-defective λ prophage into the bacterial genome.

55. The method of claim 54, wherein the bacteriophage comprises *exo*, *bet*, and *gam* genes,

56. A method of barcoding a cell comprising transfecting a cell with the engineered retron of claim 8.

57. A method of producing an *in vivo* molecular recording system comprising:

- a) introducing a Cas1 protein or a Cas2 protein of a CRISPR adaptation system into a host cell;
- b) introducing a CRISPR array nucleic acid sequence comprising a leader sequence and at least one repeat sequence into the host cell, wherein the CRISPR array nucleic acid sequence is integrated into genomic DNA or a vector in the host cell; and
- c) introducing a plurality of engineered retrons according to claim 10 or 11 into the host cell, wherein each retron comprises a different protospacer DNA sequence that can be processed and inserted into the CRISPR array nucleic acid sequence.

58. The method of claim 57, wherein the Cas1 protein or the Cas2 protein are provided by a vector.

59. The method of claim 57, wherein the engineered retron is provided by a vector.

60. The method of claims 57, wherein the plurality of engineered retrons comprises at least three different protospacer DNA sequences.

61. An engineered cell comprising an *in vivo* molecular recording system comprising:
- a) a Cas1 protein or a Cas2 protein of a CRISPR adaptation system;
 - b) a CRISPR array nucleic acid sequence comprising a leader sequence and at least one repeat sequence into the host cell, wherein the CRISPR array nucleic acid sequence is integrated into genomic DNA or a vector in the engineered cell; and
 - c) a plurality of engineered retrons according to claim 6, wherein each retron comprises a different protospacer DNA sequence that can be processed and inserted into the CRISPR array nucleic acid sequence.
62. The engineered cell of claim 61, wherein the Cas1 protein or the Cas2 protein are provided by a vector.
63. The engineered cell of claim 61, wherein the engineered retron is provided by a vector.
64. The engineered cell of claim 61, wherein the plurality of engineered retrons comprises at least three different protospacer DNA sequences.
65. A kit comprising the engineered cell of claim 61 and instructions for *in vivo* molecular recording.
66. A method of producing recombinant msDNA comprising:
- a) transfecting a host cell with the engineered retron of claim 1 or the vector system of claim 20; and
 - b) culturing the host cell under suitable conditions, wherein the msDNA is produced.