CLAIMS

1. A~~n isolated~~ fusion polypeptide comprising (A) a~~n~~ first amino acid sequence having:

a) at least 80% sequence identity to any one of SEQ ID NOs: 1, 2, 4, 5, and 7-15;

b) at least 81% sequence identity to SEQ ID NO: 3 or 16; or

c) at least 82% sequence identity to SEQ ID NO: 6;

wherein said first amino acid sequence encodes a polypeptide that has uracil stabilizing activity and (B) ~~wherein said polypeptide further comprises~~ a ~~heterologous~~ second amino acid sequence that is heterologous to the first amino acid sequence.

2. The ~~isolated~~ fusion polypeptide of claim 1, wherein the ~~polypeptide has~~first amino acid sequence comprises the sequence of any one of SEQ ID NOs: 33-39.

~~3. A pharmaceutical composition comprising a non-naturally occurring pharmaceutically acceptable carrier and a polypeptide comprising an amino acid sequence having:~~

~~a) at least 80% sequence identity to any one of SEQ ID NOs: 1, 2, 4, 5, and 7-15;~~

~~b) at least 81% sequence identity to SEQ ID NO: 3 or 16; or~~

~~c) at least 82% sequence identity to SEQ ID NO: 6;~~

~~wherein said polypeptide has uracil stabilizing activity.~~

~~4. A pharmaceutical composition comprising a non-naturally occurring pharmaceutically acceptable carrier and a nucleic acid molecule comprising a polynucleotide encoding a polypeptide comprising an amino acid sequence having:~~

~~a) at least 80% sequence identity to any one of SEQ ID NOs: 1, 2, 4, 5, and 7-15;~~

~~b) at least 81% sequence identity to SEQ ID NO: 3 or 16; or~~

~~c) at least 82% sequence identity to SEQ ID NO: 6;~~

~~wherein said polypeptide has uracil stabilizing activity.~~

~~5. The pharmaceutical composition of claim 3 or 4, wherein the polypeptide has the sequence of any one of SEQ ID NOs: 33-39.~~

~~6. The pharmaceutical composition of any one of claims 3-5, further comprising a fluoropyrimidine.~~

~~7~~3. A nucleic acid molecule comprising a polynucleotide sequence encoding a polypeptide comprising an amino acid sequence having:

a) at least 80% sequence identity to any one of SEQ ID NOs: 1, 2, 4, 5, and 7-15;

b) at least 81% sequence identity to SEQ ID NO: 3 or 16; or

c) at least 82% sequence identity to SEQ ID NO: 6;

wherein said polypeptide has uracil stabilizing activity; and

wherein said nucleic acid molecule further comprises a heterologous promoter operably linked to said polynucleotide sequence.

4. The nucleic acid molecule of claim 3, wherein the polynucleotide sequence comprises a nucleotide sequence having at least 80% sequence identity to the nucleotide sequence set forth as SEQ ID NO: 50.

~~8. The nucleic acid molecule of claim 7, wherein the polypeptide has the sequence of any one of SEQ ID NOs: 33-39.~~

~~9. A composition comprising a fluoropyrimidine and a polypeptide comprising an amino acid sequence having:~~

~~a) at least 80% sequence identity to any one of SEQ ID NOs: 1, 2, 4, 5, and 7-15;~~

~~b) at least 81% sequence identity to SEQ ID NO: 3 or 16; or~~

~~c) at least 82% sequence identity to SEQ ID NO: 6;~~

~~wherein said polypeptide has uracil stabilizing activity.~~

~~10. A composition comprising a fluoropyrimidine and a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence having:~~

~~a) at least 80% sequence identity to any one of SEQ ID NOs: 1, 2, 4, 5, and 7-15;~~

~~b) at least 81% sequence identity to SEQ ID NO: 3 or 16; or~~

~~c) at least 82% sequence identity to SEQ ID NO: 6;~~

~~wherein said polypeptide has uracil stabilizing activity.~~

~~11. The composition of claim 9 or 10, wherein the polypeptide has the sequence of any one of SEQ ID NOs: 33-39.~~

~~5~~12. A fusion protein comprising: (i) a DNA-binding polypeptide; (ii) a deaminase; and (iii) at least one uracil stabilizing polypeptide (USP) having at least 80% sequence identity to any one of SEQ ID NOs: 1-16.

~~1~~36. The fusion protein of claim 5~~1~~2, wherein the USP has the sequence of any one of SEQ ID NOs: 33-39.

~~14. The fusion protein of claim 12 or 13, wherein the deaminase is a cytidine deaminase.~~

~~15. The fusion protein of claim 14, wherein the cytidine deaminase is an activation-induced cytidine deaminase (AID) or a member of the apolipoprotein B mRNA-editing complex (APOBEC) family of deaminases.~~

~~16~~7. The fusion protein of claim ~~1~~5 or 6, wherein the ~~cytidine~~ deaminase comprises an amino acid sequence having at least 80% sequence identity to any one of SEQ ID NOs: 47, 48 and 76-94.

~~17. The fusion protein of any one of claims 12-16, wherein the DNA-binding polypeptide is a meganuclease, zinc finger fusion protein, or a TALEN.~~

~~18. The fusion protein of any one of claims 12-16, wherein the DNA-binding polypeptide is an RNA-guided, DNA-binding polypeptide.~~

~~19~~8. The fusion protein of any one of claims ~~1~~85-7, wherein the ~~RNA-guided,~~ DNA-binding polypeptide is an RNA-guided nuclease polypeptide (RGN).

~~20. The fusion protein of claim 19, wherein the RGN is a Type II CRISPR-Cas polypeptide.~~

~~21. The fusion protein of claim 19, wherein the RGN is a Type V CRISPR-Cas polypeptide.~~

~~22~~9. The fusion protein of claim ~~19~~8, wherein the RGN comprises an amino acid sequence having at least 80% sequence identity to any one of SEQ ID NOs: 40 and 95-142.

~~23~~10. The fusion protein of ~~any one of claims 19-22~~claim 8 or 9, wherein the RGN is an RGN nickase.

~~24. The fusion protein of any one of claims 19-23, wherein the fusion protein comprises an RGN, a cytidine deaminase, and a USP.~~

~~25. The fusion protein of claim 24, wherein said RGN has at least 80% sequence identity to any one of SEQ ID NOs: 40, 41, and 95-142, said cytidine deaminase has at least 80% sequence identity to any one of SEQ ID NOs: 47, 48, and 76-94, and said USP has at least 80% sequence identity to any one of SEQ ID NOs: 1-16.~~

~~26~~11. The fusion protein of any of claims ~~12-25~~5-10, wherein the fusion protein further comprises at least one nuclear localization signal (NLS).

12. The fusion protein of claim 10 or 11, wherein said RGN nickase has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 41, said deaminase has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 47, and said USP has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 1.

13. The fusion protein of claim 10 or 11, wherein said RGN nickase has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 41, said deaminase has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 77, and said USP has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 1.

~~27~~14. A nucleic acid molecule comprising a polynucleotide sequence encoding a fusion protein comprising: (i) a DNA-binding polypeptide; (ii) a deaminase; and (iii) at least one uracil stabilizing polypeptide (USP), wherein the USP is encoded by a nucleotide sequence that:

a) has at least 80% sequence identity to any one of SEQ ID NOs: 17-32,

b) is set forth in any one of SEQ ID NOs: 17-32,

c) encodes an amino acid sequence at least 80% identical to SEQ ID NOs: 1-16 and further possesses the sequence of any one of SEQ ID NOs: 33-39,

d) encodes an amino acid sequence at least 80% identical to an amino acid sequence set forth in any one of SEQ ID NOs: 1-16, or

e) encodes an amino acid sequence set forth in any one of SEQ ID NOs: 1-16.

15. The nucleic acid molecule of claim 14, wherein the polynucleotide sequence comprises a nucleotide sequence having at least 80% sequence identity to the nucleotide sequence set forth as SEQ ID NO: 50.

~~28. The nucleic acid molecule of claim 27, wherein the deaminase is a cytidine deaminase.~~

~~29. The nucleic acid molecule of claim 28, wherein the cytidine deaminase is an activation-induced cytidine deaminase (AID) or a member of the apolipoprotein B mRNA-editing complex (APOBEC) family of deaminases.~~

~~30~~16. The nucleic acid molecule of claim ~~29~~14, wherein the ~~cytidine~~ deaminase comprises an amino acid sequence having at least 80% sequence identity to any one of SEQ ID NOs: 47, 48 and 76-94.

~~31. The nucleic acid molecule of any one of claims 27-30, wherein the DNA-binding polypeptide is a meganuclease, zinc finger fusion protein, or a TALEN.~~

~~32. The nucleic acid molecule of any one of claims 27-30, wherein the DNA-binding polypeptide is an RNA-guided, DNA-binding polypeptide.~~

~~33~~17. The nucleic acid molecule of claim ~~32~~14, wherein the ~~RNA-guided,~~ DNA-binding polypeptide is an RNA-guided nuclease polypeptide (RGN).

~~34. The nucleic acid molecule of claim 33, wherein the RGN is a Type II CRISPR-Cas polypeptide.~~

~~35. The nucleic acid molecule of claim 33, wherein the RGN is a Type V CRISPR-Cas polypeptide.~~

~~36~~18. The nucleic acid molecule of claim ~~33~~17, wherein the RGN comprises an amino acid sequence having at least 80% sequence identity to any one of SEQ ID NOs: 40 and 95-142.

~~37~~19. The nucleic acid molecule of ~~any one of claims 33-36~~claim 17 or 18, wherein the RGN is an RGN nickase.

~~38. The nucleic acid molecule of any one of claims 33-36, wherein the fusion protein comprises an RGN, a cytidine deaminase, and a USP.~~

~~39. The nucleic acid molecule of claim 38, wherein said RGN has at least 80% sequence identity to any one of SEQ ID NOs: 40, 41, and 95-142, said cytidine deaminase has at least 80% sequence identity to any one of SEQ ID NOs: 47, 48, and 76-94, and said USP has at least 80% sequence identity to any one of SEQ ID NOs: 1-16.~~

~~40~~20. The nucleic acid molecule of any of claims ~~27-39~~14-19, wherein the polynucleotide sequence encoding the fusion protein is operably linked at its 5' end to a heterologous promoter.

~~41. The nucleic acid molecule of any of claims 27-39, wherein the polynucleotide encoding the fusion protein is operably linked at its 3' end to a heterologous terminator.~~

~~42. The nucleic acid molecule of any of claims 29-41, wherein the fusion protein comprises one or more nuclear localization signals.~~

~~43. The nucleic acid molecule of any of claims 27-42, wherein the fusion protein is codon optimized for expression in a eukaryotic cell.~~

~~44. The nucleic acid molecule of any of claims 27-43, wherein the fusion protein is codon optimized for expression in a prokaryotic cell.~~

~~45~~21. A vector comprising the nucleic acid molecule of any one of claims 3, 4, and 14-20~~27-44~~.

~~46~~22. A vector comprising the nucleic acid molecule of any one of claims 17-20~~33-39~~, further comprising at least one nucleotide sequence encoding a guide RNA (gRNA) capable of hybridizing to a target sequence.

~~47. The vector of claim 46, wherein the gRNA is a single guide RNA.~~

~~48. The vector of claim 46, wherein the gRNA is a dual guide RNA.~~

~~49~~23. A cell comprising the fusion protein of any one of claims 5-13, the nucleic acid molecule of any one of claims 3, 4, and 14-20, or the vector of claim 21 or 22~~12-26~~.

~~50~~24. A cell comprising the fusion protein of any one of claims 8-13~~18-25~~, wherein the cell further comprises a guide RNA.

~~51. A cell comprising the nucleic acid molecule of any of claims 27-44.~~

~~52. A cell comprising the vector of any of claims 45 through 48.~~

~~53. The cell of any one of claims 49-52, wherein the cell is a prokaryotic cell.~~

~~54. The cell of any one of claims 49-52, wherein the cell is a eukaryotic cell.~~

~~55. The cell of claim 54, wherein the cell is an insect, avian, or mammalian cell.~~

~~56. The cell of claim 54, wherein the cell is a plant or fungal cell.~~

~~57. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the nucleic acid molecule of any one of claims 7, 8, 27-44, the composition of any one of claims 9-11, the~~

~~fusion protein of any one of claims 12-26, the vector of any one of claims 45-48, or the cell of any one of claims 49-55.~~

~~58. A method for making a fusion protein comprising culturing the cell of any one of claims 49-56 under conditions in which the fusion protein is expressed.~~

~~59. A method for making a fusion protein comprising introducing into a cell the nucleic acid molecule of any of claims 27-44 or a vector of any one of claims 45-48 and culturing the cell under conditions in which the fusion protein is expressed.~~

~~60. The method of claim 58 or 59, further comprising purifying said fusion protein.~~

~~61. A method for making an RGN fusion ribonucleoprotein complex, comprising introducing into a cell the nucleic acid molecule of any one of claims 33-39 and a nucleic acid molecule comprising an expression cassette encoding for a guide RNA, or the vector of any of claims 46-48, and culturing the cell under conditions in which the fusion protein and the gRNA are expressed and form an RGN fusion ribonucleoprotein complex.~~

~~62. The method of claim 61, further comprising purifying said RGN fusion ribonucleoprotein complex.~~

~~63~~25. A system for modifying a target DNA molecule comprising a target DNA sequence, said system comprising:

a) ~~a~~ the fusion protein ~~comprising an RNA-guided nuclease polypeptide (RGN), a cytidine deaminase, and at least one uracil stabilizing polypeptide (USP), wherein the USP is at least 80% identical to any one of SEQ ID NOs: 1-16~~of any one of claims 8-13, or a nucleotide sequence encoding said fusion protein; and

b) one or more guide RNAs capable of hybridizing to said target DNA sequence or one or more nucleotide sequences encoding the one or more guide RNAs (gRNAs);

wherein said nucleotide sequences encoding the one or more guide RNAs and encoding the fusion protein are each operably linked to a promoter heterologous to said nucleotide sequence;

and

wherein the one or more guide RNAs are capable of forming a complex with the fusion protein in order to direct said fusion protein to bind to said target DNA sequence and modify the target DNA molecule.

~~64. The system of claim 63, wherein the target DNA sequence is located adjacent to a protospacer adjacent motif (PAM) that is recognized by the RGN.~~

~~65~~26. The system of claim ~~63 or 64~~25, wherein the target DNA molecule is within a cell.

~~66. The system of claim 65, wherein the cell is a eukaryotic cell.~~

~~67. The system of claim 66, wherein the eukaryotic cell is a plant cell.~~

~~68. The system of claim 66, wherein the eukaryotic cell is a mammalian cell.~~

~~69. The system of claim 66, wherein the eukaryotic cell is an insect cell.~~

~~70. The system of claim 65, wherein the cell is a prokaryotic cell.~~

~~71. The system of any one of claims 63-70, wherein the RGN of the fusion protein is a Type II CRISPR-Cas polypeptide.~~

~~72. The system of any one of claims 63-70, wherein the RGN of the fusion protein is a Type V CRISPR-Cas polypeptide.~~

~~73. The system of any one of claims 63-70, wherein the RGN of the fusion protein is at least 80% identical to any one of SEQ ID NOs: 40 and 95-142.~~

~~74. The system of any one of claims 63-73, wherein the RGN of the fusion protein is an RGN nickase.~~

~~75. The system of any of claims 63-74, wherein the cytidine deaminase is at least 80% identical to any one of SEQ ID NOs: 47, 48 and 76-94.~~

~~76. The system of any of claims 63-75, wherein the USP comprises the sequence of any one of SEQ ID NOs: 33-39.~~

~~77. The system of any one of claims 63-76, wherein the RGN has at least 80% sequence identity to any one of SEQ ID NOs: 40, 41, and 95-142, the cytidine deaminase has at least 80% sequence identity to any one of SEQ ID NOs: 47, 48, and 76-94, and the USP has at least 80% sequence identity to any one of SEQ ID NOs: 1-16.~~

~~78. The system of any of claims 63-77, wherein the fusion protein comprises one or more nuclear localization signals.~~

~~79. The system of any of claims 63-78, wherein the fusion protein is codon optimized for expression in a eukaryotic cell.~~

~~80~~27. The system of ~~any of claims 63-79~~claim 25 or 26, wherein nucleotide sequences encoding the one or more guide RNAs and the nucleotide sequence encoding ~~a~~ the fusion protein are located on one vector.

~~81~~28. A method for modifying a target DNA molecule comprising a target DNA sequence, said method comprising delivering a system according to any one of claims ~~63-80~~25-27 to said target DNA molecule or a cell comprising the target DNA molecule.

~~82. The method of claim 81, wherein said modified target DNA molecule comprises a C>T mutation of at least one nucleotide within the target DNA molecule.~~

~~83. The method of claim 81, wherein said modified target DNA molecule comprises a C>T mutation of at least one nucleotide within the target DNA sequence.~~

~~84~~29. A method for modifying a target DNA molecule comprising a target sequence comprising:

a) assembling an RGN-deaminase-USP ribonucleotide complex *in vitro* by combining:

i) one or more guide RNAs capable of hybridizing to the target DNA sequence; and

ii) ~~a~~ the fusion protein ~~comprising an RNA-guided nuclease polypeptide (RGN), a cytidine deaminase, and at least one uracil stabilizing polypeptide (USP), wherein the USP is at least 80% identical to any one of SEQ ID NOs: 1-16~~of any one of claims 8-13;

under conditions suitable for formation of the RGN-deaminase-USP ribonucleotide complex; and

b) contacting said target DNA molecule or a cell comprising said target DNA molecule with the *in vitro*-assembled RGN-deaminase-USP ribonucleotide complex;

wherein the one or more guide RNAs hybridize to the target DNA sequence, thereby directing said fusion protein to bind to said target DNA sequence and modification of the target DNA molecule occurs.

~~85. The method of claim 84, wherein said modified target DNA molecule comprises a C>T mutation of at least one nucleotide within the target DNA molecule.~~

~~86~~30. The method of claim ~~84~~29, wherein said modified target DNA molecule comprises a C>T mutation of at least one nucleotide within the target DNA sequence.

~~87. The method of any one of claims 84-86, wherein the RGN of the fusion protein is a Type II CRISPR-Cas polypeptide.~~

~~88. The method of any of claims 84-86, wherein the RGN of the fusion protein is a Type V CRISPR-Cas polypeptide.~~

~~89. The method of any of claims 84-86, wherein the RGN of the fusion protein is at least 80% identical to any one of SEQ ID NOs: 40 and 95-142.~~

~~90. The method of any of claims 84-89, wherein the RGN of the fusion protein is an RGN nickase.~~

~~91. The method of any of claims 84-90, wherein the cytidine deaminase is at least 80% identical to any one of SEQ ID NOs: 47, 48 and 76-94.~~

~~92. The method of any of claims 84-91, wherein the USP comprises the sequence of any one of SEQ ID NOs: 33-39.~~

~~93. The method of any of claims 84-92, wherein the RGN has at least 80% sequence identity to any one of SEQ ID NOs: 40, 41, and 95-142, the cytidine deaminase has at least 80% sequence identity to any one of SEQ ID NOs: 47, 48, and 76-94, and the USP has at least 80% sequence identity to any one of SEQ ID NOs: 1-16.~~

~~94. The method of any of claims 84-93, wherein the fusion protein comprises one or more nuclear localization signals.~~

~~95. The method of any of claims 84-94, wherein the fusion protein is codon optimized for expression in a eukaryotic cell.~~

~~96. The method of any of claims 84-95, wherein said target DNA sequence is located adjacent to a protospacer adjacent motif (PAM).~~

~~97~~31. The method of ~~any of claims 84-96~~claim 29 or 30, wherein the target DNA molecule is within a cell.

~~98. The method of claim 97, wherein the cell is a eukaryotic cell.~~

~~99. The method of claim 98, wherein the eukaryotic cell is a plant cell.~~

~~100. The method of claim 98, wherein the eukaryotic cell is a mammalian cell.~~

~~101. The method of claim 98, wherein the eukaryotic cell is an insect cell.~~

~~102. The method of claim 97, wherein the cell is a prokaryotic cell.~~

~~103~~32. The method of ~~any one of claims 97-102~~claim 31, further comprising selecting a cell comprising said modified DNA molecule.

~~104. A cell comprising a modified target DNA sequence according to the method of claim 103.~~

~~105. The cell of claim 104, wherein the cell is a eukaryotic cell.~~

~~106. The cell of claim 105, wherein the eukaryotic cell is a plant cell.~~

~~107. A plant comprising the cell of claim 106.~~

~~108. A seed comprising the cell of claim 106.~~

~~109. The cell of claim 105, wherein the eukaryotic cell is a mammalian cell.~~

~~110. The cell of claim 105, wherein the eukaryotic cell is an insect cell.~~

~~111. The cell of claim 104, wherein the cell is a prokaryotic cell.~~

~~112~~33. A method for producing a genetically modified cell with a correction in a causal mutation for a genetically inherited disease, the method comprising introducing into ~~the~~ a cell the system of any one of claims 25-27~~:~~.

~~a) a fusion protein comprising an RNA-guided nuclease polypeptide (RGN), a cytidine deaminase, and at least one uracil stabilizing polypeptide (USP), wherein the USP is at least 80% identical to any one of SEQ ID NOs: 1-16, or a polynucleotide encoding said fusion protein, wherein said polynucleotide encoding the fusion protein is operably linked to a promoter to enable expression of the fusion protein in the cell; and~~

~~b) one or more guide RNAs (gRNA) capable of hybridizing to a target DNA sequence, or a polynucleotide encoding said gRNA, wherein said polynucleotide encoding the gRNA is operably linked to a promoter to enable expression of the gRNA in the cell;~~

whereby the fusion protein and the one or more gRNAs of the system target to the genomic location of the causal mutation and modify the genomic sequence to remove the causal mutation.

~~113. The method of claim 112, wherein said RGN of the fusion protein is a nickase.~~

~~114. The method of claim 112 or 113, wherein the USP comprises the sequence of any one of SEQ ID NOs: 33-39.~~

~~115~~34. The method of ~~any of claims 112-114~~claim 33, wherein the genome modification comprises introducing a C>T mutation of at least one nucleotide within the target DNA sequence.

~~116. The method of any of claims 112-115, wherein the cell is an animal cell.~~

~~117. The method of claim 116, wherein the animal cell is a mammalian cell.~~

~~118. The method of claim 117, wherein the cell is derived from a dog, cat, mouse, rat, rabbit, horse, sheep, goat, cow, pig, or human.~~

~~119. The method of any of claims 112-118, wherein the correction of the causal mutation comprises introducing a stop codon.~~

~~120~~35. A composition comprising:

a) a fusion protein comprising: (i) a DNA-binding polypeptide; and (ii) a deaminase; or a nucleic acid molecule encoding the fusion protein; and

b) a uracil stabilizing polypeptide (USP) having at least 80% sequence identity to any one of SEQ ID NOs: 1-16; or a nucleic acid molecule encoding the USP.

~~121~~36. The composition of claim ~~120~~35, wherein the fusion protein further comprises a uracil stabilizing polypeptide (USP) having at least 80% sequence identity to any one of SEQ ID NOs: 1-16.

~~122. The composition of claim 120 or 121, wherein the DNA-binding polypeptide is a meganuclease, zinc finger fusion protein, or a TALEN.~~

~~123. The composition of claim 120 or 121, wherein the DNA-binding polypeptide is an RNA-guided, DNA-binding polypeptide.~~

~~124~~37. The composition of claim ~~123~~35 or 36, wherein the ~~RNA-guided,~~ DNA-binding polypeptide is an RNA-guided nuclease polypeptide (RGN).

~~125~~38. The composition of claim ~~124~~37, wherein the RGN is an RGN nickase.

39. The composition of any one of claims 35-38, wherein the deaminase comprises an amino acid sequence having at least 80% sequence identity to any one of SEQ ID NOs: 47, 48 and 76-94.

40. The composition of claim 38 or 39, wherein said RGN nickase has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 41, said deaminase has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 47, and said USP has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 1.

41. The composition of claim 38 or 39, wherein said RGN nickase has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 41, said deaminase has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 77, and said USP has an amino acid sequence having at least 80% sequence identity to the amino acid sequence set forth as SEQ ID NO: 1.

~~126. A vector comprising a nucleic acid molecule encoding a fusion protein and a nucleic acid molecule encoding a uracil stabilizing polypeptide (USP), wherein said fusion protein comprises a DNA-binding polypeptide and a deaminase, and wherein said USP has at least 80% sequence identity to any one of SEQ ID NOs: 1-16.~~

~~127. The vector of claim 126, wherein the fusion protein further comprises a uracil stabilizing polypeptide (USP) having at least 80% sequence identity to any one of SEQ ID NOs: 1-16.~~

~~128. The vector of claim 126 or 127, wherein the DNA-binding polypeptide is a meganuclease, zinc finger fusion protein, or a TALEN.~~

~~129. The vector of claim 126 or 127, wherein the DNA-binding polypeptide is an RNA-guided, DNA-binding polypeptide.~~

~~130. The vector of claim 129, wherein the RNA-guided, DNA-binding polypeptide is an RNA-guided nuclease polypeptide (RGN).~~

~~131. The vector of claim 130, wherein the RGN is an RGN nickase.~~

~~132. A cell comprising the vector of any one of claims 126-131.~~

~~133. A cell comprising:~~

~~a) a fusion protein comprising: (i) a DNA-binding polypeptide; and (ii) a deaminase; or a nucleic acid molecule encoding the fusion protein; and~~

~~b) a uracil stabilizing polypeptide (USP) having at least 80% sequence identity to any one of SEQ ID NOs: 1-16; or a nucleic acid molecule encoding the USP.~~

~~134. The cell of claim 133, wherein the fusion protein further comprises a uracil stabilizing polypeptide (USP) having at least 80% sequence identity to any one of SEQ ID NOs: 1-16.~~

~~135. The cell of claim 134, wherein the DNA-binding polypeptide is a meganuclease, zinc finger fusion protein, or a TALEN.~~

~~136. The cell of claim 134, wherein the DNA-binding polypeptide is an RNA-guided, DNA-binding polypeptide.~~

~~137. The cell of claim 136, wherein the RNA-guided, DNA-binding polypeptide is an RNA-guided nuclease polypeptide (RGN).~~

~~138. The cell of claim 137, wherein the RGN is an RGN nickase.~~