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(54) Title: MODIFIED GUIDE RNAS FOR GENE EDITING

(57) Abstract: This disclosure relates to modified guide RNAs having improved in vitro and in vivo activity in gene editing methods.

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MODIFIED GUIDE RNAS FOR GENE EDITING

[0001] This application claims the benefit of US Provisional Patent Application No. 62/682,838, filed June 8, 2018, and US Provisional Patent Application No. 62/682,820, filed June 8, 2018, each of which is incorporated herein by reference for all purposes.

[0002] This disclosure relates to the field of gene editing using CRISPR/Cas systems, a part of the prokaryotic immune system that recognizes and cuts exogenous genetic elements. The CRISPR/Cas system relies on a single nuclease, termed CRISPR-associated protein 9 (Cas9), which induces site-specific breaks in DNA. Cas9 is guided to specific DNA sequences by small RNA molecules termed guide RNA (gRNA). A complete guide RNA comprises tracrRNA (trRNA) and crisprRNA (crRNA). A crRNA comprising a guide region may also be referred to as a gRNA, with the understanding that to form a complete gRNA it should be or become associated covalently or noncovalently with a trRNA. The trRNA and crRNA may be contained within a single guide RNA (sgRNA) or in two separate RNA molecules of a dual guide RNA (dgRNA). Cas9 in combination with trRNA and crRNA or an sgRNA is termed the Cas9 ribonucleoprotein complex (RNP).

[0003] Oligonucleotides, and in particular RNA, are sometimes degraded in cells and in serum by non-enzymatic, endonuclease or exonuclease cleavage. Improved methods and compositions for preventing such degradation, improving stability of gRNAs and enhancing gene editing efficiency is desired, especially for therapeutic applications.

SUMMARY

[0004] In some embodiments, genome editing tools are provided comprising modified guide RNA (gRNA). The modifications of gRNAs described herein may improve the stability of the gRNA and the gRNA/Cas9 complex and improve the activity of Cas9 (e.g., SaCas9, SpyCas9, and equivalents) to cleave target DNA.

[0005] In some embodiments, modified crisprRNA (crRNA) and/or modified tracrRNA (trRNA) are provided. In some embodiments, the modified crRNA and/or modified trRNA comprise a dual guide RNA (dgRNA). In some embodiments, the modified crRNA and/or modified trRNA comprise a single guide RNA (sgRNA). The modifications of crRNA and/or trRNA described herein may improve the stability of the gRNA and the gRNA/Cas9 complex and improve the activity of Cas9 (e.g., SauCas9, SpyCas9, and equivalents) to cleave target DNA. In some embodiments, the crRNA portion of a dgRNA or an sgRNA is modified in the targeting domain.

[0006] In some embodiments, genome editing tools are provided comprising short-single guide RNA (short-sgRNA). In some embodiments, the short-sgRNA is modified. The short-sgRNAs described herein may improve the stability of the short-sgRNA and the short-sgRNA/Cas9 complex and improve the activity of Cas9 (e.g., SauCas9, SpyCas9, and equivalents) to cleave target DNA.

[0007] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, dgRNA, or crRNA) comprises a modification at one or more YA sites, e.g., as set forth in the embodiments below, Table 1, and in the Examples and associated Figures. For the avoidance of doubt, sgRNAs include but are not limited to short-sgRNAs. As discussed in the Examples section, it has been found that gRNAs can be susceptible to an RNase A-like degradation pattern, e.g., including cleavage at unmodified YA sites. It has further been found that YA site modifications can reduce or eliminate such cleavage and that many YA site modifications appear to be tolerated without adversely affecting the ability of the gRNA to direct cleavage by a nuclease such as Cas9. It has also been found that certain gRNA positions, including but not limited to YA sites, can be modified despite statements by others (*see* Yin et al., *Nature Biotechnol.* 35:1179-1187 (2017)) that they are contacted by Cas9 and should not be modified out of concern for loss of activity. Such modifications may further reduce undesirable gRNA degradation while not compromising activity.

[0008] The following embodiments are encompassed.

Embodiment 01 is a guide RNA (gRNA) which is a short-single guide RNA (short-sgRNA) comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides and wherein the short-sgRNA comprises a 5' end modification or a 3' end modification.

Embodiment 02 is the gRNA of embodiment 1, wherein the short-sgRNA comprises a 5' end modification.

Embodiment 03 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA comprises a 3' end modification.

Embodiment 04 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA comprises a 5' end modification and a 3' end modification.

Embodiment 05 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA comprises a 3' tail.

Embodiment 06 is the gRNA of embodiment 5, wherein the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

Embodiment 07 is the gRNA of embodiment 5, wherein the 3' tail comprises about 1-2, 1-3, 1-4, 1-5, 1-7, 1-10, at least 1-5, at least 1-3, at least 1-4, at least 1-5, at least 1-5, at least 1-7, or at least 1-10 nucleotides.

Embodiment 08 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA does not comprise a 3' tail.

Embodiment 09 is the gRNA of any one of the preceding embodiments, comprising a modification in the hairpin region.

Embodiment 10 is the gRNA of any one of the preceding embodiments, comprising a 3' end modification, and a modification in the hairpin region.

Embodiment 11 is the gRNA of any one of the preceding embodiments, comprising a 3' end modification, a modification in the hairpin region, and a 5' end modification.

Embodiment 12 is the gRNA of any one of the preceding embodiments, comprising a 5' end modification, and a modification in the hairpin region.

Embodiment 13 is the gRNA of any one of the preceding embodiments, wherein the at least 5-10 lacking nucleotides are consecutive.

Embodiment 14 is the gRNA of any one of the preceding embodiments, wherein the at least 5-10 lacking nucleotides:

i. are within hairpin 1;
ii. are within hairpin 1 and the "N" between hairpin 1 and hairpin 2;
iii. are within hairpin 1 and the two nucleotides immediately 3' of hairpin 1;
iv. include at least a portion of hairpin 1;
v. are within hairpin 2;
vi. include at least a portion of hairpin 2;
vii. are within hairpin 1 and hairpin 2;
viii. include at least a portion of hairpin 1 and include the "N" between hairpin 1 and hairpin 2;
ix. include at least a portion of hairpin 2 and include the "N" between hairpin 1 and hairpin 2;
x. include at least a portion of hairpin 1, include the "N" between hairpin 1 and hairpin 2, and include at least a portion of hairpin 2;
xi. are within hairpin 1 or hairpin 2, optionally including the "N" between hairpin 1 and hairpin 2;
xii. are consecutive;

xiii. are consecutive and include the "N" between hairpin 1 and hairpin 2;

xiv. are consecutive and span at least a portion of hairpin 1 and a portion of hairpin 2;

xv. are consecutive and span at least a portion of hairpin 1 and the "N" between hairpin 1 and hairpin 2; or

xvi. are consecutive and span at least a portion of hairpin 1 and two nucleotides immediately 3' of hairpin 1.

Embodiment 15 is the gRNA of any one of the preceding embodiments, further comprising a guide region.

Embodiment 16 is the gRNA of any one of the preceding embodiments, wherein the 3' and/or 5' end modification comprises a protective end modification, such as a modified nucleotide selected from 2'-O-methyl (2'-OMe) modified nucleotide, 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, an inverted abasic modified nucleotide, or combinations thereof.

Embodiment 17 is the gRNA of any one of the preceding embodiments, wherein the modification in the hairpin region comprises a modified nucleotide selected from 2'-O-methyl (2'-OMe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, or combinations thereof.

Embodiment 18 is the gRNA of any one of the preceding embodiments, wherein the 3' and/or 5' end modification comprises or further comprises a 2'-O-methyl (2'-OMe) modified nucleotide.

Embodiment 19 is the gRNA of any one of the preceding embodiments, wherein the 3' and/or 5' end modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

Embodiment 20 is the gRNA of any one of the preceding embodiments, wherein the 3' and/or 5' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides.

Embodiment 21 is the gRNA of any one of the preceding embodiments, wherein the 3' and/or 5' end modification comprises or further comprises an inverted abasic modified nucleotide.

Embodiment 22 is the gRNA of any one of the preceding embodiments, wherein the modification in the hairpin region comprises or further comprises a 2'-O-methyl (2'-OMe) modified nucleotide.

Embodiment 23 is the gRNA of any one of the preceding embodiments, wherein the modification in the hairpin region comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

Embodiment 24 is the gRNA of any one of the preceding embodiments, wherein the 3' end modification comprises any of:

i. a modification of any one or more of the last 7, 6, 5, 4, 3, 2, or 1 nucleotides;
ii. one modified nucleotide;
iii. two modified nucleotides;
iv. three modified nucleotides;
v. four modified nucleotides;
vi. five modified nucleotides;
vii. six modified nucleotides; and
viii. seven modified nucleotides.

Embodiment 25 is the gRNA of any one of the preceding embodiments, wherein the at least 5-10 nucleotides comprise nucleotides 54-61 of SEQ ID NO:400, nucleotides 53-60 of SEQ ID NO:400; or nucleotides 54-58 of SEQ ID NO:400, optionally wherein the short-sgRNA comprises modifications at least H1-1 to H1-5 and H2-1 to H2-12.

Embodiment 26 is the gRNA of any one of the preceding embodiments, wherein the at least 5-10 nucleotides:

i. consist of 5-10 nucleotides;
ii. consist of 6-10 nucleotides;
iii. consist of 5 nucleotides;
iv. consist of 6 nucleotides;
v. consist of 7 nucleotides;
vi. consist of 8 nucleotides;
vii. consist of 9 nucleotides;
viii. consist of 10 nucleotides;
ix. consist of 5-10 consecutive nucleotides;
x. consist of 6-10 consecutive nucleotides;
xi. consist of 5 consecutive nucleotides;
xii. consist of 6 consecutive nucleotides;
xiii. consist of 7 consecutive nucleotides;

xiv. consist of 8 consecutive nucleotides;

xv. consist of 9 consecutive nucleotides; or

xvi. consist of 10 consecutive nucleotides.

Embodiment 27 is the gRNA of any one of the preceding embodiments, wherein the 3' end modification comprises one or more of:

i. a phosphorothioate (PS) linkage between nucleotides;

ii. a 2'-OMe modified nucleotide;

iii. a 2'-O-moe modified nucleotide;

iv. a 2'-F modified nucleotide;

v. an inverted abasic modified nucleotide; and

vi. a combination of one or more of (i.) - (v.).

Embodiment 28 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA comprises a 3' tail comprising one or more of:

i. a phosphorothioate (PS) linkage between nucleotides;

ii. a 2'-OMe modified nucleotide;

iii. a 2'-O-moe modified nucleotide;

iv. a 2'-F modified nucleotide;

v. an inverted abasic modified nucleotide; and

vi. a combination of one or more of (i.) - (v.).

Embodiment 29 is the gRNA any one of the preceding embodiments, wherein the short-sgRNA comprises one or more of:

i. 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 PS linkages between nucleotides;

ii. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, or 18 PS linkages between nucleotides;

iii. about 1-3, 1-5, 1-6, 1-7, 1-8, 1-9, or 1-10 PS linkages between nucleotides;

iv. about 1-3, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 1-12, 1-14, 1-16, 1-18, or 1-20 PS linkages between nucleotides; and

v. PS linkages between each nucleotide.

Embodiment 30 is the gRNA of any one of the preceding embodiments, wherein the 3' end modification comprises at least one PS linkage, and wherein one or more of:

i. there is one PS linkage, and the linkage is between the last and second to last nucleotide;

ii. there are two PS linkages between the last three nucleotides;

iii. there are PS linkages between any one or more of the last four nucleotides;

iv. there are PS linkages between any one or more of the last five nucleotides; and

v. there are PS linkages between any one or more of the last 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

Embodiment 31 is the gRNA of embodiment 31, wherein the 3' end modification further comprises at least one 2'-OMe, 2'-O-moe, inverted abasic, or 2'-F modified nucleotide.

Embodiment 32 is the gRNA of any one of the preceding embodiments, wherein the 3' end modification comprises:

i. a modification of one or more of the last 1-7 nucleotides, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof;

ii. a modification to the last nucleotide with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and an optional one or two PS linkages to the next nucleotide and/or the first nucleotide of the 3' tail;

iii. a modification to the last and/or second to last nucleotide with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages;

iv. a modification to the last, second to last, and/or third to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages;

v. a modification to the last, second to last, third to last, and/or fourth to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages; or

vi. a modification to the last, second to last, third to last, fourth to last, and/or fifth to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

Embodiment 33 is the gRNA of any one of the preceding embodiments, wherein the sgRNA comprise a 3' tail, wherein the 3' tail comprises a modification of any one or more of the nucleotides present in the 3' tail.

Embodiment 34 is the gRNA of embodiment 33, wherein the 3' tail is fully modified.

Embodiment 35 is the gRNA of embodiment 33, wherein the at least 5-10 nucleotides comprise nucleotides 54-61 of SEQ ID NO:400, nucleotides 53-60 of SEQ ID NO:400; or nucleotides 54-58 of SEQ ID NO:400, optionally wherein the short-sgRNA comprises modifications at least H1-1 to H1-5 and H2-1 to H2-12.

Embodiment 36 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA comprises any one or more of:

i. the 3' end modification as shown in any one of SEQ ID Nos: 1-54;

ii. (i) a 2'-OMe modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, (ii) three consecutive 2'O-moe modified nucleotides immediately 5' to the 2'-OMe modified nucleotide, and (iii) three consecutive PS linkages between the last three nucleotides;

iii. (i) five consecutive 2'-OMe modified nucleotides from the 3' end of the 3' terminus, and (ii) three PS linkages between the last three nucleotides;

iv. an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA;

v. (i) an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, and (ii) three consecutive 2'-OMe modified nucleotides at the last three nucleotides of the conserved region of an sgRNA or short-sgRNA;

vi. (i) 15 consecutive 2'-OMe modified nucleotides from the 3' end of the 3' terminus, (ii) five consecutive 2'-F modified nucleotides immediately 5' to the 2'-OMe modified nucleotides, and (iii) three PS linkages between the last three nucleotides;

vii. (i) alternating 2'-OMe modified nucleotides and 2'-F modified nucleotides at the last 20 nucleotides of the conserved region of an sgRNA or short-sgRNA, and (ii) three PS linkages between the last three nucleotides;

viii. (i) two or three consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides;

ix. one PS linkage between the last and next to last nucleotides; and

x. 15 or 20 consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

Embodiment 37 is the gRNA of any one of the preceding embodiments, wherein the 5' end modification comprises any one or more of:

i. a modification of any one or more of nucleotides 1-7 of the guide region;
ii. one modified nucleotide;
iii. two modified nucleotides;
iv. three modified nucleotides;
v. four modified nucleotides;
vi. five modified nucleotides;
vii. six modified nucleotides; and
viii. seven modified nucleotides.

Embodiment 38 is the gRNA of any one of the preceding embodiments, wherein the 5' end modification comprises a modification of between 1 and 7, between 1 and 5, between 1 and 4, between 1 and 3, or between 1 and 2 nucleotides.

Embodiment 39 is the gRNA of any one of the preceding embodiments, wherein the at least 5-10 nucleotides:

i. comprise nucleotides 54-61 of SEQ ID NO:400;
ii. comprise nucleotides 53-60 of SEQ ID NO:400;
iii. comprise nucleotides 54-58 of SEQ ID NO:400.
iv. consist of nucleotides 54-61 of SEQ ID NO:400;
v. consist of nucleotides 53-60 of SEQ ID NO:400; or
vi. consist of nucleotides 54-58 of SEQ ID NO:400.

Embodiment 40 is the gRNA of any one of the preceding embodiments, wherein the 5' end modification comprises one or more of:

i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-OMe modified nucleotide;
iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide;
vi. a deoxyribonucleotide;
vii. an inosine; and
viii. combinations of one or more of (i.) – (vii.).

Embodiment 41 is the gRNA any one of the preceding embodiments, wherein the 5' end modification comprises:

i. 1, 2, 3, 4, 5, 6, and/or 7 PS linkages between nucleotides; or

ii. about 1-2, 1-3, 1-4, 1-5, 1-6, or 1-7 PS linkages between nucleotides.

Embodiment 42 is the gRNA of any one of the preceding embodiments, wherein the 5' end modification comprises at least one PS linkage, and wherein:

i. there is one PS linkage, and the linkage is between nucleotides 1 and 2 of the guide region;

ii. there are two PS linkages, and the linkages are between nucleotides 1 and 2, and 2 and 3 of the guide region;

iii. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

iv. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, and 4 and 5 of the guide region;

v. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region;

vi. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, 5 and 6, and 6 and 7 of the guide region; or

vii. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, 5 and 6, 6 and 7, and 7 and 8 of the guide region.

Embodiment 43 is the gRNA of embodiment 42, wherein the 5' end modification further comprises at least one 2'-OMe, 2'-O-moe, inverted abasic, or 2'-F modified nucleotide.

Embodiment 44 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA comprises:

i. a modification of one or more of nucleotides 1-7 of the variable region, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-OMe, 2'-O-moe, 2'-F, 2'-H (a deoxyribonucleotide), an inosine, and/or combinations thereof;

ii. a modification to the first nucleotide of the guide region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and an optional PS linkage to the next nucleotide;

iii. a modification to the first and/or second nucleotide of the variable region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and optionally one or more PS linkages;

iv. a modification to the first, second, and/or third nucleotides of the variable region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and optionally one or more PS linkages;

v. a modification to the first, second, third, and/or fourth nucleotides of the variable region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and optionally one or more PS linkages; or

vi. a modification to the first, second, third, fourth, and/or fifth nucleotides of the variable region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and optionally one or more PS linkages.

Embodiment 45 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA comprises any one or more of:

i. a 5' end modification as shown in any one of SEQ ID Nos: 1-54;

ii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region;

iii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

iv. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region;

v. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region;

vi. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region;

vii. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

viii. an inverted abasic modified nucleotide at nucleotide 1 of the guide region;

ix. an inverted abasic modified nucleotide at nucleotide 1 of the guide region and 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region; and

x. an inverted abasic modified nucleotide at nucleotide 1 of the guide region, 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the

guide region, and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the variable region.

Embodiment 46 is the gRNA of any one of the preceding embodiments, wherein the upper stem region comprises at least one modification.

Embodiment 47 is the gRNA of any one of the preceding embodiments, wherein the upper stem modification comprises any one or more of:

i. a modification to any one or more of US1-US12 in the upper stem region;

ii. a modification of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all 12 nucleotides in the upper stem region; and

iii. a modification of about 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, or 1-12 nucleotides in the upper stem region.

Embodiment 48 is the gRNA of embodiment 47, wherein the upper stem modification comprises one or more of:

i. a 2'-OMe modified nucleotide;

ii. a 2'-O-moe modified nucleotide;

iii. a 2'-F modified nucleotide; and

iv. combinations of one or more of (i.) – (iii.).

Embodiment 49 is a guide RNA which is a short-sgRNA comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides and wherein the short-sgRNA comprises a 5' end modification and one or more modification in one or more of:

i. the upper stem region;

ii. the hairpin 1 region; and

iii. the hairpin 2 region,

wherein the 5' end modification comprises a 5' protective end modification, such as at least two phosphorothioate (PS) linkages within the first seven nucleotides.

Embodiment 50 is the gRNA of embodiment 49, wherein at least one modification comprises a 2'-O-methyl (2'-OMe) modified nucleotide.

Embodiment 51 is the gRNA of embodiment 49 or embodiment 50, wherein at least one modification comprises a 2'-fluoro (2'-F) modified nucleotide.

Embodiment 52 is the gRNA of any one of embodiments 49-51, wherein at least one modification comprises a phosphorothioate (PS) bond between nucleotides.

Embodiment 53 is the gRNA of any one of embodiments 49-52, wherein the short-sgRNA comprises one or more modifications in the upper stem region.

Embodiment 54 is the gRNA of embodiment 53, comprising modifications at any one of US1 to US12.

Embodiment 55 is the gRNA of any one of embodiments 49-54, wherein the short-sgRNA comprises one or more modifications in the hairpin 1 region.

Embodiment 56 is the gRNA of embodiment 55, wherein the short-sgRNA comprises a modification at H1-1.

Embodiment 57 is the gRNA of any one of embodiments 49-56, wherein the short-sgRNA comprises one or more modifications in the hairpin 2 region.

Embodiment 58 is the gRNA of embodiment 57, wherein the short-sgRNA comprises a modification at H2-1.

Embodiment 59 is the gRNA of any one of embodiments 49-58, wherein the short-sgRNA comprises modifications at H1-1 to H1-12.

Embodiment 60 is the gRNA of any one of embodiments 49-59, wherein the short-sgRNA comprises modifications at H2-1 to H2-15.

Embodiment 61 is the gRNA of any one of embodiments 49-60, wherein the short-sgRNA comprises one or more modifications in each of the upper stem region, the hairpin 1 region, and the hairpin 2 region.

Embodiment 62 is the gRNA of any one of embodiments 49-61, wherein the short-sgRNA comprises a modified nucleotide between hairpin 1 and hairpin 2 regions.

Embodiment 63 is the gRNA of any one of embodiments 49-62, further comprising a lower stem region comprising a modification.

Embodiment 64 is the gRNA of any one of embodiments 49-63, further comprising a 3' end modification.

Embodiment 65 is the gRNA of embodiment 64, wherein at least two of the last four nucleotides at the 3' end of the 3' terminus are modified.

Embodiment 66 is the gRNA of embodiment 64, wherein at least two of the last four nucleotides at the 3' end of the 3' terminus are modified with 2'-OMe, 2'-F, or 2'-O-moe.

Embodiment 67 is the gRNA of any one of embodiments 64-66, further comprising phosphorothioate (PS) bonds between one or more of the last four nucleotides at the 3' end of the 3' terminus.

Embodiment 68 is the gRNA of any one of embodiments 49-67, further comprising a bulge region comprising a modification.

Embodiment 69 is the gRNA of any one of embodiments 49-68, further comprising a nexus region comprising a modification.

Embodiment 70 is the gRNA of any one of embodiments 49-69, wherein at least the first three nucleotides at the 5' end of the variable region, and the last three nucleotides at the 3' end of the 3' terminus are modified.

Embodiment 71 is the gRNA of any one of embodiments 49-70, wherein the first four nucleotides at the 5' end of the variable region, and the last four nucleotides at the 3' end of the 3' terminus are linked with phosphorothioate (PS) bonds.

Embodiment 72 is the gRNA of any one of embodiments 70-71, wherein the end modifications comprise 2'-OMe.

Embodiment 73 is the gRNA of any one of embodiments 70-71, wherein the end modifications comprise 2'-F.

Embodiment 74 is the gRNA of any one of embodiments 49-73, wherein the first four nucleotides at the 5' end of the variable region and the last four nucleotides at the 3' end of the 3' terminus are linked with a PS bond, and wherein the first three nucleotides at the 5' end of the variable region and the last three nucleotides at the 3' end of the 3' terminus comprise 2'-OMe modifications.

Embodiment 75 is the gRNA of any one of embodiments 49-74, wherein the first four nucleotides at the 5' terminus and the last four nucleotides at the 3' terminus are linked with a PS bond, and wherein the first three nucleotides at the 5' terminus and the last three nucleotides at the 3' terminus comprise 2'-OMe, 2'-F, and/or 2'-O-moe modifications.

Embodiment 76 is the gRNA of any one of embodiments 49-75, wherein LS1, LS6, LS7, LS8, LS11, and/or LS12 are modified with 2'-OMe.

Embodiment 77 is the gRNA of any one of embodiments 49-76, wherein each of the nucleotides in the bulge region are modified with 2'-OMe.

Embodiment 78 is the gRNA of any one of embodiments 49-77, wherein at least 50% of the nucleotides in the bulge region are modified with 2'-OMe.

Embodiment 79 is the gRNA of any one of embodiments 49-78, wherein each of the nucleotides in the upper stem region are modified with 2'-OMe.

Embodiment 80 is the gRNA of any one of embodiments 49-79, wherein N16, N17, and/or N18 in the nexus region are modified with 2'-OMe.

Embodiment 81 is the gRNA of any one of embodiments 49-80, wherein N15, N16, N17, and/or N18 in the nexus region are modified.

Embodiment 82 is the gRNA of embodiment 80 or 81, wherein the modifications in the nexus region are selected from 2'-OMe and 2'F.

Embodiment 83 is the gRNA of any one of embodiments 80-82, wherein N16, N17, and N18 are linked with PS bonds.

Embodiment 84 is the gRNA of any one of embodiments 49-83, wherein each of the nucleotides remaining in the hairpin 1 region are modified with 2'-OMe.

Embodiment 85 is the gRNA of any one of embodiments 49-84, wherein each of the nucleotides in the hairpin 2 region are modified with 2'-OMe.

Embodiment 86 is a guide RNA which is a short-sgRNA comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides and wherein the short-sgRNA comprises a 5' end modification and a 3' end modification, wherein the short-sgRNA further comprises any one or more of:

i. at least one modification in the upper stem region; and

ii. a 3' tail.

Embodiment 87 is the gRNA of embodiment 86, wherein the upper stem modification comprises any one or more of:

i. a modification of each nucleotide (US1-US12) in the upper stem region;

ii. a modification to any one or more of US1-US12 in the upper stem region;

iii. a modification of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all 12 nucleotides in the upper stem region; and

iv. a modification of about 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, or 1-12 nucleotides in the upper stem region.

Embodiment 88 is the gRNA of any one of embodiments 86-87, wherein the 5' end modification comprises any one or more of:

i. a modification of any one or more of nucleotides 1-7 of the variable region;

ii. one modified nucleotide;

iii. two modified nucleotides;

iv. three modified nucleotides;

v. four modified nucleotides;

vi. five modified nucleotides;

vii. six modified nucleotides; and

viii. seven modified nucleotides.

Embodiment 89 is the gRNA of any one of embodiments 86-88, wherein the 5' end modification comprises any one or more of:

i. a 5' end modification as shown in any one of SEQ ID Nos: 1-54, 401-532, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, 3388-3430, or 3549-3552;

ii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the variable region;

iii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the variable region;

iv. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the variable region;

v. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the variable region;

vi. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the variable region;

vii. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the variable region;

viii. an inverted abasic modified nucleotide at nucleotide 1 of the variable region;

ix. an inverted abasic modified nucleotide at nucleotide 1 of the variable region and 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the variable region; and

x. an inverted abasic modified nucleotide at nucleotide 1 of the variable region, 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the variable region, and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the variable region.

Embodiment 90 is the gRNA of embodiment 89, comprising 2'-OMe modified nucleotides at at least nucleotides 1, 2, and 3, of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the variable region.

Embodiment 91 is the gRNA of embodiment 89, comprising 2'-OMe modified nucleotides at at least nucleotides 1, 2, 3, and 4 of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the variable region.

Embodiment 92 is the gRNA of any one of embodiments 86-91, comprising a 3' end modification comprising any one or more of:

i. a modification of any one or more of the last 7, 6, 5, 4, 3, 2, or 1 nucleotides;
ii. one modified nucleotide;
iii. two modified nucleotides;
iv. three modified nucleotides;
v. four modified nucleotides;
vi. five modified nucleotides;
vii. six modified nucleotides; and
viii. seven modified nucleotides.

Embodiment 93 is the gRNA of any one of embodiments 86-92, wherein the short-sgRNA comprises any one or more of:

i. a 3' end modification shown in any one of SEQ ID Nos: 1-54, 401-532, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, 3388-3430, or 3549-3552;
ii. (i) a 2'-OMe modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, (ii) three consecutive 2'O-moe modified nucleotides immediately 5' to the 2'-OMe modified nucleotide, and (iii) three consecutive PS linkages between the last three nucleotides;
iii. (i) five consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides;
iv. an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA;
v. (i) an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, and (ii) three

consecutive 2'-OMe modified nucleotides at the last three nucleotides of the conserved region of an sgRNA or short-sgRNA;

vi. (i) 15 consecutive 2'-OMe modified nucleotides, (ii) five consecutive 2'-F modified nucleotides immediately 5' to the 2'-OMe modified nucleotides, and (iii) three PS linkages between the last three nucleotides;

vii. (i) alternating 2'-OMe modified nucleotides and 2'-F modified nucleotides at the last 20 nucleotides of the conserved region of an sgRNA or short-sgRNA, and (ii) three PS linkages between the last three nucleotides;

viii. (i) two or three consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides;

ix. one PS linkage between the last and next to last nucleotides; and

x. 15 or 20 consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

Embodiment 94 is the gRNA of any one of embodiments 86-93, wherein the sgRNA comprise a 3' tail, wherein the 3' tail comprises a modification of any one or more of the nucleotides present in the 3' tail.

Embodiment 95 is the gRNA of embodiment 94, wherein the 3' tail is fully modified.

Embodiment 96 is the gRNA of embodiment 94 wherein the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, or 1-10 nucleotides, optionally where any one or more of these nucleotides are modified.

Embodiment 97 is a guide RNA which is a short-sgRNA comprising any of SEQ ID Nos: 1-54, 201-254, and 301-354, including the modifications of Table 1.

Embodiment 98 is a guide RNA which is a short-sgRNA comprising nucleic acids having at least 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% identity to the nucleic acids of any one of SEQ ID Nos: 1-54, 201-254, and 301-354, wherein the modification at each nucleotide of the short-sgRNA that corresponds to a nucleotide of the reference sequence identifier in Table 1, is identical to or equivalent to the modification shown in the reference sequence identifier in Table 1.

Embodiment 99 is the gRNA of any one of the preceding embodiments, comprising a YA modification at at least one guide region YA site.

Embodiment 100 is the gRNA of any one of the preceding embodiments, comprising a YA modification at at least one guide region YA site that is not a 5' end modification.

Embodiment 101 is the gRNA of any one of the preceding embodiments, comprising a YA modification at one or more guide region YA sites, wherein the guide region YA site is at or after nucleotide 8 from the 5' end of the 5' terminus.

Embodiment 102 is the gRNA of any one of the preceding embodiments comprising a YA modification at one or more guide region YA sites, wherein the short-sgRNA comprises one or more of:

a. a modification at one or more of H1-1 and H2-1;
b. a YA modification at 1, 2, 3, 4, or 5 guide region YA sites;
c. a YA modification at 1, 2, 3, 4, or 5 guide region YA sites, wherein the modification of at least one guide region YA site is different from any 5' end modification of the sgRNA;
d. a YA modification at one or more guide region YA sites, wherein the guide region YA site is at or after nucleotide 8 from the 5' end of the 5' terminus;
e. a YA modification at one or more guide region YA sites, wherein the guide region YA site is within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;
f. a YA modification at one or more guide region YA sites, wherein the guide region YA site is within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;
g. a YA modification at a guide region YA site other than a 5' end modification;
h. a YA modification at two or more guide region YA sites, wherein the guide region YA sites are at or after nucleotide 8 from the 5' end of the 5' terminus;
i. a YA modification at two or more guide region YA sites, wherein the two guide region YA sites are within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;
j. a YA modification at two or more guide region YA sites, wherein the guide region YA sites are within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;
k. a YA modification at two or more guide region YA sites other than a 5' end modification; and
l. a YA modification at two or more guide region YA sites, wherein the modifications of the guide region YA sites comprise a modification that at least one nucleotide located 5' of the guide region YA site does not comprise.

Embodiment 103 is the gRNA of any one of the preceding embodiments, comprising a YA modification wherein the modification comprises 2'-fluoro, 2'-H, 2'-OMe, ENA, UNA, inosine, or PS.

Embodiment 104 is the gRNA of any one of the preceding embodiments, comprising a YA modification wherein the modification alters the structure of the dinucleotide motif to reduce RNA endonuclease activity.

Embodiment 105 is the gRNA of any one of the preceding embodiments, comprising a YA modification wherein the modification interferes with recognition or cleavage of a YA site by an RNase and/or stabilizes an RNA structure.

Embodiment 106 is the gRNA of any one of the preceding embodiments, comprising a YA modification wherein the modification comprises one or more of:

a. a ribose modification selected from 2'-O-alkyl, 2'-F, 2'-moe, 2'-F arabinose, and 2'-H (deoxyribose);
b. a bicyclic ribose analog, such as LNA, BNA, and ENA;
c. an unlocked nucleic acid modification;
d. a base modification, such as inosine, pseudouridine, and 5'-methylcytosine; and
e. an internucleoside linkage modification such as phosphorothioate.

Embodiment 107 is the gRNA of any one of the preceding embodiments, comprising a YA modification at one or more conserved region YA sites.

Embodiment 108 is the gRNA of any one of the preceding embodiments, comprising a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10.

Embodiment 109 is the gRNA of any one of the preceding embodiments, comprising a YA modification at one or more of conserved region YA sites 1 and 8.

Embodiment 110 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 1.

Embodiment 111 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 2.

Embodiment 112 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 3.

Embodiment 113 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 4.

Embodiment 114 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 5.

Embodiment 115 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 6.

Embodiment 116 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 7.

Embodiment 117 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 8.

Embodiment 118 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 9.

Embodiment 119 is the gRNA of any one of the preceding embodiments, comprising a YA modification of conserved region YA site 10.

Embodiment 120 is the gRNA of any one of the preceding embodiments, comprising one or more of:

a. YA modifications of conserved region YA sites 2, 3, 4, and 10;
b. YA modifications of conserved region YA sites 2, 3, and 4;
c. YA modifications of conserved region YA sites 2, 3, and 10;
d. YA modifications of conserved region YA sites 2, 4, and 10;
e. YA modifications of conserved region YA sites 3, 4, and 10;
f. YA modifications of conserved region YA sites 2 and 10;
g. YA modifications of conserved region YA sites 2 and 4;
h. YA modifications of conserved region YA sites 2 and 3;
i. YA modifications of conserved region YA sites 3 and 4;
j. YA modifications of conserved region YA sites 3 and 10;
k. YA modifications of conserved region YA sites 4 and 10
l. YA modifications of conserved region YA sites 1 and 5;
m. YA modifications of conserved region YA sites 1 and 6;
n. YA modifications of conserved region YA sites 1 and 7;
o. YA modifications of conserved region YA sites 1 and 8;
p. YA modifications of conserved region YA sites 1 and 9;
q. YA modifications of conserved region YA sites 8 and 5;
r. YA modifications of conserved region YA sites 8 and 6;
s. YA modifications of conserved region YA sites 8 and 7; and
t. YA modifications of conserved region YA sites 8 and 9;

optionally wherein the sgRNA further comprises YA modifications of conserved region YA sites 2, 3, 4, and/or 10.

Embodiment 121 is the gRNA of any one of the preceding embodiments, wherein at least one modified YA site comprises a 2'-OMe modification, optionally at the pyrimidine of the YA site.

Embodiment 122 is the gRNA of any one of the preceding embodiments, wherein at least one modified YA site comprises a 2'-fluoro modification, optionally at the pyrimidine of the YA site.

Embodiment 123 is the gRNA of any one of the preceding embodiments, wherein at least one modified YA site comprises a PS modification, optionally at the pyrimidine of the YA site.

Embodiment 124 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises modifications at at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or all of the following nucleotides: 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18, optionally wherein the modifications are 2'-OMe, 2'-fluoro, 2'-H, inosine, or phosphorothioate modifications.

Embodiment 125 is the gRNA of any one of the preceding embodiments, wherein the short-sgRNA comprises a guide region that comprises modifications at nucleotides 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18, optionally wherein the modifications are 2'-OMe, 2'-fluoro, 2'-H, inosine, or phosphorothioate modifications.

Embodiment 126 is the gRNA of embodiments 124-125, wherein 2'-OMe modifications are not present in the guide region at nucleotides 6-11 and 13-end.

Embodiment 127 is the gRNA of embodiments 124-126, wherein 2'-fluoro modifications are not present in the guide region at nucleotides 1-7, 15, 16, and 19-end.

Embodiment 128 is the gRNA of embodiments 124-127, wherein phosphorothioate modifications are not present in the guide region at nucleotides 4, 5, 11-14, 17, and 18.

Embodiment 129 is the gRNA of embodiments 124-128, wherein the guide region comprises an unmodified nucleotide 20.

Embodiment 130 is the gRNA of embodiments 124-129, wherein the guide region consists of 20 nucleotides.

Embodiment 131 is the gRNA of embodiments 124-130, wherein the guide region comprises a YA site at nucleotides 5-6 and a modification at nucleotide 5.

Embodiment 132 is the gRNA of embodiments 124-131, wherein the guide region comprises a YA site at nucleotides 12-13 and a modification at nucleotide 12.

Embodiment 133 is the gRNA of embodiments 124-132, wherein the guide region comprises a YA site at nucleotides 15-16 and a modification at nucleotide 15.

Embodiment 134 is the gRNA of embodiments 124-133, wherein the guide region comprises a YA site at nucleotides 16-17 and a modification at nucleotide 16.

Embodiment 135 is the gRNA of embodiments 124-134, wherein the guide region comprises a YA site at nucleotides 19-20 and a modification at nucleotide 19.

Embodiment 136 is the gRNA of embodiments 124-130 or 132-135, wherein the guide region does not comprise a YA site at nucleotides 5-6 and nucleotide 5 is unmodified.

Embodiment 137 is the gRNA of embodiments 124-131 or 133-136, wherein the guide region does not comprise a YA site at nucleotides 12-13 and nucleotide 12 is unmodified.

Embodiment 138 is the gRNA of embodiments 124-132 or 134-137, wherein the guide region does not comprise a YA site at nucleotides 15-16 and nucleotide 15 is unmodified.

Embodiment 139 is the gRNA of embodiments 124-133 or 135-138, wherein the guide region does not comprise a YA site at nucleotides 16-17 and nucleotide 16 is unmodified.

Embodiment 140 is the gRNA of embodiments 124-134 or 136-139, wherein the guide region does not comprise a YA site at nucleotides 19-20 and nucleotide 19 is unmodified.

Embodiment 141 is the gRNA of embodiments 124-140, wherein the short-sgRNA comprises a guide region that comprises one or more of the following:

(a) 2'-OMe and phosphorothioate modifications at nucleotide 1;
(b) 2'-OMe and phosphorothioate modifications at nucleotide 2;
(c) 2'-OMe and phosphorothioate modifications at nucleotide 3;
(d) a 2'-OMe modification at nucleotide 4;
(e) a phosphorothioate modification at nucleotide 6;
(f) a phosphorothioate modification at nucleotide 7;
(g) 2'-fluoro and phosphorothioate modifications at nucleotide 8;
(h) 2'-fluoro and phosphorothioate modifications at nucleotide 9;
(i) 2'-fluoro and phosphorothioate modifications at nucleotide 10;
(j) a 2'-fluoro modification at nucleotide 11;
(k) a 2'-fluoro modifications at nucleotide 13;
(l) a 2'-fluoro modifications at nucleotide 14;

(m)a 2'-fluoro modifications at nucleotide 17; and

(n) a 2'-fluoro modifications at nucleotide 18.

Embodiment 142 is the gRNA of embodiments 124-141, wherein the guide region comprises each of the modifications set forth in the preceding embodiment.

Embodiment 143 is the gRNA of embodiments 124-142, wherein the guide region comprises at least 1, 2, 3, or 4 of the following:

(a) a 2'-OMe modification at nucleotide 5 if nucleotides 5 and 6 form a YA site;

(b) a 2'-OMe modification at nucleotide 12 if nucleotides 12 and 13 form a YA site;

(c) a phosphorothioate or 2'-H modification at nucleotide 15 if nucleotides 15 and 16 form a YA site;

(d) a phosphorothioate modification at nucleotide 16 if nucleotides 16 and 17 form a YA site; and

(e) a phosphorothioate or 2'-fluoro modification at nucleotide 19 if nucleotides 19 and 20 form a YA site.

Embodiment 144 is the gRNA of embodiments 124-143, wherein the guide region comprises a YA site at nucleotides 5-6 and a 2'-OMe modification at nucleotide 5.

Embodiment 145 is the gRNA of embodiments 124-144, wherein the guide region comprises a YA site at nucleotides 12-13 and a 2'-OMe modification at nucleotide 12.

Embodiment 146 is the gRNA of embodiments 124-145, wherein the guide region comprises a YA site at nucleotides 15-16 and a phosphorothioate modification at nucleotide 15.

Embodiment 147 is the gRNA of embodiments 124-146, wherein the guide region comprises a YA site at nucleotides 16-17 and a phosphorothioate modification at nucleotide 16.

Embodiment 148 is the gRNA of embodiments 124-147, wherein the guide region comprises a YA site at nucleotides 19-20 and a phosphorothioate modification at nucleotide 19.

Embodiment 149 is the gRNA of embodiments 124-148, wherein the guide region comprises a 2'-fluoro modification at nucleotide 19.

Embodiment 150 is the gRNA of embodiments 124-149, wherein the guide region comprises an unmodified nucleotide 15 or only a phosphorothioate modification at nucleotide 15.

Embodiment 151 is the gRNA of embodiments 124-150, wherein the guide region comprises an unmodified nucleotide 16 or only a phosphorothioate modification at nucleotide 16.

Embodiment 152 is a guide RNA which is a single guide RNA (sgRNA) comprising:

a. a YA modification at two or more guide region YA sites;
b. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
c. a YA modification at one or more of conserved region YA sites 1 and 8.

Embodiment 153 is a guide RNA which is a single guide RNA (sgRNA) comprising:

a. a YA modification at one or more guide region YA sitesthat are at or after nucleotide 8 from the 5' end of the 5' terminus;
b. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and optionally
c. a YA modification at one or more of conserved region YA sites 1 and 8.

Embodiment 154 is a guide RNA which is a single guide RNA (sgRNA) comprising:

a. a YA modification at one or more guide region YA sitesthat are within 13 nucleotides of the 3' terminal nucleotide of the guide region;
b. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
c. a YA modification at one or more of conserved region YA sites 1 and 8.

Embodiment 155 is a guide RNA which is a single guide RNA (sgRNA) comprising:

a. a 5' end modification and a 3' end modification;
b. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
c. a YA modification at one or more of conserved region YA sites 1 and 8.

Embodiment 156 is a guide RNA which is a single guide RNA (sgRNA) comprising:

a. a YA modification at at least one guide region YA site, wherein the modification of the guide region YA site comprises a modification at at least one nucleotide located 5' of the guide region YA site does not comprise;
b. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
c. a YA modification at one or more of conserved region YA sites 1 and 8.

Embodiment 157 is a guide RNA which is a single guide RNA (sgRNA) comprising:

a. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
b. a YA modification at conserved region YA sites 1 and 8.

Embodiment 158 is a guide RNA which is a single guide RNA (sgRNA) comprising:

a. a YA modification at one or more guide region YA sitesthat are at or after nucleotide 8 from the 5' end of the 5' terminus;
b. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
c. a modification at one or more of H1-1 and H2-1.

Embodiment 159 is a guide RNA which is a single guide RNA (sgRNA) comprising:

a. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10;
b. a YA modification at one or more of conserved region YA sites 1, 5, 6, 7, 8, and 9; and
c. a modification at one or more of H1-1 and H2-1.

Embodiment 160 is a guide RNA which is an sgRNA comprising any one or more of the following:

a. a modification, such as a YA modification, at one or more nucleotides located at or after nucleotide 6 from the 5' end of the 5' terminus;
b. a YA modification at one or more guide sequence YA sites;
c. a modification at one or more of B3, B4, and B5, wherein B6 does not comprise a 2'-OMe modification or comprises a modification other than 2'-OMe;
d. a modification at LS10, wherein LS10 comprises a modification other than 2'-fluoro; and/or
e. a modification at N2, N3, N4, N5, N6, N7, N10, or N11;

and

wherein at least one of the following is true:

i. at least one of nucleotides 8-11, 13, 14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
ii. at least one of nucleotides 6-10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
iii. at least one of B2, B3, B4, or B5 does not comprise a 2'-OMe modification;
iv. at least one of LS1, LS8, or LS10 does not comprise a 2'-OMe modification;
v. at least one of N2, N3, N4, N5, N6, N7, N10, N11, N16, or N17 does not comprise a 2'-OMe modification;

vi. H1-1 comprises a modification;

vii. H2-1 comprises a modification; or

viii. at least one of H1-2, H1-3, H1-4, H1-5, H1-6, H1-7, H1-8, H1-9, H1-10, H2-1, H2-2, H2-3, H2-4, H2-5, H2-6, H2-7, H2-8, H2-9, H2-10, H2-11, H2-12, H2-13, H2-14, or H2-15 does not comprise a phosphorothioate linkage.

Embodiment 161 is a guide RNA comprising any one or more of the following:

i. a modification, such as a YA modification, at one or more nucleotides located at or after nucleotide 6 from the 5' end of the 5' terminus; or

ii. a YA modification at one or more guide sequence YA sites;

wherein at least one of the following is true:

a. at least one of nucleotides 8-11, 13, 14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification; or

b. at least one of nucleotides 6-10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;

and wherein at least one of the following is also true:

c. at least one of nucleotides 7-10 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification;

d. nucleotide 20 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification; or

e. the guide RNA comprises a 2'-fluoro modification at any one or more of nucleotides 1-20 from the 5' end of the 5' terminus and at least one of nucleotides 11, 12, 13, 14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification, optionally wherein nucleotide 12 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

Embodiment 162 is a guide RNA which is an sgRNA comprising a guanosine at N14 and/or one or more of the following:

a. a YA modification at one or more guide region YA sitesthat are at or after nucleotide 8 from the 5' end of the 5' terminus;

b. a YA modification at one or more of conserved region YA sites 1, 5, and 6, wherein if YA site 6 is modified at LS12 and LS9is not modified, then the modification of LS12 is other than 2'-OMe;

c. a modification at LS9, wherein if LS9 is modified and LS5, LS7, and LS12 are not modified, then the modification of LS9 is other than 2'-fluoro,

d. a modification at LS12, wherein if LS12 is modified and LS9 is not modified, then the modification of LS12 is other than 2'-OMe;
e. a modification at LS8 or LS11, wherein at least one of LS8 and LS11 comprises a modification other than 2'-OMe; and/or
f. a modification at N6, N14, or N17, wherein if N17 is modified and N6 and N14 are not modified, then the modification of N17 is other than 2'-fluoro and other than 2'-OMe;

and wherein at least one of the following is true:

i. at least one of nucleotides 8-11, 13-14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
ii. at least one of nucleotides 6-10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
iii. at least one of B2, B3, B4, or B5 does not comprise a 2'-OMe modification;
iv. at least one of LS1, LS8, or LS10 does not comprise a 2'-OMe modification;
v. at least one of N2, N3, N4, N5, N6, N7, N10, N11, N16, or N17 does not comprise a 2'-OMe modification;
vi. H1-1 comprises a modification;
vii. H2-1 comprises a modification; or
viii. at least one of H1-2, H1-3, H1-4, H1-5, H1-6, H1-7, H1-8, H1-9, H1-10, H2-1, H2-2, H2-3, H2-4, H2-5, H2-6, H2-7, H2-8, H2-9, H2-10, H2-11, H2-12, H2-13, H2-14, or H2-15 does not comprise a phosphorothioate linkage.

Embodiment 163 is the gRNA of embodiments 161 or 162, comprising:

a. a YA modification at 1, 2, 3, 4, or 5 guide region YA sites;
b. a YA modification at 1, 2, 3, 4, or 5 guide region YA sites, wherein the modification of at least one guide region YA site is different from any 5' end modification of the sgRNA;
c. a YA modification at one or more guide region YA sites that are at or after nucleotide 8 from the 5' end of the 5' terminus;
d. a YA modification at one or more guide region YA sites that are is within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;
e. a YA modification at one or more guide region YA sites that are within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;

f. a YA modification at a guide region YA site other than a 5' end modification; or

g. a YA modification at a guide region YA site, wherein the modification of the guide region YA site comprises a modification at at least one nucleotide located 5' of the guide region YA site does not comprise.

Embodiment 164 is the gRNA of embodiment 163, comprising:

a. a YA modification at two or more guide region YA sites that are at or after nucleotide 8 from the 5' end of the 5' terminus;

b. a YA modification at two or more guide region YA sites that are within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;

c. a YA modification at two or more guide region YA sites that are within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;

d. a YA modification at two or more guide region YA sites other than a 5' end modification; or

e. a YA modification at a two or more guide region YA sites, wherein the modifications of the guide region YA sites comprise a modification at at least one nucleotide located 5' of the guide region YA site does not comprise.

Embodiment 165 is the gRNA of embodiment 163, comprising:

a. a YA modification at three or more guide region YA sites that are at or after nucleotide 8 from the 5' end of the 5' terminus;

b. a YA modification at three or more guide region YA sites that are within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;

c. a YA modification at three or more guide region YA sites that are within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;

d. a YA modification at three or more guide region YA sites other than a 5' end modification; or

e. a YA modification at a three or more guide region YA sites, wherein the modifications of the guide region YA sites comprise a modification at at least one nucleotide located 5' of the guide region YA site does not comprise.

Embodiment 166 is the gRNA of any one of embodiments 161-165, comprising at least one YA modification at nucleotide 6 from the 5' end of the 5' terminus.

Embodiment 167 is the gRNA of any one of embodiments 161-166, comprising at least one YA modification at nucleotide 7 from the 5' end of the 5' terminus.

Embodiment 168 is the gRNA of any one of embodiments 161-167, comprising at least one YA modification at nucleotide 8 from the 5' end of the 5' terminus.

Embodiment 169 is the gRNA of any one of embodiments 161-168, comprising at least one YA modification at nucleotide 9 from the 5' end of the 5' terminus.

Embodiment 170 is the gRNA of any one of embodiments 161-169, comprising at least one YA modification at nucleotide 10 from the 5' end of the 5' terminus.

Embodiment 171 is the gRNA of any one of embodiments 161-170, comprising at least one YA modification at nucleotide 11 from the 5' end of the 5' terminus.

Embodiment 172 is the gRNA of any one of embodiments 161-171, comprising at least one YA modification at nucleotide 12 from the 5' end of the 5' terminus.

Embodiment 173 is the gRNA of any one of embodiments 161-172, comprising at least one YA modification at nucleotide 13 from the 5' end of the 5' terminus.

Embodiment 174 is the gRNA of any one of embodiments 161-173, comprising at least one YA modification at nucleotide 14 from the 5' end of the 5' terminus.

Embodiment 175 is the gRNA of any one of embodiments 161-174, comprising at least one YA modification at nucleotide 15 from the 5' end of the 5' terminus.

Embodiment 176 is the gRNA of any one of embodiments 161-175, comprising at least one YA modification at nucleotide 16 from the 5' end of the 5' terminus.

Embodiment 177 is the gRNA of any one of embodiments 161-176, comprising at least one YA modification at nucleotide 17 from the 5' end of the 5' terminus.

Embodiment 178 is the gRNA of any one of embodiments 161-177, comprising at least one YA modification at nucleotide 18 from the 5' end of the 5' terminus.

Embodiment 179 is the gRNA of any one of embodiments 161-178, comprising at least one YA modification at nucleotide 19 from the 5' end of the 5' terminus.

Embodiment 180 is the gRNA of any one of embodiments 161-179, comprising at least one YA modification at nucleotide 20 from the 5' end of the 5' terminus.

Embodiment 181 is the gRNA of any one of embodiments 161-180, wherein at least 1, 2, 3, 4, 5, 6, 7, or 8 of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus comprise a YA modification, optionally wherein the modification comprises 2'-fluoro, 2'-H, 2'-OMe, or PS.

Embodiment 182 is the gRNA of embodiment 181, wherein the modification is 2'-fluoro.

Embodiment 183 is the gRNA of embodiment 181, wherein the modification is 2'-OMe or 2'-H.

Embodiment 184 is the gRNA of embodiment 181, wherein the modification is PS.

Embodiment 185 is the gRNA of any one of embodiments 161-184, wherein at least 1, 2, 3, 4, or 5 of nucleotides 6-10 from the 5' terminus comprise a YA modification, optionally wherein the modification comprises 2'-fluoro, 2'-H, 2'-OMe, inosine, or PS.

Embodiment 186 is the gRNA of embodiment 185, wherein the modification is PS.

Embodiment 187 is the gRNA of embodiment 185, wherein the modification is 2'-fluoro or 2'-H.

Embodiment 188 is the gRNA of embodiment 185, wherein the modification is 2'-OMe.

Embodiment 189 is the gRNA of any one of embodiments 161-188, comprising any one or more of the following:

a. 1, 2, 3, 4, 5, 6, 7, or 8 YA modifications of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, wherein the YA modifications are optionally 2'-fluoro modifications, and a modification other than 2'-fluoro at one or more of nucleotides 6-10 from the 5' end of the 5' terminus;
b. a YA modification other than PS at one or more of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, and 1, 2, 3, 4, or 5 YA modifications at nucleotides 6-10 from the 5' end of the 5' end of the 5' terminus, optionally wherein the modifications are PS modifications;
c. 1, 2, 3, 4, 5, 6, 7, or 8 YA modifications at nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, wherein the YA modifications are optionally 2'-fluoro modifications, and modifications other than 2'-fluoro at nucleotides 6-10 from the 5' end of the 5' terminus;
d. YA modifications other than PS at each of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' end of the 5' terminus, and 1, 2, 3, 4, or 5 YA modifications at nucleotides 6-10 from the 5' end of the 5' terminus, wherein the modifications are optionally PS modifications;

e. 1, 2, 3, 4, 5, 6, 7, or 8 YA modifications at nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, wherein the YA modifications are optionally 2'-fluoro modifications, and one or more PS modification at any one of nucleotides 6-10 from the 5' end of the 5' terminus;
f. at least one 2'-fluoro modification at any one of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, and 1, 2, 3, 4, or 5 YA modifications of nucleotides 6-10 from the 5' end of the 5' terminus, wherein the modifications are optionally PS modifications;
g. 1, 2, 3, 4, 5, 6, 7, or 8 YA modifications of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, wherein the YA modifications are optionally 2'-fluoro modifications, and a PS modification at each of nucleotides 6-10 from the 5' end of the 5' terminus; or
h. a 2'-fluoro modification at each of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, and 1, 2, 3, 4, or 5 YA modifications of nucleotides 6-10 from the 5' end of the 5' terminus, wherein the modifications are optionally PS modifications.

Embodiment 190 is the gRNA of any one of embodiments 161-189, wherein:

a. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, or 4 modified YA sites including a first modified YA site comprising a 2'-OMe modification and a second modified YA site comprising a 2'-fluoro modification or a PS modification;
b. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, or 4 modified YA sites including a first modified YA site comprising a 2'-fluoro modification and a second modified YA site comprising a 2'-OMe modification or a PS modification;
c. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, or 4 modified YA sites including a first modified YA site comprising a PS modification and a second modified YA site comprising a 2'-OMe modification or a 2'-fluoro modification;
d. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, or 4 modified YA sites including a YA modification;

e. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 3 or 4 modified YA sites including a first modified YA site comprising a 2'-OMe modification, a second modified YA site comprising a 2'-fluoro modification, and a third modified YA site comprising a PS modification;
f. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 3 or 4 modified YA sites including a first modified YA site comprising a 2'-OMe modification, a second modified YA site comprising a 2'-fluoro modification, a third modified YA site comprising a 2'-fluoro modification, and a fourth modified YA site comprising a PS modification;
g. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 3 or 4 modified YA sites including a YA modification;
h. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 4 modified YA sites including a first modified YA site comprising a 2'-OMe modification, a second modified YA site comprising a 2'-fluoro modification, a third modified YA site comprising a PS modification, and a fourth modified YA site comprising a PS modification; or
i. nucleotides 4-40 from the 5' end of the 5' terminus comprise at least 4 modified YA sites including a YA modification.

Embodiment 191 is the gRNA of any one of embodiments 161-190, wherein nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 5 modified YA sites.

Embodiment 192 is the gRNA of any one of embodiments 161-191, wherein the at least 5 modified YA sites include a fifth modified YA site comprising a PS modification, optionally wherein the third modified YA site comprises a 2'-fluoro modification.

Embodiment 193 is the gRNA of any one of embodiments 161-192, wherein the first, second, and (if applicable) third, fourth, and fifth of the at least 5 modified YA sites are arranged in the 5' to 3' direction.

Embodiment 194 is the gRNA of any one of embodiments 161-193, wherein the first, second, and (if applicable) third, fourth, and fifth of the at least 5 modified YA sites are not arranged in the 5' to 3' direction.

Embodiment 195 is the gRNA of any one of embodiments 161-194, wherein nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, 4, or 5 modified YA sites comprising a deoxyribonucleotide, optionally wherein the deoxyribonucleotide is the pyrimidine of the YA sites.

Embodiment 196 is the gRNA of any one of embodiments 161-195, wherein:

a. at least 1, 2, 3, or 4 of nucleotides 8-11 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-fluoro modification;
b. at least 1, 2, 3, 4, 5, 6, 7, or 8 of nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus comprise a YA modification, optionally wherein the YA modifications are 2'-OMe if present at nucleotides 8-11 and 2'-fluoro if present at nucleotides 13, 14, 17, or 18;
c. at least one or both of nucleotides 17 and 18 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-fluoro modification;
d. at least one or both of nucleotides 17 and 18 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-fluoro modification; or
e. at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 of nucleotides 4-14, 17, and 18 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-fluoro modification.

Embodiment 197 is the gRNA of any one of embodiments 161-196, wherein at least 1, 2, 3, 4, 5, or 6 of nucleotides 4-10 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-OMe modification.

Embodiment 198 is the gRNA of any one of embodiments 161-197, wherein nucleotides 4-10 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-OMe modification.

Embodiment 199 is the gRNA of any one of embodiments 161-198, wherein:

a. at least one of nucleotides 1-3 from the 5' end of the 5' terminus comprise a 5' protective end modification, which is optionally a 2'-OMe modification;
b. at least two of nucleotides 1-3 from the 5' end of the 5' terminus comprise a 5' protective end modification, which is optionally a 2'-OMe modification; or
c. each of nucleotides 1-3 from the 5' end of the 5' terminus comprise a 5' protective end modification, which is optionally a 2'-OMe modification.

Embodiment 200 is the gRNA of any one of embodiments 161-199, wherein at least 1, 2, 3, 4, or 5 of nucleotides 11, 13, 14, 17, and 18 from the 5' end of the 5' terminus comprise a 5' end modification, which is optionally a 2'-fluoro modification.

Embodiment 201 is the gRNA of any one of embodiments 161-200, wherein nucleotide 15 from the 5' end of the 5' terminus is unmodified or modified only with phosphorothioate.

Embodiment 202 is the gRNA of any one of embodiments 161-200, wherein nucleotide 16 from the 5' end of the 5' terminus is unmodified or modified only with phosphorothioate.

Embodiment 203 is the gRNA of any one of the preceding embodiments, wherein nucleotide 3 from the 5' end of the 5' terminus is unmodified or modified only with phosphorothioate.

Embodiment 204 is the gRNA of any one of embodiments 161-203, which is a crRNA or dgRNA.

Embodiment 205 is the gRNA of any one of embodiments 161-203, which is an sgRNA.

Embodiment 206 is the gRNA of any one of embodiments 161-203, which is a short-sgRNA.

Embodiment 207 is the gRNA of any one of embodiment 205 or 206, comprising a YA modification of conserved region YA site 1.

Embodiment 208 is the gRNA of any one of embodiments 205-207, comprising a YA modification of conserved region YA site 2.

Embodiment 209 is the gRNA of any one of embodiments 205-208, comprising a YA modification of conserved region YA site 3.

Embodiment 210 is the gRNA of any one of embodiments 205-209, comprising a YA modification of conserved region YA site 4.

Embodiment 211 is the gRNA of any one of embodiments 205-210, comprising a YA modification of conserved region YA site 5.

Embodiment 212 is the gRNA of any one of embodiments 205-211, comprising a YA modification of conserved region YA site 6.

Embodiment 213 is the gRNA of any one of embodiments 205-212, comprising a YA modification of conserved region YA site 7.

Embodiment 214 is the gRNA of any one of embodiments 205-213, comprising a YA modification of conserved region YA site 8.

Embodiment 215 is the gRNA of any one of embodiments 205-214, comprising a YA modification of conserved region YA site 9.

Embodiment 216 is the gRNA of any one of embodiments 205-215, comprising a YA modification of conserved region YA site 10.

Embodiment 217 is the gRNA of any one of embodiments 205-216, comprising:

a. YA modifications of conserved region YA sites 2, 3, 4, and 10;
b. YA modifications of conserved region YA sites 2, 3, and 4;

c. YA modifications of conserved region YA sites 2, 3, and 10;
d. YA modifications of conserved region YA sites 2, 4, and 10;
e. YA modifications of conserved region YA sites 3, 4, and 10;
f. YA modifications of conserved region YA sites 2 and 10;
g. YA modifications of conserved region YA sites 2 and 4;
h. YA modifications of conserved region YA sites 2 and 3;
i. YA modifications of conserved region YA sites 3 and 4;
j. YA modifications of conserved region YA sites 3 and 10; or
k. YA modifications of conserved region YA sites 4 and 10.

Embodiment 218 is the gRNA of any one of embodiments 205-217, comprising:

a. YA modifications of conserved region YA sites 1 and 5;
b. YA modifications of conserved region YA sites 1 and 6;
c. YA modifications of conserved region YA sites 1 and 7;
d. YA modifications of conserved region YA sites 1 and 8;
e. YA modifications of conserved region YA sites 1 and 9;
f. YA modifications of conserved region YA sites 8 and 5;
g. YA modifications of conserved region YA sites 8 and 6;
h. YA modifications of conserved region YA sites 8 and 7; or
i. YA modifications of conserved region YA sites 8 and 9;

optionally wherein the sgRNA further comprises YA modifications of conserved region YA sites 2, 3, 4, and 10.

Embodiment 219 is the gRNA of any one of embodiments 205-218, wherein at least one modified YA site comprises a 2'-OMe modification, optionally at the pyrimidine of the YA site.

Embodiment 220 is the gRNA of any one of embodiments 205-219, wherein at least one modified YA site comprises a 2'-fluoro modification, optionally at the pyrimidine of the YA site.

Embodiment 221 is the gRNA of any one of embodiments 205-220, wherein at least one modified YA site comprises a PS modification, optionally at the pyrimidine of the YA site.

Embodiment 222 is the gRNA of any one of embodiments 205-221, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified YA sites comprise a 2'-OMe modification, optionally at the pyrimidines of the YA sites.

Embodiment 223 is the gRNA of any one of embodiments205-222, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified YA sites comprise a 2'-fluoro modification, optionally at the pyrimidines of the YA sites.

Embodiment 224 is the gRNA of any one of embodiments205-223, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified YA sites comprise a PS modification, optionally at the pyrimidines of the YA sites.

Embodiment 225 is the gRNA of any one of embodiments205-224, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified YA sites comprise a ribose modification at the 2' position, optionally at the pyrimidines of the YA sites, and optionally chosen from a 2'-O-alkyl, 2'-H, and 2'-fluoro modification.

Embodiment 226 is the gRNA of any one of embodiments 205-225, wherein:

a. conserved region YA sites 1 and 8 comprise 2'-fluoro modifications, optionally at the pyrimidines of the YA sites;
b. conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
c. conserved region YA site 1 comprises a 2'-fluoro modification and conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
d. conserved region YA site 8 comprises a 2'-fluoro modification and conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
e. conserved region YA site 1 comprises a 2'-fluoro modification at the pyrimidine of the YA sites and YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
f. conserved region YA site 8 comprises a 2'-fluoro modification at the pyrimidine of the YA site and YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
g. conserved region YA sites 1 and 8 comprise 2'-fluoro modifications and conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6,

and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites; or

h. conserved region YA sites 1 and 8 comprise 2'-fluoro modifications at the pyrimidines of the YA sites and conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites.

Embodiment 227 is the gRNA of any one of embodiments 205-226, wherein conserved region YA sites 7 and 9 comprise YA modifications, which are optionally 2'-OMe modifications.

Embodiment 228 is the gRNA of any one of embodiments 205-227, wherein conserved region YA sites 5, 6, 7, and 9 comprise YA modifications, which are optionally 2'-OMe modifications.

Embodiment 229 is the gRNA of any one of embodiments 205-228, wherein conserved region YA site 8 comprises a 2'-fluoro modification.

Embodiment 230 is the gRNA of any one of embodiments 205-229, wherein conserved region YA site 8 comprises a deoxyribonucleotide modification.

Embodiment 231 is the gRNA of any one of embodiments 205-230, wherein conserved region YA site 8 is abolished by a base substitution, optionally wherein the base substitution eliminates the uracil of YA site 8, further optionally wherein the base substitution is a uracil to guanine substitution.

Embodiment 232 is the gRNA of any one of embodiments 205-231, wherein conserved region YA site 1 comprises a 2'-fluoro modification.

Embodiment 233 is the gRNA of any one of embodiments 205-232, wherein conserved region YA site 1 comprises a PS modification.

Embodiment 234 is the gRNA of any one of embodiments 205-233, wherein 1, 2, 3, 4, 5, 6, or 7 of LS5, LS7, LS8, LS9, LS10, LS11, and LS12 comprise modifications, optionally wherein the modifications are 2'-fluoro and/or 2'-OMe modifications.

Embodiment 235 is the gRNA of any one of embodiments 205-234, wherein modifications at LS5, LS7, LS9, and LS11, if present, comprise 2'-fluoro modifications, optionally wherein each of LS5, LS7, LS9, and LS11 comprise 2'-fluoro modifications.

Embodiment 236 is the gRNA of any one of embodiments 205-235, wherein modifications at LS8, LS10, and LS12, if present, comprise 2'-OMe modifications, optionally wherein each of LS8, LS10, and LS12 comprise 2'-OMe modifications.

Embodiment 237 is the gRNA of any one of embodiments 205-236, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of N2, N3, N4, N5, N6, N7, N10, N11, N16, and N17 comprise modifications, which are optionally 2'-OMe modifications.

Embodiment 238 is the gRNA of any one of embodiments 205-237, wherein H2-2 comprises a modification, optionally wherein H2 is otherwise unmodified.

Embodiment 239 is the gRNA of any one of embodiments 205-238, wherein H2-2 comprises a 2'-OMe modification.

Embodiment 240 is the gRNA of any one of embodiments 205-239, wherein US3, US9, and US12 comprise modifications, optionally wherein the US is otherwise unmodified.

Embodiment 241 is the gRNA of any one of embodiments 205-240, wherein US3, US9, and US12 comprise 2'-OMe modifications.

Embodiment 242 is the gRNA of any one of embodiments 205-241, wherein nucleotides 6-10 from the 5' end of the 5' terminus comprise a PS modification and nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus comprise a 2'-fluoro modification.

Embodiment 243 is the gRNA of any one of embodiments 205-242, wherein each guide region YA site comprises a 2'-fluoro modification, optionally excepting nucleotides 15 and/or 16 from the 5' end of the 5' terminus.

Embodiment 244 is the gRNA of any one of embodiments 205-243, wherein nucleotides 4, 8, and 11 from the 5' end of the 5' terminus comprise YA modifications, optionally wherein nucleotide 4 comprises a 2'-OMe modification and nucleotides 8 and 11 comprise a 2'-fluoro modification.

Embodiment 245 is the gRNA of any one of embodiments 205-244, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or more modified YA sites comprise a YA modification at the pyrimidine position of the YA site.

Embodiment 246 is the gRNA of embodiment 245, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified conserved region YA sites comprise a YA modification at the pyrimidine position of the YA site.

Embodiment 247 is the gRNA of any one of embodiments 205-246, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or more modified YA sites comprise a YA modification at the adenine position of the YA site.

Embodiment 248 is the gRNA of embodiment 247, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified conserved region YA sites comprise a YA site modification at the adenine position of the YA site.

Embodiment 249 is the gRNA of any one of embodiments 205-248, comprising:

a. a modification of H1-1;
b. a modification of H2-1; or
c. modifications of H1-1 and H2-1.

Embodiment 250 is the gRNA of embodiment 249, wherein H1-1 and/or H2-1 comprises a 2'-OMe modification.

Embodiment 251 is the gRNA of embodiment 250, wherein H1-1 and/or H2-1 comprises a 2'-fluoro modification.

Embodiment 252 is the gRNA of embodiment 251, wherein H1-1 and/or H2-1 comprises a PS modification.

Embodiment 253 is the gRNA of any one of embodiments 205-252, comprising a modification at B3, optionally wherein B6 does not comprise a 2'-OMe modification or comprises a modification other than 2'-OMe.

Embodiment 254 is the gRNA of any one of embodiments 205-253, comprising a modification at B4, optionally wherein B6 does not comprise a 2'-OMe modification or comprises a modification other than 2'-OMe.

Embodiment 255 is the gRNA of any one of embodiments 205-254, comprising a modification at B5, optionally wherein B6 does not comprise a 2'-OMe modification or comprises a modification other than 2'-OMe.

Embodiment 256 is the gRNA of any one of embodiments 205-255, comprising a modification at LS10, optionally wherein LS10 comprises a modification other than 2'-fluoro.

Embodiment 257 is the gRNA of any one of embodiments 205-256, comprising a modification at N2.

Embodiment 258 is the gRNA of any one of embodiments 205-257, comprising a modification at N3.

Embodiment 259 is the gRNA of any one of embodiments 205-258, comprising a modification at N4.

Embodiment 260 is the gRNA of any one of embodiments 205-259, comprising a modification at N5.

Embodiment 261 is the gRNA of any one of embodiments 205-260, comprising a modification at N6.

Embodiment 262 is the gRNA of any one of embodiments 205-261, comprising a modification at N7.

Embodiment 263 is the gRNA of any one of embodiments 205-262, comprising a modification at N10.

Embodiment 264 is the gRNA of any one of embodiments 205-263, comprising a modification at N11.

Embodiment 265 is the gRNA of any one of embodiments 205-264,, wherein:

a. nucleotide 8 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
b. nucleotide 9 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
c. nucleotide 10 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
d. nucleotide 11 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
e. nucleotide 13 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
f. nucleotide 14 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
g. nucleotide 17 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification; and/or
h. nucleotide 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

Embodiment 266 is the gRNA of any one of embodiments 205-265, wherein:

a. nucleotide 6 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
b. nucleotide 7 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
c. nucleotide 8 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
d. nucleotide 9 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification; and/or

e. nucleotide 10 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

Embodiment 267 is the gRNA of any one of embodiments 205-266, wherein:

a. nucleotide 6 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
b. nucleotide 7 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
c. nucleotide 8 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
d. nucleotide 9 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage; and/or
e. nucleotide 10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage.

Embodiment 268 is the gRNA of any one of embodiments 205-267, wherein:

a. nucleotide 7 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification;
b. nucleotide 8 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification;
c. nucleotide 9 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification; and/or
d. nucleotide 10 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification.

Embodiment 269 is the gRNA of any one of embodiments 205-268, wherein nucleotide 20 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification.

Embodiment 270 is the gRNA of any one of embodiments 205-269, wherein the guide RNA comprises a 2'-fluoro modification at any one or more of nucleotides 1-11 and 13-20 from the 5' end of the 5' terminus and nucleotide 12 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

Embodiment 271 is the gRNA of any one of embodiments 205-270, wherein the guide RNA comprises a 2'-fluoro modification at any one or more of nucleotides 1-20 from the 5' end of the 5' terminus and:

a. nucleotide 11 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;

b. nucleotide 12 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
c. nucleotide 13 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
d. nucleotide 14 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
e. nucleotide 17 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification; and/or
f. nucleotide 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

Embodiment 272 is the gRNA of any one of embodiments 205-271, wherein:

a. B2 does not comprise a 2'-OMe modification;
b. B3 does not comprise a 2'-OMe modification;
c. B4 does not comprise a 2'-OMe modification; and/or
d. B5 does not comprise a 2'-OMe modification.

Embodiment 273 is the gRNA of any one of embodiments 205-272, wherein:

a. LS1 does not comprise a 2'-OMe modification;
b. LS8 does not comprise a 2'-OMe modification; and/or
c. LS10 does not comprise a 2'-OMe modification.

Embodiment 274 is the gRNA of any one of embodiments 205-273, wherein:

a. N2 does not comprise a 2'-OMe modification;
b. N3 does not comprise a 2'-OMe modification;
c. N4 does not comprise a 2'-OMe modification;
d. N5 does not comprise a 2'-OMe modification;
e. N6 does not comprise a 2'-OMe modification;
f. N7 does not comprise a 2'-OMe modification;
g. N10 does not comprise a 2'-OMe modification;
h. N11 does not comprise a 2'-OMe modification;
i. N16 does not comprise a 2'-OMe modification; and/or
j. N17 does not comprise a 2'-OMe modification.

Embodiment 275 is the gRNA of any one of embodiments 205-274, wherein:

a. H1-2 does not comprise a phosphorothioate linkage;
b. H1-3 does not comprise a phosphorothioate linkage;

c. H1-4 does not comprise a phosphorothioate linkage;
d. H1-5 does not comprise a phosphorothioate linkage;
e. H1-6 does not comprise a phosphorothioate linkage;
f. H1-7 does not comprise a phosphorothioate linkage;
g. H1-8 does not comprise a phosphorothioate linkage;
h. H1-9 does not comprise a phosphorothioate linkage;
i. H1-10 does not comprise a phosphorothioate linkage;
j. H2-1 does not comprise a phosphorothioate linkage;
k. H2-2 does not comprise a phosphorothioate linkage;
l. H2-3 does not comprise a phosphorothioate linkage;
m. H2-4 does not comprise a phosphorothioate linkage;
n. H2-5 does not comprise a phosphorothioate linkage;
o. H2-6 does not comprise a phosphorothioate linkage;
p. H2-7 does not comprise a phosphorothioate linkage;
q. H2-8 does not comprise a phosphorothioate linkage;
r. H2-9 does not comprise a phosphorothioate linkage;
s. H2-10 does not comprise a phosphorothioate linkage;
t. H2-11 does not comprise a phosphorothioate linkage;
u. H2-12 does not comprise a phosphorothioate linkage;
v. H2-13 does not comprise a phosphorothioate linkage;
w. H2-14 does not comprise a phosphorothioate linkage; and/or
x. H2-15 does not comprise a phosphorothioate linkage.

Embodiment 276 is a gRNA which is an sgRNA comprising modifications at:

a. nucleotides 6-10 from the 5' end of the 5' terminus, which are optionally PS modifications;
b. nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus, which are optionally 2'-fluoro modifications; and
c. H1-1 and H2-1, which are optionally 2'-OMe modifications, or conserved region YA site 1 or 8.

Embodiment 277 is a gRNA which is an sgRNA comprising YA modifications at:

a. conserved region YA sites 1, 5, 6, 7, and 9, which are optionally 2'-OMe modifications; and
b. conserved region YA site 8, which is optionally a 2'-fluoro modification.

Embodiment 278 is a gRNA comprising YA modifications at four guide region YA sites, wherein at least one of the YA sites is at or after nucleotide 8 from the 5' end of the 5' terminus, and wherein:

a. the first YA site comprises a 2'-OMe modification;
b. the second YA site comprises a 2'-fluoro modification;
c. the third YA site comprises a 2'-fluoro or PS modification; and
d. the fourth YA site comprises a PS modification,

optionally wherein the first, second, third, and fourth YA sites are arranged in the 5' to 3' direction.

Embodiment 279 is the gRNA of embodiment 278, wherein the third YA site comprises a PS modification.

Embodiment 280 is the gRNA of any one of embodiments 278-279, wherein the third YA site comprises a 2'-fluoro modification.

Embodiment 281 is the gRNA of any one of embodiments 278-280, further comprising a fifth YA site comprising a PS modification, which is optionally 3' of the fourth YA site.

Embodiment 282 is the gRNA of any one of the embodiments 205-281, wherein conserved region YA sites 1, 5, 6, 7, and 9 comprise YA modifications, which are optionally 2'-OMe modifications; and conserved region YA site 8 comprises a modification, which is optionally a 2'-fluoro modification.

Embodiment 283 is a gRNA which is an sgRNA comprising YA modifications at:

a. nucleotide 4 from the 5' end of the 5' terminus, wherein the YA modification is optionally a 2'-OMe modification;
b. nucleotides 6-10 from the 5' end of the 5' terminus, which are optionally PS modifications;
c. nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus, which are optionally 2'-fluoro modifications;
d. LS5, LS7, LS9, and LS11, which are optionally 2'-fluoro modifications;
e. LS8, LS10, and LS12, which are optionally 2'-OMe modifications;
f. N2, N3, N4, N5, N6, N7, N10, N11, N16, and N17, which are optionally 2'-OMe modifications; and
g. N14, which is optionally a 2'-fluoro modification.

Embodiment 284 is the gRNA of any one of embodiment 161-, wherein one or more of the following are true:

a. nucleotide 4 from the 5' end of the 5' terminus comprises a 2'-OMe modification;
b. nucleotides 6-10 from the 5' end of the 5' terminus comprise PS modifications;
c. nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus comprise 2'-fluoro modifications;
d. LS5, LS7, LS9, and LS11 comprise 2'-fluoro modifications;
e. LS8, LS10, and LS12 comprise 2'-OMe modifications;
f. N2, N3, N4, N5, N6, N7, N10, N11, N16, and N17 comprise 2'-OMe modifications; and
g. N14 comprises a 2'-fluoro modification.

Embodiment 285 is the gRNA of any one of embodiments 161-284, wherein at least one YA modification comprises a modification of the pyrimidine position of the YA site.

Embodiment 286 is the gRNA of any one of embodiments 161-285, wherein at least one YA modification comprises a modification of the adenine position of the YA site.

Embodiment 287 is the gRNA of any one of embodiments 161-286, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 YA sites comprise YA modifications at the pyrimidines positions of the YA sites.

Embodiment 288 is the gRNA of any one of embodiments 161-287, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 YA sites comprise YA modifications at the adenine positions of the YA sites.

Embodiment 289 is the gRNA of any one of embodiments 161-288, wherein at least one YA modification comprises a 2'-OMe modification.

Embodiment 290 is the gRNA of any one of embodiments 161-289, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 YA sites comprise a 2'-OMe modification.

Embodiment 291 is the gRNA of any one of embodiments 161-290, wherein each modified conserved region YA site comprises a modification at the pyrimidine position of the YA site.

Embodiment 292 is the gRNA of any one of embodiments 161-291, wherein each modified guide region YA site, or each modified conserved region and guide region YA site, comprises a modification at the pyrimidine position of the YA site.

Embodiment 293 is the gRNA of any one of embodiments 161-292, wherein each modified conserved region YA site comprises a modification at the adenine position of the YA site.

Embodiment 294 is the gRNA of any one of embodiments 161-293, wherein each modified guide region YA site, or each modified conserved region and guide region YA site, comprises a modification at the adenine position of the YA site.

Embodiment 295 is the gRNA of any one of embodiments 161-294, which is an sgRNA comprising a modification at LS5.

Embodiment 296 is the gRNA of any one of embodiments 161-295, which is an sgRNA comprising a modification at LS7.

Embodiment 297 is the gRNA of any one of embodiments 161-296, which is an sgRNA comprising a modification at LS9, optionally wherein if LS9 is modified and LS5, LS7, and LS12 are not, then the modification of LS9 is other than 2'-fluoro.

Embodiment 298 is the gRNA of any one of embodiments 161-297, which is an sgRNA comprising a modification at LS12, optionally wherein if LS12 is modified and LS9 is not, then the modification of LS12 is other than 2'-OMe.

Embodiment 299 is the gRNA of any one of embodiments 161-298, which is an sgRNA comprising at least one YA modification that stabilizes a secondary structure, optionally wherein the secondary structure is the lower stem.

Embodiment 300 is the gRNA of any one of embodiments 161-299, which is an sgRNA comprising at least one modification of LS8 and/or LS11, optionally wherein the modification of LS8 and/or LS11 stabilizes a secondary structure.

Embodiment 301 is the gRNA of any one of embodiments 161-300, comprising a YA modification that stabilizes a secondary structure chosen from:

a. ENA;
b. LNA; or
c. a bicyclic ribose modification.

Embodiment 302 is the gRNA of any one of embodiments 161-301, which is an sgRNA comprising a modification at N6.

Embodiment 303 is the gRNA of any one of embodiments 161-302, which is an sgRNA comprising a modification at N14.

Embodiment 304 is the gRNA of any one of embodiments 161-303, which is an sgRNA comprising a modification at N17, optionally wherein if N17 is modified and N6 and N14 are not, then the modification of N17 is other than 2'-fluoro and other than 2'-OMe.

Embodiment 305 is the gRNA of any one of embodiments 161-304, wherein at least 1, 2, or 3 of nucleotides 1-3 from the 5' end of the 5' terminus comprise

deoxyribonucleotides, optionally wherein nucleotides 1-3 from the 5' end of the 5' terminus comprise PS modifications.

Embodiment 306 is the gRNA of any one of embodiments 161-305, wherein the gRNA is an sgRNA and at least 1, 2, or 3 of nucleotides 1-3 from the 3' end of the 3' terminus comprise deoxyribonucleotides, optionally wherein nucleotides 2-3 from the 3' end of the 3' terminus comprise PS modifications.

Embodiment 307 is the gRNA of any one of embodiments 161-306, wherein the gRNA is an sgRNA and nucleotide 4 from the 3' end of the 3' terminus comprises a PS modification, optionally wherein nucleotide 4 from the 3' end of the 3' terminus comprises a 2'-OMe modification.

Embodiment 308 is the gRNA of any one of embodiments 161-307, wherein the gRNA is an sgRNA and hairpin 2 comprises deoxyribonucleotides, optionally wherein all or all but 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides of hairpin 1 and hairpin 2 are deoxyribonucleotides.

Embodiment 309 is the gRNA of any one of embodiments 161-308, wherein the gRNA is an sgRNA and hairpin 1 and hairpin 2 comprise deoxyribonucleotides, optionally wherein all or all but 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 nucleotides of hairpin 1 and hairpin 2 are deoxyribonucleotides.

Embodiment 310 is the gRNA of any one of embodiments 161-309, wherein the gRNA is an sgRNA and all or all but 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 nucleotides from the beginning of hairpin 1 to the 3' end of the sgRNA are deoxyribonucleotides, optionally wherein nucleotides 1-3 from the 3' end of the 3' terminus are deoxyribonucleotides.

Embodiment 311 is the gRNA of any one of embodiments 161-310, wherein the gRNA is an sgRNA and the upper stem comprises deoxyribonucleotides.

Embodiment 312 is the gRNA of any one of embodiments 161-311, wherein the gRNA is an sgRNA and all or all but 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides of the upper stem are deoxyribonucleotides.

Embodiment 313 is the gRNA of any one of embodiments 161-312, wherein at least 1, 2, or 3 of nucleotides 1-3 from the 5' end of the 5' terminus comprise ENA, optionally wherein nucleotides 1-3 from the 5' end of the 5' terminus comprise PS modifications.

Embodiment 314 is the gRNA of any one of embodiments 161-313, wherein the gRNA is an sgRNA and at least 1, 2, or 3 of nucleotides 2-4 from the 3' end of the 3' terminus

comprise ENA, optionally wherein nucleotides 2-3 from the 3' end of the 3' terminus comprise PS modifications.

Embodiment 315 is the gRNA of any one of embodiments 161-314, wherein at least 1, 2, or 3 of nucleotides 1-3 from the 5' end of the 5' terminus comprise UNA, optionally wherein nucleotides 1-3 from the 5' end of the 5' terminus comprise PS modifications.

Embodiment 316 is the gRNA of any one of embodiments 161-315, wherein the gRNA is an sgRNA and at least 1, 2, or 3 of nucleotides 2-4 from the 3' end of the 3' terminus comprise UNA, optionally wherein nucleotides 2-3 from the 3' end of the 3' terminus comprise PS modifications.

Embodiment 317 is the gRNA of any one of embodiments 161-316, wherein the gRNA is an sgRNA and nucleotide 4 from the 3' end of the 3' terminus comprises a PS modification, optionally wherein nucleotide 4 from the 3' end of the 3' terminus comprises a 2'-OMe modification.

Embodiment 318 is the gRNA of any one embodiments 161-317, wherein the gRNA is an sgRNA that comprises a 3' end modification.

Embodiment 319 is the gRNA of any one of embodiments 161-318, which is an sgRNA comprising a 3' end modification, wherein the 3' end modification is a protective 3' end modification.

Embodiment 320 is the gRNA of any one embodiments 161-319, wherein the gRNA is an sgRNA that comprises a 3' tail.

Embodiment 321 is the gRNA of embodiment 320, wherein the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

Embodiment 322 is the gRNA of embodiment 320, wherein the 3' tail comprises about 1-2, 1-3, 1-4, 1-5, 1-7, 1-10, at least 1-5, at least 1-3, at least 1-4, at least 1-5, at least 1-5, at least 1-7, or at least 1-10 nucleotides.

Embodiment 323 is the gRNA of any one of embodiments 161-322, which is an sgRNA comprising a modification in the hairpin region.

Embodiment 324 is the gRNA of any one of embodiments 161-323, which is an sgRNA comprising a 3' end modification, and a modification in the hairpin region.

Embodiment 325 is the gRNA of embodiment 323 or 324, wherein the modification in the hairpin region comprises a modified nucleotide selected from 2'-O-methyl (2'-O-Me) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, or combinations thereof.

Embodiment 326 is the gRNA of any one of embodiments 323-325, wherein the modification in the hairpin region comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

Embodiment 327 is the gRNA of any one of embodiments 323-326, wherein the modification in the hairpin region comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

Embodiment 328 is the gRNA of any one of embodiments 161-327, comprising 3' and/or 5' protective end modification(s).

Embodiment 329 is the gRNA of embodiment 328, wherein the 3' and/or 5' end modification comprises a modified nucleotide selected from 2'-O-methyl (2'-O-Me) modified nucleotide, 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, an inverted abasic modified nucleotide, or combinations thereof.

Embodiment 330 is the gRNA of embodiment 328 or 329, wherein the 3' and/or 5' end modification comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

Embodiment 331 is the gRNA of embodiment 328 or 329, wherein the 3' and/or 5' end modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

Embodiment 332 is the gRNA of embodiment 328 or 329, wherein the 3' and/or 5' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides.

Embodiment 333 is the gRNA of embodiment 328 or 329, wherein the 3' and/or 5' end modification comprises or further comprises an inverted abasic modified nucleotide.

Embodiment 334 is the gRNA of any one any one of embodiments 161-333, wherein the gRNA is an sgRNA and if the sgRNA comprises a 3' end modification, the 3' end modification comprises any one or more of the following:

i. a modification of any one or more of the last 7, 6, 5, 4, 3, 2, or 1 nucleotides;
ii. one modified nucleotide;
iii. two modified nucleotides;
iv. three modified nucleotides;
v. four modified nucleotides;
vi. five modified nucleotides;
vii. six modified nucleotides; and

viii. seven modified nucleotides.

Embodiment 335 is the gRNA of embodiment 334, wherein the 3' end modification comprises a modification of between 1 and 7, between 1 and 5, between 1 and 4, or between 2 and 4 nucleotides.

Embodiment 336 is the gRNA of any one of embodiments 161-335, wherein the gRNA is an sgRNA comprising a 3' end modification and the 3' end modification comprises one or more of the following:

i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-O-Me modified nucleotide;
iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide
vi. ENA, UNA, and/or DNA; and
vii. or a combination thereof.

Embodiment 337 is the gRNA of any one of embodiments 161-336, wherein the gRNA is an sgRNA comprising a 3' tail, and the 3' tail comprises any one or more of:

i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-O-Me modified nucleotide;
iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide
vi. ENA, UNA, and/or DNA; and
vii. or a combination thereof.

Embodiment 338 is the gRNA of embodiment 336, wherein the 3' end modification comprises:

i. 1, 2, 3, 4, 5, 6, or 7 PS linkages between nucleotides;
ii. about 1-3, 1-5, 1-6, or 1-7 PS linkages between nucleotides; or
iii. PS linkages between each nucleotide.

Embodiment 339 is the gRNA of any one of embodiments embodiment 326-328, wherein the 3' end modification further comprises at least one 2'-O-Me, 2'-O-moe, inverted abasic, or 2'-F modified nucleotide.

Embodiment 340 is the gRNA of any one of embodiments 326-329, wherein the 3' end modification comprises at least one PS linkage, and wherein:

i. there is one PS linkage, and the linkage is between the last and second to last nucleotide;

ii. there are two PS linkages between the last three nucleotides;

iii. there are PS linkages between any one or more of the last four nucleotides;

iv. there are PS linkages between any one or more of the last five nucleotides; or

v. there are PS linkages between any one or more of the last 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

Embodiment 341 is the gRNA of any one of embodiments 336-340, wherein the 3' end modification comprises:

i. a modification of one or more of the last 1-7 nucleotides, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof;

ii. a modification to the last nucleotide with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and an optional one or two PS linkages to the next nucleotide and/or the first nucleotide of the 3' tail;

iii. a modification to the last and/or second to last nucleotide with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages;

iv. a modification to the last, second to last, and/or third to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages;

v. a modification to the last, second to last, third to last, and/or fourth to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages; or

vi. a modification to the last, second to last, third to last, fourth to last, and/or fifth to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

Embodiment 342 is the gRNA of any one of embodiments 161-341, wherein the gRNA is an sgRNA comprising a 3' tail, wherein the 3' tail comprises a modification of any one or more of the nucleotides present in the 3' tail.

Embodiment 343 is the gRNA of embodiment 342, wherein the 3' tail is fully modified.

Embodiment 344 is the gRNA of embodiment 342, wherein the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, or 1-10 nucleotides, optionally where any one or more of these nucleotides are modified.

Embodiment 345 is the gRNA of any one of embodiments 336-344, wherein the 3' end modification comprises any one or more of the following:

i. the 3' end modification as shown in any one of SEQ ID Nos: 401-532;

ii. (i) a 2'O-Me modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, (ii) three consecutive 2'O-moe modified nucleotides immediately 5' to the 2'O-Me modified nucleotide, and (iii) three consecutive PS linkages between the last three nucleotides;

iii. (i) five consecutive 2'O-Me modified nucleotides from the 3' end of the 3' terminus, and (ii) three PS linkages between the last three nucleotides;

iv. an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA;

v. (i) an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, and (ii) three consecutive 2'O-Me modified nucleotides at the last three nucleotides of the conserved region of an sgRNA or short-sgRNA;

vi. (i) 15 consecutive 2'O-Me modified nucleotides from the 3' end of the 3' terminus, (ii) five consecutive 2'-F modified nucleotides immediately 5' to the 2'O-Me modified nucleotides, and (iii) three PS linkages between the last three nucleotides;

vii. (i) alternating 2'O-Me modified nucleotides and 2'-F modified nucleotides at the last 20 nucleotides of the conserved region of an sgRNA or short-sgRNA, and (ii) three PS linkages between the last three nucleotides;

viii. (i) two or three consecutive 2'O-Me modified nucleotides, and (ii) three PS linkages between the last three nucleotides;

ix. one PS linkage between the last and next to last nucleotides; and

x. 15 or 20 consecutive 2'O-Me modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

Embodiment 346 is the gRNA of any one of embodiments 161-345, comprising a 5' end modification comprising any one or more of the following:

i. a modification of any one or more of nucleotides 1-7 of the guide region;
ii. one modified nucleotide;
iii. two modified nucleotides;
iv. three modified nucleotides;
v. four modified nucleotides;
vi. five modified nucleotides;
vii. six modified nucleotides; and
viii. seven modified nucleotides.

Embodiment 347 is the gRNA of any one of embodiments 161-346, comprising a 5' end modification, wherein the 5' end modification is a protective 5' end modification.

Embodiment 348 is the gRNA of any one of embodiments 161-347, comprising a 5' end modification, wherein the 5' end modification comprises a modification of between 1 and 7, between 1 and 5, between 1 and 4, between 1 and 3, or between 1 and 2 nucleotides.

Embodiment 349 is the gRNA of any one of embodiments 161-348, comprising a 5' end modification wherein the 5' end modification comprises any one or more of the following:

i. modifications of 1, 2, 3, 4, 5, 6, or 7 of the first 7 nucleotides;
ii. modifications of about 1-3, 1-4, 1-5, 1-6, or 1-7 of the first 7 nucleotides; and
iii. modifications at the first, second, third, fourth, fifth, sixth, and/or seventh nucleotide at the 5' end, optionally wherein the modifications are consecutive.

Embodiment 350 is the gRNA of any one of embodiments 161-349, comprising a 5' end modification, wherein the 5' end modification comprises one or more of:

i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-O-Me modified nucleotide;
iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide
vi. ENA, UNA, and/or DNA; and

vii. combinations thereof.

Embodiment 351 is the gRNA any one of embodiments 161-350, comprising a 5' end modification wherein the 5' end modification comprises:

i. 1, 2, 3, 4, 5, 6, and/or 7 PS linkages between nucleotides; or

ii. about 1-2, 1-3, 1-4, 1-5, 1-6, or 1-7 PS linkages between nucleotides.

Embodiment 352 is the gRNA of any one of embodiments 161-351, wherein the sgRNA comprises a 5' end modification and the 5' end modification comprises at least one 2'-O-Me, 2'-O-moe, inverted abasic, 2'-H, inosine, or 2'-F modified nucleotide.

Embodiment 353 is the gRNA of embodiment 352, wherein the 5' end modification comprises at least one PS linkage, and wherein:

i. there is one PS linkage, and the linkage is at nucleotide 1 of the guide region;

ii. there are two PS linkages, and the linkages are at nucleotides 1 and 2 of the guide region;

iii. there are PS linkages at any one or more of nucleotides 1, 2, and 3 of the guide region;

iv. there are PS linkages at any one or more of nucleotides 1, 2, 3, and 4 of the guide region;

v. there are PS linkages at any one or more of nucleotides 1, 2, 3, 4, and 5 of the guide region;

vi. there are PS linkages at any one or more of nucleotides 1, 2, 3, 4, 5, and 6 of the guide region; or

vii. there are PS linkages at any one or more of nucleotides 1, 2, 3, 4, 5, 6, and 7 of the guide region.

Embodiment 354 is the gRNA of any one of embodiments 352-353, wherein the 5' end modification comprises:

i. a modification of one or more of nucleotides 1-7 of the variable region, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, and/or combinations thereof;

ii. a modification to the first nucleotide of the guide region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and an optional PS linkage to the next nucleotide;

iii. a modification to the first and/or second nucleotide of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and optionally one or more PS linkages;

iv. a modification to the first, second, and/or third nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and optionally one or more PS linkages;

v. a modification to the first, second, third, and/or fourth nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and optionally one or more PS linkages; or

vi. a modification to the first, second, third, fourth, and/or fifth nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and optionally one or more PS linkages.

Embodiment 355 is the gRNA of any one of embodiments 161-354, comprising a 5' end modification, wherein the 5' end modification comprises any one or more of the following:

i. a 5' end modification as shown in any one of SEQ ID Nos: 1-54, 401-532, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, 3388-3430, or 3549-3552;

ii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region;

iii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

iv. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region;

v. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region;

vi. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region;

vii. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

viii. an inverted abasic modified nucleotide at nucleotide 1 of the guide region;

ix. an inverted abasic modified nucleotide at nucleotide 1 of the guide region and 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region; and

x. an inverted abasic modified nucleotide at nucleotide 1 of the guide region, 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region, and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the variable region.

Embodiment 356 is the gRNA of any one of embodiments 161-355, wherein the gRNA is an sgRNA and the upper stem region comprises at least one modification.

Embodiment 357 is the gRNA of embodiment 346, wherein the upper stem modification comprises any one or more of the following:

i. a modification to any one or more of US1-US12 in the upper stem region;

ii. a modification of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all 12 nucleotides in the upper stem region; and

iii. a modification of about 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, or 1-12 nucleotides in the upper stem region.

Embodiment 358 is the gRNA of any one of embodiments 356-357, wherein the upper stem modification comprises one or more of:

i. a 2'-O-Me modified nucleotide;

ii. a 2'-H modified nucleotide;

iii. a 2'-F modified nucleotide; and

iv. combinations thereof.

Embodiment 359 is the gRNA of any one of embodiments 161-358, wherein the gRNA is an sgRNA comprising one or more modifications in the hairpin 1 region.

Embodiment 360 is the gRNA of embodiment 359 wherein the sgRNA comprises a modification at H1-1.

Embodiment 361 is the gRNA of any one of embodiments 161-360, wherein the gRNA is an sgRNA comprising one or more modifications in the hairpin 2 region.

Embodiment 362 is the gRNA of embodiment 361, wherein the sgRNA comprises a modification at H2-1.

Embodiment 363 is the gRNA of any one of embodiments 161-362, wherein the gRNA is an sgRNA comprising comprises modifications at H1-1 to H1-12.

Embodiment 364 is the gRNA of any one of embodiments 161-363, wherein the gRNA is an sgRNA comprising comprises modifications at H2-1 to H2-15.

Embodiment 365 is the gRNA of any one of embodiments 161-364, wherein the gRNA is an sgRNA comprising one or more modifications in each of the upper stem region, the hairpin 1 region, and the hairpin 2 region.

Embodiment 366 is the gRNA of any one of embodiments 161-365, wherein the gRNA is an sgRNA comprising a modified nucleotide between hairpin 1 and hairpin 2 regions.

Embodiment 367 is the gRNA of any one of embodiments 161-366, which is an sgRNA further comprising a lower stem region comprising a modification.

Embodiment 368 is the gRNA of any one of embodiments 161-367, further comprising a 3' end modification.

Embodiment 369 is the gRNA of embodiment 368, wherein at least two of the last four nucleotides at the 3' end of the 3' terminus are modified.

Embodiment 370 is the gRNA of embodiment 369, wherein at least two of the last four nucleotides at the 3' end of the 3' terminus are modified with 2'-O-Me, 2'-F, or 2'-O-moe.

Embodiment 371 is the gRNA of any one of embodiments 368-370, further comprising phosphorothioate (PS) bonds between one or more of the last four nucleotides at the 3' end of the 3' terminus.

Embodiment 372 is the gRNA of any one of embodiments 161-371, which is an sgRNA further comprising a bulge region comprising a modification.

Embodiment 373 is the gRNA of any one of embodiments 161-372, which is an sgRNA further comprising a nexus region comprising a modification.

Embodiment 374 is an sgRNA comprising any of SEQ ID Nos: 401-535, 601, 607-732, 801, 807-932, 1001, or 1007-1132, including the modifications of Table 1.

Embodiment 375 is an sgRNA comprising nucleic acids having at least 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% identity to the nucleic acids of any one of SEQ ID Nos: 401-535, 601, 607-732, 801, 807-932, 1001, or 1007-1132, wherein the modification at each nucleotide of the sgRNA that corresponds to a nucleotide of the

reference sequence identifier in Table 1, is identical to or equivalent to the modification shown in the reference sequence identifier in Table 1.

Embodiment 376 is the gRNA of any one of embodiments 161-375, wherein the modification reduces gRNA degradation without significantly altering the ability of the guide to cleave a target nucleic acid.

Embodiment 377 is the gRNA of any one of embodiments 161-376, comprising a YA modification wherein the modification comprises 2'-fluoro, 2'-H, 2'-O-Me, ENA, UNA, or PS.

Embodiment 378 is the gRNA of any one of embodiments 161-377, comprising a YA modification wherein the modification alters the structure of the dinucleotide motif to reduce RNA endonuclease activity.

Embodiment 379 is the gRNA of any one of embodiments 161-378, comprising a YA modification wherein the modification interferes with recognition or cleavage of a YA site by an RNase and/or stabilizes an RNA structure.

Embodiment 380 is the gRNA of any one of embodiments 161-379, comprising a YA modification wherein the modification comprises one or more of:

a. a ribose modification selected from 2'-O-alkyl, 2'-F, 2'-moe, 2'-F arabinose, and 2'-H (deoxyribose);
b. a bicyclic ribose analog, such as LNA, BNA, and ENA;
c. an unlocked nucleic acid modification;
d. a base modification, such as inosine, pseudouridine, and 5'-methylcytosine; and
e. an internucleoside linkage modification such as phosphorothioate.

Embodiment 381 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises a modification at nucleotide 5, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

Embodiment 382 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises a modification at nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

Embodiment 383 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises a 2'-OMe modification at nucleotide 5 and/or nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

Embodiment 384 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises a 2'-F modification at nucleotide 5 and/or nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

Embodiment 385 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises a 2'-H modification at nucleotide 5 and/or nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

Embodiment 386 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises a phosphorothioate modification at nucleotide 5 and/or nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

Embodiment 387 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises modifications at:

i. nucleotides 8-10;

ii. nucleotides 8 and 9;

iii. nucleotides 8 and 10; or

iv. nucleotides 9 and 10,

optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

Embodiment 388 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-F modifications at:

i. nucleotides 8-10;

ii. nucleotides 8 and 9;

iii. nucleotides 8 and 10;

iv. nucleotides 9 and 10; or

v. nucleotide 8;

optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

Embodiment 389 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-F modifications at:

i. nucleotides 8-10;

ii. nucleotides 8 and 9;

iii. nucleotides 8 and 10;

iv. nucleotides 9 and 10; or

v. nucleotide 8;

wherein nucleotides 8-10 do not comprise phosphorothioate modifications, and optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

Embodiment 390 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-F modifications at nucleotides 8-10 and:

i. phosphorothioate modifications at 1, 2, or 3 of nucleotides 8-10;

ii. a phosphorothioate modification at nucleotide 8;

iii. a phosphorothioate modification at nucleotide 9;

iv. a phosphorothioate modification at nucleotide 10;

v. a phosphorothioate modification at nucleotides 8 and 9;

vi. a phosphorothioate modification at nucleotides 8 and 10;

vii. a phosphorothioate modification at nucleotides 9 and 10; or

vii. a phosphorothioate modification at nucleotides 8-10

optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

Embodiment 391 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises:

i. a 2'-F or phosphorothioate modification at nucleotides 5 and 6;

ii. a 2'-F modification at nucleotides 5 and 6;

iii. a phosphorothioate modification at nucleotides 5 and 6;

iv. a 2'-F modification at nucleotide 5 and a phosphorothioate modification at nucleotide 6; or

v. a 2'-F modification at nucleotide 6 and a phosphorothioate modification at nucleotide 5;

optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 7-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

Embodiment 392 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-F modifications at at least 1, 2, 3, 4, 5, or 6 of nucleotides 6-11, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3, and/or 2'-F modifications at nucleotides 13, 14, 17, and 18.

Embodiment 393 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-F modifications at at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of nucleotides 1-4 and 6-11, optionally wherein the guide region comprises phosphorothioate modifications at nucleotides 1-3 and/or 2'-F modifications at nucleotides 13, 14, 17, and 18.

Embodiment 394 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-F modifications at nucleotides 6-11, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3, and/or 2'-F modifications at nucleotides 13, 14, 17, and 18.

Embodiment 395 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-F modifications at nucleotides 1-4, optionally wherein the guide region comprises phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 6-11, 13, 14, 17, and 18.

Embodiment 396 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises a 2'-F modification at nucleotide 9 and not a phosphorothioate modification at nucleotide 9, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-8 and 10, and/or 2'-F modifications at nucleotides 8, 10, 11, 13, 14, 17, and 18.

Embodiment 397 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that does not comprise 2'-F modifications at at least 1, 2, 3, 4, 5, 6, 7, or 8 of nucleotides 8-11, 13, 14, 17, and 18, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

Embodiment 398 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that does not comprise 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

Embodiment 399 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-OMe modifications at at least 1, 2, 3, or 4 of nucleotides 9, 11, 13, and 14, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

Embodiment 400 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises 2'-OMe modifications at nucleotides 9, 11, 13, and 14, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

Embodiment 401 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises phosphorothioate modifications at one or both of nucleotides 8 and 10, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

Embodiment 402 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises modifications at at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or all of the following nucleotides: 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18, optionally wherein the modifications are 2'-OMe, 2'-fluoro, or phosphorothioate modifications.

Embodiment 403 is the gRNA of any one of the the preceding embodiments, wherein the gRNA comprises a guide region that comprises modifications at nucleotides 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18, optionally wherein the modifications are 2'-OMe, 2'-fluoro, or phosphorothioate modifications.

Embodiment 404 is the gRNA of any one of the preceding embodiments, wherein 2'-OMe modifications are not present in the guide region at nucleotides 6-11 and 13-end.

Embodiment 405 is the gRNA of any one of the preceding embodiments, wherein 2'-fluoro modifications are not present in the guide region at nucleotides 1-7, 15, 16, and 19-end.

Embodiment 406 is the gRNA of any one of the preceding embodiments, wherein phosphorothioate modifications are not present in the guide region at nucleotides 4, 5, 11-14, 17, and 18.

Embodiment 407 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises an unmodified nucleotide 20.

Embodiment 408 is the gRNA of any one of the preceding embodiments, wherein the guide region consists of 20 nucleotides.

Embodiment 409 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 5-6 and a modification at nucleotide 5.

Embodiment 410 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 12-13 and a modification at nucleotide 12.

Embodiment 411 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 15-16 and a modification at nucleotide 15.

Embodiment 412 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 16-17 and a modification at nucleotide 16.

Embodiment 413 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 19-20 and a modification at nucleotide 19.

Embodiment 414 is the gRNA of any one of the preceding embodiments, wherein the guide region does not comprise a YA site at nucleotides 5-6 and nucleotide 5 is unmodified.

Embodiment 415 is the gRNA of any one of the preceding embodiments, wherein the guide region does not comprise a YA site at nucleotides 12-13 and nucleotide 12 is unmodified.

Embodiment 416 is the gRNA of any one of the preceding embodiments, wherein the guide region does not comprise a YA site at nucleotides 15-16 and nucleotide 15 is unmodified.

Embodiment 417 is the gRNA of any one of the preceding embodiments, wherein the guide region does not comprise a YA site at nucleotides 16-17 and nucleotide 16 is unmodified.

Embodiment 418 is the gRNA of any one of the preceding embodiments, wherein the guide region does not comprise a YA site at nucleotides 19-20 and nucleotide 19 is unmodified.

Embodiment 419 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a guide region that comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or all of the following:

a. 2'-OMe and phosphorothioate modifications at nucleotide 1;
b. 2'-OMe and phosphorothioate modifications at nucleotide 2;
c. 2'-OMe and phosphorothioate modifications at nucleotide 3;
d. a 2'-OMe modification at nucleotide 4;
e. a phosphorothioate modification at nucleotide 6;
f. a phosphorothioate modification at nucleotide 7;
g. 2'-fluoro and phosphorothioate modifications at nucleotide 8;
h. 2'-fluoro and phosphorothioate modifications at nucleotide 9;
i. 2'-fluoro and phosphorothioate modifications at nucleotide 10;
j. a 2'-fluoro modification at nucleotide 11;
k. a 2'-fluoro modifications at nucleotide 13;
l. a 2'-fluoro modifications at nucleotide 14;
m. a 2'-fluoro modifications at nucleotide 17; and
n. a 2'-fluoro modifications at nucleotide 18.

Embodiment 420 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises each of the modifications set forth in the preceding embodiment.

Embodiment 421 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises at least 1, 2, 3, or 4 of the following:

i. a 2'-OMe modification at nucleotide 5 if nucleotides 5 and 6 form a YA site;

ii. a 2'-OMe modification at nucleotide 12 if nucleotides 12 and 13 form a YA site;

iii. a phosphorothioate modification at nucleotide 15 if nucleotides 15 and 16 form a YA site;

iv. a phosphorothioate modification at nucleotide 16 if nucleotides 16 and 17 form a YA site; and

v. a phosphorothioate or 2'-fluoro modification at nucleotide 19 if nucleotides 19 and 20 form a YA site.

Embodiment 422 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 5-6 and a a 2'-OMe modification at nucleotide 5.

Embodiment 423 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 12-13 and a 2'-OMe modification at nucleotide 12.

Embodiment 424 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 15-16 and a phosphorothioate modification at nucleotide 15.

Embodiment 425 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 16-17 and a phosphorothioate modification at nucleotide 16.

Embodiment 426 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a YA site at nucleotides 19-20 and a phosphorothioate modification at nucleotide 19.

Embodiment 427 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises a 2'-fluoro modification at nucleotide 19.

Embodiment 428 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises an unmodified nucleotide 15 or only a phosphorothioate modification at nucleotide 15.

Embodiment 429 is the gRNA of any one of the preceding embodiments, wherein the guide region comprises an unmodified nucleotide 16 or only a phosphorothioate modification at nucleotide 16.

Embodiment 430 is the gRNA of any one of the preceding embodiments, wherein the gRNA is an sgRNA comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides.

Embodiment 431 is the gRNA of embodiment 430, wherein the at least 5-10 lacking nucleotides are consecutive.

Embodiment 432 is the gRNA of embodiment 430 or 431, wherein the at least 5-10 lacking nucleotides:

i. are within hairpin 1;
ii. are within hairpin 1 and the "N" between hairpin 1 and hairpin 2;
iii. are within hairpin 1 and the two nucleotides immediately 3' of hairpin 1;
iv. include at least a portion of hairpin 1;
v. are within hairpin 2;
vi. include at least a portion of hairpin 2;
vii. are within hairpin 1 and hairpin 2;
viii. include at least a portion of hairpin 1 and include the "N" between hairpin 1 and hairpin 2;
ix. include at least a portion of hairpin 2 and include the "N" between hairpin 1 and hairpin 2;
x. include at least a portion of hairpin 1, include the "N" between hairpin 1 and hairpin 2, and include at least a portion of hairpin 2;
xi. are within hairpin 1 or hairpin 2, optionally including the "N" between hairpin 1 and hairpin 2;
xii. are consecutive;
xiii. are consecutive and include the "N" between hairpin 1 and hairpin 2;

xiv. are consecutive and span at least a portion of hairpin 1 and a portion of hairpin 2;

xv. are consecutive and span at least a portion of hairpin 1 and the "N" between hairpin 1 and hairpin 2; or

xvi. are consecutive and span at least a portion of hairpin 1 and two nucleotides immediately 3' of hairpin 1.

Embodiment 433 is the gRNA of any one of embodiments 430-432, wherein the at least 5-10 nucleotides comprise nucleotides 54-61 of SEQ ID NO:400, nucleotides 53-60 of SEQ ID NO:400; or nucleotides 54-58 of SEQ ID NO:400, optionally wherein the sgRNA comprises modifications at least H1-1 to H1-5 and H2-1 to H2-12.

Embodiment 434 is the gRNA of any one of embodiments 430-433, wherein the at least 5-10 nucleotides:

i. consist of 5-10 nucleotides;

ii. consist of 6-10 nucleotides;

iii. consist of 5 nucleotides;

iv. consist of 6 nucleotides;

v. consist of 7 nucleotides;

vi. consist of 8 nucleotides;

vii. consist of 9 nucleotides;

viii. consist of 10 nucleotides;

ix. consist of 5-10 consecutive nucleotides;

x. consist of 6-10 consecutive nucleotides;

xi. consist of 5 consecutive nucleotides;

xii. consist of 6 consecutive nucleotides;

xiii. consist of 7 consecutive nucleotides;

xiv. consist of 8 consecutive nucleotides;

xv. consist of 9 consecutive nucleotides; or

xvi. consist of 10 consecutive nucleotides.

Embodiment 435 is the gRNA of embodiment 434, wherein the at least 5-10 nucleotides comprise nucleotides 54-61 of SEQ ID NO:400, nucleotides 53-60 of SEQ ID NO:400; or nucleotides 54-58 of SEQ ID NO:400, optionally wherein the sgRNA comprises modifications at least H1-1 to H1-5 and H2-1 to H2-12.

Embodiment 436 is the gRNA of any one of embodiments 430-435, wherein the at least 5-10 nucleotides:

i. comprise nucleotides 54-61 of SEQ ID NO:400;
ii. comprise nucleotides 53-60 of SEQ ID NO:400;
iii. comprise nucleotides 54-58 of SEQ ID NO:400.
iv. consist of nucleotides 54-61 of SEQ ID NO:400;
v. consist of nucleotides 53-60 of SEQ ID NO:400; or
vi. consist of nucleotides 54-58 of SEQ ID NO:400.

Embodiment 437 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 15 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

Embodiment 438 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 16 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

Embodiment 439 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 17 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of a gRNA, wherein the gRNA is any one of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

Embodiment 440 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 18 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

Embodiment 441 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 19 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

Embodiment 442 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises modifications and/or unmodified nucleotides at nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

Embodiment 443 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises a modification pattern that matches at least 75% of the modification pattern of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

Embodiment 444 is the gRNA of any one of the preceding embodiments, wherein the gRNA comprises the modification pattern of any one of the gRNAs in Table 1, wherein the modification pattern is the same as any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

Embodiment 445 is the gRNA of any one of embodiments 437-444, further comprising a sequence having at least 75% identity to the sequence of nucleotides 21-end of the gRNA.

Embodiment 446 is the gRNA of any one of embodiments 437-444, further comprising a sequence having at least 80% identity to the sequence of nucleotides 21-end of the gRNA.

Embodiment 447 is the gRNA of any one of embodiments 437-444, further comprising a sequence having at least 85% identity to the sequence of nucleotides 21-end of the gRNA.

Embodiment 448 is the gRNA of any one of embodiments 437-444, further comprising a sequence having at least 90% identity to the sequence of nucleotides 21-end of the gRNA.

Embodiment 449 is the gRNA of any one of embodiments 437-444, further comprising a sequence having at least 95% identity to the sequence of nucleotides 21-end of the gRNA.

Embodiment 450 is the gRNA of any one of embodiments 437-444, further comprising a sequence having at least 98% identity to the sequence of nucleotides 21-end of the gRNA.

Embodiment 451 is the gRNA of any one of embodiments 437-444, further comprising a sequence having 100% identity to the sequence of nucleotides 21-end of the gRNA.

Embodiment 452 is an LNP composition comprising a gRNA of any one of the preceding embodiments.

Embodiment 453 is a composition comprising a gRNA of any one of embodiments 1-451 associated with a lipid nanoparticle (LNP).

Embodiment 454 is a composition comprising the gRNA of any one of embodiments 1-451, or the composition of any one of embodiments 452-453, further comprising a nuclease or an mRNA which encodes the nuclease.

Embodiment 455 is the composition of embodiment 454, wherein the nuclease is a Cas protein.

Embodiment 456 is the composition of embodiment 455, wherein the Cas protein is a Cas9.

Embodiment 457 is the composition of embodiment 456, wherein the Cas9 is an *S. pyogenes* Cas9 or an *S. aureus* Cas9.

Embodiment 458 is the composition of any one of embodiments 453-457, wherein the nuclease is a nickase or a dCas.

Embodiment 459 is the composition of any one of embodiments 453-458, wherein the nuclease is modified.

Embodiment 460 is the composition of embodiment 459 wherein the modified nuclease comprises a nuclear localization signal (NLS).

Embodiment 461 is the composition of any one of embodiments 452-460, comprising an mRNA which encodes the nuclease.

Embodiment 462 is the composition of embodiment 461, wherein the mRNA comprises the sequence of any one of SEQ ID NOs: 3499-3527 or 3529-3546.

Embodiment 463 is a pharmaceutical formulation comprising the gRNA of any one of embodiments 1-451 or the composition of any one of embodiments 452-462 and a pharmaceutically acceptable carrier.

Embodiment 464 is a method of modifying a target DNA comprising, delivering a Cas protein or a nucleic acid encoding a Cas protein, and any one or more of the following to a cell:

i. the gRNA of any one of embodiments 1-451;
ii. the composition of any one of embodiments 452-462; and
iii. the pharmaceutical formulation of embodiment 463.

Embodiment 465 is the method of embodiment 464, wherein the method results in an insertion or deletion in a gene.

Embodiment 466 is the method of embodiment 464 or embodiment 465, further comprising delivering to the cell a template, wherein at least a part of the template incorporates into a target DNA at or near a double strand break site induced by the Cas protein.

Embodiment 467 is the gRNA of any one of embodiments 1-451, the composition of embodiments 452-462, or the pharmaceutical formulation of embodiment 463 for use in preparing a medicament for treating a disease or disorder.

Embodiment 468 is the use of the gRNA of any one of embodiments 1-451, the composition of embodiments 452-462, or the pharmaceutical formulation of embodiment 463 in the manufacture of a medicament for treating a disease or disorder.

FIGURE LEGENDS

[0009] FIGs 1A and 1B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0010] FIGs 2A and 2B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0011] FIGs 3A and 3B show in vivo % editing and serum TTR results, respectively, for the indicated guides. FIGs 3C and 3D show in vivo % editing and serum TTR results,

respectively, for the indicated guides. FIGs 3E and 3F show in vivo % editing and serum TTR results, respectively, for the indicated guides in rats.

[0012] FIGs 4A and 4B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0013] FIG 5 show % editing in neuro2A cells in vitro.

[0014] FIGs 6A and 6B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0015] FIGs 7A and 7B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0016] FIGs 8A and 8B show in vivo % editing and serum TTR results, respectively, for the indicated guides. FIGs 8C and 8D show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0017] FIGs 9A, 9B, and 9C show % editing by concentration in PHH (9A), PCH (9B), and HepG2 (9C) cells, respectively, for the indicated guides.

[0018] FIG 10A shows an exemplary sgRNA (SEQ ID NO: 801, methylation not shown) in a possible secondary structure with labels designating individual nucleotides of the conserved region of the sgRNA, including the lower stem, bulge, upper stem, nexus (the nucleotides of which can be referred to as N1 through N18, respectively, in the 5' to 3' direction), and the hairpin region which includes hairpin 1 and hairpin 2 regions. A nucleotide between hairpin 1 and hairpin 2 is labeled n. A guide region may be present on an sgRNA and is indicated in this figure as "(N)x" preceding the conserved region of the sgRNA.

[0019] FIG 10B labels the 10 conserved region YA sites in an exemplary sgRNA sequence (SEQ ID NO: 801, methylation not shown) from 1 to 10. The numbers 25, 45, 50, 56, 64, 67, and 83 indicate the position of the pyrimidine of YA sites 1, 5, 6, 7, 8, 9, and 10 in an sgRNA with a guide region indicated as $(N)_x$, e.g., wherein x is optionally 20.

[0020] FIG 11A-E show results of nuclease stability assays in which the indicated guides were incubated with 0.01 mg/mL human liver cytosol (HLC) and cleavage sites were determined. FLP indicates signal from full-length product.

[0021] FIG 11F illustrates the location of cleavage sites observed in FIGs 11A-E mapped onto an exemplary guide sequence and possible secondary structure of SEQ ID NO: 401 (not all modifications are shown). Open triangles show YA cleavage sites in the guide region. Closed triangles show YA cleavage sites in the conserved region.

[0022] FIGs 12A-G show results of nuclease stability assays in which the indicated guides were incubated with 0.01 mg/mL human liver cytosol (HLC) and cleavage sites were determined.

[0023] FIGs 13A-B show results of nuclease stability assays in which G010039 was incubated with 0.01 mg/mL (A) or 8.5 mg/mL (B) human liver cytosol (HLC).

[0024] FIG 14 shows % editing results from experiments in which lipoplexes comprising the indicated guides were transfected into primary mouse hepatocytes (PMH).

[0025] FIG 15A-C show % editing results from experiments in which lipoplexes comprising the indicated guides were transfected into PMH, primary cynomolgous macaque hepatocytes (PCH), or primary human hepatocytes (PHH), respectively.

[0026] FIG 16A shows a scatter plot and correlation values for % editing results from experiments in which sgRNA was administered to mice in vivo or delivered to PMH via lipoplex transfection of the sgRNA.

[0027] FIGs 16B-F show correlation of in vivo and in vitro % editing results in which the in vitro results were generated by delivering the sgRNAs in LNPs to PHH.

[0028] FIG 16G shows a comparison of % editing with the indicated guides delivered to PMH by lipoplex transfection (data above left box), to PMH in LNP (data above center box), or to mice in vivo (data above right box).

[0029] FIG 16H shows a comparison of % editing with the indicated guides delivered to PMH in LNP (1 ng, 3 ng, 10 ng) or to mice in vivo (0.1 mpk, 0.3 mpk).

[0030] FIG 16I shows the results from Fig. 16G replotted to indicate differences in editing between G000282 and G000211. The barplot values were generated by dividing % editing of the G000282 value by the % editing of the G000211 value to indicate fold differences in editing. The indicated guides were delivered to PMH by lipoplex transfection (data above left box), to PMH in LNP (data above center box), or to mice in vivo (data above right box).

[0031] FIG 16J shows the results from Fig. 16H replotted to indicate differences in editing between G000283 and G000269. The barplot values were generated by dividing % editing of the G000283 value by the % editing of the G000269 value to indicate fold differences in editing. The indicated guides were delivered to PMH in LNP (data above left box) or to mice in vivo (data above right box).

[0032] FIGs 17A-B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0033] FIGs 18A-B show in vivo % editing and serum TTR results, respectively, for the indicated guides. FIGs 18C-D show in vivo % editing and serum TTR results, respectively, for the indicated guides. FIGs 18E-F show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0034] FIGs 19A-B show in vivo % editing and serum TTR results, respectively, for the indicated guides. FIGs 19C-D show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0035] FIGs 20A-B show in vivo % editing and serum TTR results, respectively, for the indicated guides at the indicated concentrations. FIGs 20C-D show in vivo % editing and serum TTR results, respectively, for the indicated guides at the indicated concentrations. FIGs 20E-F show in vivo % editing and serum TTR results, respectively, for the indicated guides at the indicated concentrations.

[0036] FIGs 21A-B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0037] FIGs 22A-B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0038] FIGs 23A-B show editing frequency for the indicated guides.

[0039] FIGs 24A-B show in vivo % editing and serum TTR results, respectively, for the indicated guides.

[0040] FIGs 25A-E show indel frequency versus guide concentration for the indicated guides.

[0041] FIGs 26A-E show indel frequency versus guide concentration for the indicated guides.

[0042] FIGs 27A-D show indel frequency versus guide concentration for the indicated guides.

[0043] FIGs 28A-D show indel frequency versus guide concentration for the indicated guides.

[0044] FIGs 29A-B and 29F show editing frequency for guides with the indicated dinucleotide modification (for a given 5' modified position, the immediately subsequent position was also modified in the same way). FIGs 29C-E show editing frequency for guides with the indicated modification at an individual nucleotide.

[0045] FIGs 30A-C show influence scores for the indicated modification at guide positions 1-20.

[0046] FIGs 31A-C show editing frequency for the indicated guides. Guides are grouped into boxes based on having similar conserved region modification patterns.

DETAILED DESCRIPTION

[0047] Provided herein are modified guide RNAs (gRNAs) for use in gene editing methods. Sequences of engineered and tested gRNAs are shown in Table 1.

[0048] Certain of the gRNAs provided herein are modified dual guide RNAs (dgRNAs) for use in gene editing methods. Sequences of engineered and tested dgRNAs are shown in Table 1. Certain of the dgRNAs have certain modifications at YA sites in the dgRNA, including modifications in the crRNA and/or the trRNA.

[0049] Certain of the gRNAs provided herein are modified single guide RNAs (sgRNAs) for use in gene editing methods. Sequences of engineered and tested sgRNAs are shown in Table 1. Certain of the sgRNAs have certain modifications at YA sites in the sgRNA, including modifications in the crRNA portion of the sgRNA and/or the trRNA portion of the sgRNA.

[0050] Also provided herein are short-single guide RNAs (short-sgRNAs), optionally modified, for use in gene editing methods. Sequences of engineered and tested short-sgRNAs are shown in Table 1. Certain of the short-sgRNAs have certain modifications at YA sites in the short-sgRNA, including modifications in the crRNA portion of the short-sgRNA and/or the trRNA portion of the short-sgRNA.

[0051] This disclosure further provides uses of these gRNAs (e.g., sgRNA, short-sgRNA, dgRNA, or crRNA) to alter the genome of a target nucleic acid *in vitro* (e.g., cells cultured *in vitro* for use in *ex vivo* therapy or other uses of genetically edited cells) or in a cell in a subject such as a human (e.g., for use in *in vivo* therapy). The present disclosure also provides methods for preventing or treating a disease in a subject by modifying a target gene associated with a disease. The disclosed gRNAs can be used with any cell type and at any genetic locus amenable to nuclease mediated genome editing technology.

Table 1 (Table of Sequences):

SEQ ID NO	Name	Sequence
1	G282	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
2	G515	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3	G621	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGC*mU*mU*mU
4	G632	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
5	G638	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
6	G639	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
7	G640	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
8	G641	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGU*mG*mC*mU
9	G211	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U
10	G269	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U
11	G620	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
12	G622	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGC*mU*mU*mU
13	G623	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
14	G624	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC

SEQ ID NO	Name	Sequence
15	G625	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAG GCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
16	G626	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAG GCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
17	G627	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAA CUUGGCACCGAGUCGGU*mG*mC*mU
18	G283	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
19	G628	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA ACUUGGCACCGAGUCGG*mU*mG*mC
20	G629	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA ACUUGGCACCGAGUCGGUGC*mU*mU*mU
21	G630	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA mAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
22	G631	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA ACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
23	G633	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
24	G634	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
25	G635	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA ACUUGGCACCGAGUCGGU*mG*mC*mU
26	G208-2	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA ACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U
27	G373-2	mC*mA*mG*GGCUCUUGAAGAUCUCCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
28	G513	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC

SEQ ID NO	Name	Sequence
29	G514	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmGmAmAmAmCAAGUUAAAAUAAGGCUAGUCCGUUAU CAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
30	G516	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGGAAACAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGG CACCGAGUCGG*mU*mG*mC
31	G517	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmA*mG*mU*mG
32	G518	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA ACUUGAAAAA*mG*mU*mG
33	G642	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG *mU*mG*mC
34	G612	moeU*moeU*moeA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGU UAUCAACUUGGCACCGAGUCGmoeG*moeU*moeG*mC
35	G613	mU*mU*mA*mC*mA*GCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUU AUCAACUUGGCACCGAGUC*mG*mU*mG*mC
36	G614	(invd)UUACAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACU UGGCACCGAGUCGGUGC(invd)
37	G615	(invd)mUmUmACAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUC AACUUGGCACCGAGUCGGmUmGmC(invd)
38	G643	(invd)mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUU AUCAACUUGGCACCGAGUCGG*mU*mG*mC(invd)
39	G616	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAf AfCfUfUfGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
40	G617	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAf AmCfUmUfGmGfCmAfCmCfGmAfGmUfCmGfG*mU*fG*mC
41	G618	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAfAfCfUfUfGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
42	G619	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAfAmCfUmUfGmGfCmAfCmCfGmAfGmUfCmGfG*mU*fG*mC

SEQ ID NO	Name	Sequence
43	G534	mA*mC*mG*CAAAUAUCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
44	G637	mA*mC*mG*CAAAUAUCAGUCCAGCGGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA ACUUGGCACCGAGUCGG*mU*mG*mC
45	G694	mA*mC*mG*CAAAUAUCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
46	G695	mA*mC*mG*CAAAUAUCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmAmGmUmCmGmG*mU*mG*mC
47	G698	mU*mC*mU*AGAACUUUGACCAUCAGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
48	G699	mU*mC*mU*AGAACUUUGACCAUCAGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmAmGmUmCmGmG*mU*mG*mC
49	G481	mU*mC*mU*AGAACUUUGACCAUCAGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
50	G700	mU*mG*mA*AUCCAAGUGUCCUCUGAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
51	G701	mU*mG*mA*AUCCAAGUGUCCUCUGAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmAmGmUmCmGmG*mU*mG*mC
52	G499	mU*mG*mA*AUCCAAGUGUCCUCUGAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
53	G12401	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
54	G12402	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
55-200	Not Used	
201	G282-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
202	G515-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
203	G621-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGC*mU*mU*mU
204	G632-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
205	G638-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
206	G639-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
207	G640-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
208	G641-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGU*mG*mC*mU
209	G211-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U
210	G269-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U
211	G620-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
212	G622-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGC*mU*mU*mU
213	G623-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
214	G624-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
215	G625-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
216	G626-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC

SEQ ID NO	Name	Sequence
217	G627-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGU*mG*mC*mU
218	G283-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmCmU*mU*mU*mU
219	G628-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
220	G629-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGC*mU*mU*mU
221	G630-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
222	G631-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
223	G633-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
224	G634-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
225	G635-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGU*mG*mC*mU
226	G208-2-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U
227	G373-2-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmCmU*mU*mU*mU
228	G513-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
229	G514-C	GUUUUAGAmGmGmAmAmAmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
230	G516-C	GUUUUAGAGGAAACAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
231	G517-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmUmGmAmAmAmAmA*mG*mU*mG
232	G518-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAA*mG*mU*mG

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233	G642-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
234	G612-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGmoeG*moeU* moeG*mC
235	G613-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUC*mG*mG*mU*m G*mC
236	G614-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGC(invd)
237	G615-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGmUmGmC(inv d)
238	G643-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC (invd)
239	G616-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAfAfCfUfUfGmGmCmAmCmCmGmAmG mUmCmGmG*mU*mG*mC
240	G617-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAfAmCfUmUfGmGfCmAfCmCfGmAfGm UfCmGfG*mU*fG*mC
241	G618-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAfAfCfUfUfUfGmG mCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
242	G619-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAfAmCfUmUfGm GfCmAfCmCfGmAfGmUfCmGfG*mU*fG*mC
243	G534-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mU*mU*mU
244	G637-C	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
245	G694-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACC GAGUCGG*mU*mG*mC
246	G695-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmC mAmCmCmGmAmGmUmCmGmG*mU*mG*mC
247	G698-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACC GAGUCGG*mU*mG*mC
248	G699-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmC mAmCmCmGmAmGmUmCmGmG*mU*mG*mC

SEQ ID NO	Name	Sequence
249	G481-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
250	G700-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
251	G701-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmGmAmGmUmCmGmG*mU*mG*mC
252	G499-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
253	G12401-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
254	G12402-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
255-300	Not Used	
301	G282-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
302	G515-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
303	G621-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGC*mU*mU*mU
304	G632-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
305	G638-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
306	G639-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
307	G640-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
308	G641-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGU*mG*mC*mU

SEQ ID NO	Name	Sequence
309	G211-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGG CACCGAGUCGGUGCmU*mU*mU*U
310	G269-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGG CACCGAGUCGGUGCmU*mU*mU*U
311	G620-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGU CGG*mU*mG*mC
312	G622-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGU CGGUGC*mU*mU*mU
313	G623-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmG mCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
314	G624-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmC mCmGmAmGmUmCmGmG*mU*mG*mC
315	G625-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAU CAACUUGGCACCGAGUCGG*mU*mG*mC
316	G626-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAU CAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
317	G627-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGU CGGU*mG*mC*mU
318	G283-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAU CAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*m U*mU
319	G628-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGU CGG*mU*mG*mC
320	G629-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGU CGGUGC*mU*mU*mU
321	G630-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmG mCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
322	G631-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmC mCmGmAmGmUmCmGmG*mU*mG*mC
323	G633-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAU CAACUUGGCACCGAGUCGG*mU*mG*mC

SEQ ID NO	Name	Sequence
324	G634-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*U
325	G635-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGU*mG*mC*mU
326	G208-2-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU
327	G373-2-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
328	G513-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
329	G514-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmGmAmAmAmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
330	G516-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGGAAACAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
331	G517-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmA*mG*mU*mG
332	G518-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAA*mG*mU*mG
333	G642-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
334	G612-Nx	moeN*moeN*moeN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGmoeG*moeU*moeG*mC
335	G613-Nx	mN*mN*mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGCmU*mG*mU*mG*mC
336	G615-Nx	(invd)mNmNmN(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGCmU*mG*mU*mG*mC(invd)
337	G614-Nx	(invd)(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGUGC(invd)
338	G643-Nx	(invd)mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC(invd)

SEQ ID NO	Name	Sequence
339	G616-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAfAfCfUfUfGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
340	G617-Nx	mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAfAmCfUmUfGmGfCmAfCmCfGmAfGmUfCmGfG*mU*fG*mC
341	G618-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAfAfCfUfUfGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
342	G619-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAfAmCfUmUfGmGfCmAfCmCfGmAfGmUfCmGfG*mU*fG*mC
343	G534-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
344	G637-Nx	mN*mN*mN*mN*(N)$_x$GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
345	G694-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGmU*mG*mC
346	G695-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
347	G698-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
348	G699-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
349	G481-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
350	G700-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
351	G701-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGmGmCmAmCmCmGmAmGmUmCmGmG*mU*mG*mC
352	G499-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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353	G12401-Nx	mN*mN*mN*(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
354	G12402-Nx	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNNfNf(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
355-399	Not Used	
400	Conserved Portion of a spyCas9 sgRNA	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGC
401	G282	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmGmCmUmCmGmGmUmGmCmU*mU*mU*mU
402	G480	mA*mA*mA*GGCUGCUGAUGACACCUGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmGmCmUmCmGmGmUmGmCmU*mU*mU*mU
403	G481	mU*mC*mU*AGAACUUUGACCAUCAGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmGmCmUmCmGmGmUmGmCmU*mU*mU*mU
404	G502	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmGmCmUmCmGmGmUmGmCmU*mU*mU*mU
405	G504	mA*mA*mA*GGCUGCUGAUGAGACCUGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmGmCmUmCmGmGmUmGmCmU*mU*mU*mU
406	G509	mA*mA*mA*GUUCUAGAUGCCGUCCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmGmCmUmCmGmGmUmGmCmU*mU*mU*mU
407	G9423	T*T*dA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmGmCmUmCmGmGmUmGmCmU*T*T*T
408	G9424	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T

SEQ ID NO	Name	Sequence
409	G9425	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAdAdCTTdGdAdAdAdAdAdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
410	G9426	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAdGdCTdAdGdAdAdATdAdGdCAAGUUAAAAUAAGGCUAGUC CGUUAUCAdAdCTTdGdAdAdAdAdAdAdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
411	G9427	T*T*dA*CAGCCACGUCUACAGCAGUUUUAGAdGdCTdAdGdAdAdATdAdGdCAAGUUAAAAUAAGGCUAGUCCGUU AUCAdAdCTTdGdAdAdAdAdAdAdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
412	G9553	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mA* mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mC*mU*mU*mU*mU
413	G9554	mU*mU*mA*CAGCCACGUCUACAGCAmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUm AAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmG G*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mC*mU*mU*mU*mU
414	G9555	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmG GmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
415	G9556	mU*mU*mA*CAGCCACGUCUACAGCAmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUm AAmAAUAmAmGmGmCmUmAmGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmC mCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
416	G9557	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmA mAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmC mAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
417	G9558	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUUmAAmAAUAAGGCUAGUCCGUUAUCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGm AmGmUmCmGmGmUmGmCmU*mU*mU*mU
418	G9559	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGm UmCmGmGmUmGmCmU*mU*mU*mU
419	G9560	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA *mG*mU*mC*mG*mG*mU*mG*mC*mU*mU*mU*mU

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420	G9561	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
421	G9562	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
422	G9563	mU*mU*mA*CAGCCACGUCUACAGCAmGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUmAAmAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
423	G9564	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mC*mU*mU*mU*mU*mU
424	G9565	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mA*mG*mU*mU*mG*mC*mU*mU*mU*mU
425	G9566	mA*mC*mA*CAAAUACCAGUCCAGCGmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mA*mG*mU*mU*mG*mC*mU*mU*mU*mU
426	G9567	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
427	G9568	mA*mC*mA*CAAAUACCAGUCCAGCGmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
428	G9569	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
429	G9570	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAGGCUAGUCCGUUAUCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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430	G9571	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGm UmCmGmGmUmGmCmU*mU*mU*mU
431	G9572	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA *mG*mU*mC*mG*mG*mU*mG*mC*mU*mU*mU*mU
432	G9573	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAm AmGmGmCmUmAGUmCmCGUUAUmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGm AmGmUmCmGmGmUmGmCmU*mU*mU*mU
433	G9574	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAA AUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCm GmGmUmGmCmU*mU*mU*mU
434	G9575	mA*mC*mA*CAAAUACCAGUCCAGCGmGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUmAAmA AUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCm GmGmUmGmCmU*mU*mU*mU
435	G9576	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC* mC*mG*mA*mG*mU*mC*mG*mG*mU*mG*mC*mU*mU*mU*mU
436	G9878	eT*eT*eA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGG CUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmU mGmCeT*eT*eT*mU
437	G9879	xU*xU*xA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGG CUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmU mGmCxU*xU*xU*mU
438	G9981	mU*mU*mA*C*AGCC*ACGUCU*AC*AGC*AGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*A AAAU*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmG mUmCmGmGmUmGmCmU*mU*mU*mU
439	G9982	mU*mU*mA*C*AGCC*ACGUCU*AC*AGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCm GmGmUmGmCmU*mU*mU*mU

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440	G9983	mU*mU*mA*CAGCCACGUCUACAGCAGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
441	G9984	mU*mU*mA*CAGCCACGUCUACAGCAGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
442	G9985	mU*mU*mA*mCAGCfCACGUCfUAC*AGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
443	G9986	mU*mU*mA*mCAGCfCACGUCfUAC*AGC*AGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
444	G9987	mU*mU*mA*mCmAmGmCmCmAmCGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
445	G9988	mU*mU*mA*mCmAmGmCmCmAmCfGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
446	G9989	mU*mU*mA*CAGCCACGUCUACAGCAGUUUmUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
447	G9990	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
448	G9991	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAmUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
449	G9992	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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450	G9993	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUmUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
451	G9994	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
452	G9995	mU*mU*mA*CAGCCACGUCUACAGCAGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
453	G9996	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
454	G9997	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAfUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
455	G9998	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCfUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
456	G9999	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUfUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
457	G10000	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUfCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
458	G10001	mU*mU*mA*CAGCCACGUCUACAGCAGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
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461	G10004	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCU*AGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
462	G10005	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUU*AUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
463	G10006	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUC*AmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
464	G10007	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUeTAAAAeTA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
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469	G10013	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU* AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmC mGmGmUmGmCmU*mU*mU*mU

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471	G10015	mA*mC*mA*mCAAAfUACfCAGUCC*AGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
472	G10016	mA*mC*mA*mCAAAfUACfCAGUCC*AGCGGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAA AAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmG mUmCmGmGmUmGmCmU*mU*mU*mU
473	G10017	mA*mC*mA*mCmAmAmAmUmAmCCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmG mUmCmGmGmUmGmCmU*mU*mU*mU
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475	G10019	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUmUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
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477	G10021	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAmUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
478	G10022	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCmUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
479	G10023	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUmUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU

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482	G10026	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
483	G10027	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAfUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
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494	G10038	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUeAAAeAUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
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496	G9565	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mA* mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mU*mG*mC*mU*mU*mU*mU
497	G9571	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm UmCmGmGmUmGmCmU*mU*mU*mU
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499	G12422	mA*mC*mA*fCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU

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501	G12424	mA*mC*AfCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAG GCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGm UmGmCmU*mU*mU*mU
502	G12425	mA*mC*mA*mCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
503	G12689	mA*mC*mA*dCAAAdUACdCAGUCdCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
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507	G12428	mA*mC*mA*CAAAUACCAGUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
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511	G12432	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
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519	G12439	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU

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520	G12440	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmG mAmGmUmCmGmGmUmGmCmU*mU*mU*mU
521	G12692	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUdUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmG mAmGmUmCmGmGmUmGmCmU*mU*mU*mU
522	G12441	mA*mC*mA*fCAAAfUACfCAGUCfCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmC mGmGmUmGmCmU*mU*mU*mU
523	G12442	mA*mC*mA*fCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCm GmGmUmGmCmU*mU*mU*mU
424	G12443	mA*mC*mA*fCAAAfUACfCAGUCfCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCm GmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
525	G12444	mA*mC*mA*fCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA mAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmG mAmGmUmCmGmGmUmGmCmU*mU*mU*mU
526	G12445	mA*mC*mA*fCAAAfUACfCAGUCfCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAA mUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmU mCmGmGmUmGmCmU*mU*mU*mU
527	G12446	mA*mC*mA*fCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAA mUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmU mCmGmGmUmGmCmU*mU*mU*mU
528	G12447	mA*mC*mA*mCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmC mGmGmUmGmCmU*mU*mU*mU
529	G12448	mA*mC*mA*mCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCm GmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
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531	G12450	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAGCmUAGAAAmUAGmCAAGUUAAAAUAAGGCU AGUCCGUUAUCAACUUGAAAAAGUGGmCACCGAGUCGGUGCmU*mU*mU*mU
532	G12451	mA*mC*mA*CAAAUACCAGUCCAGCGGUUUUAGAGCmUAGAAAmUAGmCAAGUUAAAAUAAGGCUAGUCCGUU AUCAACUUGAAAAAGUGGmCACCGAGUCGGUGCmU*mU*mU*mU
533	G211	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCA ACUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*mU
534	G269	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAA CUUGAAAAAGUGGCACCGAGUCGGUGCmU*mU*mU*U
535	G283	mC*mC*mC*AUACUCCUACAGCACCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAG GCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGm UmGmCmU*mU*mU*mU
536-600	Not Used	
601	G282-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
607	G9423-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*T*T*T
608	G9424-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
609	G9425-C	GUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAdAdCTTdGdAd AdAdAdAdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
610	G9426-C	GUUUUAGAdGdCTdAdGdAdAdATdAdGdCAAGUUAAAAUAAGGCUAGUCCGUUAUCAdAdCTTdGdAdAdAdAdG TdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
611	G9427-C	GUUUUAGAdGdCTdAdGdAdAdATdAdGdCAAGUUAAAAUAAGGCUAGUCCGUUAUCAdAdCTTdGdAdAdAdAdG TdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
612	G9553-C	GUUUUAGmAmGmCmUmAmGmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*m C*mG*mG*mU*mG*mC*mU*mU*mU*mU

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613	G9554-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*m C*mG*mG*mU*mU*mG*mC*mU*mU*mU*mU
614	G9555-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU *mU*mU*mU
615	G9556-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU *mU*mU*mU
616	G9557-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAmAmGmGmCmUmAGUmCmCGU UAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*m U*mU*mU
617	G9558-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAGGCUAGUCCGUUAUCAAmC mUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
618	G9559-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
619	G9560-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAAmC*mU*m U*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mC *mU*mU*mU*mU
620	G9561-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmU mCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU* mU*mU
621	G9562-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCm UmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmGmCmU*mU*mU*mU
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623	G9564-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*m U*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mC *mU*mU*mU*mU
624	G9565-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*m C*mG*mG*mU*mG*mC*mU*mU*mU*mU

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625	G9566-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*m C*mG*mG*mU*mG*mC*mU*mU*mU*mU
626	G9567-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU *mU*mU*mU
627	G9568-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU *mU*mU*mU
628	G9569-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAmAmGmGmCmUmAGUmCmCGU UAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*m U*mU*mU
629	G9570-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAGGCUAGUCCGUUAUCAAmC mUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
630	G9571-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
631	G9572-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*m U*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA*mG*mU*mU*mG*mG*mC *mU*mU*mU*mU
632	G9573-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmU mCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU* mU*mU
633	G9574-C	GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCm UmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
634	G9575-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUmAAmAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
635	G9576-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*m U*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA*mG*mU*mU*mG*mG*mC *mU*mU*mU*mU
636	G9878-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCeT*eT*eT*mU

SEQ ID NO	Name	Sequence
637	G9879-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCxU*xU*xU*mU
638	G9981-C	GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmC mUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
639	G9982-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
640	G9983-C	GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmC mUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
641	G9984-C	GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAm CmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
642	G9985-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
643	G9986-C	GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAm CmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
644	G9987-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
645	G9988-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
646	G9989-C	GUUUmUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
647	G9990-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
648	G9991-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAmUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
649	G9992-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
650	G9993-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUmUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
651	G9994-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUmCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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652	G9995-C	GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
653	G9996-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUAAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
654	G9997-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAfUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
655	G9998-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAUAAGGCfUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
656	G9999-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAUAAGGCUAGUCCGUfUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
657	G10000-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAUAAGGCUAGUCCGUUAUfCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
658	G10001-C	GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
659	G10002-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
660	G10003-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU*AAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
661	G10004-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAUAAGGCU*AGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
662	G10005-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAUAAGGCUAGUCCGUU*AUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
663	G10006-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAUAAGGCUAGUCCGUUAUC*AmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
664	G10007-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUeTAAAAeTAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
665	G10008-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUeAAAeAUAAGGCUAGUCCGUUAUCAmAmCmUm UmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmGmGmCmU*mU*mU*mU
666	G10009-C	GUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUm CmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmGmCmGmGmU mGmCmU*mU*mU*mU

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667	G10011-C	GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmC mUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
668	G10012-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
669	G10013-C	GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmC mUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
670	G10014-C	GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAm CmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
671	G10015-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
672	G10016-C	GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAm CmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
673	G10017-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
674	G10018-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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677	G10021-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAmUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
678	G10022-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
679	G10023-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUmUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
680	G10024-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUmCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
681	G10025-C	GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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682	G10026-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
683	G10027-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAfUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
684	G10028-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCfUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
685	G10029-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUfUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
686	G10030-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUfCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
687	G10031-C	GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
688	G10032-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAUAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
689	G10033-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU*AAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
690	G10034-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCU*AGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
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692	G10036-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUC*AmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
693	G10037-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUeTAAAAeTAAGGCUAGUCCGUUAUCAmAmCmUmU mGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
694	G10038-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUeAAAeAUAAGGCUAGUCCGUUAUCAmAmCmUm UmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
695	G10039-C	GUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUm CmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmU mGmCmU*mU*mU*mU

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697	G9571-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
698	G12421-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
699	G12422-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
700	G12423-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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703	G12689-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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705	G12426-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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708	G12429-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
709	G12430-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
710	G12431-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUm GmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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711	G12432-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
712	G12433-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAmGmGmCmUmAGUmCmCGUUAmU mCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU* mU*mU
713	G12434-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
714	G12435-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUmAfAmAfAmUAAGGCmUAGUCCGUUAUmCAmA mCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*m U
715	G12436-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUmUAUmCAmAm CmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
716	G12437-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
717	G12438-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUGAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
718	G12691-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUdUAUmCAmAm CmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
719	G12439-C	GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
720	G12440-C	GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
721	G12692-C	GUUUdUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAm CmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
722	G12441-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
723	G12442-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
724	G12443-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAmGmGmCmUmAGUmCmCGUUAmU mCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU* mU*mU

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726	G12445-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAAGGCmUAGUCCGUUAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
727	G12446-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAAGGCmUAGUCCGUUAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
728	G12447-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
729	G12448-C	GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAmGUmCmCGUUAmU mCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU* mU*mU
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731	G12450-C	GUUUUAGAGCmUAGAAAmUAGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGmCACCGAG UCGGUGCmU*mU*mU*mU
732	G12451-C	GUUUUAGAGCmUAGAAAmUAGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGmCACCGAG UCGGUGCmU*mU*mU*mU
733-800	Not Used	
801	G282-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
802-806	Not Used	
807	G9423-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*T*T*T
808	G9424-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
809	G9425-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAdAdCTTdGd AdAdAdAdAdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
810	G9426-Nx	(N)$_x$GUUUUAGAdGdCTdAdGdAdAdATdAdGdCAAGUUAAAAUAAGGCUAGUCCGUUAUCAdAdCTTdGdAdAdAd AdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T

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811	G9427-Nx	(N)$_x$GUUUUAGAdGdCTdAdGdAdAdATdAdGdCAAGUUAAAAUAAGGCUAGUCCGUUAUCAdAdCTTdGdAdAdAdAd AdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
812	G9553-Nx	(N)$_x$GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmC mCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU *mC*mG*mG*mU*mG*mC*mC*mU*mU*mU*mU
813	G9554-Nx	(N)$_x$GUUUUAGmAmGmCmUmAmGmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmC mCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU *mC*mG*mG*mU*mG*mC*mC*mU*mU*mU*mU
814	G9555-Nx	(N)$_x$GUUUUAGmAmGmCmUmAmGmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmC mCGUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmC mU*mU*mU*mU
815	G9556-Nx	(N)$_x$GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmC mCGUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmC mU*mU*mU*mU
816	G9557-Nx	(N)$_x$GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAmAmGmGmCmUmAGUmCmC GUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU *mU*mU*mU
817	G9558-Nx	(N)$_x$GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAGGCUAGUCCGUUAUCAA mCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmGmCmU*mU*mU*mU
818	G9559-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmGmCmU*mU*mU*mU
819	G9560-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU *mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mC*mG*mA*mG*mU*mC*mG* mC*mU*mU*mU*mU
820	G9561-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUA mUmCAmAmCmUmUmGmAmAmAmAmGmUmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU* mU*mU*mU
821	G9562-Nx	(N)$_x$GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAAGGCUAGUCCGUUAUCAmAm CmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmGmCmU*mU*mU*mU
822	G9563-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUmAAmAAUAAGGCUAGUCCGUUAUCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU

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823	G9564-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA*mG*mU*mG*mC*mU*mU*mU*mU
824	G9565-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mU*mU*mG*mC*mU*mU*mU
825	G9566-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mA*mG*mU*mC*mG*mG*mU*mU*mG*mC*mU*mU*mU
826	G9567-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU
827	G9568-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU
828	G9569-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU
829	G9570-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAAGGCUAGUCCGUUAUCAAmCmUmUmGmAmAmAmAmGmUmGGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU
830	G9571-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU
831	G9572-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA*mG*mU*mU*mG*mC*mU*mU*mU*mU
832	G9573-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUAAAAUAAmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU
833	G9574-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU
834	G9575-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUmAAmAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmUmGmCmU*mU*mU*mU

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835	G9576-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG*mA*mA*mG*mU*mC*mG*mG*mU*mC*mU*mU*mU
836	G9878-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCeT*eT*eT*mU
837	G9879-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCxU*xU*xU*mU
838	G9981-Nx	(N)$_x$GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
839	G9982-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
840	G9983-Nx	(N)$_x$GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
841	G9984-Nx	(N)$_x$GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
842	G9985-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
843	G9986-Nx	(N)$_x$GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
844	G9987-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
845	G9988-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
846	G9989-Nx	(N)$_x$GUUUmUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
847	G9990-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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848	G9991-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAmUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
849	G9992-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
850	G9993-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUmUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
851	G9994-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
852	G9995-Nx	(N)$_x$GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
853	G9996-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
854	G9997-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAfUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
855	G9998-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCfUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
856	G9999-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUfUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
857	G10000-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUfCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
858	G10001-Nx	(N)$_x$GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
859	G10002-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
860	G10003-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAAU*AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
861	G10004-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCU*AGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
862	G10005-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUU*AUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU

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863	G10006-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
864	G10007-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUeTAAAAeTAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
865	G10008-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUeAAAeAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
866	G10009-Nx	(N)$_x$GUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
867	G10011-Nx	(N)$_x$GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
868	G10012Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
869	G10013-Nx	(N)$_x$GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
870	G10014-Nx	(N)$_x$GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
871	G10015-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
872	G10016-Nx	(N)$_x$GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
873	G10017-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
874	G10018-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
875	G10019-Nx	(N)$_x$GUUUmUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU

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876	G10020-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAUAAGGCUAGUCCGUUAUCAmAmCm UmUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
877	G10021-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAmUAAGGCUAGUCCGUUAUCAmAmCm UmUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
878	G10022-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUCAmAmCm UmUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
879	G10023-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUmUAUCAmAmCm UmUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
880	G10024-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUmCAmAmCm UmUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
881	G10025-Nx	(N)$_x$GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
882	G10026-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
883	G10027-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAfUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
884	G10028-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCfUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
885	G10029-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUfUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
886	G10030-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUfCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
887	G10031-Nx	(N)$_x$GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
888	G10032-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
889	G10033-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU*AAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
890	G10034-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCU*AGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU

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891	G10035-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUU*AUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
892	G10036-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUC*AmAmCmU mUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
893	G10037-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUeTAAAAeTAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
894	G10038-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUeAAAeAUAAGGCUAGUCCGUUAUCAmAmCm UmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
895	G10039-Nx	(N)$_x$GUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAG UmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmG mUmGmCmU*mU*mU*mU
896	G9565-Nx	(N)$_x$GUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmC mCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU *mC*mG*mG*mU*mG*mC*mU*mU*mU*mU
897	G9571-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
898	G12421-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
899	G12422-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
900	G12423-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
901	G12424-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
902	G12425-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
903	G12689-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
904	G12690-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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905	G12426-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
906	G12427-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
907	G12428-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
908	G12429-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
909	G12430-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
910	G12431-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmU mUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
911	G12432-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
912	G12433-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUA mUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU* mU*mU*mU
913	G12434-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmA mCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*m U
914	G12435-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUmAfAmAfAmUAAGGCmUAGUCCGUUAUmC AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*m U*mU
915	G12436-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUmUAUmCAm AmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*m U
916	G12437-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmA mCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*m U

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917	G12438-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUGAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
918	G12691-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUdUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
919	G12439-Nx	(N)$_x$GUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
920	G12440-Nx	(N)$_x$GUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
921	G12692-Nx	(N)$_x$GUUUdUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
922	G12441-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
923	G12442-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
924	G12443-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAmGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
925	G12444-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAmGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
926	G12445-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
927	G12446-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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928	G12447-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUmCAmAmC mUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmGmCmU*mU*mU*mU
929	G12448-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAmGmGmCmUmAGUmCmCGUUA mUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmGmCmU* mU*mU*mU
930	G12449-Nx	(N)$_x$GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmA mCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmGmCmU*mU*mU*m U
931	G12450-Nx	(N)$_x$GUUUUAGAGCmUAGAAAmUAGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGmCACCG AGUCGGUGCmU*mU*mU*mU
932	G12451-Nx	(N)$_x$GUUUUAGAGCmUAGAAAmUAGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGmCACCG AGUCGGUGCmU*mU*mU*mU
933-1000	Not Used	
1001	G282-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1002-1006	Not Used	
1007	G9423-N20	N*N*dN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAG GCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGm UmGmCmU*T*T*T
1008	G9424-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT *T*T*T
1009	G9425-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAdAdCTTdGdAdAdAdAdAdGTdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
1010	G9426-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAdGdCTdAdGdAdAdATdAdGdCAAGUUAAAAUAAGGCUAG UCCGUUAUCAdAdCTTdGdAdAdAdAdAdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T
1011	G9427-N20	N*N*dN*NNNNNNNNNNNNNNNNGUUUUAGAdGdCTdAdGdAdAdATdAdGdCAAGUUAAAAUAAGGCUAGUCC GUUAUCAdAdCTTdGdAdAdAdAdAdGTdGdGdCdAdCdCdGdAdGTdCdGdGTdGdCT*T*T*T

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1012	G9553-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA* mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*mU*mG*mG*mC*mU*mU*mU*mU
1013	G9554-N20	mN*mN*mN*NNNNNNNNNNNNNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUU mAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUm GG*mC*mA*mC*mC*mG*mA*mA*mG*mU*mU*mG*mG*mU*mG*mC*mU*mU*mU*mU
1014	G9555-N20	mN*mN*mN*NNN*N*fN*fN*fNNfNfNNNfNfNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmU mGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1015	G9556-N20	mN*mN*mN*NNNNNNNNNNNNNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUU mAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGmCmAm CmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1016	G9557-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmGmUmGG mCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1017	G9558-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUUmAAmAAUAAGGCUAGUCCGUUAUCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCm GmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1018	G9559-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmCmAmCmCmGmAmG mUmCmGmGmUmGmCmU*mU*mU*mU
1019	G9560-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG* mA*mG*mU*mC*mG*mG*mU*mG*mC*mU*mU*mU*mU
1020	G9561-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmCmAmCmCm GmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1021	G9562-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUA AAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU

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1022	G9563-N20	mN*mN*mN*NNNNNNNNNNNNNNNmGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUmAA mAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU
1023	G9564-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*m C*mC*mG*mA*mG*mU*mC*mG*mG*mU*mC*mU*mU*mU*mU
1024	G9565-N20	mN*mN*mN*NNN*N*fN*fN*fNNfNfNNNNfNfNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUUmAAmAmAAUAAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA* mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mU*mC*mU*mU*mU*mU
1025	G9566-N20	mN*mN*mN*NNNNNNNNNNNNNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUU mAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA*mGmUm GG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mU*mC*mU*mU*mU*mU
1026	G9567-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNNfNfNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmU mGGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1027	G9568-N20	mN*mN*mN*NNNNNNNNNNNNNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUU mAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAm CmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1028	G9569-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNNfNfNNNGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmCmUmUmGmAmAmAmAmAmGmUmGG mCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1029	G9570-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNNfNfNNNmGUUUUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUUmAAmAAUAAGGCUAGUCCGUUAUCAAmCmUmUmGmAmAmAmAmAmGmUmGGmCmAmCmCm GmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1030	G9571-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmAmGmCmGmAmGmG mUmCmGmGmUmGmCmU*mU*mU*mU
1031	G9572-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*mC*mC*mG* mA*mG*mU*mC*mG*mG*mU*mG*mC*mU*mU*mU*mU

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1032	G9573-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCm GmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1033	G9574-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAmAGUUA AAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU
1034	G9575-N20	mN*mN*mN*NNNNNNNNNNNNNNNNmGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUmAA mAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU
1035	G9576-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAmAmC*mU*mU*mG*mA*mA*mA*mA*mGmUmGmG*mC*mA*m C*mC*mG*mA*mG*mU*mC*mG*mG*mU*mG*mC*mU*mU*mU*mU
1036	G9878-N20	eN*eN*eN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmGmUmCmGmG mUmGmCeT*eT*eT*eT*mU
1037	G9879-N20	xN*xN*xN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCxU*xU*xU*xU*mU
1038	G9981-N20	mN*mN*mN*N*NNNN*NNNNNN*NN*NNN*NGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU *AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAm GmUmCmGmGmUmGmCmU*mU*mU*mU
1039	G9982-N20	mN*mN*mN*N*NNNN*NNNNNN*NN*NNN*NGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUA AAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU
1040	G9983-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAA U*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU
1041	G9984-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAA AmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGm UmCmGmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
1042	G9985-N20	mN*mN*mN*mNNNNfNNNNNfNNN*NNN*NGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUA AAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU
1043	G9986-N20	mN*mN*mN*mNNNNfNNNNNfNNN*NNN*NGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUm UAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmA mGmUmCmGmGmUmGmCmU*mU*mU*mU
1044	G9987-N20	mN*mN*mN*mNmNmNmNmNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAm GmUmCmGmGmUmGmCmU*mU*mU*mU
1045	G9988-N20	mN*mN*mN*mNmNmNmNmNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmG mCAAGUUAAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmG mAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1046	G9989-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUmUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmG mGmUmGmCmU*mU*mU*mU
1047	G9990-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmG mGmUmGmCmU*mU*mU*mU
1048	G9991-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAm UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1049	G9992-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCmUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCm GmGmUmGmCmU*mU*mU*mU
1050	G9993-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUmUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCm GmGmUmGmCmU*mU*mU*mU
1051	G9994-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCm GmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
1052	G9995-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1053	G9996-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUAAAAU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1054	G9997-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAfU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1055	G9998-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCfUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1056	G9999-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUfUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1057	G10000-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUfCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1058	G10001-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1059	G10002-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1060	G10003-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU *AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1061	G10004-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCU*AGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU

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1062	G10005-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUU*AUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1063	G10006-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1064	G10007-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUeTAAAAe TAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1065	G10008-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUeAAAeA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1066	G10009-N20	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNNN*fNfNN*NmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmA mGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm AmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1067	G10011-N20	mN*mN*mN*N*NNNN*NNN*NNNNN*NNNNGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU* AAAAU*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAm GmUmCmGmGmUmGmCmU*mU*mU*mU
1068	G10012-N20	mN*mN*mN*N*NNNN*NNN*NNNNN*NNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmC mGmGmUmGmCmU*mU*mU*mU
1069	G10013-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAA U*AAGGCU*AGUCCGUU*AUC*AmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU
1070	G10014-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAA AmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGm UmCmGmGmUmGmCmU*mU*mU*mU
1071	G10015-N20	mN*mN*mN*mNNNNfNNNfNNNNNN*NNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmC mGmGmUmGmCmU*mU*mU*mU

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1072	G10016-N20	mN*mN*mN*mNNNNfNNNfNNNNNN*NNNNGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1073	G10017-N20	mN*mN*mN*mNmNmNmNmNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1074	G10018-N20	mN*mN*mN*mNmNmNmNmNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1075	G10019-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUmUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1076	G10020-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1077	G10021-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAmUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1078	G10022-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1079	G10023-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUmUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1080	G10024-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1081	G10025-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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1082	G10026-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUfUAAAAU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1083	G10027-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAfU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1084	G10028-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCfUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1085	G10029-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUfUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1086	G10030-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUfCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1087	G10031-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1088	G10032-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU*AAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1089	G10033-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU *AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1090	G10034-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCU*AGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1091	G10035-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUU*AUCAmAmCmUmUmGmAmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU

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1092	G10036-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUC*AmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1093	G10037-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUeTAAAAe TAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1094	G10038-N20	mN*mN*mN*NNNNNNNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUeAAAeA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1095	G10039-N20	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNNN*fNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1096	G9565-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNmGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUUmAAmAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAAmC*mU*mU*mG*mA*mA*mA*mA* mA*mGmUmGG*mC*mA*mC*mC*mG*mA*mG*mU*mC*mG*mG*mU*mG*mC*mC*mU*mU*mU*mU
1097	G9571-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmG mUmCmGmGmUmGmCmU*mU*mU*mU
1098	G12421-N20	mN*mN*mN*fNNNNfNNNfNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCm GmGmUmGmCmU*mU*mU*mU
1099	G12422-N20	mN*mN*mN*fNNNNfNNNfNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1100	G12423-N20	mN*mN*NfNNNNfNNNfNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
1101	G12424-N20	mN*mN*NfNNNNfNNNfNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU

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1102	G12425-N20	mN*mN*mN*mNNNNfNNNfNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1103	G12689-N20	mN*mN*mN*dNNNNdNNNdNNNNNNdNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
1104	G12690-N20	mN*mN*mN*dNNNNdNNNdNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
1105	G12426-N20	mN*mN*mN*NNNNfNfNfNNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
1106	G12427-N20	mN*mN*mN*NNNNmNmNmNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
1107	G12428-N20	mN*mN*mN*NNNNNNNNNNNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
1108	G12429-N20	mN*mN*mN*NNNNNNNNNNNNNfNfNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
1109	G12430-N20	mN*mN*mN*fNfNfNfNfNfNfNfNfNfNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
1110	G12431-N20	mN*mN*mN*fNfNfNfNfNfNfNfNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
1111	G12432-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNfNNNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCmUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU

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1112	G12433-N20	mN*mN*mN*NNN*N*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmC mAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1113	G12434-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmCmAmCmCm GmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1114	G12435-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUfUmAfAmAfAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmC mCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
1115	G12436-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUmUAAAAmUAAGGCmUAGUCCGUmUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmC mGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1116	G12437-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUmUAAAAmUAAGGCmUAGUCCGUfUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmC mGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1117	G12438-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUmUAAAAmUAAGGCmUAGUCCGUGAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCm GmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1118	G12691-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUmUAAAAmUAAGGCmUAGUCCGUdUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmC mGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1119	G12439-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUfUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmC mGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1120	G12440-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUU*AGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmC mGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1121	G12692-N20	mN*mN*mN*NNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUdUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUmUAAAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmC mGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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1122	G12441-N20	mN*mN*mN*fNNNNfNNNNfNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmU mCmGmGmUmGmCmU*mU*mU*mU
1123	G12442-N20	mN*mN*mN*fNNNNfNNNNfNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUm CmGmGmUmGmCmU*mU*mU*mU
1124	G12443-N20	mN*mN*mN*fNNNNfNNNNfNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCm CmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1125	G12444-N20	mN*mN*mN*fNNNNfNNNNfNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmC mGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1126	G12445-N20	mN*mN*mN*fNNNNfNNNNfNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAA AAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmG mUmCmGmGmUmGmCmU*mU*mU*mU
1127	G12446-N20	mN*mN*mN*fNNNNfNNNNfNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUAA AAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmG mUmCmGmGmUmGmCmU*mU*mU*mU
1128	G12447-N20	mN*mN*mN*mNNNNfNNNNfNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmU mCmGmGmUmGmCmU*mU*mU*mU
1129	G12448-N20	mN*mN*mN*mNNNNfNNNNfNNNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCm CmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1130	G12449-N20	mN*mN*mN*mNNNNfNNNNfNNNNNN*NNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUmUA AAAmUAAGGCmUAGUCCGUUAUmCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmG mUmCmGmGmUmGmCmU*mU*mU*mU
1131	G12450-N20	mN*mN*mN*NNN*N*fN*fN*fNNfNfNNNfNNNGUUUUAGAGCmUAGAAAmUAGmCAAGUUAAAAUAAGG CUAGUCCGUUAUCAACUUGAAAAAGUGGmCACCGAGUCGGUGCmU*mU*mU*mU
1132	G12451-N20	mN*mN*mN*NNNNNNNNNNNNNNNGUUUUAGAGCmUAGAAAmUAGmCAAGUUAAAAUAAGGCUAGUCCG UUAUCAACUUGAAAAAGUGGmCACCGAGUCGGUGCmU*mU*mU*mU

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1133-1199	Not Used	
1200	Conserved Portion of a spyCas9 sgRNA	GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCAC CGAGUCGGUGC
1201	G009428	mA*mA*mC*CUGUGAAAAUGCUCCCCGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
1202	G009429	mU*mG*mU*UCUGCCAGAAAUUGUGGGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
1203	G009430	mG*mC*mC*CGUUCCCAGGGACUGACGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
1204	G009432	mA*mA*mU*AGACCCAUCUAUCAGCUGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
1205	G013964	mA*mA*mC*mCUG*U*fG*fA*fA*fAAfUfGCUfCfCCCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1206	G013965	mU*mG*mU*mUCU*G*fC*fC*fA*fGAfAfAUUfGfUGGmGUUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1207	G013966	mG*mC*mC*mCGU*U*fC*fC*fC*fAGfGfGACfUfGACmGUUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1208	G013967	mA*mA*mU*mAGA*C*fC*fC*fA*fUCfUfAUC*fAfGCUmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
1209	G013968	mA*mA*mC*CUGUGAAAAUGCUCCCCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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1210	G013969	mU*mG*mU*UCUGCCAGAAAUUGUGGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
1211	G013970	mG*mC*mC*CGUUCCCAGGGACUGACGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
1212	G013971	mA*mA*mU*AGACCCAUCUAUCAGCUGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
1213	TR000002	AACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAGUGGCACCGAGUCGGUGCUUUUUUU
1214	CR000309	CACGCCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1215	CR003102	CGCCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1216	CR005081	CCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1217	CR005082	GCCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1218	CR005083	ACGCCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1219	CR005084	mCmACGCCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1220	CR005085	CAmCmGCCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1221	CR005086	CACGmCmCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1222	CR005087	CACGCCmCmCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1223	CR005088	CACGCCCCmCmACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1224	CR005089	CACGCCCCCAmCmCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1225	CR005090	CACGCCCCCACCmCmUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
1226	CR005091	CACGCCCCCACCCUmAmAUCAGGUUUUAGAGCUAUGCUGUUUUG
1227	CR005092	CACGCCCCCACCCUAAmUmCAGGUUUUAGAGCUAUGCUGUUUUG
1228	CR005093	CACGCCCCCACCCUAAUCmAmGGUUUUAGAGCUAUGCUGUUUUG
1229	CR005094	GGCACGCCCCCACCCUAAUCAGGUUUUAGAGCUAUGCUGUUUUG
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1323	CR010416	mU*mG*mA*AUCCAAGUGUCCUCUfGAGUUUUAGAGCUAUGCUGUUUUG
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1333	CR010426	mU*mG*mA*AUCCAAGUGUCfCUCUGAGUUUUAGAGCUAUGCUGUUUUG
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1351	CR010444	mU*mG*mA*AUCfCAAGUGUCCUCUGfAGUUUUUAGAGCUAUGCUGUUUUG
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1386	CR010479	mU*mG*mA*AUCCfAAGUfGUCCUCfUGAGUUUUUAGAGCUAUGCUGUUUUG
1387	CR010480	mU*mG*mA*AUfCCAAGUGUCfCUCUfGAGUUUUUAGAGCUAUGCUGUUUUG
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1440	CR010996	mU*mG*mA*AmUCCAAGUGUCCUmCUGAGUUUUAGAGCUAUGCUGUUUUG
1441	CR010997	mU*mG*mA*AUCCAAmGUGUCCUCUGmAGUUUUAGAGCUAUGCUGUUUUG
1442	CR010998	mU*mG*mA*AUmCCAAGUmGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
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1445	CR011001	mU*mG*mA*AUCCAAGUGUCCUmCmUGAGUUUUAGAGCUAUGCUGUUUUG
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1447	CR011003	mU*mG*mA*AUmCCAAGUGUmCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1448	CR011004	mU*mG*mA*AmUCCAAGUGUCmCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1449	CR011005	mU*mG*mA*AUCCmAAGUGUCCmUCUGAGUUUUAGAGCUAUGCUGUUUUG
1450	CR011006	mU*mG*mA*mAUCCAAmGUGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1451	CR011007	mU*mG*mA*mAUCCAAGUGUCmCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1452	CR011008	mU*mG*mA*AUCCmAAGUGUmCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1453	CR011009	mU*mG*mA*AUCCAmAGUGUCCUCUmGAGUUUUAGAGCUAUGCUGUUUUG
1454	CR011010	mU*mG*mA*AUCCAAGUGUCCmUCUGmAGUUUUAGAGCUAUGCUGUUUUG
1455	CR011011	mU*mG*mA*AUCCAAGmUGUCCUCmUGAGUUUUAGAGCUAUGCUGUUUUG
1456	CR011012	mU*mG*mA*AUCCAAGUGmUCCUmCUGAGUUUUAGAGCUAUGCUGUUUUG
1457	CR011013	mU*mG*mA*AUCCAAmGUmGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1458	CR011014	mU*mG*mA*AmUCmCAAGUGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1459	CR011015	mU*mG*mA*AUmCCAAGUGUCCUCUmGAGUUUUAGAGCUAUGCUGUUUUG
1460	CR011016	mU*mG*mA*AUCCAmAGUGUCCmUCUGAGUUUUAGAGCUAUGCUGUUUUG
1461	CR011017	mU*mG*mA*AUCCmAAGUmGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1462	CR011018	mU*mG*mA*AUCCAAGUGUCCUCmUGmAGUUUUAGAGCUAUGCUGUUUUG

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1463	CR011019	mU*mG*mA*AUCCAAmGUGUmCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1464	CR011020	mU*mG*mA*AUCCAAGUGmUCmCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1465	CR011021	mU*mG*mA*AmUmCCAAGUGUCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1466	CR011022	mU*mG*mA*mAUCCAAGmUGUCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1467	CR011023	mU*mG*mA*AUCmCAAGUGUCCUmCUGAGUUUUUAGAGCUAUGCUGUUUUG
1468	CR011024	mU*mG*mA*AUCmCAAGUGUCCUmCUGmAGUUUUUAGAGCUAUGCUGUUUUG
1469	CR011025	mU*mG*mA*mAUCCAAGUmGUCmCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1470	CR011026	mU*mG*mA*AUCCAAGUGUCCmUCmUmGAGUUUUUAGAGCUAUGCUGUUUUG
1471	CR011027	mU*mG*mA*AUCCmAAGUGmUmCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1472	CR011028	mU*mG*mA*AUmCCAmAmGUGUCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1473	CR011029	mU*mG*mA*AmUCCAAGmUGUCCmUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1474	CR011030	mU*mG*mA*AmUCCAAGUGUmCCUCUmGAGUUUUUAGAGCUAUGCUGUUUUG
1475	CR011031	mU*mG*mA*AUCCAAGmUGUCCUCmUGmAGUUUUUAGAGCUAUGCUGUUUUG
1476	CR011032	mU*mG*mA*AUCCAAGUGmUCmCUmCUGAGUUUUUAGAGCUAUGCUGUUUUG
1477	CR011033	mU*mG*mA*AUCmCAmAGUmGUCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1478	CR011034	mU*mG*mA*mAUCCmAAmGUGUCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1479	CR011035	mU*mG*mA*AUmCCAAGUGmUCCUmCUGAGUUUUUAGAGCUAUGCUGUUUUG
1480	CR011036	mU*mG*mA*AUCCAmAmGUGUCCUCUGmAGUUUUUAGAGCUAUGCUGUUUUG
1481	CR011037	mU*mG*mA*AUCCmAAGUmGUCCUCmUGAGUUUUUAGAGCUAUGCUGUUUUG
1482	CR011038	mU*mG*mA*AUmCCAAGUGUCCmCUCUmGAGUUUUUAGAGCUAUGCUGUUUUG
1483	CR011039	mU*mG*mA*AmUCmCAAGUGUCCmUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1484	CR011040	mU*mG*mA*mAUCCAAGmUGUmCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1485	CR011041	mU*mG*mA*AUCmCmAAmGUGUCCmUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1486	CR011042	mU*mG*mA*AUCCAAGUGUmCCUmCmUmGAGUUUUUAGAGCUAUGCUGUUUUG
1487	CR011043	mU*mG*mA*AUCCAmAGmUGmUCCUCUGmAGUUUUUAGAGCUAUGCUGUUUUG
1488	CR011044	mU*mG*mA*mAUmCCAAGUmGUCmCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1489	CR011045	mU*mG*mA*AmUCCmAAGUmGmUCCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1490	CR011046	mU*mG*mA*AUCCAAmGmUGUmCmCUCUGAGUUUUUAGAGCUAUGCUGUUUUG
1491	CR011047	mU*mG*mA*mAUCmCAmAGUGUCCUCmUGAGUUUUUAGAGCUAUGCUGUUUUG

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1493	CR011049	mU*mG*mA*AUmCCAAmGUGUCCUCUmGmAGUUUUAGAGCUAUGCUGUUUUG
1494	CR011050	mU*mG*mA*AUCmCAAGUGmUCmCmUCUGAGUUUUAGAGCUAUGCUGUUUUG
1495	CR011051	mU*mG*mA*AUCCmAmAGUmGUCCUCUmGAGUUUUAGAGCUAUGCUGUUUUG
1496	CR011052	mU*mG*mA*AmUmCCAAGUGUmCCUCmUGAGUUUUAGAGCUAUGCUGUUUUG
1497	CR011053	mU*mG*mA*mAUCCAAGmUmGUCCUmCUGAGUUUUAGAGCUAUGCUGUUUUG
1498	CR011054	mU*mG*mA*AmUCCAmAGUGUCmCUCmUGAGUUUUAGAGCUAUGCUGUUUUG
1499	CR011055	mU*mG*mA*AUCCmAAGmUGUmCCUCUGmAGUUUUAGAGCUAUGCUGUUUUG
1500	CR011056	mU*mG*mA*mAUCCAAGUGmUCCUmCUmGAGUUUUAGAGCUAUGCUGUUUUG
1501	CR011057	mU*mG*mA*AUmCmCAAmGUGUCCmUCUGAGUUUUAGAGCUAUGCUGUUUUG
1502	CR011058	UGAAUCCAAGUGUCCUmCUGAGUUUUAGAGCUAUGCUGUUUUG
1503	CR011059	UGAAUmCCAAGUGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1504	CR011060	UGAAUCCAmAGUGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1505	CR011061	UGAAUCCmAAGUGUCCmUCUGAGUUUUAGAGCUAUGCUGUUUUG
1506	CR011062	UGAAUCCAAmGUmGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1507	CR011063	UGAmAUCCAAGmUGUmCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1508	CR011064	UGAAUCmCAAGUGUCCUmCUGmAGUUUUAGAGCUAUGCUGUUUUG
1509	CR011065	UGAAmUCCAmAGUGUCmCUCmUGAGUUUUAGAGCUAUGCUGUUUUG
1510	CR011066	UGAmAUCCAAGUGmUCCUmCUmGAGUUUUAGAGCUAUGCUGUUUUG
1511	CR011534	mU*mG*mA*A*UCCAAGUGUCCUCU*GAGUUUUAGAGCUAUGCUGUUUUG
1512	CR011535	mU*mG*mA*AUCCAAGUG*UCCU*CUGAGUUUUAGAGCUAUGCUGUUUUG
1513	CR011536	mU*mG*mA*AUCC*AAGUGUC*CUCUGAGUUUUAGAGCUAUGCUGUUUUG
1514	CR011537	mU*mG*mA*AUCCAAGU*GU*CCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1515	CR011538	mU*mG*mA*AUCCAA*GUGUCC*UCUGAGUUUUAGAGCUAUGCUGUUUUG
1516	CR011539	mU*mG*mA*AUCCA*AGUGUCCUCUG*AGUUUUAGAGCUAUGCUGUUUUG
1517	CR011540	mU*mG*mA*AU*CCAAGUGUCCUC*UGAGUUUUAGAGCUAUGCUGUUUUG
1518	CR011541	mU*mG*mA*AUCCAAG*UGUCCUCUGA*GUUUUAGAGCUAUGCUGUUUUG
1519	CR011542	mU*mG*mA*AUCC*AAGUGUCCUC*UGA*GUUUUAGAGCUAUGCUGUUUUG
1520	CR011543	mU*mG*mA*A*UCCAAGUG*UCC*UCUGAGUUUUAGAGCUAUGCUGUUUUG

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1521	CR011544	mU*mG*mA*AUCCAAGUGUCCU*CU*G*AGUUUUAGAGCUAUGCUGUUUUG
1522	CR011545	mU*mG*mA*AUCCA*AGUGU*C*CUCUGAGUUUUAGAGCUAUGCUGUUUUG
1523	CR011546	mU*mG*mA*AUC*CAA*G*UGUCCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1524	CR011547	mU*mG*mA*AU*CCAAGU*GUCCU*CUGAGUUUUAGAGCUAUGCUGUUUUG
1525	CR011548	mU*mG*mA*AU*CCAAGUGUC*CUCUG*AGUUUUAGAGCUAUGCUGUUUUG
1526	CR011549	mU*mG*mA*AUCCAAGU*GUCCUCU*GA*GUUUUAGAGCUAUGCUGUUUUG
1527	CR011550	mU*mG*mA*AUCC*A*AG*UGUCCU*CUGAGUUUUAGAGCUAUGCUGUUUUG
1528	CR011551	mU*mG*mA*AUCCAAGUGUC*CUC*U*G*AGUUUUAGAGCUAUGCUGUUUUG
1529	CR011552	mU*mG*mA*AUCCAA*GU*GU*CCUCUGA*GUUUUAGAGCUAUGCUGUUUUG
1530	CR011553	mU*mG*mA*A*UC*CAAGUG*UCC*UCUGAGUUUUAGAGCUAUGCUGUUUUG
1531	CR011554	mU*mG*mA*AU*CCA*AGUG*U*CCUCUGAGUUUUAGAGCUAUGCUGUUUUG
1532	CR011555	mU*mG*mA*AUCCAAG*U*GUC*C*UCUGAGUUUUAGAGCUAUGCUGUUUUG
1533	CR011556	mU*mG*mA*A*UCC*AA*GUGUCCUCU*GAGUUUUAGAGCUAUGCUGUUUUG
1534	CR011557	mU*mG*mA*AU*CCAAGUGUCCU*C*UGA*GUUUUAGAGCUAUGCUGUUUUG
1535	CR011558	mU*mG*mA*AUCC*A*AG*UGUCCUC*U*GAGUUUUAGAGCUAUGCUGUUUUG
1536	CR011559	mU*mG*mA*AUCCAA*GUG*U*CC*UCUG*AGUUUUAGAGCUAUGCUGUUUUG
1537	CR011560	mU*mG*mA*A*UCCAAGU*GUC*CU*CUGA*GUUUUAGAGCUAUGCUGUUUUG
1538	CR011561	mU*mG*mA*AU*C*CAAGU*GUCC*UC*UGAGUUUUAGAGCUAUGCUGUUUUG
1539	CR011562	mU*mG*mA*A*UC*CAAG*UGU*CCU*CUGAGUUUUAGAGCUAUGCUGUUUUG
1540	CR011563	mU*mG*mA*AU*CCAAGUGUC*CUCU*G*A*GUUUUAGAGCUAUGCUGUUUUG
1541	CR011564	mU*mG*mA*AUCC*A*A*GUG*UCCU*CUGAGUUUUAGAGCUAUGCUGUUUUG
1542	CR011565	mU*mG*mA*AUC*C*AA*GUGU*CCUCUGA*GUUUUAGAGCUAUGCUGUUUUG
1543	CR011566	mU*mG*mA*AUC*C*A*AGUGU*CCUC*U*GAGUUUUAGAGCUAUGCUGUUUUG
1544	CR011567	mU*mG*mA*AU*CCAA*G*UG*UC*CU*CUGAGUUUUAGAGCUAUGCUGUUUUG
1545	CR011568	mU*mG*mA*A*UCCAAGU*GUC*C*UCUG*A*GUUUUAGAGCUAUGCUGUUUUG
1546	CR011569	mU*mG*mA*A*UC*CA*A*GUG*UCC*UCUGAGUUUUAGAGCUAUGCUGUUUUG
1547	CR011570	mU*mG*mA*A*UCCAAG*UGUCCUC*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1548	CR011571	mU*mG*mA*AUCC*AA*GU*GU*CCU*CUGA*GUUUUAGAGCUAUGCUGUUUUG
1549	CR011572	mU*mG*mA*AU*CC*AAGU*G*UCC*UCU*GAGUUUUAGAGCUAUGCUGUUUUG

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1552	CR011575	mU*mG*mA*A*UCCAAG*U*G*UCC*U*CUG*AGUUUUAGAGCUAUGCUGUUUUG
1553	CR011576	mU*mG*mA*AU*C*CA*AG*UGUC*CU*C*UGAGUUUUAGAGCUAUGCUGUUUUG
1554	CR011577	mU*mG*mA*A*U*C*CAAGUG*UCCUC*U*GA*GUUUUAGAGCUAUGCUGUUUUG
1555	CR011578	mU*mG*mA*AU*CC*AA*GU*GU*CC*UCUG*AGUUUUAGAGCUAUGCUGUUUUG
1556	CR011579	mU*mG*mA*AUCCAA*G*UG*UC*CUC*U*G*AGUUUUAGAGCUAUGCUGUUUUG
1557	CR011580	mU*mG*mA*A*UC*CA*AGU*GU*CC*UCUGA*GUUUUAGAGCUAUGCUGUUUUG
1558	CR011581	mU*mG*mA*AUC*C*AAGUG*UCC*U*C*U*GAGUUUUAGAGCUAUGCUGUUUUG
1559	CR011582	mU*mG*mA*A*U*CC*AA*GU*GUC*CU*CUGAGUUUUAGAGCUAUGCUGUUUUG
1560	CR011583	mU*mG*mA*A*U*CCAA*G*U*GU*CCUCUG*A*GUUUUAGAGCUAUGCUGUUUUG
1561	CR011584	mU*mG*mA*AUC*C*A*AGUG*UC*CU*C*U*GAGUUUUAGAGCUAUGCUGUUUUG
1562	CR011585	mU*mG*mA*AUCC*AAG*UG*U*CC*U*CU*G*AGUUUUAGAGCUAUGCUGUUUUG
1563	CR011586	mU*mG*mA*A*U*C*CA*AGU*GUCC*UC*UGA*GUUUUAGAGCUAUGCUGUUUUG
1564	CR011587	mU*mG*mA*AUC*CA*A*G*UGU*C*CU*CUGA*GUUUUAGAGCUAUGCUGUUUUG
1565	CR011588	mU*mG*mA*AU*CC*AA*GU*GUC*CUC*U*G*AGUUUUAGAGCUAUGCUGUUUUG
1566	CR011589	mU*mG*mA*A*UC*C*AAGU*G*U*C*C*UCUGAGUUUUAGAGCUAUGCUGUUUUG
1567	CR011590	mU*mG*mA*A*UCCA*A*G*UG*UCC*UC*U*GAGUUUUAGAGCUAUGCUGUUUUG
1568	CR011591	mU*mG*mA*AU*CC*A*AGU*G*UCCU*CUG*A*GUUUUAGAGCUAUGCUGUUUUG
1569	CR011592	mU*mG*mA*AUC*CA*A*GUG*UC*C*U*C*UGA*GUUUUAGAGCUAUGCUGUUUUG
1570	CR011593	mU*mG*mA*A*U*CC*A*AG*U*GU*CCUCU*G*AGUUUUAGAGCUAUGCUGUUUUG
1571	CR011594	mU*mG*mA*AUC*C*AAGU*GU*C*C*U*CU*G*AGUUUUAGAGCUAUGCUGUUUUG
1572	CR011595	mU*mG*mA*A*U*CCAA*G*U*G*UCCUC*U*GA*GUUUUAGAGCUAUGCUGUUUUG
1573	CR011596	mU*mG*mA*AU*C*CA*A*G*UGUC*C*U*CU*GA*GUUUUAGAGCUAUGCUGUUUUG
1574	CR011597	mU*mG*mA*A*UCC*AA*GU*G*U*CC*UC*UG*A*GUUUUAGAGCUAUGCUGUUUUG
1575	CR011598	mU*mG*mA*A*U*CCAAG*U*G*U*C*CU*C*U*GAGUUUUAGAGCUAUGCUGUUUUG
1576	CR011599	mU*mG*mA*AUC*C*A*AG*UG*U*CCU*C*U*G*AGUUUUAGAGCUAUGCUGUUUUG
1577	CR011600	mU*mG*mA*A*UC*CA*A*G*U*G*UCCU*C*U*G*AGUUUUAGAGCUAUGCUGUUUUG
1578	CR011601	mU*mG*mA*AU*C*C*A*AGU*GU*C*C*UC*U*GA*GUUUUAGAGCUAUGCUGUUUUG

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1579	CR011602	mU*mG*mA*A*U*CC*AA*G*UG*U*C*C*UCUG*A*GUUUUAGAGCUAUGCUGUUUUG
1580	CR011603	mU*mG*mA*AUC*CA*A*GUG*U*C*C*U*C*UG*A*GUUUUAGAGCUAUGCUGUUUUG
1581	CR011604	mU*mG*mA*AUCC*A*A*GU*G*U*CC*U*C*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1582	CR011605	mU*mG*mA*A*U*C*CAAG*UG*U*C*C*UC*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1583	CR011606	mU*mG*mA*A*U*C*C*A*A*G*U*GUC*C*U*CUG*AGUUUUAGAGCUAUGCUGUUUUG
1584	CR011607	mU*mG*mA*A*U*C*C*C*A*AGU*G*U*C*CU*C*UGA*GUUUUAGAGCUAUGCUGUUUUG
1585	CR011608	mU*mG*mA*A*U*C*C*CA*AGU*G*UC*C*U*C*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1586	CR011609	mU*mG*mA*AU*C*C*C*A*A*G*U*G*U*C*C*U*CUGA*GUUUUAGAGCUAUGCUGUUUUG
1587	CR011610	mU*mG*mA*A*U*C*C*C*A*A*G*UG*U*CC*UC*U*G*AGUUUUAGAGCUAUGCUGUUUUG
1588	CR011611	mU*mG*mA*A*U*C*C*C*AA*G*U*GU*C*CU*C*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1589	CR011612	mU*mG*mA*A*U*C*CC*A*AG*U*GU*C*C*U*C*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1590	CR011613	mU*mG*mA*A*U*C*CAA*G*U*G*U*C*C*U*C*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1591	CR011614	mU*mG*mA*AU*C*C*C*A*A*G*UG*U*C*C*UC*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1592	CR011615	mU*mG*mA*A*U*C*C*C*A*A*GU*G*UC*C*U*CU*G*A*GUUUUAGAGCUAUGCUGUUUUG
1593	CR011616	mU*mG*mA*A*U*C*C*C*AA*G*U*G*U*C*C*U*C*UG*A*GUUUUAGAGCUAUGCUGUUUUG
1594	CR011617	mU*mG*mA*AU*C*C*C*A*A*G*U*G*U*C*C*U*C*U*GA*GUUUUAGAGCUAUGCUGUUUUG
1595	CR011618	mU*mG*mA*A*UC*C*A*A*G*U*G*U*CC*U*C*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1596	CR011619	mU*mG*mA*A*U*C*C*C*A*A*GU*GU*C*C*U*C*U*G*A*GUUUUAGAGCUAUGCUGUUUUG
1597	CR011620	UGAAU*CCAAGUGUCCUC*UGAGUUUUAGAGCUAUGCUGUUUUG
1598	CR011621	UGAAUCCA*AGUGU*C*CUCUGAGUUUUAGAGCUAUGCUGUUUUG
1599	CR011622	UGAA*UCC*AA*GUGUCCUCU*GAGUUUUAGAGCUAUGCUGUUUUG
1600	CR011623	UGAA*UCCAAGU*GUC*CU*CUGA*GUUUUAGAGCUAUGCUGUUUUG
1601	CR011624	UGAA*UC*CA*A*GUG*UCC*UCUGAGUUUUAGAGCUAUGCUGUUUUG
1602	CR011625	UGAA*UCCAAG*U*G*UCC*U*CUG*AGUUUUAGAGCUAUGCUGUUUUG
1603	CR011626	UGAAU*CC*AA*GU*GUC*CUC*U*G*AGUUUUAGAGCUAUGCUGUUUUG
1604	CR011627	UGAAUC*C*AAGU*GU*C*C*U*CU*G*AGUUUUAGAGCUAUGCUGUUUUG
1605	CR010320	mG*mU*mG*AfGUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1606	CR010321	mG*mU*mG*AGUCUGGAGAGCUGCfAUGUUUUAGAGCUAUGCUGUUUUG
1607	CR010322	mG*mU*mG*AGUCUGGAGAGCfUGCAUGUUUUAGAGCUAUGCUGUUUUG

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1609	CR010324	mG*mU*mG*AGUCUGGAGAGCUGCAfUGUUUUAGAGCUAUGCUGUUUUG
1610	CR010325	mG*mU*mG*AGUCUGGAGAGCUfGCAUGUUUUAGAGCUAUGCUGUUUUG
1611	CR010326	mG*mU*mG*AGUCUGGAGfAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1612	CR010327	mG*mU*mG*AGUCUfGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1613	CR010328	mG*mU*mG*AGUCUGGAGAfGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1614	CR010329	mG*mU*mG*AGUCUGGfAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1615	CR010330	mG*mU*mG*fAGUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1616	CR010331	mG*mU*mG*AGUCUGGAGAGfCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1617	CR010332	mG*mU*mG*AGUCUGGAfGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1618	CR010333	mG*mU*mG*AGUCUGfGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1619	CR010334	mG*mU*mG*AGfUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
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1621	CR010336	mG*mU*mG*AGUCUGGAGAGCUGfCAUGUUUUAGAGCUAUGCUGUUUUG
1622	CR010337	mG*mU*mG*fAGUCUGGAGAGCUGfCAUGUUUUAGAGCUAUGCUGUUUUG
1623	CR010338	mG*mU*mG*AGUCUGGAfGAGCfUGCAUGUUUUAGAGCUAUGCUGUUUUG
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1625	CR010340	mG*mU*mG*AGUCUGGfAGfAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1626	CR010341	mG*mU*mG*AGUCUfGGAGAGfCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1627	CR010342	mG*mU*mG*AGUCfUGGAGAGCUGCfAUGUUUUAGAGCUAUGCUGUUUUG
1628	CR010343	mG*mU*mG*AfGUCUGGAGAGCUfGCAUGUUUUAGAGCUAUGCUGUUUUG
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1635	CR010350	mG*mU*mG*AGfUCUGGAGAfGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
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SEQ ID NO	Name	Sequence
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1640	CR010355	mG*mU*mG*AGUCfUGGAGAfGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1641	CR010356	mG*mU*mG*AGUCUfGGAGAGCUGCfAUGUUUUAGAGCUAUGCUGUUUUG
1642	CR010357	mG*mU*mG*AGUCUGGAGAGCfUGCAfUGUUUUAGAGCUAUGCUGUUUUG
1643	CR010358	mG*mU*mG*AGUCUGGfAGAGCUGfCAUGUUUUAGAGCUAUGCUGUUUUG
1644	CR010359	mG*mU*mG*AGUCUGGAGfAGCUfGCAUGUUUUAGAGCUAUGCUGUUUUG
1645	CR010360	mG*mU*mG*AGUCUGfGAfGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1646	CR010361	mG*mU*mG*AfGUfCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1647	CR010362	mG*mU*mG*AGfUCUGGAGAGCUGCfAUGUUUUAGAGCUAUGCUGUUUUG
1648	CR010363	mG*mU*mG*AGUCUfGGAGAGCfUGCAUGUUUUAGAGCUAUGCUGUUUUG
1649	CR010364	mG*mU*mG*AGUCfUGGAfGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1650	CR010365	mG*mU*mG*AGUCUGGAGAGCUGfCAfUGUUUUAGAGCUAUGCUGUUUUG
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1652	CR010367	mG*mU*mG*AGUCUGGAGfAGfCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1653	CR010368	mG*mU*mG*AfGfUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1654	CR010369	mG*mU*mG*fAGUCUGGfAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1655	CR010370	mG*mU*mG*AGUfCUGGAGAGCUfGCAUGUUUUAGAGCUAUGCUGUUUUG
1656	CR010371	mG*mU*mG*AGUfCUGGAGAGCUfGCAfUGUUUUAGAGCUAUGCUGUUUUG
1657	CR010372	mG*mU*mG*fAGUCUGGAfGAGfCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1658	CR010373	mG*mU*mG*AGUCUGGAGAGCfUGfCfAUGUUUUAGAGCUAUGCUGUUUUG
1659	CR010374	mG*mU*mG*AGUCfUGGAGfAfGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1660	CR010375	mG*mU*mG*AGfUCUfGfGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1661	CR010376	mG*mU*mG*AfGUCUGGfAGAGCfUGCAUGUUUUAGAGCUAUGCUGUUUUG
1662	CR010377	mG*mU*mG*AfGUCUGGAGAfGCUGCfAUGUUUUAGAGCUAUGCUGUUUUG
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1664	CR010379	mG*mU*mG*AGUCUGGAGfAGfCUfGCAUGUUUUAGAGCUAUGCUGUUUUG
1665	CR010380	mG*mU*mG*AGUfCUfGGAfGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG

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1668	CR010383	mG*mU*mG*AGUCUfGfGAGAGCUGCAfUGUUUUAGAGCUAUGCUGUUUUG
1669	CR010384	mG*mU*mG*AGUCfUGGAfGAGCUGfCAUGUUUUAGAGCUAUGCUGUUUUG
1670	CR010385	mG*mU*mG*AGfUCUGGAGAGfCUGCfAUGUUUUAGAGCUAUGCUGUUUUG
1671	CR010386	mG*mU*mG*AfGUfCUGGAGAGCfUGCAUGUUUUAGAGCUAUGCUGUUUUG
1672	CR010387	mG*mU*mG*fAGUCUGGfAGAfGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1673	CR010388	mG*mU*mG*AGUfCfUGfGAGAGCfUGCAUGUUUUAGAGCUAUGCUGUUUUG
1674	CR010389	mG*mU*mG*AGUCUGGAGAfGCUfGfCfAUGUUUUAGAGCUAUGCUGUUUUG
1675	CR010390	mG*mU*mG*AGUCUfGGfAGfAGCUGCAfUGUUUUAGAGCUAUGCUGUUUUG
1676	CR010391	mG*mU*mG*fAGfUCUGGGAfGAGfCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1677	CR010392	mG*mU*mG*AfGUCfUGGAfGfAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1678	CR010393	mG*mU*mG*AGUCUGfGfAGAfGfCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1679	CR010394	mG*mU*mG*fAGUfCUfGGAGAGCUGfCAUGUUUUAGAGCUAUGCUGUUUUG
1680	CR010395	mG*mU*mG*AfGUCUGGAGAGCfUfGCAfUGUUUUAGAGCUAUGCUGUUUUG
1681	CR010396	mG*mU*mG*AGfUCUGfGAGAGCUGCfAfUGUUUUAGAGCUAUGCUGUUUUG
1682	CR010397	mG*mU*mG*AGUfCUGGAGfAGfCfUGCAUGUUUUAGAGCUAUGCUGUUUUG
1683	CR010398	mG*mU*mG*AGUCfUfGGAfGAGCUGCfAUGUUUUAGAGCUAUGCUGUUUUG
1684	CR010399	mG*mU*mG*AfGfUCUGGAGAfGCUGfCAUGUUUUAGAGCUAUGCUGUUUUG
1685	CR010400	mG*mU*mG*fAGUCUGGfAfGAGCUfGCAUGUUUUAGAGCUAUGCUGUUUUG
1686	CR010401	mG*mU*mG*AfGUCUfGGAGAGfCUGfCAUGUUUUAGAGCUAUGCUGUUUUG
1687	CR010402	mG*mU*mG*AGUCfUGGfAGAfGCUGCAfUGUUUUAGAGCUAUGCUGUUUUG
1688	CR010403	mG*mU*mG*fAGUCUGGAGfAGCUfGfCfAUGUUUUAGAGCUAUGCUGUUUUG
1689	CR010404	mG*mU*mG*AGfUfCUGfGAGAGCfUGCAUGUUUUAGAGCUAUGCUGUUUUG
1690	CR010405	GUGAGUCUGGGAGAGCUfGCAUGUUUUAGAGCUAUGCUGUUUUG
1691	CR010406	GUGAGfUCUGGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1692	CR010407	GUGAGUCUfGGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1693	CR010408	GUGAGUCfUGGGAGAGCfUGCAUGUUUUAGAGCUAUGCUGUUUUG
1694	CR010409	GUGAGUCUGfGAfGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG

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1696	CR010411	GUGAGUfCUGGAGAGCUfGCAfUGUUUUAGAGCUAUGCUGUUUUG
1697	CR010412	GUGAfGUCUfGGAGAGfCUGfCAUGUUUUAGAGCUAUGCUGUUUUG
1698	CR010413	GUGfAGUCUGGAGfAGCUfGCfAUGUUUUAGAGCUAUGCUGUUUUG
1699	CR010414	mG*mU*mG*AGUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1700	CR010879	mG*mU*mG*AmGUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1701	CR010880	mG*mU*mG*AGUCUGGAGAGCUGCmAUGUUUUAGAGCUAUGCUGUUUUG
1702	CR010881	mG*mU*mG*AGUCUGGAGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1703	CR010882	mG*mU*mG*AGUmCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1704	CR010883	mG*mU*mG*AGUCUGGAGAGCUGCAmUGUUUUAGAGCUAUGCUGUUUUG
1705	CR010884	mG*mU*mG*AGUCUGGAGAGCUmGCAUGUUUUAGAGCUAUGCUGUUUUG
1706	CR010885	mG*mU*mG*AGUCUGGAGmAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1707	CR010886	mG*mU*mG*AGUCUmGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1708	CR010887	mG*mU*mG*AGUCUGGAGAmGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1709	CR010888	mG*mU*mG*AGUCUGGmAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1710	CR010889	mG*mU*mG*mAGUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1711	CR010890	mG*mU*mG*AGUCUGGAGAGmCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1712	CR010891	mG*mU*mG*AGUCUGGAmGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
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1714	CR010893	mG*mU*mG*AGmUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1715	CR010894	mG*mU*mG*AGUCmUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1716	CR010895	mG*mU*mG*AGUCUGGAGAGCUGmCAUGUUUUAGAGCUAUGCUGUUUUG
1717	CR010896	mG*mU*mG*mAGUCUGGAGAGCUGmCAUGUUUUAGAGCUAUGCUGUUUUG
1718	CR010897	mG*mU*mG*AGUCUGGAmGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1719	CR010898	mG*mU*mG*AGUmCUGGAGAmGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1720	CR010899	mG*mU*mG*AGUCUGGmAGmAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1721	CR010900	mG*mU*mG*AGUCUmGGAGAGmCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1722	CR010901	mG*mU*mG*AGUCmUGGAGAGCUGCmAUGUUUUAGAGCUAUGCUGUUUUG
1723	CR010902	mG*mU*mG*AmGUCUGGAGAGCUmGCAUGUUUUAGAGCUAUGCUGUUUUG

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1725	CR010904	mG*mU*mG*AGmUCUGGAmGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1726	CR010905	mG*mU*mG*AGUCUGGAGmAGCUGCmAUGUUUUAGAGCUAUGCUGUUUUG
1727	CR010906	mG*mU*mG*AGUCUmGGmAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1728	CR010907	mG*mU*mG*AGUCUGGAGAGCUmGmCAUGUUUUAGAGCUAUGCUGUUUUG
1729	CR010908	mG*mU*mG*AGUmCUGGAGAGCUGCAmUGUUUUAGAGCUAUGCUGUUUUG
1730	CR010909	mG*mU*mG*AGmUCUGGAGAmGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1731	CR010910	mG*mU*mG*AmGUCUGGAGAGmCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1732	CR010911	mG*mU*mG*AGUCmUGGAGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1733	CR010912	mG*mU*mG*mAGUCUGmGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1734	CR010913	mG*mU*mG*mAGUCUGGAGAGmCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1735	CR010914	mG*mU*mG*AGUCmUGGAGAmGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1736	CR010915	mG*mU*mG*AGUCUmGGAGAGCUGCmAUGUUUUAGAGCUAUGCUGUUUUG
1737	CR010916	mG*mU*mG*AGUCUGGAGAGCmUGCAmUGUUUUAGAGCUAUGCUGUUUUG
1738	CR010917	mG*mU*mG*AGUCUGGmAGAGCUGmCAUGUUUUAGAGCUAUGCUGUUUUG
1739	CR010918	mG*mU*mG*AGUCUGGAGmAGCUmGCAUGUUUUAGAGCUAUGCUGUUUUG
1740	CR010919	mG*mU*mG*AGUCUGmGAmGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1741	CR010920	mG*mU*mG*AmGUmCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1742	CR010921	mG*mU*mG*AGmUCUGGAGAGCUGCmAUGUUUUAGAGCUAUGCUGUUUUG
1743	CR010922	mG*mU*mG*AGUCUmGGAGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1744	CR010923	mG*mU*mG*AGUCmUGGAmGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1745	CR010924	mG*mU*mG*AGUCUGGAGAGCUGmCAmUGUUUUAGAGCUAUGCUGUUUUG
1746	CR010925	mG*mU*mG*AGUCUGmGAGAmGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1747	CR010926	mG*mU*mG*AGUCUGGAGmAGmCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1748	CR010927	mG*mU*mG*AmGmUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1749	CR010928	mG*mU*mG*mAGUCUGGmAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1750	CR010929	mG*mU*mG*AGUmCUGGAGAGCUmGCAUGUUUUAGAGCUAUGCUGUUUUG
1751	CR010930	mG*mU*mG*AGUmCUGGAGAGCUmGCAmUGUUUUAGAGCUAUGCUGUUUUG
1752	CR010931	mG*mU*mG*mAGUCUGGAmGAGmCUGCAUGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
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1754	CR010933	mG*mU*mG*AGUCmUGGAGmAmGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1755	CR010934	mG*mU*mG*AGmUCUmGmGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1756	CR010935	mG*mU*mG*AmGUCUGGmAGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1757	CR010936	mG*mU*mG*AmGUCUGGAGAmGCUGCmAUGUUUUAGAGCUAUGCUGUUUUG
1758	CR010937	mG*mU*mG*AGUCUGGmAGAGCUGmCAmUGUUUUAGAGCUAUGCUGUUUUG
1759	CR010938	mG*mU*mG*AGUCUGGAGmAGmCUmGCAUGUUUUAGAGCUAUGCUGUUUUG
1760	CR010939	mG*mU*mG*AGUmCUmGGAmGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1761	CR010940	mG*mU*mG*mAGUCmUGmGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1762	CR010941	mG*mU*mG*AGmUCUGGAGmAGCUmGCAUGUUUUAGAGCUAUGCUGUUUUG
1763	CR010942	mG*mU*mG*AGUCUmGmGAGAGCUGCAmUGUUUUAGAGCUAUGCUGUUUUG
1764	CR010943	mG*mU*mG*AGUCmUGGAmGAGCUGmCAUGUUUUAGAGCUAUGCUGUUUUG
1765	CR010944	mG*mU*mG*AGmUCUGGAGAGmCUGCmAUGUUUUAGAGCUAUGCUGUUUUG
1766	CR010945	mG*mU*mG*AmGUmCUGGAGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1767	CR010946	mG*mU*mG*mAGUCUGGmAGAmGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1768	CR010947	mG*mU*mG*AGUmCmUGmGAGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1769	CR010948	mG*mU*mG*AGUCUGGAGAmGCUmGmCmAUGUUUUAGAGCUAUGCUGUUUUG
1770	CR010949	mG*mU*mG*AGUCUmGGmAGmAGCUGCAmUGUUUUAGAGCUAUGCUGUUUUG
1771	CR010950	mG*mU*mG*mAGmUCUGGAmGAGmCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1772	CR010951	mG*mU*mG*AmGUCmUGGAmGmAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1773	CR010952	mG*mU*mG*AGUCUGmGmAGAmGmCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1774	CR010953	mG*mU*mG*mAGUmCUmGGAGAGCUGmCAUGUUUUAGAGCUAUGCUGUUUUG
1775	CR010954	mG*mU*mG*AmGUCUGGAGAGCmUmGCAmUGUUUUAGAGCUAUGCUGUUUUG
1776	CR010955	mG*mU*mG*AGmUCUGmGAGAGCUGCmAmUGUUUUAGAGCUAUGCUGUUUUG
1777	CR010956	mG*mU*mG*AGUmCUGGAGmAGmCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1778	CR010957	mG*mU*mG*AGUCmUmGGAmGAGCUGCmAUGUUUUAGAGCUAUGCUGUUUUG
1779	CR010958	mG*mU*mG*AmGmUCUGGAGAmGCUGmCAUGUUUUAGAGCUAUGCUGUUUUG
1780	CR010959	mG*mU*mG*mAGUCUGGmAmGAGCUmGCAUGUUUUAGAGCUAUGCUGUUUUG
1781	CR010960	mG*mU*mG*AmGUCUmGGAGAGmCUGmCAUGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
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1783	CR010962	mG*mU*mG*mAGUCUGGAGmAGCUmGCmAUGUUUUAGAGCUAUGCUGUUUUG
1784	CR010963	mG*mU*mG*AGmUmCUGmGAGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1785	CR010964	GUGAGUCUGGAGAGCUmGCAUGUUUUAGAGCUAUGCUGUUUUG
1786	CR010965	GUGAGmUCUGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1787	CR010966	GUGAGUCUmGGAGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1788	CR010967	GUGAGUCmUGGAGAGCmUGCAUGUUUUAGAGCUAUGCUGUUUUG
1789	CR010968	GUGAGUCUGmGAmGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1790	CR010969	GUGmAGUCUGGmAGAmGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1791	CR010970	GUGAGUmCUGGAGAGCUmGCAmUGUUUUAGAGCUAUGCUGUUUUG
1792	CR010971	GUGAmGUCUmGGAGAGmCUGmCAUGUUUUAGAGCUAUGCUGUUUUG
1793	CR010972	GUGmAGUCUGGAGmAGCUmGCmAUGUUUUAGAGCUAUGCUGUUUUG
1794	CR011440	mG*mU*mG*A*GUCUGGAGAGCUGC*AUGUUUUAGAGCUAUGCUGUUUUG
1795	CR011441	mG*mU*mG*AGUCUGGAG*AGCU*GCAUGUUUUAGAGCUAUGCUGUUUUG
1796	CR011442	mG*mU*mG*AGUC*UGGAGAG*CUGCAUGUUUUAGAGCUAUGCUGUUUUG
1797	CR011443	mG*mU*mG*AGUCUGGA*GA*GCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1798	CR011444	mG*mU*mG*AGUCUG*GAGAGC*UGCAUGUUUUAGAGCUAUGCUGUUUUG
1799	CR011445	mG*mU*mG*AGUCU*GGAGAGCUGCA*UGUUUUAGAGCUAUGCUGUUUUG
1800	CR011446	mG*mU*mG*AG*UCUGGAGAGCUG*CAUGUUUUAGAGCUAUGCUGUUUUG
1801	CR011447	mG*mU*mG*AGUCUGG*AGAGCUGCAU*GUUUUAGAGCUAUGCUGUUUUG
1802	CR011448	mG*mU*mG*AGUC*UGGAGAGCUG*CAU*GUUUUAGAGCUAUGCUGUUUUG
1803	CR011449	mG*mU*mG*A*GUCUGGAG*AGC*UGCAUGUUUUAGAGCUAUGCUGUUUUG
1804	CR011450	mG*mU*mG*AGUCUGGAGAGCU*GC*A*UGUUUUAGAGCUAUGCUGUUUUG
1805	CR011451	mG*mU*mG*AGUCU*GGAGA*G*CUGCAUGUUUUAGAGCUAUGCUGUUUUG
1806	CR011452	mG*mU*mG*AGU*CUG*G*AGAGCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1807	CR011453	mG*mU*mG*AG*UCUGGA*GAGCU*GCAUGUUUUAGAGCUAUGCUGUUUUG
1808	CR011454	mG*mU*mG*AG*UCUGGAGAG*CUGCA*UGUUUUAGAGCUAUGCUGUUUUG
1809	CR011455	mG*mU*mG*AGUCUGGA*GAGCUGC*AU*GUUUUAGAGCUAUGCUGUUUUG
1810	CR011456	mG*mU*mG*AGUC*U*GG*AGAGCU*GCAUGUUUUAGAGCUAUGCUGUUUUG

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1812	CR011458	mG*mU*mG*AGUCUG*GA*GA*GCUGCAU*GUUUUAGAGCUAUGCUGUUUUG
1813	CR011459	mG*mU*mG*A*GU*CUGGAG*AGC*UGCAUGUUUUAGAGCUAUGCUGUUUUG
1814	CR011460	mG*mU*mG*AG*UCU*GGAG*A*GCUGCAUGUUUUAGAGCUAUGCUGUUUUG
1815	CR011461	mG*mU*mG*AGUCUGG*A*GAG*C*UGCAUGUUUUAGAGCUAUGCUGUUUUG
1816	CR011462	mG*mU*mG*A*GUC*UG*GAGAGCUGC*AUGUUUUAGAGCUAUGCUGUUUUG
1817	CR011463	mG*mU*mG*AG*UCUGGAGAGCU*G*CAU*GUUUUAGAGCUAUGCUGUUUUG
1818	CR011464	mG*mU*mG*AGUC*U*GG*AGAGCUG*C*AUGUUUUAGAGCUAUGCUGUUUUG
1819	CR011465	mG*mU*mG*AGUCUG*GAG*A*GC*UGCA*UGUUUUAGAGCUAUGCUGUUUUG
1820	CR011466	mG*mU*mG*A*GUCUGGA*GAG*CU*GCAU*GUUUUAGAGCUAUGCUGUUUUG
1821	CR011467	mG*mU*mG*AG*U*CUGGA*GAGC*UG*CAUGUUUUAGAGCUAUGCUGUUUUG
1822	CR011468	mG*mU*mG*A*GU*CUGG*AGA*GCU*GCAUGUUUUAGAGCUAUGCUGUUUUG
1823	CR011469	mG*mU*mG*AG*UCUGGAGAG*CUGC*A*U*GUUUUAGAGCUAUGCUGUUUUG
1824	CR011470	mG*mU*mG*AGUC*U*G*GAG*AGCU*GCAUGUUUUAGAGCUAUGCUGUUUUG
1825	CR011471	mG*mU*mG*AGU*C*UG*GAGA*GCUGCAU*GUUUUAGAGCUAUGCUGUUUUG
1826	CR011472	mG*mU*mG*AGU*C*U*GGAGA*GCUG*C*AUGUUUUAGAGCUAUGCUGUUUUG
1827	CR011473	mG*mU*mG*AG*UCUG*G*AG*AG*CU*GCAUGUUUUAGAGCUAUGCUGUUUUG
1828	CR011474	mG*mU*mG*A*GUCUGGA*GAG*C*UGCA*U*GUUUUAGAGCUAUGCUGUUUUG
1829	CR011475	mG*mU*mG*A*GU*CU*G*GAG*AGC*UGCAUGUUUUAGAGCUAUGCUGUUUUG
1830	CR011476	mG*mU*mG*AG*UCUGG*AGAGCUG*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1831	CR011477	mG*mU*mG*AGUC*UG*GA*GA*GCU*GCAU*GUUUUAGAGCUAUGCUGUUUUG
1832	CR011478	mG*mU*mG*AG*UC*UGGA*G*AGC*UGC*AUGUUUUAGAGCUAUGCUGUUUUG
1833	CR011479	mG*mU*mG*A*GUCU*GGAGA*GCU*G*CA*UGUUUUAGAGCUAUGCUGUUUUG
1834	CR011480	mG*mU*mG*AGUC*U*G*GAGA*G*CUGC*AU*GUUUUAGAGCUAUGCUGUUUUG
1835	CR011481	mG*mU*mG*A*GUCUGG*A*G*AGC*U*GCA*UGUUUUAGAGCUAUGCUGUUUUG
1836	CR011482	mG*mU*mG*AG*U*CU*GG*AGAG*CU*G*CAUGUUUUAGAGCUAUGCUGUUUUG
1837	CR011483	mG*mU*mG*A*G*U*CUGGAG*AGCUG*C*AU*GUUUUAGAGCUAUGCUGUUUUG
1838	CR011484	mG*mU*mG*AG*UC*UG*GA*GA*GC*UGCA*UGUUUUAGAGCUAUGCUGUUUUG
1839	CR011485	mG*mU*mG*AGUCUG*G*AG*AG*CUG*C*A*UGUUUUAGAGCUAUGCUGUUUUG

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1840	CR011486	mG*mU*mG*A*GU*CU*GGA*GA*GC*UGCAU*GUUUUAGAGCUAUGCUGUUUUG
1841	CR011487	mG*mU*mG*AGU*C*UGGAG*AGC*U*G*C*AUGUUUUAGAGCUAUGCUGUUUUG
1842	CR011488	mG*mU*mG*A*G*UC*UG*GA*GAG*CU*GCAUGUUUUAGAGCUAUGCUGUUUUG
1843	CR011489	mG*mU*mG*A*G*UCUG*G*A*GA*GCUGCA*U*GUUUUAGAGCUAUGCUGUUUUG
1844	CR011490	mG*mU*mG*AGU*C*U*GGAG*AG*CU*G*C*AUGUUUUAGAGCUAUGCUGUUUUG
1845	CR011491	mG*mU*mG*AGUC*UGG*AG*A*GC*U*GC*A*UGUUUUAGAGCUAUGCUGUUUUG
1846	CR011492	mG*mU*mG*A*G*U*CU*GGA*GAGC*UG*CAU*GUUUUAGAGCUAUGCUGUUUUG
1847	CR011493	mG*mU*mG*AGU*CU*G*G*AGA*G*CU*GCAU*GUUUUAGAGCUAUGCUGUUUUG
1848	CR011494	mG*mU*mG*AG*UC*UG*GA*GAG*CUG*C*A*UGUUUUAGAGCUAUGCUGUUUUG
1849	CR011495	mG*mU*mG*A*GU*C*UGGA*G*A*G*C*UGCAUGUUUUAGAGCUAUGCUGUUUUG
1850	CR011496	mG*mU*mG*A*GUCU*G*G*AG*AGC*UG*C*AUGUUUUAGAGCUAUGCUGUUUUG
1851	CR011497	mG*mU*mG*AG*UC*U*GGA*G*AGCU*GCA*U*GUUUUAGAGCUAUGCUGUUUUG
1852	CR011498	mG*mU*mG*AGU*CU*G*GAG*AG*C*U*G*CAU*GUUUUAGAGCUAUGCUGUUUUG
1853	CR011499	mG*mU*mG*A*G*UC*U*GG*A*GA*GCUGC*A*UGUUUUAGAGCUAUGCUGUUUUG
1854	CR011500	mG*mU*mG*AGU*C*UGGA*GA*G*C*U*GC*A*UGUUUUAGAGCUAUGCUGUUUUG
1855	CR011501	mG*mU*mG*A*G*UCUG*G*A*G*AGCUG*C*AU*GUUUUAGAGCUAUGCUGUUUUG
1856	CR011502	mG*mU*mG*AG*U*CU*G*G*AGAG*C*U*GC*AU*GUUUUAGAGCUAUGCUGUUUUG
1857	CR011503	mG*mU*mG*A*GUC*UG*GA*G*A*GC*UG*CA*U*GUUUUAGAGCUAUGCUGUUUUG
1858	CR011504	mG*mU*mG*A*G*UCUGG*A*G*A*G*CU*G*C*AUGUUUUAGAGCUAUGCUGUUUUG
1859	CR011505	mG*mU*mG*AGU*C*U*GG*AG*A*GCU*G*C*A*UGUUUUAGAGCUAUGCUGUUUUG
1860	CR011506	mG*mU*mG*A*GU*CU*G*G*A*G*AGCU*G*C*A*UGUUUUAGAGCUAUGCUGUUUUG
1861	CR011507	mG*mU*mG*AG*U*C*U*GGA*GA*G*C*UG*C*AU*GUUUUAGAGCUAUGCUGUUUUG
1862	CR011508	mG*mU*mG*A*G*UC*UG*G*AG*A*G*C*UGCA*U*GUUUUAGAGCUAUGCUGUUUUG
1863	CR011509	mG*mU*mG*AGU*CU*G*GAG*A*G*C*U*G*CA*U*GUUUUAGAGCUAUGCUGUUUUG
1864	CR011510	mG*mU*mG*AGUC*U*G*GA*G*A*GC*U*G*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1865	CR011511	mG*mU*mG*A*G*U*CUGG*AG*A*G*C*UG*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1866	CR011512	mG*mU*mG*A*G*U*C*U*G*G*A*GAG*C*U*GCA*UGUUUUAGAGCUAUGCUGUUUUG
1867	CR011513	mG*mU*mG*A*G*U*C*U*GGA*G*A*G*CU*G*CAU*GUUUUAGAGCUAUGCUGUUUUG
1868	CR011514	mG*mU*mG*A*G*U*CU*GGA*G*AG*C*U*G*C*A*U*GUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
1869	CR011515	mG*mU*mG*AG*U*C*U*G*G*A*G*A*G*C*U*GCAU*GUUUUAGAGCUAUGCUGUUUUG
1870	CR011516	mG*mU*mG*A*G*U*C*U*G*G*AG*A*GC*UG*C*A*UGUUUUAGAGCUAUGCUGUUUUG
1871	CR011517	mG*mU*mG*A*GU*C*UG*G*A*GA*G*CU*G*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1872	CR011518	mG*mU*mG*A*G*UC*U*GG*A*GA*G*C*U*G*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1873	CR011519	mG*mU*mG*A*GU*CUG*G*A*G*A*G*C*U*G*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1874	CR011520	mG*mU*mG*AG*U*C*U*G*G*AG*A*G*C*UG*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1875	CR011521	mG*mU*mG*A*G*U*C*U*G*GA*G*AG*C*U*GC*A*U*GUUUUAGAGCUAUGCUGUUUUG
1876	CR011522	mG*mU*mG*A*G*U*C*UG*G*A*G*A*G*C*U*G*CA*U*GUUUUAGAGCUAUGCUGUUUUG
1877	CR011523	mG*mU*mG*AG*U*C*U*G*G*A*G*A*G*C*U*G*C*AU*GUUUUAGAGCUAUGCUGUUUUG
1878	CR011524	mG*mU*mG*A*GU*C*U*G*G*A*G*A*GC*U*G*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1879	CR011525	mG*mU*mG*A*G*U*C*U*G*GA*GA*G*C*U*G*C*A*U*GUUUUAGAGCUAUGCUGUUUUG
1880	CR011526	GUGAG*UCUGGAGAGCUG*CAUGUUUUAGAGCUAUGCUGUUUUG
1881	CR011527	GUGAGUCU*GGAGA*G*CUGCAUGUUUUAGAGCUAUGCUGUUUUG
1882	CR011528	GUGA*GUC*UG*GAGAGCUGC*AUGUUUUAGAGCUAUGCUGUUUUG
1883	CR011529	GUGA*GUCUGGA*GAG*CU*GCAU*GUUUUAGAGCUAUGCUGUUUUG
1884	CR011530	GUGA*GU*CU*G*GAG*AGC*UGCAUGUUUUAGAGCUAUGCUGUUUUG
1885	CR011531	GUGA*GUCUGG*A*G*AGC*U*GCA*UGUUUUAGAGCUAUGCUGUUUUG
1886	CR011532	GUGAG*UC*UG*GA*GAG*CUG*C*A*UGUUUUAGAGCUAUGCUGUUUUG
1887	CR011533	GUGAGU*C*UGGA*GA*G*C*U*GC*A*UGUUUUAGAGCUAUGCUGUUUUG
1888	CR010225	mA*mA*mA*UfAGACACCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
1889	CR010226	mA*mA*mA*UAGACACCAAAUCUUfACGUUUUAGAGCUAUGCUGUUUUG
1890	CR010227	mA*mA*mA*UAGACACCAAAUfCUUACGUUUUAGAGCUAUGCUGUUUUG
1891	CR010228	mA*mA*mA*UAGfACACCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
1892	CR010229	mA*mA*mA*UAGACACCAAAUCUUAfCGUUUUAGAGCUAUGCUGUUUUG
1893	CR010230	mA*mA*mA*UAGACACCAAAUCfUUACGUUUUAGAGCUAUGCUGUUUUG
1894	CR010231	mA*mA*mA*UAGACACCAfAUCUUACGUUUUAGAGCUAUGCUGUUUUG
1895	CR010232	mA*mA*mA*UAGACfACCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
1896	CR010233	mA*mA*mA*UAGACACCAAfAUCUUACGUUUUAGAGCUAUGCUGUUUUG
1897	CR010234	mA*mA*mA*UAGACACfCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
1898	CR010235	mA*mA*mA*fUAGACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1899	CR010236	mA*mA*mA*UAGACACCAAAfUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1900	CR010237	mA*mA*mA*UAGACACCfAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1901	CR010238	mA*mA*mA*UAGACAfCCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1902	CR010239	mA*mA*mA*UAfGACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1903	CR010240	mA*mA*mA*UAGAfCACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1904	CR010241	mA*mA*mA*UAGACACCAAAUCUfUACGUUUUUAGAGCUAUGCUGUUUUG
1905	CR010242	mA*mA*mA*fUAGACACCAAAUCUfUACGUUUUUAGAGCUAUGCUGUUUUG
1906	CR010243	mA*mA*mA*UAGACACCfAAAUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1907	CR010244	mA*mA*mA*UAGfACACCAAfAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1908	CR010245	mA*mA*mA*UAGACACfCAfAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1909	CR010246	mA*mA*mA*UAGACfACCAAAfUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1910	CR010247	mA*mA*mA*UAGAfCACCAAAUCUUfACGUUUUUAGAGCUAUGCUGUUUUG
1911	CR010248	mA*mA*mA*UfAGACACCAAAUCfUUACGUUUUUAGAGCUAUGCUGUUUUG
1912	CR010249	mA*mA*mA*UAGACAfCCAAAUCUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1913	CR010250	mA*mA*mA*UAfGACACCfAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1914	CR010251	mA*mA*mA*UAGACACCAfAUCUUfACGUUUUUAGAGCUAUGCUGUUUUG
1915	CR010252	mA*mA*mA*UAGACfACfCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1916	CR010253	mA*mA*mA*UAGACACCAAAUCfUfUACGUUUUUAGAGCUAUGCUGUUUUG
1917	CR010254	mA*mA*mA*UAGfACACCAAAUCUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1918	CR010255	mA*mA*mA*UAfGACACCAAfAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1919	CR010256	mA*mA*mA*UfAGACACCAAAfUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1920	CR010257	mA*mA*mA*UAGAfCACCAAAUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1921	CR010258	mA*mA*mA*fUAGACAfCCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1922	CR010259	mA*mA*mA*fUAGACACCAAAfUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1923	CR010260	mA*mA*mA*UAGAfCACCAAfAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1924	CR010261	mA*mA*mA*UAGACfACCAAAUCUUfACGUUUUUAGAGCUAUGCUGUUUUG
1925	CR010262	mA*mA*mA*UAGACACCAAAUfCUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1926	CR010263	mA*mA*mA*UAGACACfCAAAUCUfUACGUUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
1927	CR010264	mA*mA*mA*UAGACACCAfAAUCfUUACGUUUUUAGAGCUAUGCUGUUUUG
1928	CR010265	mA*mA*mA*UAGACAfCCfAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1929	CR010266	mA*mA*mA*UfAGfACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1930	CR010267	mA*mA*mA*UAfGACACCAAAUCUUfACGUUUUUAGAGCUAUGCUGUUUUG
1931	CR010268	mA*mA*mA*UAGACfACCAAAUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1932	CR010269	mA*mA*mA*UAGAfCACCfAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1933	CR010270	mA*mA*mA*UAGACACCAAAUCUfUAfCGUUUUUAGAGCUAUGCUGUUUUG
1934	CR010271	mA*mA*mA*UAGACAfCCAAfAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1935	CR010272	mA*mA*mA*UAGACACCAfAAfUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1936	CR010273	mA*mA*mA*UfAfGACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1937	CR010274	mA*mA*mA*fUAGACACfCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1938	CR010275	mA*mA*mA*UAGfACACCAAAUCfUUACGUUUUUAGAGCUAUGCUGUUUUG
1939	CR010276	mA*mA*mA*UAGfACACCAAAUCfUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1940	CR010277	mA*mA*mA*fUAGACACCfAAAfUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1941	CR010278	mA*mA*mA*UAGACACCAAAUfCUfUfACGUUUUUAGAGCUAUGCUGUUUUG
1942	CR010279	mA*mA*mA*UAGAfCACCAfAfAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1943	CR010280	mA*mA*mA*UAfGACfAfCCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1944	CR010281	mA*mA*mA*UfAGACACfCAAAUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1945	CR010282	mA*mA*mA*UfAGACACCAAfAUCUUfACGUUUUUAGAGCUAUGCUGUUUUG
1946	CR010283	mA*mA*mA*UAGACACfCAAAUCUfUAfCGUUUUUAGAGCUAUGCUGUUUUG
1947	CR010284	mA*mA*mA*UAGACACCAfAAfUCfUUACGUUUUUAGAGCUAUGCUGUUUUG
1948	CR010285	mA*mA*mA*UAGfACfACCfAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1949	CR010286	mA*mA*mA*fUAGAfCAfCCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1950	CR010287	mA*mA*mA*UAfGACACCAfAAUCfUUACGUUUUUAGAGCUAUGCUGUUUUG
1951	CR010288	mA*mA*mA*UAGACfAfCCAAAUCUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1952	CR010289	mA*mA*mA*UAGAfCACCfAAAUCUfUACGUUUUUAGAGCUAUGCUGUUUUG
1953	CR010290	mA*mA*mA*UAfGACACCAAAfUCUUfACGUUUUUAGAGCUAUGCUGUUUUG
1954	CR010291	mA*mA*mA*UfAGfACACCAAAUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1955	CR010292	mA*mA*mA*fUAGACACfCAAfAUCUUACGUUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
1956	CR010293	mA*mA*mA*UAGfAfCAfCCAAAUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1957	CR010294	mA*mA*mA*UAGACACCAAfAUCfUfUfACGUUUUUAGAGCUAUGCUGUUUUG
1958	CR010295	mA*mA*mA*UAGACfACfCAfAAUCUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1959	CR010296	mA*mA*mA*fUAfGACACCfAAAfUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1960	CR010297	mA*mA*mA*UfAGAfCACCfAfAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1961	CR010298	mA*mA*mA*UAGACAfCfCAAfAfUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1962	CR010299	mA*mA*mA*fUAGfACfACCAAAUCUfUACGUUUUUAGAGCUAUGCUGUUUUG
1963	CR010300	mA*mA*mA*UfAGACACCAAAUfCfUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1964	CR010301	mA*mA*mA*UAfGACAfCCAAAUCUUfAfCGUUUUUAGAGCUAUGCUGUUUUG
1965	CR010302	mA*mA*mA*UAGfACACCAfAAfUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1966	CR010303	mA*mA*mA*UAGAfCfACCfAAAUCUUfAfCGUUUUUAGAGCUAUGCUGUUUUG
1967	CR010304	mA*mA*mA*UfAfGACACCAAfAUCUfUACGUUUUUAGAGCUAUGCUGUUUUG
1968	CR010305	mA*mA*mA*fUAGACACfCfAAAUCfUUACGUUUUUAGAGCUAUGCUGUUUUG
1969	CR010306	mA*mA*mA*UfAGACfACCAAAfUCUfUACGUUUUUAGAGCUAUGCUGUUUUG
1970	CR010307	mA*mA*mA*UAGAfCACfCAAfAUCUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1971	CR010308	mA*mA*mA*fUAGACACCAfAAUCfUUfACGUUUUUAGAGCUAUGCUGUUUUG
1972	CR010309	mA*mA*mA*UAfGfACAfCCAAAUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1973	CR010310	AAAUAGACACCAAAUCfUUACGUUUUUAGAGCUAUGCUGUUUUG
1974	CR010311	AAAUAfGACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1975	CR010312	AAAUAGACfACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1976	CR010313	AAAUAGAfCACCAAAUfCUUACGUUUUUAGAGCUAUGCUGUUUUG
1977	CR010314	AAAUAGACAfCCfAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1978	CR010315	AAAfUAGACACfCAAfAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1979	CR010316	AAAUAGfACACCAAAUCfUUAfCGUUUUUAGAGCUAUGCUGUUUUG
1980	CR010317	AAAUfAGACfACCAAAfUCUfUACGUUUUUAGAGCUAUGCUGUUUUG
1981	CR010318	AAAfUAGACACCAfAAUCfUUfACGUUUUUAGAGCUAUGCUGUUUUG
1982	CR010319	mA*mA*mA*UAGACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1983	CR010785	mA*mA*mA*UmAGACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1984	CR010786	mA*mA*mA*UAGACACCAAAUCUUmACGUUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
1985	CR010787	mA*mA*mA*UAGACACCAAAUmCUUACGUUUUUAGAGCUAUGCUGUUUUG
1986	CR010788	mA*mA*mA*UAGmACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1987	CR010789	mA*mA*mA*UAGACACCAAAUCUUAmCGUUUUUAGAGCUAUGCUGUUUUG
1988	CR010790	mA*mA*mA*UAGACACCAAAUCmUUACGUUUUUAGAGCUAUGCUGUUUUG
1989	CR010791	mA*mA*mA*UAGACACCAmAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1990	CR010792	mA*mA*mA*UAGACmACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1991	CR010793	mA*mA*mA*UAGACACCAAmAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1992	CR010794	mA*mA*mA*UAGACACmCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1993	CR010795	mA*mA*mA*mUAGACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1994	CR010796	mA*mA*mA*UAGACACCAAAmUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1995	CR010797	mA*mA*mA*UAGACACCmAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1996	CR010798	mA*mA*mA*UAGACAmCCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1997	CR010799	mA*mA*mA*UAmGACACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1998	CR010800	mA*mA*mA*UAGAmCACCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
1999	CR010801	mA*mA*mA*UAGACACCAAAUCUmUACGUUUUUAGAGCUAUGCUGUUUUG
2000	CR010802	mA*mA*mA*mUAGACACCAAAUCUmUACGUUUUUAGAGCUAUGCUGUUUUG
2001	CR010803	mA*mA*mA*UAGACACCmAAAUmCUUACGUUUUUAGAGCUAUGCUGUUUUG
2002	CR010804	mA*mA*mA*UAGmACACCAAmAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
2003	CR010805	mA*mA*mA*UAGACACmCAmAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
2004	CR010806	mA*mA*mA*UAGACmACCAAAmUCUUACGUUUUUAGAGCUAUGCUGUUUUG
2005	CR010807	mA*mA*mA*UAGAmCACCAAAUCUUmACGUUUUUAGAGCUAUGCUGUUUUG
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2007	CR010809	mA*mA*mA*UAGACAmCCAAAUCUUAmCGUUUUUAGAGCUAUGCUGUUUUG
2008	CR010810	mA*mA*mA*UAmGACACCmAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
2009	CR010811	mA*mA*mA*UAGACACCAmAAUCUUmACGUUUUUAGAGCUAUGCUGUUUUG
2010	CR010812	mA*mA*mA*UAGACmACmCAAAUCUUACGUUUUUAGAGCUAUGCUGUUUUG
2011	CR010813	mA*mA*mA*UAGACACCAAAUCmUmUACGUUUUUAGAGCUAUGCUGUUUUG
2012	CR010814	mA*mA*mA*UAGmACACCAAAUCUUAmCGUUUUUAGAGCUAUGCUGUUUUG
2013	CR010815	mA*mA*mA*UAmGACACCAAmAUCUUACGUUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2014	CR010816	mA*mA*mA*UmAGACACCAAAmUCUUACGUUUUAGAGCUAUGCUGUUUUG
2015	CR010817	mA*mA*mA*UAGAmCACCAAAUmCUUACGUUUUAGAGCUAUGCUGUUUUG
2016	CR010818	mA*mA*mA*mUAGACAmCCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2017	CR010819	mA*mA*mA*mUAGACACCAAAmUCUUACGUUUUAGAGCUAUGCUGUUUUG
2018	CR010820	mA*mA*mA*UAGAmCACCAAmAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2019	CR010821	mA*mA*mA*UAGACmACCAAAUCUUmACGUUUUAGAGCUAUGCUGUUUUG
2020	CR010822	mA*mA*mA*UAGACACCAAAUmCUUAmCGUUUUAGAGCUAUGCUGUUUUG
2021	CR010823	mA*mA*mA*UAGACACmCAAAUCUmUACGUUUUAGAGCUAUGCUGUUUUG
2022	CR010824	mA*mA*mA*UAGACACCAmAAUCmUUACGUUUUAGAGCUAUGCUGUUUUG
2023	CR010825	mA*mA*mA*UAGACAmCCmAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2024	CR010826	mA*mA*mA*UmAGmACACCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2025	CR010827	mA*mA*mA*UAmGACACCAAAUCUUmACGUUUUAGAGCUAUGCUGUUUUG
2026	CR010828	mA*mA*mA*UAGACmACCAAAUmCUUACGUUUUAGAGCUAUGCUGUUUUG
2027	CR010829	mA*mA*mA*UAGAmCACCmAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2028	CR010830	mA*mA*mA*UAGACACCAAAUCUmUAmCGUUUUAGAGCUAUGCUGUUUUG
2029	CR010831	mA*mA*mA*UAGACAmCCAAmAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2030	CR010832	mA*mA*mA*UAGACACCAmAAmUCUUACGUUUUAGAGCUAUGCUGUUUUG
2031	CR010833	mA*mA*mA*UmAmGACACCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2032	CR010834	mA*mA*mA*mUAGACACmCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
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2036	CR010838	mA*mA*mA*UAGACACCAAAUmCUmACGUUUUAGAGCUAUGCUGUUUUG
2037	CR010839	mA*mA*mA*UAGAmCACCAmAmAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2038	CR010840	mA*mA*mA*UAmGACmAmCCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2039	CR010841	mA*mA*mA*UmAGACACmCAAAUmCUUACGUUUUAGAGCUAUGCUGUUUUG
2040	CR010842	mA*mA*mA*UmAGACACCAAmAUCUUmACGUUUUAGAGCUAUGCUGUUUUG
2041	CR010843	mA*mA*mA*UAGACACmCAAAUCUmUAmCGUUUUAGAGCUAUGCUGUUUUG
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SEQ ID NO	Name	Sequence
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2045	CR010847	mA*mA*mA*UAmGACACCAmAAUCmUUACGUUUUAGAGCUAUGCUGUUUUG
2046	CR010848	mA*mA*mA*UAGACmAmCCAAAUCUUAmCGUUUUAGAGCUAUGCUGUUUUG
2047	CR010849	mA*mA*mA*UAGAmCACCmAAAUCUmUACGUUUUAGAGCUAUGCUGUUUUG
2048	CR010850	mA*mA*mA*UAmGACACCAAAmUCUUmACGUUUUAGAGCUAUGCUGUUUUG
2049	CR010851	mA*mA*mA*UmAGmACACCAAAUmCUUACGUUUUAGAGCUAUGCUGUUUUG
2050	CR010852	mA*mA*mA*mUAGACACmCAAmAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2051	CR010853	mA*mA*mA*UAGmAmCAmCCAAAUmCUUACGUUUUAGAGCUAUGCUGUUUUG
2052	CR010854	mA*mA*mA*UAGACACCAAmAUCmUmUmACGUUUUAGAGCUAUGCUGUUUUG
2053	CR010855	mA*mA*mA*UAGACmACmCAmAAUCUUAmCGUUUUAGAGCUAUGCUGUUUUG
2054	CR010856	mA*mA*mA*mUAmGACACCmAAAmUCUUACGUUUUAGAGCUAUGCUGUUUUG
2055	CR010857	mA*mA*mA*UmAGAmCACCmAmAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2056	CR010858	mA*mA*mA*UAGACAmCmCAAmAmUCUUACGUUUUAGAGCUAUGCUGUUUUG
2057	CR010859	mA*mA*mA*mUAGmACmACCAAAUCUmUACGUUUUAGAGCUAUGCUGUUUUG
2058	CR010860	mA*mA*mA*UmAGACACCAAAUmCmUUAmCGUUUUAGAGCUAUGCUGUUUUG
2059	CR010861	mA*mA*mA*UAmGACAmCCAAAUCUUmAmCGUUUUAGAGCUAUGCUGUUUUG
2060	CR010862	mA*mA*mA*UAGmACACCAmAAmUmCUUACGUUUUAGAGCUAUGCUGUUUUG
2061	CR010863	mA*mA*mA*UAGAmCmACCmAAAUCUUmACGUUUUAGAGCUAUGCUGUUUUG
2062	CR010864	mA*mA*mA*UmAmGACACCAAmAUCUmUACGUUUUAGAGCUAUGCUGUUUUG
2063	CR010865	mA*mA*mA*mUAGACACmCmCmAAAUCmUUACGUUUUAGAGCUAUGCUGUUUUG
2064	CR010866	mA*mA*mA*UmAGACmACCAAAmUCUmUACGUUUUAGAGCUAUGCUGUUUUG
2065	CR010867	mA*mA*mA*UAGAmCACmCAAmAUCUUAmCGUUUUAGAGCUAUGCUGUUUUG
2066	CR010868	mA*mA*mA*mUAGACACCAmAAUCmUUmACGUUUUAGAGCUAUGCUGUUUUG
2067	CR010869	mA*mA*mA*UAmGmACAmCCAAAUmCUUACGUUUUAGAGCUAUGCUGUUUUG
2068	CR010870	AAAUAGACACCAAAUCmUUACGUUUUAGAGCUAUGCUGUUUUG
2069	CR010871	AAAUAmGACACCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2070	CR010872	AAAUAGACmACCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2071	CR010873	AAAUAGAmCACCAAAUmCUUACGUUUUAGAGCUAUGCUGUUUUG

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2072	CR010874	AAAUAGACAmCCmAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2073	CR010875	AAAmUAGACACmCAAmAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2074	CR010876	AAAUAGmACACCAAAUCmUUAmCGUUUUAGAGCUAUGCUGUUUUG
2075	CR010877	AAAUmAGACmACCAAAmUCUmUACGUUUUAGAGCUAUGCUGUUUUG
2076	CR010878	AAAmUAGACACCAmAAUCmUUmACGUUUUAGAGCUAUGCUGUUUUG
2077	CR011346	mA*mA*mA*U*AGACACCAAAUCUU*ACGUUUUAGAGCUAUGCUGUUUUG
2078	CR011347	mA*mA*mA*UAGACACCA*AAUC*UUACGUUUUAGAGCUAUGCUGUUUUG
2079	CR011348	mA*mA*mA*UAGA*CACCAAA*UCUUACGUUUUAGAGCUAUGCUGUUUUG
2080	CR011349	mA*mA*mA*UAGACACC*AA*AUCUUACGUUUUAGAGCUAUGCUGUUUUG
2081	CR011350	mA*mA*mA*UAGACA*CCAAAU*CUUACGUUUUAGAGCUAUGCUGUUUUG
2082	CR011351	mA*mA*mA*UAGAC*ACCAAAUCUUA*CGUUUUAGAGCUAUGCUGUUUUG
2083	CR011352	mA*mA*mA*UA*GACACCAAAUCU*UACGUUUUAGAGCUAUGCUGUUUUG
2084	CR011353	mA*mA*mA*UAGACAC*CAAAUCUUAC*GUUUUAGAGCUAUGCUGUUUUG
2085	CR011354	mA*mA*mA*UAGA*CACCAAAUCU*UAC*GUUUUAGAGCUAUGCUGUUUUG
2086	CR011355	mA*mA*mA*U*AGACACCA*AAU*CUUACGUUUUAGAGCUAUGCUGUUUUG
2087	CR011356	mA*mA*mA*UAGACACCAAAUC*UU*A*CGUUUUAGAGCUAUGCUGUUUUG
2088	CR011357	mA*mA*mA*UAGAC*ACCAA*A*UCUUACGUUUUAGAGCUAUGCUGUUUUG
2089	CR011358	mA*mA*mA*UAG*ACA*C*CAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
2090	CR011359	mA*mA*mA*UA*GACACC*AAAUC*UUACGUUUUAGAGCUAUGCUGUUUUG
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2092	CR011361	mA*mA*mA*UAGACACC*AAAUCUU*AC*GUUUUAGAGCUAUGCUGUUUUG
2093	CR011362	mA*mA*mA*UAGA*C*AC*CAAAUC*UUACGUUUUAGAGCUAUGCUGUUUUG
2094	CR011363	mA*mA*mA*UAGACACCAAA*UCU*U*A*CGUUUUAGAGCUAUGCUGUUUUG
2095	CR011364	mA*mA*mA*UAGACA*CC*AA*AUCUUAC*GUUUUAGAGCUAUGCUGUUUUG
2096	CR011365	mA*mA*mA*U*AG*ACACCA*AAU*CUUACGUUUUAGAGCUAUGCUGUUUUG
2097	CR011366	mA*mA*mA*UA*GAC*ACCA*A*AUCUUACGUUUUAGAGCUAUGCUGUUUUG
2098	CR011367	mA*mA*mA*UAGACAC*C*AAA*U*CUUACGUUUUAGAGCUAUGCUGUUUUG
2099	CR011368	mA*mA*mA*U*AGA*CA*CCAAAUCUU*ACGUUUUAGAGCUAUGCUGUUUUG
2100	CR011369	mA*mA*mA*UA*GACACCAAAUC*U*UAC*GUUUUAGAGCUAUGCUGUUUUG

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2101	CR011370	mA*mA*mA*UAGA*C*AC*CAAAUCU*U*ACGUUUUAGAGCUAUGCUGUUUUG
2102	CR011371	mA*mA*mA*UAGACA*CCA*A*AU*CUUA*CGUUUUAGAGCUAUGCUGUUUUG
2103	CR011372	mA*mA*mA*U*AGACACC*AAA*UC*UUAC*GUUUUAGAGCUAUGCUGUUUUG
2104	CR011373	mA*mA*mA*UA*G*ACACC*AAAU*CU*UACGUUUUAGAGCUAUGCUGUUUUG
2105	CR011374	mA*mA*mA*U*AG*ACAC*CAA*AUC*UUACGUUUUAGAGCUAUGCUGUUUUG
2106	CR011375	mA*mA*mA*UA*GACACCAAA*UCUU*A*C*GUUUUAGAGCUAUGCUGUUUUG
2107	CR011376	mA*mA*mA*UAGA*C*A*CCA*AAUC*UUACGUUUUAGAGCUAUGCUGUUUUG
2108	CR011377	mA*mA*mA*UAG*A*CA*CCAA*AUCUUAC*GUUUUAGAGCUAUGCUGUUUUG
2109	CR011378	mA*mA*mA*UAG*A*C*ACCAA*AUCU*U*ACGUUUUAGAGCUAUGCUGUUUUG
2110	CR011379	mA*mA*mA*UA*GACA*C*CA*AA*UC*UUACGUUUUAGAGCUAUGCUGUUUUG
2111	CR011380	mA*mA*mA*U*AGACACC*AAA*U*CUUA*C*GUUUUAGAGCUAUGCUGUUUUG
2112	CR011381	mA*mA*mA*U*AG*AC*A*CCA*AAU*CUUACGUUUUAGAGCUAUGCUGUUUUG
2113	CR011382	mA*mA*mA*UA*GACAC*CAAAUCU*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2114	CR011383	mA*mA*mA*UAGA*CA*CC*AA*AUC*UUAC*GUUUUAGAGCUAUGCUGUUUUG
2115	CR011384	mA*mA*mA*UA*GA*CACC*A*AAU*CUU*ACGUUUUAGAGCUAUGCUGUUUUG
2116	CR011385	mA*mA*mA*U*AGAC*ACCAA*AUC*U*UA*CGUUUUAGAGCUAUGCUGUUUUG
2117	CR011386	mA*mA*mA*UAGA*C*A*CCAA*A*UCUU*AC*GUUUUAGAGCUAUGCUGUUUUG
2118	CR011387	mA*mA*mA*U*AGACAC*C*A*AAU*C*UUA*CGUUUUAGAGCUAUGCUGUUUUG
2119	CR011388	mA*mA*mA*UA*G*AC*AC*CAAA*UC*U*UACGUUUUAGAGCUAUGCUGUUUUG
2120	CR011389	mA*mA*mA*U*A*G*ACACCA*AAUCU*U*AC*GUUUUAGAGCUAUGCUGUUUUG
2121	CR011390	mA*mA*mA*UA*GA*CA*CC*AA*AU*CUUA*CGUUUUAGAGCUAUGCUGUUUUG
2122	CR011391	mA*mA*mA*UAGACA*C*CA*AA*UCU*U*A*CGUUUUAGAGCUAUGCUGUUUUG
2123	CR011392	mA*mA*mA*U*AG*AC*ACC*AA*AU*CUUAC*GUUUUAGAGCUAUGCUGUUUUG
2124	CR011393	mA*mA*mA*UAG*A*CACCA*AAU*C*U*U*ACGUUUUAGAGCUAUGCUGUUUUG
2125	CR011394	mA*mA*mA*U*A*GA*CA*CC*AAA*UC*UUACGUUUUAGAGCUAUGCUGUUUUG
2126	CR011395	mA*mA*mA*U*A*GACA*C*C*AA*AUCUUA*C*GUUUUAGAGCUAUGCUGUUUUG
2127	CR011396	mA*mA*mA*UAG*A*C*ACCA*AA*UC*U*U*ACGUUUUAGAGCUAUGCUGUUUUG
2128	CR011397	mA*mA*mA*UAGA*CAC*CA*A*AU*C*UU*A*CGUUUUAGAGCUAUGCUGUUUUG
2129	CR011398	mA*mA*mA*U*A*G*AC*ACC*AAAU*CU*UAC*GUUUUAGAGCUAUGCUGUUUUG

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2130	CR011399	mA*mA*mA*UAG*AC*A*C*CAA*A*UC*UUAC*GUUUUAGAGCUAUGCUGUUUUG
2131	CR011400	mA*mA*mA*UA*GA*CA*CC*AAA*UCU*U*A*CGUUUUAGAGCUAUGCUGUUUUG
2132	CR011401	mA*mA*mA*U*AG*A*CACC*A*A*A*U*CUUACGUUUUAGAGCUAUGCUGUUUUG
2133	CR011402	mA*mA*mA*U*AGAC*A*C*CA*AAU*CU*U*ACGUUUUAGAGCUAUGCUGUUUUG
2134	CR011403	mA*mA*mA*UA*GA*C*ACC*A*AAUC*UUA*C*GUUUUAGAGCUAUGCUGUUUUG
2135	CR011404	mA*mA*mA*UAG*AC*A*CCA*AA*U*C*U*UAC*GUUUUAGAGCUAUGCUGUUUUG
2136	CR011405	mA*mA*mA*U*A*GA*C*AC*C*AA*AUCUU*A*CGUUUUAGAGCUAUGCUGUUUUG
2137	CR011406	mA*mA*mA*UAG*A*CACC*AA*A*U*C*UU*A*CGUUUUAGAGCUAUGCUGUUUUG
2138	CR011407	mA*mA*mA*U*A*GACA*C*C*A*AAUCU*U*AC*GUUUUAGAGCUAUGCUGUUUUG
2139	CR011408	mA*mA*mA*UA*G*AC*A*C*CAAA*U*C*UU*AC*GUUUUAGAGCUAUGCUGUUUUG
2140	CR011409	mA*mA*mA*U*AGA*CA*CC*A*A*AU*CU*UA*C*GUUUUAGAGCUAUGCUGUUUUG
2141	CR011410	mA*mA*mA*U*A*GACAC*C*A*A*A*UC*U*U*ACGUUUUAGAGCUAUGCUGUUUUG
2142	CR011411	mA*mA*mA*UAG*A*C*AC*CA*A*AUC*U*U*A*CGUUUUAGAGCUAUGCUGUUUUG
2143	CR011412	mA*mA*mA*U*AG*AC*A*C*C*A*AAUC*U*U*A*CGUUUUAGAGCUAUGCUGUUUUG
2144	CR011413	mA*mA*mA*UA*G*A*C*ACC*AA*A*U*CU*U*AC*GUUUUAGAGCUAUGCUGUUUUG
2145	CR011414	mA*mA*mA*U*A*GA*CA*C*CA*A*A*U*CUUA*C*GUUUUAGAGCUAUGCUGUUUUG
2146	CR011415	mA*mA*mA*UAG*AC*A*CCA*A*A*U*C*U*UA*C*GUUUUAGAGCUAUGCUGUUUUG
2147	CR011416	mA*mA*mA*UAGA*C*A*CC*A*A*AU*C*U*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2148	CR011417	mA*mA*mA*U*A*G*ACAC*CA*A*A*U*CU*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2149	CR011418	mA*mA*mA*U*A*G*A*C*A*C*C*AAA*U*C*UUA*CGUUUUAGAGCUAUGCUGUUUUG
2150	CR011419	mA*mA*mA*U*A*G*A*C*ACC*A*A*A*UC*U*UAC*GUUUUAGAGCUAUGCUGUUUUG
2151	CR011420	mA*mA*mA*U*A*G*AC*ACC*A*AA*U*C*U*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2152	CR011421	mA*mA*mA*UA*G*A*C*A*C*C*A*A*A*U*C*UUAC*GUUUUAGAGCUAUGCUGUUUUG
2153	CR011422	mA*mA*mA*U*A*G*A*C*A*C*CA*A*AU*CU*U*A*CGUUUUAGAGCUAUGCUGUUUUG
2154	CR011423	mA*mA*mA*U*AG*A*CA*C*C*AA*A*UC*U*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2155	CR011424	mA*mA*mA*U*A*GA*C*AC*C*AA*A*U*C*U*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2156	CR011425	mA*mA*mA*U*AG*ACA*C*C*A*A*A*U*C*U*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2157	CR011426	mA*mA*mA*UA*G*A*C*A*C*CA*A*A*U*CU*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2158	CR011427	mA*mA*mA*U*A*G*A*C*A*CC*A*AA*U*C*UU*A*C*GUUUUAGAGCUAUGCUGUUUUG

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2159	CR011428	mA*mA*mA*U*A*G*A*CA*C*C*A*A*A*U*C*U*UA*C*GUUUUAGAGCUAUGCUGUUUUG
2160	CR011429	mA*mA*mA*UA*G*A*C*A*C*C*A*A*A*U*C*U*U*AC*GUUUUAGAGCUAUGCUGUUUUG
2161	CR011430	mA*mA*mA*U*AG*A*C*A*C*C*A*A*A*AU*C*U*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2162	CR011431	mA*mA*mA*U*A*G*A*C*A*CC*AA*A*U*C*U*U*A*C*GUUUUAGAGCUAUGCUGUUUUG
2163	CR011432	AAAUA*GACACCAAAUCU*UACGUUUUAGAGCUAUGCUGUUUUG
2164	CR011433	AAAUAGAC*ACCAA*A*UCUUACGUUUUAGAGCUAUGCUGUUUUG
2165	CR011434	AAAU*AGA*CA*CCAAAUCUU*ACGUUUUAGAGCUAUGCUGUUUUG
2166	CR011435	AAAU*AGACACC*AAA*UC*UUAC*GUUUUAGAGCUAUGCUGUUUUG
2167	CR011436	AAAU*AG*AC*A*CCA*AAU*CUUACGUUUUAGAGCUAUGCUGUUUUG
2168	CR011437	AAAU*AGACAC*C*A*AAU*C*UUA*CGUUUUAGAGCUAUGCUGUUUUG
2169	CR011438	AAAUA*GA*CA*CC*AAA*UCU*U*A*CGUUUUAGAGCUAUGCUGUUUUG
2170	CR011439	AAAUAG*A*CACC*AA*A*U*C*UU*A*CGUUUUAGAGCUAUGCUGUUUUG
2171	CR010130	mA*mA*mA*GfUUCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2172	CR010131	mA*mA*mA*GUUCUAGAUGCUGUCfCGGUUUUAGAGCUAUGCUGUUUUG
2173	CR010132	mA*mA*mA*GUUCUAGAUGCUfGUCCGGUUUUAGAGCUAUGCUGUUUUG
2174	CR010133	mA*mA*mA*GUUfCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2175	CR010134	mA*mA*mA*GUUCUAGAUGCUGUCCfGGUUUUAGAGCUAUGCUGUUUUG
2176	CR010135	mA*mA*mA*GUUCUAGAUGCUGfUCCGGUUUUAGAGCUAUGCUGUUUUG
2177	CR010136	mA*mA*mA*GUUCUAGAUfGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2178	CR010137	mA*mA*mA*GUUCUfAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2179	CR010138	mA*mA*mA*GUUCUAGAUGfCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2180	CR010139	mA*mA*mA*GUUCUAGfAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2181	CR010140	mA*mA*mA*fGUUCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2182	CR010141	mA*mA*mA*GUUCUAGAUGCfUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2183	CR010142	mA*mA*mA*GUUCUAGAfUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2184	CR010143	mA*mA*mA*GUUCUAfGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2185	CR010144	mA*mA*mA*GUfUCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2186	CR010145	mA*mA*mA*GUUCfUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2187	CR010146	mA*mA*mA*GUUCUAGAUGCUGUfCCGGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2188	CR010147	mA*mA*mA*fGUUCUAGAUGCUGUfCCGGUUUUAGAGCUAUGCUGUUUUG
2189	CR010148	mA*mA*mA*GUUCUAGAfUGCUfGUCCGGUUUUAGAGCUAUGCUGUUUUG
2190	CR010149	mA*mA*mA*GUUfCUAGAUGfCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2191	CR010150	mA*mA*mA*GUUCUAGfAUfGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2192	CR010151	mA*mA*mA*GUUCUfAGAUGCfUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2193	CR010152	mA*mA*mA*GUUCfUAGAUGCUGUCfCGGUUUUAGAGCUAUGCUGUUUUG
2194	CR010153	mA*mA*mA*GfUUCUAGAUGCUGfUCCGGUUUUAGAGCUAUGCUGUUUUG
2195	CR010154	mA*mA*mA*GUUCUAfGAUGCUGUCCfGGUUUUAGAGCUAUGCUGUUUUG
2196	CR010155	mA*mA*mA*GUfUCUAGAfUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2197	CR010156	mA*mA*mA*GUUCUAGAUfGCUGUCfCGGUUUUAGAGCUAUGCUGUUUUG
2198	CR010157	mA*mA*mA*GUUCUfAGfAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2199	CR010159	mA*mA*mA*GUUfCUAGAUGCUGUCCfGGUUUUAGAGCUAUGCUGUUUUG
2200	CR010160	mA*mA*mA*GUfUCUAGAUGfCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2201	CR010161	mA*mA*mA*GfUUCUAGAUGCfUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2202	CR010162	mA*mA*mA*GUUCfUAGAUGCUfGUCCGGUUUUAGAGCUAUGCUGUUUUG
2203	CR010163	mA*mA*mA*fGUUCUAfGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2204	CR010164	mA*mA*mA*fGUUCUAGAUGCfUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2205	CR010165	mA*mA*mA*GUUCfUAGAUGfCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2206	CR010166	mA*mA*mA*GUUCUfAGAUGCUGUCfCGGUUUUAGAGCUAUGCUGUUUUG
2207	CR010167	mA*mA*mA*GUUCUAGAUGCUfGUCCfGGUUUUAGAGCUAUGCUGUUUUG
2208	CR010168	mA*mA*mA*GUUCUAGfAUGCUGUfCCGGUUUUAGAGCUAUGCUGUUUUG
2209	CR010169	mA*mA*mA*GUUCUAGAUfGCUGfUCCGGUUUUAGAGCUAUGCUGUUUUG
2210	CR010170	mA*mA*mA*GUUCUAfGAfUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2211	CR010171	mA*mA*mA*GfUUfCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2212	CR010172	mA*mA*mA*GUfUCUAGAUGCUGUCfCGGUUUUAGAGCUAUGCUGUUUUG
2213	CR010173	mA*mA*mA*GUUCUfAGAUGCUfGUCCGGUUUUAGAGCUAUGCUGUUUUG
2214	CR010174	mA*mA*mA*GUUCfUAGAfUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2215	CR010175	mA*mA*mA*GUUCUAGAUGCUGUfCCfGGUUUUAGAGCUAUGCUGUUUUG
2216	CR010176	mA*mA*mA*GUUCUAfGAUGfCUGUCCGGUUUUAGAGCUAUGCUGUUUUG

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2218	CR010178	mA*mA*mA*GfUfUCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2219	CR010179	mA*mA*mA*fGUUCUAGfAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2220	CR010180	mA*mA*mA*GUUfCUAGAUGCUGfUCCGGUUUUAGAGCUAUGCUGUUUUG
2221	CR010181	mA*mA*mA*GUUfCUAGAUGCUGfUCCfGGUUUUAGAGCUAUGCUGUUUUG
2222	CR010182	mA*mA*mA*fGUUCUAGAfUGCfUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2223	CR010183	mA*mA*mA*GUUCUAGAUGCUfGUfCfCGGUUUUAGAGCUAUGCUGUUUUG
2224	CR010184	mA*mA*mA*GUUCfUAGAUfGfCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2225	CR010185	mA*mA*mA*GUfUCUfAfGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2226	CR010186	mA*mA*mA*GfUUCUAGfAUGCUfGUCCGGUUUUAGAGCUAUGCUGUUUUG
2227	CR010187	mA*mA*mA*GfUUCUAGAUGfCUGUCfCGGUUUUAGAGCUAUGCUGUUUUG
2228	CR010188	mA*mA*mA*GUUCUAGfAUGCUGUfCCfGGUUUUAGAGCUAUGCUGUUUUG
2229	CR010189	mA*mA*mA*GUUCUAGAUfGCfUGfUCCGGUUUUAGAGCUAUGCUGUUUUG
2230	CR010190	mA*mA*mA*GUUfCUfAGAfUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2231	CR010191	mA*mA*mA*fGUUCfUAfGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2232	CR010192	mA*mA*mA*GUfUCUAGAUfGCUGfUCCGGUUUUAGAGCUAUGCUGUUUUG
2233	CR010193	mA*mA*mA*GUUCUfAfGAUGCUGUCCfGGUUUUAGAGCUAUGCUGUUUUG
2234	CR010194	mA*mA*mA*GUUCfUAGAfUGCUGUfCCGGUUUUAGAGCUAUGCUGUUUUG
2235	CR010195	mA*mA*mA*GUfUCUAGAUGCfUGUCfCGGUUUUAGAGCUAUGCUGUUUUG
2236	CR010196	mA*mA*mA*GfUUfCUAGAUGCUfGUCCGGUUUUAGAGCUAUGCUGUUUUG
2237	CR010197	mA*mA*mA*fGUUCUAGfAUGfCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2238	CR010198	mA*mA*mA*GUUfCfUAfGAUGCUfGUCCGGUUUUAGAGCUAUGCUGUUUUG
2239	CR010199	mA*mA*mA*GUUCUAGAUGfCUGfUfCfCGGUUUUAGAGCUAUGCUGUUUUG
2240	CR010200	mA*mA*mA*GUUCUfAGfAUfGCUGUCCfGGUUUUAGAGCUAUGCUGUUUUG
2241	CR010201	mA*mA*mA*fGUfUCUAGAfUGCfUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2242	CR010202	mA*mA*mA*GfUUCfUAGAfUfGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2243	CR010203	mA*mA*mA*GUUCUAfGfAUGfCfUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2244	CR010204	mA*mA*mA*fGUUfCUfAGAUGCUGUfCCGGUUUUAGAGCUAUGCUGUUUUG
2245	CR010205	mA*mA*mA*GfUUCUAGAUGCUfGfUCCfGGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2246	CR010206	mA*mA*mA*GUfUCUAfGAUGCUGUCfCfGGUUUUUAGAGCUAUGCUGUUUUG
2247	CR010207	mA*mA*mA*GUUfCUAGAUfGCfUfGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2248	CR010208	mA*mA*mA*GUUCfUfAGAfUGCUGUCfCGGUUUUUAGAGCUAUGCUGUUUUG
2249	CR010209	mA*mA*mA*GfUfUCUAGAUGfCUGUfCCGGUUUUUAGAGCUAUGCUGUUUUG
2250	CR010210	mA*mA*mA*fGUUCUAGfAfUGCUGfUCCGGUUUUUAGAGCUAUGCUGUUUUG
2251	CR010211	mA*mA*mA*GfUUCUfAGAUGCfUGUfCCGGUUUUUAGAGCUAUGCUGUUUUG
2252	CR010212	mA*mA*mA*GUUCfUAGfAUGfCUGUCCfGGUUUUUAGAGCUAUGCUGUUUUG
2253	CR010213	mA*mA*mA*fGUUCUAGAUfGCUGfUCfCGGUUUUUAGAGCUAUGCUGUUUUG
2254	CR010214	mA*mA*mA*GUfUfCUAfGAUGCUfGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2255	CR010215	AAAGUUCUAGAUGCUGfUCCGGUUUUUAGAGCUAUGCUGUUUUG
2256	CR010216	AAAGUfUCUAGAUGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2257	CR010217	AAAGUUCUfAGAUGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2258	CR010218	AAAGUUCfUAGAUGCUfGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2259	CR010219	AAAGUUCUAfGAfUGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2260	CR010220	AAAfGUUCUAGfAUGfCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2261	CR010221	AAAGUUfCUAGAUGCUGfUCCfGGUUUUUAGAGCUAUGCUGUUUUG
2262	CR010222	AAAGfUUCUfAGAUGCfUGUfCCGGUUUUUAGAGCUAUGCUGUUUUG
2263	CR010223	AAAfGUUCUAGAUfGCUGfUCfCGGUUUUUAGAGCUAUGCUGUUUUG
2264	CR010224	mA*mA*mA*GUUCUAGAUGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2265	CR010691	mA*mA*mA*GmUUCUAGAUGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2266	CR010692	mA*mA*mA*GUUCUAGAUGCUGUCmCGGUUUUUAGAGCUAUGCUGUUUUG
2267	CR010693	mA*mA*mA*GUUCUAGAUGCUmGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2268	CR010694	mA*mA*mA*GUUmCUAGAUGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2269	CR010695	mA*mA*mA*GUUCUAGAUGCUGUCCmGGUUUUUAGAGCUAUGCUGUUUUG
2270	CR010696	mA*mA*mA*GUUCUAGAUGCUGmUCCGGUUUUUAGAGCUAUGCUGUUUUG
2271	CR010697	mA*mA*mA*GUUCUAGAUmGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2272	CR010698	mA*mA*mA*GUUCUmAGAUGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2273	CR010699	mA*mA*mA*GUUCUAGAUGmCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG
2274	CR010700	mA*mA*mA*GUUCUAGmAUGCUGUCCGGUUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
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2276	CR010702	mA*mA*mA*GUUCUAGAUGCmUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2277	CR010703	mA*mA*mA*GUUCUAGAmUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2278	CR010704	mA*mA*mA*GUUCUAmGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2279	CR010705	mA*mA*mA*GUmUCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2280	CR010706	mA*mA*mA*GUUCmUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2281	CR010707	mA*mA*mA*GUUCUAGAUGCUGUmCCGGUUUUAGAGCUAUGCUGUUUUG
2282	CR010708	mA*mA*mA*mGUUCUAGAUGCUGUmCCGGUUUUAGAGCUAUGCUGUUUUG
2283	CR010709	mA*mA*mA*GUUCUAGAmUGCUmGUCCGGUUUUAGAGCUAUGCUGUUUUG
2284	CR010710	mA*mA*mA*GUUmCUAGAUGmCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2285	CR010711	mA*mA*mA*GUUCUAGmAUmGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2286	CR010712	mA*mA*mA*GUUCUmAGAUGCmUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2287	CR010713	mA*mA*mA*GUUCmUAGAUGCUGUCmCGGUUUUAGAGCUAUGCUGUUUUG
2288	CR010714	mA*mA*mA*GmUUCUAGAUGCUGmUCCGGUUUUAGAGCUAUGCUGUUUUG
2289	CR010715	mA*mA*mA*GUUCUAmGAUGCUGUCCmGGUUUUAGAGCUAUGCUGUUUUG
2290	CR010716	mA*mA*mA*GUmUCUAGAmUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2291	CR010717	mA*mA*mA*GUUCUAGAUmGCUGUCmCGGUUUUAGAGCUAUGCUGUUUUG
2292	CR010718	mA*mA*mA*GUUCUmAGmAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2293	CR010719	mA*mA*mA*GUUCUAGAUGCUGmUmCCGGUUUUAGAGCUAUGCUGUUUUG
2294	CR010720	mA*mA*mA*GUUmCUAGAUGCUGUCCmGGUUUUAGAGCUAUGCUGUUUUG
2295	CR010721	mA*mA*mA*GUmUCUAGAUGmCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2296	CR010722	mA*mA*mA*GmUUCUAGAUGCmUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2297	CR010723	mA*mA*mA*GUUCmUAGAUGCUmGUCCGGUUUUAGAGCUAUGCUGUUUUG
2298	CR010724	mA*mA*mA*mGUUCUAmGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2299	CR010725	mA*mA*mA*mGUUCUAGAUGCmUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2300	CR010726	mA*mA*mA*GUUCmUAGAUGmCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2301	CR010727	mA*mA*mA*GUUCUmAGAUGCUGUCmCGGUUUUAGAGCUAUGCUGUUUUG
2302	CR010728	mA*mA*mA*GUUCUAGAUGCUmGUCCmGGUUUUAGAGCUAUGCUGUUUUG
2303	CR010729	mA*mA*mA*GUUCUAGmAUGCUGUmCCGGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2304	CR010730	mA*mA*mA*GUUCUAGAUmGCUGmUCCGGUUUUAGAGCUAUGCUGUUUUG
2305	CR010731	mA*mA*mA*GUUCUAmGAmUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2306	CR010732	mA*mA*mA*GmUUmCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2307	CR010733	mA*mA*mA*GUmUCUAGAUGCUGUCmCGGUUUUAGAGCUAUGCUGUUUUG
2308	CR010734	mA*mA*mA*GUUCUmAGAUGCUmGUCCGGUUUUAGAGCUAUGCUGUUUUG
2309	CR010735	mA*mA*mA*GUUCmUAGAmUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2310	CR010736	mA*mA*mA*GUUCUAGAUGCUGUmCCmGGUUUUAGAGCUAUGCUGUUUUG
2311	CR010737	mA*mA*mA*GUUCUAmGAUGmCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2312	CR010738	mA*mA*mA*GUUCUAGAUmGCmUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2313	CR010739	mA*mA*mA*GmUmUCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2314	CR010740	mA*mA*mA*mGUUCUAGmAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2315	CR010741	mA*mA*mA*GUUmCUAGAUGCUGmUCCGGUUUUAGAGCUAUGCUGUUUUG
2316	CR010742	mA*mA*mA*GUUmCUAGAUGCUGmUCCmGGUUUUAGAGCUAUGCUGUUUUG
2317	CR010743	mA*mA*mA*mGUUCUAGAmUGCmUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2318	CR010744	mA*mA*mA*GUUCUAGAUGCUmGUmCmCGGUUUUAGAGCUAUGCUGUUUUG
2319	CR010745	mA*mA*mA*GUUCmUAGAUmGmCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2320	CR010746	mA*mA*mA*GUmUCUmAmGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2321	CR010747	mA*mA*mA*GmUUCUAGmAUGCUmGUCCGGUUUUAGAGCUAUGCUGUUUUG
2322	CR010748	mA*mA*mA*GmUUCUAGAUGmCUGUCmCGGUUUUAGAGCUAUGCUGUUUUG
2323	CR010749	mA*mA*mA*GUUCUAGmAUGCUGUmCCmGGUUUUAGAGCUAUGCUGUUUUG
2324	CR010750	mA*mA*mA*GUUCUAGAUmGCmUGmUCCGGUUUUAGAGCUAUGCUGUUUUG
2325	CR010751	mA*mA*mA*GUUmCUmAGAmUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2326	CR010752	mA*mA*mA*mGUUCmUAmGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2327	CR010753	mA*mA*mA*GUmUCUAGAUmGCUGmUCCGGUUUUAGAGCUAUGCUGUUUUG
2328	CR010754	mA*mA*mA*GUUCUmAmGAUGCUGUCCmGGUUUUAGAGCUAUGCUGUUUUG
2329	CR010755	mA*mA*mA*GUUCmUAGAmUGCUGUmCCGGUUUUAGAGCUAUGCUGUUUUG
2330	CR010756	mA*mA*mA*GUmUCUAGAUGCmUGUCmCGGUUUUAGAGCUAUGCUGUUUUG
2331	CR010757	mA*mA*mA*GmUUmCUAGAUGCUmGUCCGGUUUUAGAGCUAUGCUGUUUUG
2332	CR010758	mA*mA*mA*mGUUCUAGmAUGmCUGUCCGGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
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2334	CR010760	mA*mA*mA*GUUCUAGAUGmCUGmUmCmCGGUUUUAGAGCUAUGCUGUUUUG
2335	CR010761	mA*mA*mA*GUUCUmAGmAUmGCUGUCCmGGUUUUAGAGCUAUGCUGUUUUG
2336	CR010762	mA*mA*mA*mGUmUCUAGAmUGCmUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2337	CR010763	mA*mA*mA*GmUUCmUAGAmUmGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2338	CR010764	mA*mA*mA*GUUCUAmGmAUGmCmUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2339	CR010765	mA*mA*mA*mGUUmCUmAGAUGCUGUmCCGGUUUUAGAGCUAUGCUGUUUUG
2340	CR010766	mA*mA*mA*GmUUCUAGAUGCUmGmUCCmGGUUUUAGAGCUAUGCUGUUUUG
2341	CR010767	mA*mA*mA*GUmUCUAmGAUGCUGUCmCmGGUUUUAGAGCUAUGCUGUUUUG
2342	CR010768	mA*mA*mA*GUUmCUAGAUmGCmUmGUCCGGUUUUAGAGCUAUGCUGUUUUG
2343	CR010769	mA*mA*mA*GUUCmUmAGAmUGCUGUCmCGGUUUUAGAGCUAUGCUGUUUUG
2344	CR010770	mA*mA*mA*GmUmUCUAGAUGmCUGUmCCGGUUUUAGAGCUAUGCUGUUUUG
2345	CR010771	mA*mA*mA*mGUUCUAGmAmUGCUGmUCCGGUUUUAGAGCUAUGCUGUUUUG
2346	CR010772	mA*mA*mA*GmUUCUmAGAUGCmUGUmCCGGUUUUAGAGCUAUGCUGUUUUG
2347	CR010773	mA*mA*mA*GUUCmUAGmAUGmCUGUCCmGGUUUUAGAGCUAUGCUGUUUUG
2348	CR010774	mA*mA*mA*mGUUCUAGAUmGCUGmUCmCGGUUUUAGAGCUAUGCUGUUUUG
2349	CR010775	mA*mA*mA*GUmUmCUAmGAUGCUmGUCCGGUUUUAGAGCUAUGCUGUUUUG
2350	CR010776	AAAGUUCUAGAUGCUGmUCCGGUUUUAGAGCUAUGCUGUUUUG
2351	CR010777	AAAGUmUCUAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2352	CR010778	AAAGUUCUmAGAUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2353	CR010779	AAAGUUCmUAGAUGCUmGUCCGGUUUUAGAGCUAUGCUGUUUUG
2354	CR010780	AAAGUUCUAmGAmUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2355	CR010781	AAAmGUUCUAGmAUGmCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2356	CR010782	AAAGUUmCUAGAUGCUGmUCCmGGUUUUAGAGCUAUGCUGUUUUG
2357	CR010783	AAAGmUUCUmAGAUGCmUGUmCCGGUUUUAGAGCUAUGCUGUUUUG
2358	CR010784	AAAmGUUCUAGAUmGCUGmUCmCGGUUUUAGAGCUAUGCUGUUUUG
2359	CR011252	mA*mA*mA*G*UUCUAGAUGCUGUC*CGGUUUUAGAGCUAUGCUGUUUUG
2360	CR011253	mA*mA*mA*GUUCUAGAU*GCUG*UCCGGUUUUAGAGCUAUGCUGUUUUG
2361	CR011254	mA*mA*mA*GUUC*UAGAUGC*UGUCCGGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
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2363	CR011256	mA*mA*mA*GUUCUA*GAUGCU*GUCCGGUUUUAGAGCUAUGCUGUUUUG
2364	CR011257	mA*mA*mA*GUUCU*AGAUGCUGUCC*GGUUUUAGAGCUAUGCUGUUUUG
2365	CR011258	mA*mA*mA*GU*UCUAGAUGCUGU*CCGGUUUUAGAGCUAUGCUGUUUUG
2366	CR011259	mA*mA*mA*GUUCUAG*AUGCUGUCCG*GUUUUAGAGCUAUGCUGUUUUG
2367	CR011260	mA*mA*mA*GUUC*UAGAUGCUGU*CCG*GUUUUAGAGCUAUGCUGUUUUG
2368	CR011261	mA*mA*mA*G*UUCUAGAU*GCU*GUCCGGUUUUAGAGCUAUGCUGUUUUG
2369	CR011262	mA*mA*mA*GUUCUAGAUGCUG*UC*C*GGUUUUAGAGCUAUGCUGUUUUG
2370	CR011263	mA*mA*mA*GUUCU*AGAUG*C*UGUCCGGUUUUAGAGCUAUGCUGUUUUG
2371	CR011264	mA*mA*mA*GUU*CUA*G*AUGCUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2372	CR011265	mA*mA*mA*GU*UCUAGA*UGCUG*UCCGGUUUUAGAGCUAUGCUGUUUUG
2373	CR011266	mA*mA*mA*GU*UCUAGAUGC*UGUCC*GGUUUUAGAGCUAUGCUGUUUUG
2374	CR011267	mA*mA*mA*GUUCUAGA*UGCUGUC*CG*GUUUUAGAGCUAUGCUGUUUUG
2375	CR011268	mA*mA*mA*GUUC*U*AG*AUGCUG*UCCGGUUUUAGAGCUAUGCUGUUUUG
2376	CR011269	mA*mA*mA*GUUCUAGAUGC*UGU*C*C*GGUUUUAGAGCUAUGCUGUUUUG
2377	CR011270	mA*mA*mA*GUUCUA*GA*UG*CUGUCCG*GUUUUAGAGCUAUGCUGUUUUG
2378	CR011271	mA*mA*mA*G*UU*CUAGAU*GCU*GUCCGGUUUUAGAGCUAUGCUGUUUUG
2379	CR011272	mA*mA*mA*GU*UCU*AGAU*G*CUGUCCGGUUUUAGAGCUAUGCUGUUUUG
2380	CR011273	mA*mA*mA*GUUCUAG*A*UGC*U*GUCCGGUUUUAGAGCUAUGCUGUUUUG
2381	CR011274	mA*mA*mA*G*UUC*UA*GAUGCUGUC*CGGUUUUAGAGCUAUGCUGUUUUG
2382	CR011275	mA*mA*mA*GU*UCUAGAUGCUG*U*CCG*GUUUUAGAGCUAUGCUGUUUUG
2383	CR011276	mA*mA*mA*GUUC*U*AG*AUGCUGU*C*CGGUUUUAGAGCUAUGCUGUUUUG
2384	CR011277	mA*mA*mA*GUUCUA*GAU*G*CU*GUCC*GGUUUUAGAGCUAUGCUGUUUUG
2385	CR011278	mA*mA*mA*G*UUCUAGA*UGC*UG*UCCG*GUUUUAGAGCUAUGCUGUUUUG
2386	CR011279	mA*mA*mA*GU*U*CUAGA*UGCU*GU*CCGGUUUUAGAGCUAUGCUGUUUUG
2387	CR011280	mA*mA*mA*G*UU*CUAG*AUG*CUG*UCCGGUUUUAGAGCUAUGCUGUUUUG
2388	CR011281	mA*mA*mA*GU*UCUAGAUGC*UGUC*C*G*GUUUUAGAGCUAUGCUGUUUUG
2389	CR011282	mA*mA*mA*GUUC*U*A*GAU*GCUG*UCCGGUUUUAGAGCUAUGCUGUUUUG
2390	CR011283	mA*mA*mA*GUU*C*UA*GAUG*CUGUCCG*GUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2391	CR011284	mA*mA*mA*GUU*C*U*AGAUG*CUGU*C*CGGUUUUAGAGCUAUGCUGUUUUG
2392	CR011285	mA*mA*mA*GU*UCUA*G*AU*GC*UG*UCCGGUUUUAGAGCUAUGCUGUUUUG
2393	CR011286	mA*mA*mA*G*UUCUAGA*UGC*U*GUCC*G*GUUUUAGAGCUAUGCUGUUUUG
2394	CR011287	mA*mA*mA*G*UU*CU*A*GAU*GCU*GUCCGGUUUUAGAGCUAUGCUGUUUUG
2395	CR011288	mA*mA*mA*GU*UCUAG*AUGCUGU*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2396	CR011289	mA*mA*mA*GUUC*UA*GA*UG*CUG*UCCG*GUUUUAGAGCUAUGCUGUUUUG
2397	CR011290	mA*mA*mA*GU*UC*UAGA*U*GCU*GUC*CGGUUUUAGAGCUAUGCUGUUUUG
2398	CR011291	mA*mA*mA*G*UUCU*AGAUG*CUG*U*CC*GGUUUUAGAGCUAUGCUGUUUUG
2399	CR011292	mA*mA*mA*GUUC*U*A*GAUG*C*UGUC*CG*GUUUUAGAGCUAUGCUGUUUUG
2400	CR011293	mA*mA*mA*G*UUCUAG*A*U*GCU*G*UCC*GGUUUUAGAGCUAUGCUGUUUUG
2401	CR011294	mA*mA*mA*GU*U*CU*AG*AUGC*UG*U*CCGGUUUUAGAGCUAUGCUGUUUUG
2402	CR011295	mA*mA*mA*G*U*U*CUAGAU*GCUGU*C*CG*GUUUUAGAGCUAUGCUGUUUUG
2403	CR011296	mA*mA*mA*GU*UC*UA*GA*UG*CU*GUCC*GGUUUUAGAGCUAUGCUGUUUUG
2404	CR011297	mA*mA*mA*GUUCUA*G*AU*GC*UGU*C*C*GGUUUUAGAGCUAUGCUGUUUUG
2405	CR011298	mA*mA*mA*G*UU*CU*AGA*UG*CU*GUCCG*GUUUUAGAGCUAUGCUGUUUUG
2406	CR011299	mA*mA*mA*GUU*C*UAGAU*GCU*G*U*C*CGGUUUUAGAGCUAUGCUGUUUUG
2407	CR011300	mA*mA*mA*G*U*UC*UA*GA*UGC*UG*UCCGGUUUUAGAGCUAUGCUGUUUUG
2408	CR011301	mA*mA*mA*G*U*UCUA*G*A*UG*CUGUCC*G*GUUUUAGAGCUAUGCUGUUUUG
2409	CR011302	mA*mA*mA*GUU*C*U*AGAU*GC*UG*U*C*CGGUUUUAGAGCUAUGCUGUUUUG
2410	CR011303	mA*mA*mA*GUUC*UAG*AU*G*CU*G*UC*C*GGUUUUAGAGCUAUGCUGUUUUG
2411	CR011304	mA*mA*mA*G*U*U*CU*AGA*UGCU*GU*CCG*GUUUUAGAGCUAUGCUGUUUUG
2412	CR011305	mA*mA*mA*GUU*CU*A*G*AUG*C*UG*UCCG*GUUUUAGAGCUAUGCUGUUUUG
2413	CR011306	mA*mA*mA*GU*UC*UA*GA*UGC*UGU*C*C*GGUUUUAGAGCUAUGCUGUUUUG
2414	CR011307	mA*mA*mA*G*UU*C*UAGA*U*G*C*U*GUCCGGUUUUAGAGCUAUGCUGUUUUG
2415	CR011308	mA*mA*mA*G*UUCU*A*G*AU*GCU*GU*C*CGGUUUUAGAGCUAUGCUGUUUUG
2416	CR011309	mA*mA*mA*GU*UC*U*AGA*U*GCUG*UCC*G*GUUUUAGAGCUAUGCUGUUUUG
2417	CR011310	mA*mA*mA*GUU*CU*A*GAU*GC*U*G*U*CCG*GUUUUAGAGCUAUGCUGUUUUG
2418	CR011311	mA*mA*mA*G*U*UC*U*AG*A*UG*CUGUC*C*GGUUUUAGAGCUAUGCUGUUUUG
2419	CR011312	mA*mA*mA*GUU*C*UAGA*UG*C*U*G*UC*C*GGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2420	CR011313	mA*mA*mA*G*U*UCUA*G*A*U*GCUGU*C*CG*GUUUUAGAGCUAUGCUGUUUUG
2421	CR011314	mA*mA*mA*GU*U*CU*A*G*AUGC*U*G*UC*CG*GUUUUAGAGCUAUGCUGUUUUG
2422	CR011315	mA*mA*mA*G*UUC*UA*GA*U*G*CU*GU*CC*G*GUUUUAGAGCUAUGCUGUUUUG
2423	CR011316	mA*mA*mA*G*U*UCUAG*A*U*G*C*UG*U*C*CGGUUUUAGAGCUAUGCUGUUUUG
2424	CR011317	mA*mA*mA*GUU*C*U*AG*AU*G*CUG*U*C*C*GGUUUUAGAGCUAUGCUGUUUUG
2425	CR011318	mA*mA*mA*G*UU*CU*A*G*A*U*GCUG*U*C*C*GGUUUUAGAGCUAUGCUGUUUUG
2426	CR011319	mA*mA*mA*GU*U*C*U*AGA*UG*C*U*GU*C*CG*GUUUUAGAGCUAUGCUGUUUUG
2427	CR011320	mA*mA*mA*G*U*UC*UA*G*AU*G*C*U*GUCC*G*GUUUUAGAGCUAUGCUGUUUUG
2428	CR011321	mA*mA*mA*GUU*CU*A*GAU*G*C*U*G*U*CC*G*GUUUUAGAGCUAUGCUGUUUUG
2429	CR011322	mA*mA*mA*GUUC*U*A*GA*U*G*CU*G*U*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2430	CR011323	mA*mA*mA*G*U*U*CUAG*AU*G*C*U*GU*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2431	CR011324	mA*mA*mA*G*U*U*C*U*A*G*A*UGC*U*G*UCC*GGUUUUAGAGCUAUGCUGUUUUG
2432	CR011325	mA*mA*mA*G*U*U*C*U*AGA*U*G*C*UG*U*CCG*GUUUUAGAGCUAUGCUGUUUUG
2433	CR011326	mA*mA*mA*G*U*U*CU*AGA*U*GC*U*G*U*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2434	CR011327	mA*mA*mA*GU*U*C*U*A*G*A*U*G*C*U*G*UCCG*GUUUUAGAGCUAUGCUGUUUUG
2435	CR011328	mA*mA*mA*G*U*U*C*U*A*G*AU*G*CU*GU*C*C*GGUUUUAGAGCUAUGCUGUUUUG
2436	CR011329	mA*mA*mA*G*UU*C*UA*G*A*UG*C*UG*U*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2437	CR011330	mA*mA*mA*G*U*UC*U*AG*A*UG*C*U*G*U*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2438	CR011331	mA*mA*mA*G*UU*CUA*G*A*U*G*C*U*G*U*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2439	CR011332	mA*mA*mA*GU*U*C*U*A*G*AU*G*C*U*GU*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2440	CR011333	mA*mA*mA*G*U*U*C*U*A*GA*U*GC*U*G*UC*C*G*GUUUUAGAGCUAUGCUGUUUUG
2441	CR011334	mA*mA*mA*G*U*U*C*UA*G*A*U*G*C*U*G*U*CC*G*GUUUUAGAGCUAUGCUGUUUUG
2442	CR011335	mA*mA*mA*GU*U*C*U*A*G*A*U*G*C*U*G*U*C*CG*GUUUUAGAGCUAUGCUGUUUUG
2443	CR011336	mA*mA*mA*G*UU*C*U*A*G*A*U*G*CU*G*U*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2444	CR011337	mA*mA*mA*G*U*U*C*U*A*GA*UG*C*U*G*U*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
2445	CR011338	AAAGU*UCUAGAUGCUGU*CCGGUUUUAGAGCUAUGCUGUUUUG
2446	CR011339	AAAGUUCU*AGAUG*C*UGUCCGGUUUUAGAGCUAUGCUGUUUUG
2447	CR011340	AAAG*UUC*UA*GAUGCUGUC*CGGUUUUAGAGCUAUGCUGUUUUG
2448	CR011341	AAAG*UUCUAGA*UGC*UG*UCCG*GUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2449	CR011342	AAAG*UU*CU*A*GAU*GCU*GUCCGGUUUUAGAGCUAUGCUGUUUUG
2450	CR011343	AAAG*UUCUAG*A*U*GCU*G*UCC*GGUUUUAGAGCUAUGCUGUUUUG
2451	CR011344	AAAGU*UC*UA*GA*UGC*UGU*C*C*GGUUUUAGAGCUAUGCUGUUUUG
2452	CR011345	AAAGUU*C*UAGA*UG*C*U*G*UC*C*GGUUUUAGAGCUAUGCUGUUUUG
2453	CR009676	AAAGGmCUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2454	CR009679	AAAGGCUGmCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2455	CR009687	AAAGGCUGCUGAUGACmACCUGUUUUAGAGCUAUGCUGUUUUG
2456	CR009711	mA*mA*mA*GGCUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2457	CR009723	AAAGGfCUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2458	CR009726	AAAGGCUGfCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2459	CR009734	AAAGGCUGCUGAUGACfACCUGUUUUAGAGCUAUGCUGUUUUG
2460	CR010040	mA*mA*mA*GfGCUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2461	CR010041	mA*mA*mA*GGCUGCUGAUGACACfCUGUUUUAGAGCUAUGCUGUUUUG
2462	CR010042	mA*mA*mA*GGCUGCUGAUGAfCACCUGUUUUAGAGCUAUGCUGUUUUG
2463	CR010043	mA*mA*mA*GGCfUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2464	CR010044	mA*mA*mA*GGCUGCUGAUGACACCfUGUUUUAGAGCUAUGCUGUUUUG
2465	CR010045	mA*mA*mA*GGCUGCUGAUGACfACCUGUUUUAGAGCUAUGCUGUUUUG
2466	CR010046	mA*mA*mA*GGCUGCUGAfUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2467	CR010047	mA*mA*mA*GGCUGfCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2468	CR010048	mA*mA*mA*GGCUGCUGAUfGACACCUGUUUUAGAGCUAUGCUGUUUUG
2469	CR010049	mA*mA*mA*GGCUGCUfGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2470	CR010050	mA*mA*mA*fGGCUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2471	CR010051	mA*mA*mA*GGCUGCUGAUGfACACCUGUUUUAGAGCUAUGCUGUUUUG
2472	CR010052	mA*mA*mA*GGCUGCUGfAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2473	CR010053	mA*mA*mA*GGCUGCfUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2474	CR010054	mA*mA*mA*GGfCUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2475	CR010055	mA*mA*mA*GGCUfGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2476	CR010056	mA*mA*mA*GGCUGCUGAUGACAfCCUGUUUUAGAGCUAUGCUGUUUUG
2477	CR010057	mA*mA*mA*fGGCUGCUGAUGACAfCCUGUUUUAGAGCUAUGCUGUUUUG

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2479	CR010059	mA*mA*mA*GGCfUGCUGAUfGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2480	CR010060	mA*mA*mA*GGCUGCUfGAfUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2481	CR010061	mA*mA*mA*GGCUGfCUGAUGfACACCUGUUUUUAGAGCUAUGCUGUUUUG
2482	CR010062	mA*mA*mA*GGCUfGCUGAUGACACfCUGUUUUUAGAGCUAUGCUGUUUUG
2483	CR010063	mA*mA*mA*GfGCUGCUGAUGACfACCUGUUUUUAGAGCUAUGCUGUUUUG
2484	CR010064	mA*mA*mA*GGCUGCfUGAUGACACCfUGUUUUUAGAGCUAUGCUGUUUUG
2485	CR010065	mA*mA*mA*GGfCUGCUGfAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2486	CR010066	mA*mA*mA*GGCUGCUGAfUGACACfCUGUUUUUAGAGCUAUGCUGUUUUG
2487	CR010067	mA*mA*mA*GGCUGfCUfGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2488	CR010068	mA*mA*mA*GGCfUGCUGAUGACACCfUGUUUUUAGAGCUAUGCUGUUUUG
2489	CR010069	mA*mA*mA*GGfCUGCUGAUfGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2490	CR010070	mA*mA*mA*GfGCUGCUGAUGfACACCUGUUUUUAGAGCUAUGCUGUUUUG
2491	CR010071	mA*mA*mA*GGCUfGCUGAUGAfCACCUGUUUUUAGAGCUAUGCUGUUUUG
2492	CR010072	mA*mA*mA*fGGCUGCfUGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2493	CR010073	mA*mA*mA*fGGCUGCUGAUGfACACCUGUUUUUAGAGCUAUGCUGUUUUG
2494	CR010074	mA*mA*mA*GGCUfGCUGAUfGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2495	CR010075	mA*mA*mA*GGCUGfCUGAUGACACfCUGUUUUUAGAGCUAUGCUGUUUUG
2496	CR010076	mA*mA*mA*GGCUGCUGAUGAfCACCfUGUUUUUAGAGCUAUGCUGUUUUG
2497	CR010077	mA*mA*mA*GGCUGCUfGAUGACAfCCUGUUUUUAGAGCUAUGCUGUUUUG
2498	CR010078	mA*mA*mA*GGCUGCUGAfUGACfACCUGUUUUUAGAGCUAUGCUGUUUUG
2499	CR010079	mA*mA*mA*GGCUGCfUGfAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2500	CR010080	mA*mA*mA*GfGCfUGCUGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2501	CR010081	mA*mA*mA*GGfCUGCUGAUGACACfCUGUUUUUAGAGCUAUGCUGUUUUG
2502	CR010082	mA*mA*mA*GGCUGfCUGAUGAfCACCUGUUUUUAGAGCUAUGCUGUUUUG
2503	CR010083	mA*mA*mA*GGCUfGCUGfAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2504	CR010084	mA*mA*mA*GGCUGCUGAUGACAfCCfUGUUUUUAGAGCUAUGCUGUUUUG
2505	CR010085	mA*mA*mA*GGCUGCfUGAUfGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2506	CR010086	mA*mA*mA*GGCUGCUGAfUGfACACCUGUUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
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2508	CR010088	mA*mA*mA*fGGCUGCUfGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2509	CR010089	mA*mA*mA*GGCfUGCUGAUGACfACCUGUUUUAGAGCUAUGCUGUUUUG
2510	CR010090	mA*mA*mA*GGCfUGCUGAUGACfACCfUGUUUUAGAGCUAUGCUGUUUUG
2511	CR010091	mA*mA*mA*fGGCUGCUGfAUGfACACCUGUUUUAGAGCUAUGCUGUUUUG
2512	CR010092	mA*mA*mA*GGCUGCUGAUGAfCAfCfCUGUUUUAGAGCUAUGCUGUUUUG
2513	CR010093	mA*mA*mA*GGCUfGCUGAfUfGACACCUGUUUUAGAGCUAUGCUGUUUUG
2514	CR010094	mA*mA*mA*GGfCUGfCfUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2515	CR010095	mA*mA*mA*GfGCUGCUfGAUGAfCACCUGUUUUAGAGCUAUGCUGUUUUG
2516	CR010096	mA*mA*mA*GfGCUGCUGAUfGACACfCUGUUUUAGAGCUAUGCUGUUUUG
2517	CR010097	mA*mA*mA*GGCUGCUfGAUGACAfCCfUGUUUUAGAGCUAUGCUGUUUUG
2518	CR010098	mA*mA*mA*GGCUGCUGAfUGfACfACCUGUUUUAGAGCUAUGCUGUUUUG
2519	CR010099	mA*mA*mA*GGCfUGfCUGfAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2520	CR010100	mA*mA*mA*fGGCUfGCfUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2521	CR010101	mA*mA*mA*GGfCUGCUGAfUGACfACCUGUUUUAGAGCUAUGCUGUUUUG
2522	CR010102	mA*mA*mA*GGCUGfCfUGAUGACACCfUGUUUUAGAGCUAUGCUGUUUUG
2523	CR010103	mA*mA*mA*GGCUfGCUGfAUGACAfCCUGUUUUAGAGCUAUGCUGUUUUG
2524	CR010104	mA*mA*mA*GGfCUGCUGAUGfACACfCUGUUUUAGAGCUAUGCUGUUUUG
2525	CR010105	mA*mA*mA*GfGCfUGCUGAUGAfCACCUGUUUUAGAGCUAUGCUGUUUUG
2526	CR010106	mA*mA*mA*fGGCUGCUfGAUfGACACCUGUUUUAGAGCUAUGCUGUUUUG
2527	CR010107	mA*mA*mA*GGCfUfGCfUGAUGAfCACCUGUUUUAGAGCUAUGCUGUUUUG
2528	CR010108	mA*mA*mA*GGCUGCUGAUfGACfAfCfCUGUUUUAGAGCUAUGCUGUUUUG
2529	CR010109	mA*mA*mA*GGCUGfCUfGAfUGACACCfUGUUUUAGAGCUAUGCUGUUUUG
2530	CR010110	mA*mA*mA*fGGfCUGCUGfAUGfACACCUGUUUUAGAGCUAUGCUGUUUUG
2531	CR010111	mA*mA*mA*GfGCUfGCUGfAfUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2532	CR010112	mA*mA*mA*GGCUGCfUfGAUfGfACACCUGUUUUAGAGCUAUGCUGUUUUG
2533	CR010113	mA*mA*mA*fGGCfUGfCUGAUGACAfCCUGUUUUAGAGCUAUGCUGUUUUG
2534	CR010114	mA*mA*mA*GfGCUGCUGAUGAfCfACCfUGUUUUAGAGCUAUGCUGUUUUG
2535	CR010115	mA*mA*mA*GGfCUGCfUGAUGACACfCfUGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2536	CR010116	mA*mA*mA*GGCfUGCUGAfUGfAfCACCUGUUUUUAGAGCUAUGCUGUUUUG
2537	CR010117	mA*mA*mA*GGCUfGfCUGfAUGACACfCUGUUUUUAGAGCUAUGCUGUUUUG
2538	CR010118	mA*mA*mA*GfGfCUGCUGAUfGACAfCCUGUUUUUAGAGCUAUGCUGUUUUG
2539	CR010119	mA*mA*mA*fGGCUGCUfGfAUGACfACCUGUUUUUAGAGCUAUGCUGUUUUG
2540	CR010120	mA*mA*mA*GfGCUGfCUGAUGfACAfCCUGUUUUUAGAGCUAUGCUGUUUUG
2541	CR010121	mA*mA*mA*GGCUfGCUfGAUfGACACCfUGUUUUUAGAGCUAUGCUGUUUUG
2542	CR010122	mA*mA*mA*fGGCUGCUGAfUGACfACfCUGUUUUUAGAGCUAUGCUGUUUUG
2543	CR010123	mA*mA*mA*GGfCfUGCfUGAUGAfCACCUGUUUUUAGAGCUAUGCUGUUUUG
2544	CR010124	AAAGGCUfGCUGAUGAfCACCUGUUUUUAGAGCUAUGCUGUUUUG
2545	CR010125	AAAGGCUGCfUGfAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2546	CR010126	AAAfGGCUGCUfGAUfGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2547	CR010127	AAAGGCfUGCUGAUGACfACCfUGUUUUUAGAGCUAUGCUGUUUUG
2548	CR010128	AAAGfGCUGfCUGAUGfACAfCCUGUUUUUAGAGCUAUGCUGUUUUG
2549	CR010129	AAAfGGCUGCUGAfUGACfACfCUGUUUUUAGAGCUAUGCUGUUUUG
2550	CR010600	mA*mA*mA*GmGCUGCUGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2551	CR010601	mA*mA*mA*GGCUGCUGAUGACACmCUGUUUUUAGAGCUAUGCUGUUUUG
2552	CR010602	mA*mA*mA*GGCUGCUGAUGAmCACCUGUUUUUAGAGCUAUGCUGUUUUG
2553	CR010603	mA*mA*mA*GGCmUGCUGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2554	CR010604	mA*mA*mA*GGCUGCUGAUGACACCmUGUUUUUAGAGCUAUGCUGUUUUG
2555	CR010605	mA*mA*mA*GGCUGCUGAUGACmACCUGUUUUUAGAGCUAUGCUGUUUUG
2556	CR010606	mA*mA*mA*GGCUGCUGAmUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2557	CR010607	mA*mA*mA*GGCUGmCUGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2558	CR010608	mA*mA*mA*GGCUGCUGAUmGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2559	CR010609	mA*mA*mA*GGCUGCUmGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2560	CR010610	mA*mA*mA*mGGCUGCUGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2561	CR010611	mA*mA*mA*GGCUGCUGAUGmACACCUGUUUUUAGAGCUAUGCUGUUUUG
2562	CR010612	mA*mA*mA*GGCUGCUGmAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2563	CR010613	mA*mA*mA*GGCUGCmUGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG
2564	CR010614	mA*mA*mA*GGmCUGCUGAUGACACCUGUUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2565	CR010615	mA*mA*mA*GGCUmGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2566	CR010616	mA*mA*mA*GGCUGCUGAUGACAmCCUGUUUUAGAGCUAUGCUGUUUUG
2567	CR010617	mA*mA*mA*mGGCUGCUGAUGACAmCCUGUUUUAGAGCUAUGCUGUUUUG
2568	CR010618	mA*mA*mA*GGCUGCUGmAUGAmCACCUGUUUUAGAGCUAUGCUGUUUUG
2569	CR010619	mA*mA*mA*GGCmUGCUGAUmGACACCUGUUUUAGAGCUAUGCUGUUUUG
2570	CR010620	mA*mA*mA*GGCUGCUmGAmUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2571	CR010621	mA*mA*mA*GGCUGmCUGAUGmACACCUGUUUUAGAGCUAUGCUGUUUUG
2572	CR010622	mA*mA*mA*GGCUmGCUGAUGACACmCUGUUUUAGAGCUAUGCUGUUUUG
2573	CR010623	mA*mA*mA*GmGCUGCUGAUGACmACCUGUUUUAGAGCUAUGCUGUUUUG
2574	CR010624	mA*mA*mA*GGCUGCmUGAUGACACCmUGUUUUAGAGCUAUGCUGUUUUG
2575	CR010625	mA*mA*mA*GGmCUGCUGmAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2576	CR010626	mA*mA*mA*GGCUGCUGAmUGACACmCUGUUUUAGAGCUAUGCUGUUUUG
2577	CR010627	mA*mA*mA*GGCUGmCUmGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2578	CR010628	mA*mA*mA*GGCUGCUGAUGACmAmCCUGUUUUAGAGCUAUGCUGUUUUG
2579	CR010629	mA*mA*mA*GGCmUGCUGAUGACACCmUGUUUUAGAGCUAUGCUGUUUUG
2580	CR010630	mA*mA*mA*GGmCUGCUGAUmGACACCUGUUUUAGAGCUAUGCUGUUUUG
2581	CR010631	mA*mA*mA*GmGCUGCUGAUGmACACCUGUUUUAGAGCUAUGCUGUUUUG
2582	CR010632	mA*mA*mA*GGCUmGCUGAUGAmCACCUGUUUUAGAGCUAUGCUGUUUUG
2583	CR010633	mA*mA*mA*mGGCUGCmUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2584	CR010634	mA*mA*mA*mGGCUGCUGAUGmACACCUGUUUUAGAGCUAUGCUGUUUUG
2585	CR010635	mA*mA*mA*GGCUmGCUGAUmGACACCUGUUUUAGAGCUAUGCUGUUUUG
2586	CR010636	mA*mA*mA*GGCUGmCUGAUGACACmCUGUUUUAGAGCUAUGCUGUUUUG
2587	CR010637	mA*mA*mA*GGCUGCUGAUGAmCACCmUGUUUUAGAGCUAUGCUGUUUUG
2588	CR010638	mA*mA*mA*GGCUGCUmGAUGACAmCCUGUUUUAGAGCUAUGCUGUUUUG
2589	CR010639	mA*mA*mA*GGCUGCUGAmUGACmACCUGUUUUAGAGCUAUGCUGUUUUG
2590	CR010640	mA*mA*mA*GGCUGCmUGmAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2591	CR010641	mA*mA*mA*GmGCmUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2592	CR010642	mA*mA*mA*GGmCUGCUGAUGACACmCUGUUUUAGAGCUAUGCUGUUUUG
2593	CR010643	mA*mA*mA*GGCUGmCUGAUGAmCACCUGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2594	CR010644	mA*mA*mA*GGCUmGCUGmAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2595	CR010645	mA*mA*mA*GGCUGCUGAUGACAmCCmUGUUUUAGAGCUAUGCUGUUUUG
2596	CR010646	mA*mA*mA*GGCUGCmUGAUmGACACCUGUUUUAGAGCUAUGCUGUUUUG
2597	CR010647	mA*mA*mA*GGCUGCUGAmUGmACACCUGUUUUAGAGCUAUGCUGUUUUG
2598	CR010648	mA*mA*mA*GmGmCUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2599	CR010649	mA*mA*mA*mGGCUGCUmGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2600	CR010650	mA*mA*mA*GGCmUGCUGAUGACmACCUGUUUUAGAGCUAUGCUGUUUUG
2601	CR010651	mA*mA*mA*GGCmUGCUGAUGACmACCmUGUUUUAGAGCUAUGCUGUUUUG
2602	CR010652	mA*mA*mA*mGGCUGCUGmAUGmACACCUGUUUUAGAGCUAUGCUGUUUUG
2603	CR010653	mA*mA*mA*GGCUGCUGAUGAmCAmCmCUGUUUUAGAGCUAUGCUGUUUUG
2604	CR010654	mA*mA*mA*GGCUmGCUGAmUmGACACCUGUUUUAGAGCUAUGCUGUUUUG
2605	CR010655	mA*mA*mA*GGmCUGmCmUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2606	CR010656	mA*mA*mA*GmGCUGCUmGAUGAmCACCUGUUUUAGAGCUAUGCUGUUUUG
2607	CR010657	mA*mA*mA*GmGCUGCUGAUmGACACmCUGUUUUAGAGCUAUGCUGUUUUG
2608	CR010658	mA*mA*mA*GGCUGCUmGAUGACAmCCmUGUUUUAGAGCUAUGCUGUUUUG
2609	CR010659	mA*mA*mA*GGCUGCUGAmUGmACmACCUGUUUUAGAGCUAUGCUGUUUUG
2610	CR010660	mA*mA*mA*GGCmUGmCUGmAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2611	CR010661	mA*mA*mA*mGGCUmGCmUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2612	CR010662	mA*mA*mA*GGmCUGCUGAmUGACmACCUGUUUUAGAGCUAUGCUGUUUUG
2613	CR010663	mA*mA*mA*GGCUGmCmUGAUGACACCmUGUUUUAGAGCUAUGCUGUUUUG
2614	CR010664	mA*mA*mA*GGCUmGCUGmAUGACAmCCUGUUUUAGAGCUAUGCUGUUUUG
2615	CR010665	mA*mA*mA*GGmCUGCUGAUGmACACmCUGUUUUAGAGCUAUGCUGUUUUG
2616	CR010666	mA*mA*mA*GmGCmUGCUGAUGAmCACCUGUUUUAGAGCUAUGCUGUUUUG
2617	CR010667	mA*mA*mA*mGGCUGCUmGAUmGACACCUGUUUUAGAGCUAUGCUGUUUUG
2618	CR010668	mA*mA*mA*GGCmUmGCmUGAUGAmCACCUGUUUUAGAGCUAUGCUGUUUUG
2619	CR010669	mA*mA*mA*GGCUGCUGAUmGACmAmCmCUGUUUUAGAGCUAUGCUGUUUUG
2620	CR010670	mA*mA*mA*GGCUGmCUmGAmUGACACCmUGUUUUAGAGCUAUGCUGUUUUG
2621	CR010671	mA*mA*mA*mGGmCUGCUGmAUGmACACCUGUUUUAGAGCUAUGCUGUUUUG
2622	CR010672	mA*mA*mA*GmGCUmGCUGmAmUGACACCUGUUUUAGAGCUAUGCUGUUUUG

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2623	CR010673	mA*mA*mA*GGCUGCmUmGAUmGmACACCUGUUUUAGAGCUAUGCUGUUUUG
2624	CR010674	mA*mA*mA*mGGCmUGmCUGAUGACAmCCUGUUUUAGAGCUAUGCUGUUUUG
2625	CR010675	mA*mA*mA*GmGCUGCUGAUGAmCmACCmUGUUUUAGAGCUAUGCUGUUUUG
2626	CR010676	mA*mA*mA*GGmCUGCmUGAUGACACmCmUGUUUUAGAGCUAUGCUGUUUUG
2627	CR010677	mA*mA*mA*GGCmUGCUGAmUGmAmCACCUGUUUUAGAGCUAUGCUGUUUUG
2628	CR010678	mA*mA*mA*GGCUmGmCUGmAUGACACmCUGUUUUAGAGCUAUGCUGUUUUG
2629	CR010679	mA*mA*mA*GmGmCUGCUGAUmGACAmCCUGUUUUAGAGCUAUGCUGUUUUG
2630	CR010680	mA*mA*mA*mGGCUGCUmGmAUGACmACCUGUUUUAGAGCUAUGCUGUUUUG
2631	CR010681	mA*mA*mA*GmGCUGmCUGAUGmACAmCCUGUUUUAGAGCUAUGCUGUUUUG
2632	CR010682	mA*mA*mA*GGCUmGCUmGAUmGACACCmUGUUUUAGAGCUAUGCUGUUUUG
2633	CR010683	mA*mA*mA*mGGCUGCUGAmUGACmACmCUGUUUUAGAGCUAUGCUGUUUUG
2634	CR010684	mA*mA*mA*GGmCmUGCmUGAUGAmCACCUGUUUUAGAGCUAUGCUGUUUUG
2635	CR010685	AAAGGCUmGCUGAUGAmCACCUGUUUUAGAGCUAUGCUGUUUUG
2636	CR010686	AAAGGCUGCmUGmAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2637	CR010687	AAAmGGCUGCUmGAUmGACACCUGUUUUAGAGCUAUGCUGUUUUG
2638	CR010688	AAAGGCmUGCUGAUGACmACCmUGUUUUAGAGCUAUGCUGUUUUG
2639	CR010689	AAAGmGCUGmCUGAUGmACAmCCUGUUUUAGAGCUAUGCUGUUUUG
2640	CR010690	AAAmGGCUGCUGAmUGACmACmCUGUUUUAGAGCUAUGCUGUUUUG
2641	CR011158	mA*mA*mA*G*GCUGCUGAUGACAC*CUGUUUUAGAGCUAUGCUGUUUUG
2642	CR011159	mA*mA*mA*GGCUGCUGA*UGAC*ACCUGUUUUAGAGCUAUGCUGUUUUG
2643	CR011160	mA*mA*mA*GGCU*GCUGAUG*ACACCUGUUUUAGAGCUAUGCUGUUUUG
2644	CR011161	mA*mA*mA*GGCUGCUG*AU*GACACCUGUUUUAGAGCUAUGCUGUUUUG
2645	CR011162	mA*mA*mA*GGCUGC*UGAUGA*CACCUGUUUUAGAGCUAUGCUGUUUUG
2646	CR011163	mA*mA*mA*GGCUG*CUGAUGACACC*UGUUUUAGAGCUAUGCUGUUUUG
2647	CR011164	mA*mA*mA*GG*CUGCUGAUGACA*CCUGUUUUAGAGCUAUGCUGUUUUG
2648	CR011165	mA*mA*mA*GGCUGCU*GAUGACACCU*GUUUUAGAGCUAUGCUGUUUUG
2649	CR011166	mA*mA*mA*GGCU*GCUGAUGACA*CCU*GUUUUAGAGCUAUGCUGUUUUG
2650	CR011167	mA*mA*mA*G*GCUGCUGA*UGA*CACCUGUUUUAGAGCUAUGCUGUUUUG
2651	CR011168	mA*mA*mA*GGCUGCUGAUGAC*AC*C*UGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2652	CR011169	mA*mA*mA*GGCUG*CUGAU*G*ACACCUGUUUUAGAGCUAUGCUGUUUUG
2653	CR011170	mA*mA*mA*GGC*UGC*U*GAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
2654	CR011171	mA*mA*mA*GG*CUGCUG*AUGAC*ACCUGUUUUAGAGCUAUGCUGUUUUG
2655	CR011172	mA*mA*mA*GG*CUGCUGAUG*ACACC*UGUUUUAGAGCUAUGCUGUUUUG
2656	CR011173	mA*mA*mA*GGCUGCUG*AUGACAC*CU*GUUUUAGAGCUAUGCUGUUUUG
2657	CR011174	mA*mA*mA*GGCU*G*CU*GAUGAC*ACCUGUUUUAGAGCUAUGCUGUUUUG
2658	CR011175	mA*mA*mA*GGCUGCUGAUG*ACA*C*C*UGUUUUAGAGCUAUGCUGUUUUG
2659	CR011176	mA*mA*mA*GGCUGC*UG*AU*GACACCU*GUUUUAGAGCUAUGCUGUUUUG
2660	CR011177	mA*mA*mA*G*GC*UGCUGA*UGA*CACCUGUUUUAGAGCUAUGCUGUUUUG
2661	CR011178	mA*mA*mA*GG*CUG*CUGA*U*GACACCUGUUUUAGAGCUAUGCUGUUUUG
2662	CR011179	mA*mA*mA*GGCUGCU*G*AUG*A*CACCUGUUUUAGAGCUAUGCUGUUUUG
2663	CR011180	mA*mA*mA*G*GCU*GC*UGAUGACAC*CUGUUUUAGAGCUAUGCUGUUUUG
2664	CR011181	mA*mA*mA*GG*CUGCUGAUGAC*A*CCU*GUUUUAGAGCUAUGCUGUUUUG
2665	CR011182	mA*mA*mA*GGCU*G*CU*GAUGACA*C*CUGUUUUAGAGCUAUGCUGUUUUG
2666	CR011183	mA*mA*mA*GGCUGC*UGA*U*GA*CACC*UGUUUUAGAGCUAUGCUGUUUUG
2667	CR011184	mA*mA*mA*G*GCUGCUG*AUG*AC*ACCU*GUUUUAGAGCUAUGCUGUUUUG
2668	CR011185	mA*mA*mA*GG*C*UGCUG*AUGA*CA*CCUGUUUUAGAGCUAUGCUGUUUUG
2669	CR011186	mA*mA*mA*G*GC*UGCU*GAU*GAC*ACCUGUUUUAGAGCUAUGCUGUUUUG
2670	CR011187	mA*mA*mA*GG*CUGCUGAUG*ACAC*C*U*GUUUUAGAGCUAUGCUGUUUUG
2671	CR011188	mA*mA*mA*GGCU*G*C*UGA*UGAC*ACCUGUUUUAGAGCUAUGCUGUUUUG
2672	CR011189	mA*mA*mA*GGC*U*GC*UGAU*GACACCU*GUUUUAGAGCUAUGCUGUUUUG
2673	CR011190	mA*mA*mA*GGC*U*G*CUGAU*GACA*C*CUGUUUUAGAGCUAUGCUGUUUUG
2674	CR011191	mA*mA*mA*GG*CUGC*U*GA*UG*AC*ACCUGUUUUAGAGCUAUGCUGUUUUG
2675	CR011192	mA*mA*mA*G*GCUGCUG*AUG*A*CACC*U*GUUUUAGAGCUAUGCUGUUUUG
2676	CR011193	mA*mA*mA*G*GC*UG*C*UGA*UGA*CACCUGUUUUAGAGCUAUGCUGUUUUG
2677	CR011194	mA*mA*mA*GG*CUGCU*GAUGACA*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2678	CR011195	mA*mA*mA*GGCU*GC*UG*AU*GAC*ACCU*GUUUUAGAGCUAUGCUGUUUUG
2679	CR011196	mA*mA*mA*GG*CU*GCUG*A*UGA*CAC*CUGUUUUAGAGCUAUGCUGUUUUG
2680	CR011197	mA*mA*mA*G*GCUG*CUGAU*GAC*A*CC*UGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
2681	CR011198	mA*mA*mA*GGCU*G*C*UGAU*G*ACAC*CU*GUUUUAGAGCUAUGCUGUUUUG
2682	CR011199	mA*mA*mA*G*GCUGCU*G*A*UGA*C*ACC*UGUUUUAGAGCUAUGCUGUUUUG
2683	CR011200	mA*mA*mA*GG*C*UG*CU*GAUG*AC*A*CCUGUUUUAGAGCUAUGCUGUUUUG
2684	CR011201	mA*mA*mA*G*G*C*UGCUGA*UGACA*C*CU*GUUUUAGAGCUAUGCUGUUUUG
2685	CR011202	mA*mA*mA*GG*CU*GC*UG*AU*GA*CACC*UGUUUUAGAGCUAUGCUGUUUUG
2686	CR011203	mA*mA*mA*GGCUGC*U*GA*UG*ACA*C*C*UGUUUUAGAGCUAUGCUGUUUUG
2687	CR011204	mA*mA*mA*G*GC*UG*CUG*AU*GA*CACCU*GUUUUAGAGCUAUGCUGUUUUG
2688	CR011205	mA*mA*mA*GGC*U*GCUGA*UGA*C*A*C*CUGUUUUAGAGCUAUGCUGUUUUG
2689	CR011206	mA*mA*mA*G*G*CU*GC*UG*AUG*AC*ACCUGUUUUAGAGCUAUGCUGUUUUG
2690	CR011207	mA*mA*mA*G*G*CUGC*U*G*AU*GACACC*U*GUUUUAGAGCUAUGCUGUUUUG
2691	CR011208	mA*mA*mA*GGC*U*G*CUGA*UG*AC*A*C*CUGUUUUAGAGCUAUGCUGUUUUG
2692	CR011209	mA*mA*mA*GGCU*GCU*GA*U*GA*C*AC*C*UGUUUUAGAGCUAUGCUGUUUUG
2693	CR011210	mA*mA*mA*G*G*C*UG*CUG*AUGA*CA*CCU*GUUUUAGAGCUAUGCUGUUUUG
2694	CR011211	mA*mA*mA*GGC*UG*C*U*GAU*G*AC*ACCU*GUUUUAGAGCUAUGCUGUUUUG
2695	CR011212	mA*mA*mA*GG*CU*GC*UG*AUG*ACA*C*C*UGUUUUAGAGCUAUGCUGUUUUG
2696	CR011213	mA*mA*mA*G*GC*U*GCUG*A*U*G*A*CACCUGUUUUAGAGCUAUGCUGUUUUG
2697	CR011214	mA*mA*mA*G*GCUG*C*U*GA*UGA*CA*C*CUGUUUUAGAGCUAUGCUGUUUUG
2698	CR011215	mA*mA*mA*GG*CU*G*CUG*A*UGAC*ACC*U*GUUUUAGAGCUAUGCUGUUUUG
2699	CR011216	mA*mA*mA*GGC*UG*C*UGA*UG*A*C*A*CCU*GUUUUAGAGCUAUGCUGUUUUG
2700	CR011217	mA*mA*mA*G*G*CU*G*CU*G*AU*GACAC*C*UGUUUUAGAGCUAUGCUGUUUUG
2701	CR011218	mA*mA*mA*GGC*U*GCUG*AU*G*A*C*AC*C*UGUUUUAGAGCUAUGCUGUUUUG
2702	CR011219	mA*mA*mA*G*G*CUGC*U*G*A*UGACA*C*CU*GUUUUAGAGCUAUGCUGUUUUG
2703	CR011220	mA*mA*mA*GG*C*UG*C*U*GAUG*A*C*AC*CU*GUUUUAGAGCUAUGCUGUUUUG
2704	CR011221	mA*mA*mA*G*GCU*GC*UG*A*U*GA*CA*CC*U*GUUUUAGAGCUAUGCUGUUUUG
2705	CR011222	mA*mA*mA*G*G*CUGCU*G*A*U*G*AC*A*C*CUGUUUUAGAGCUAUGCUGUUUUG
2706	CR011223	mA*mA*mA*GGC*U*G*CU*GA*U*GAC*A*C*C*UGUUUUAGAGCUAUGCUGUUUUG
2707	CR011224	mA*mA*mA*G*GC*UG*C*U*G*A*UGAC*A*C*C*UGUUUUAGAGCUAUGCUGUUUUG
2708	CR011225	mA*mA*mA*GG*C*U*G*CUG*AU*G*A*CA*C*CU*GUUUUAGAGCUAUGCUGUUUUG
2709	CR011226	mA*mA*mA*G*G*CU*GC*U*GA*U*G*A*CACC*U*GUUUUAGAGCUAUGCUGUUUUG

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2710	CR011227	mA*mA*mA*GGC*UG*C*UGA*U*G*A*C*A*CC*U*GUUUUAGAGCUAUGCUGUUUUG
2711	CR011228	mA*mA*mA*GGCU*G*C*UG*A*U*GA*C*A*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2712	CR011229	mA*mA*mA*G*G*C*UGCU*GA*U*G*A*CA*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2713	CR011230	mA*mA*mA*G*G*C*U*G*C*U*G*AUG*A*C*ACC*UGUUUUAGAGCUAUGCUGUUUUG
2714	CR011231	mA*mA*mA*G*G*C*U*G*CUG*A*U*G*AC*A*CCU*GUUUUAGAGCUAUGCUGUUUUG
2715	CR011232	mA*mA*mA*G*G*C*UG*CUG*A*UG*A*C*A*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2716	CR011233	mA*mA*mA*GG*C*U*G*C*U*G*A*U*G*A*C*ACCU*GUUUUAGAGCUAUGCUGUUUUG
2717	CR011234	mA*mA*mA*G*G*C*U*G*C*U*GA*U*GA*CA*C*C*UGUUUUAGAGCUAUGCUGUUUUG
2718	CR011235	mA*mA*mA*G*GC*U*G*AU*G*AC*A*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2719	CR011236	mA*mA*mA*G*G*CU*G*AU*G*A*C*A*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2720	CR011237	mA*mA*mA*G*GC*UGC*U*G*A*U*G*A*C*A*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2721	CR011238	mA*mA*mA*GG*C*U*G*C*U*GA*U*G*A*CA*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2722	CR011239	mA*mA*mA*G*G*C*U*G*C*UG*A*UG*A*C*AC*C*U*GUUUUAGAGCUAUGCUGUUUUG
2723	CR011240	mA*mA*mA*G*G*C*U*GC*U*G*A*U*G*A*C*A*CC*U*GUUUUAGAGCUAUGCUGUUUUG
2724	CR011241	mA*mA*mA*GG*C*U*G*C*U*G*A*U*G*A*C*A*C*CU*GUUUUAGAGCUAUGCUGUUUUG
2725	CR011242	mA*mA*mA*G*GC*U*G*C*U*G*A*U*GA*C*A*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2726	CR011243	mA*mA*mA*G*G*C*U*G*C*UG*AU*G*A*C*A*C*C*U*GUUUUAGAGCUAUGCUGUUUUG
2727	CR011244	AAAGG*CUGCUGAUGACA*CCUGUUUUAGAGCUAUGCUGUUUUG
2728	CR011245	AAAGGCUG*CUGAU*G*ACACCUGUUUUAGAGCUAUGCUGUUUUG
2729	CR011246	AAAG*GCU*GC*UGAUGACAC*CUGUUUUAGAGCUAUGCUGUUUUG
2730	CR011247	AAAG*GCUGCUG*AUG*AC*ACCU*GUUUUAGAGCUAUGCUGUUUUG
2731	CR011248	AAAG*GC*UG*C*UGA*UGA*CACCUGUUUUAGAGCUAUGCUGUUUUG
2732	CR011249	AAAG*GCUGCU*G*A*UGA*C*ACC*UGUUUUAGAGCUAUGCUGUUUUG
2733	CR011250	AAAGG*CU*GC*UG*AUG*ACA*C*C*UGUUUUAGAGCUAUGCUGUUUUG
2734	CR011251	AAAGGC*U*GCUG*AU*G*A*C*AC*C*UGUUUUAGAGCUAUGCUGUUUUG
2735	CR000689	ACACAAAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2736	CR009583	ACACAmAAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2737	CR009586	ACACAAAUmACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2738	CR009594	ACACAAAUACCAGUCCmAGCGGUUUUAGAGCUAUGCUGUUUUG

SEQ ID NO	Name	Sequence
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2741	CR009633	ACACAAAUfACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2742	CR009641	ACACAAAUACCAGUCCfAGCGGUUUUAGAGCUAUGCUGUUUUG
2743	CR010510	mA*mC*mA*CfAAAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2744	CR010511	mA*mC*mA*CAAAUACCAGUCCAGfCGGUUUUAGAGCUAUGCUGUUUUG
2745	CR010512	mA*mC*mA*CAAAUACCAGUCfCAGCGGUUUUAGAGCUAUGCUGUUUUG
2746	CR010513	mA*mC*mA*CAAfAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2747	CR010514	mA*mC*mA*CAAAUACCAGUCCAGCfGGUUUUAGAGCUAUGCUGUUUUG
2748	CR010515	mA*mC*mA*CAAAUACCAGUCCfAGCGGUUUUAGAGCUAUGCUGUUUUG
2749	CR010516	mA*mC*mA*CAAAUACCAfGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2750	CR010517	mA*mC*mA*CAAAUfACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2751	CR010518	mA*mC*mA*CAAAUACCAGfUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2752	CR010519	mA*mC*mA*CAAAUACfCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2753	CR010520	mA*mC*mA*fCAAAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2754	CR010521	mA*mC*mA*CAAAUACCAGUfCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2755	CR010522	mA*mC*mA*CAAAUACCfAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2756	CR010523	mA*mC*mA*CAAAUAfCCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2757	CR010524	mA*mC*mA*CAfAAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2758	CR010525	mA*mC*mA*CAAAfUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2759	CR010526	mA*mC*mA*CAAAUACCAGUCCAfGCGGUUUUAGAGCUAUGCUGUUUUG
2760	CR010527	mA*mC*mA*fCAAAUACCAGUCCAfGCGGUUUUAGAGCUAUGCUGUUUUG
2761	CR010528	mA*mC*mA*CAAAUACCfAGUCfCAGCGGUUUUAGAGCUAUGCUGUUUUG
2762	CR010529	mA*mC*mA*CAAfAUACCAGfUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2763	CR010530	mA*mC*mA*CAAAUACfCAfGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2764	CR010531	mA*mC*mA*CAAAUfACCAGUfCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2765	CR010532	mA*mC*mA*CAAAfUACCAGUCCAGfCGGUUUUAGAGCUAUGCUGUUUUG
2766	CR010533	mA*mC*mA*CfAAAUACCAGUCCfAGCGGUUUUAGAGCUAUGCUGUUUUG
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2770	CR010537	mA*mC*mA*CAAAUfACfCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2771	CR010538	mA*mC*mA*CAAfAUACCAGUCCAGCfGGUUUUAGAGCUAUGCUGUUUUG
2772	CR010539	mA*mC*mA*CAfAAUACCAGfUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2773	CR010540	mA*mC*mA*CfAAAUACCAGUfCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2774	CR010541	mA*mC*mA*CAAAfUACCAGUCfCAGCGGUUUUAGAGCUAUGCUGUUUUG
2775	CR010542	mA*mC*mA*fCAAAUAfCCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2776	CR010543	mA*mC*mA*fCAAAUACCAGUfCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2777	CR010544	mA*mC*mA*CAAAfUACCAGfUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2778	CR010545	mA*mC*mA*CAAAUfACCAGUCCAGfCGGUUUUAGAGCUAUGCUGUUUUG
2779	CR010546	mA*mC*mA*CAAAUACCAGUCfCAGCfGGUUUUAGAGCUAUGCUGUUUUG
2780	CR010547	mA*mC*mA*CAAAUACfCAGUCCAfGCGGUUUUAGAGCUAUGCUGUUUUG
2781	CR010548	mA*mC*mA*CAAAUACCAfGUCCfAGCGGUUUUAGAGCUAUGCUGUUUUG
2782	CR010549	mA*mC*mA*CAAAUAfCCfAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2783	CR010550	mA*mC*mA*CfAAfAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2784	CR010551	mA*mC*mA*CAfAAUACCAGUCCAGfCGGUUUUAGAGCUAUGCUGUUUUG
2785	CR010552	mA*mC*mA*CAAAUfACCAGUCfCAGCGGUUUUAGAGCUAUGCUGUUUUG
2786	CR010553	mA*mC*mA*CAAAfUACCfAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2787	CR010554	mA*mC*mA*CAAAUACCAGUCCAfGCfGGUUUUAGAGCUAUGCUGUUUUG
2788	CR010555	mA*mC*mA*CAAAUAfCCAGfUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2789	CR010556	mA*mC*mA*CAAAUACCAfGUfCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2790	CR010557	mA*mC*mA*CfAfAAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
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2792	CR010559	mA*mC*mA*CAAfAUACCAGUCCfAGCGGUUUUAGAGCUAUGCUGUUUUG
2793	CR010560	mA*mC*mA*CAAfAUACCAGUCCfAGCfGGUUUUAGAGCUAUGCUGUUUUG
2794	CR010561	mA*mC*mA*fCAAAUACCfAGUfCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2795	CR010562	mA*mC*mA*CAAAUACCAGUCfCAfGfCGGUUUUAGAGCUAUGCUGUUUUG
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2798	CR010565	mA*mC*mA*CfAAAUACfCAGUCfCAGCGGUUUUAGAGCUAUGCUGUUUUG
2799	CR010566	mA*mC*mA*CfAAAUACCAGfUCCAGfCGGUUUUAGAGCUAUGCUGUUUUG
2800	CR010567	mA*mC*mA*CAAAUACfCAGUCCAfGCfGGUUUUAGAGCUAUGCUGUUUUG
2801	CR010568	mA*mC*mA*CAAAUACCAfGUfCCfAGCGGUUUUAGAGCUAUGCUGUUUUG
2802	CR010569	mA*mC*mA*CAAfAUfACCfAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2803	CR010570	mA*mC*mA*fCAAAfUAfCCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2804	CR010571	mA*mC*mA*CAfAAUACCAfGUCCfAGCGGUUUUAGAGCUAUGCUGUUUUG
2805	CR010572	mA*mC*mA*CAAAUfAfCCAGUCCAGCfGGUUUUAGAGCUAUGCUGUUUUG
2806	CR010573	mA*mC*mA*CAAAfUACCfAGUCCAfGCGGUUUUAGAGCUAUGCUGUUUUG
2807	CR010574	mA*mC*mA*CAfAAUACCAGUfCCAGfCGGUUUUAGAGCUAUGCUGUUUUG
2808	CR010575	mA*mC*mA*CfAAfAUACCAGUCfCAGCGGUUUUAGAGCUAUGCUGUUUUG
2809	CR010576	mA*mC*mA*fCAAAUACfCAGfUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2810	CR010577	mA*mC*mA*CAAfAfUAfCCAGUCfCAGCGGUUUUAGAGCUAUGCUGUUUUG
2811	CR010578	mA*mC*mA*CAAAUACCAGfUCCfAfGfCGGUUUUAGAGCUAUGCUGUUUUG
2812	CR010579	mA*mC*mA*CAAAUfACfCAfGUCCAGCfGGUUUUAGAGCUAUGCUGUUUUG
2813	CR010580	mA*mC*mA*fCAfAAUACCfAGUfCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2814	CR010581	mA*mC*mA*CfAAAfUACCfAfGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2815	CR010582	mA*mC*mA*CAAAUAfCfCAGfUfCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2816	CR010583	mA*mC*mA*fCAAfAUfACCAGUCCAfGCGGUUUUAGAGCUAUGCUGUUUUG
2817	CR010584	mA*mC*mA*CfAAAUACCAGUCfCfAGCfGGUUUUAGAGCUAUGCUGUUUUG
2818	CR010585	mA*mC*mA*CAfAAUAfCCAGUCCAGfCfGGUUUUAGAGCUAUGCUGUUUUG
2819	CR010586	mA*mC*mA*CAAfAUACCAfGUfCfCAGCGGUUUUAGAGCUAUGCUGUUUUG
2820	CR010587	mA*mC*mA*CAAAfUfACCfAGUCCAGfCGGUUUUAGAGCUAUGCUGUUUUG
2821	CR010588	mA*mC*mA*CfAfAAUACCAGfUCCAfGCGGUUUUAGAGCUAUGCUGUUUUG
2822	CR010589	mA*mC*mA*fCAAAUACfCfAGUCCfAGCGGUUUUAGAGCUAUGCUGUUUUG
2823	CR010590	mA*mC*mA*CfAAAUfACCAGUfCCAfGCGGUUUUAGAGCUAUGCUGUUUUG
2824	CR010591	mA*mC*mA*CAAAfUACfCAGfUCCAGCfGGUUUUAGAGCUAUGCUGUUUUG
2825	CR010592	mA*mC*mA*fCAAAUACCAfGUCCfAGfCGGUUUUAGAGCUAUGCUGUUUUG

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2828	CR010595	ACACAAAUAfCCfAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2829	CR010596	ACAfCAAAUACfCAGfUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2830	CR010597	ACACAAfAUACCAGUCCfAGCfGGUUUUAGAGCUAUGCUGUUUUG
2831	CR010598	ACACfAAAUfACCAGUfCCAfGCGGUUUUAGAGCUAUGCUGUUUUG
2832	CR010599	ACAfCAAAUACCAfGUCCfAGfCGGUUUUAGAGCUAUGCUGUUUUG
2833	CR011067	mA*mC*mA*CmAAAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
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2835	CR011069	mA*mC*mA*CAAAUACCAGUCmCAGCGGUUUUAGAGCUAUGCUGUUUUG
2836	CR011070	mA*mC*mA*CAAmAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2837	CR011071	mA*mC*mA*CAAAUACCAGUCCAGCmGGUUUUAGAGCUAUGCUGUUUUG
2838	CR011072	mA*mC*mA*CAAAUACCAGUCCmAGCGGUUUUAGAGCUAUGCUGUUUUG
2839	CR011073	mA*mC*mA*CAAAUACCAmGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2840	CR011074	mA*mC*mA*CAAAUmACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2841	CR011075	mA*mC*mA*CAAAUACCAGmUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2842	CR011076	mA*mC*mA*CAAAUACmCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
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2844	CR011078	mA*mC*mA*CAAAUACCAGUmCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2845	CR011079	mA*mC*mA*CAAAUACCmAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2846	CR011080	mA*mC*mA*CAAAUAmCCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
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2853	CR011087	mA*mC*mA*CAAAUACmCAmGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
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2868	CR011102	mA*mC*mA*CAAAmUACCAGmUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2869	CR011103	mA*mC*mA*CAAAUmACCAGUCCAGmCGGUUUUAGAGCUAUGCUGUUUUG
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2874	CR011108	mA*mC*mA*CmAAmAUACCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
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2887	CR011121	mA*mC*mA*CAAAmUACCAmGmUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2888	CR011122	mA*mC*mA*CAmAAUmAmCCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2889	CR011123	mA*mC*mA*CmAAAUACmCAGUCmCAGCGGUUUUAGAGCUAUGCUGUUUUG
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2892	CR011126	mA*mC*mA*CAAAUACCAmGUmCCmAGCGGUUUUAGAGCUAUGCUGUUUUG
2893	CR011127	mA*mC*mA*CAAmAUmACCmAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2894	CR011128	mA*mC*mA*mCAAAmUAmCCAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2895	CR011129	mA*mC*mA*CAmAAUACCAmGUCCmAGCGGUUUUAGAGCUAUGCUGUUUUG
2896	CR011130	mA*mC*mA*CAAAUmAmCCAGUCCAGCmGGUUUUAGAGCUAUGCUGUUUUG
2897	CR011131	mA*mC*mA*CAAAmUACCmAGUCCAmGCGGUUUUAGAGCUAUGCUGUUUUG
2898	CR011132	mA*mC*mA*CAmAAUACCAGUmCCAGmCGGUUUUAGAGCUAUGCUGUUUUG
2899	CR011133	mA*mC*mA*CmAAmAUACCAGUCmCAGCGGUUUUAGAGCUAUGCUGUUUUG
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2903	CR011137	mA*mC*mA*CAAAUmACmCAmGUCCAGCmGGUUUUAGAGCUAUGCUGUUUUG
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2910	CR011144	mA*mC*mA*CAAmAUACCAmGUmCmCAGCGGUUUUAGAGCUAUGCUGUUUUG
2911	CR011145	mA*mC*mA*CAAAmUmACCmAGUCCAGmCGGUUUUAGAGCUAUGCUGUUUUG
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2915	CR011149	mA*mC*mA*CAAAmUACmCAGmUCCAGCmGGUUUUAGAGCUAUGCUGUUUUG
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2917	CR011151	mA*mC*mA*CAmAmAUAmCCAGUCmCAGCGGUUUUAGAGCUAUGCUGUUUUG
2918	CR011152	ACACAAAmUACCAGUCmCAGCGGUUUUAGAGCUAUGCUGUUUUG
2919	CR011153	ACACAAAUAmCCmAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2920	CR011154	ACAmCAAAUACmCAGmUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2921	CR011155	ACACAAmAUACCAGUCCmAGCmGGUUUUAGAGCUAUGCUGUUUUG
2922	CR011156	ACACmAAAUmACCAGUmCCAmGCGGUUUUAGAGCUAUGCUGUUUUG
2923	CR011157	ACAmCAAAUACCAmGUCCmAGmCGGUUUUAGAGCUAUGCUGUUUUG
2924	CR011628	mA*mC*mA*C*AAAUACCAGUCCAG*CGGUUUUAGAGCUAUGCUGUUUUG
2925	CR011629	mA*mC*mA*CAAAUACCA*GUCC*AGCGGUUUUAGAGCUAUGCUGUUUUG
2926	CR011630	mA*mC*mA*CAAA*UACCAGU*CCAGCGGUUUUAGAGCUAUGCUGUUUUG
2927	CR011631	mA*mC*mA*CAAAUACC*AG*UCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2928	CR011632	mA*mC*mA*CAAAUA*CCAGUC*CAGCGGUUUUAGAGCUAUGCUGUUUUG
2929	CR011633	mA*mC*mA*CAAAU*ACCAGUCCAGC*GGUUUUAGAGCUAUGCUGUUUUG
2930	CR011634	mA*mC*mA*CA*AAUACCAGUCCA*GCGGUUUUAGAGCUAUGCUGUUUUG
2931	CR011635	mA*mC*mA*CAAAUAC*CAGUCCAGCG*GUUUUAGAGCUAUGCUGUUUUG
2932	CR011636	mA*mC*mA*CAAA*UACCAGUCCA*GCG*GUUUUAGAGCUAUGCUGUUUUG
2933	CR011637	mA*mC*mA*C*AAAUACCA*GUC*CAGCGGUUUUAGAGCUAUGCUGUUUUG
2934	CR011638	mA*mC*mA*CAAAUACCAGUCC*AG*C*GGUUUUAGAGCUAUGCUGUUUUG
2935	CR011639	mA*mC*mA*CAAAU*ACCAG*U*CCAGCGGUUUUAGAGCUAUGCUGUUUUG
2936	CR011640	mA*mC*mA*CAA*AUA*C*CAGUCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2937	CR011641	mA*mC*mA*CA*AAUACC*AGUCC*AGCGGUUUUAGAGCUAUGCUGUUUUG
2938	CR011642	mA*mC*mA*CA*AAUACCAGU*CCAGC*GGUUUUAGAGCUAUGCUGUUUUG
2939	CR011643	mA*mC*mA*CAAAUACC*AGUCCAG*CG*GUUUUAGAGCUAUGCUGUUUUG
2940	CR011644	mA*mC*mA*CAAA*U*AC*CAGUCC*AGCGGUUUUAGAGCUAUGCUGUUUUG
2941	CR011645	mA*mC*mA*CAAAUACCAGU*CCA*G*C*GGUUUUAGAGCUAUGCUGUUUUG

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2942	CR011646	mA*mC*mA*CAAAUA*CC*AG*UCCAGCG*GUUUUAGAGCUAUGCUGUUUUG
2943	CR011647	mA*mC*mA*C*AA*AUACCA*GUC*CAGCGGUUUUAGAGCUAUGCUGUUUUG
2944	CR011648	mA*mC*mA*CA*AAU*ACCA*G*UCCAGCGGUUUUAGAGCUAUGCUGUUUUG
2945	CR011649	mA*mC*mA*CAAAUAC*C*AGU*C*CAGCGGUUUUAGAGCUAUGCUGUUUUG
2946	CR011650	mA*mC*mA*C*AAA*UA*CCAGUCCAG*CGGUUUUAGAGCUAUGCUGUUUUG
2947	CR011651	mA*mC*mA*CA*AAUACCAGUCC*A*GCG*GUUUUAGAGCUAUGCUGUUUUG
2948	CR011652	mA*mC*mA*CAAA*U*AC*CAGUCCA*G*CGGUUUUAGAGCUAUGCUGUUUUG
2949	CR011653	mA*mC*mA*CAAAUA*CCA*G*UC*CAGC*GGUUUUAGAGCUAUGCUGUUUUG
2950	CR011654	mA*mC*mA*C*AAAUACC*AGU*CC*AGCG*GUUUUAGAGCUAUGCUGUUUUG
2951	CR011655	mA*mC*mA*CA*A*AUACC*AGUC*CA*GCGGUUUUAGAGCUAUGCUGUUUUG
2952	CR011656	mA*mC*mA*C*AA*AUAC*CAG*UCC*AGCGGUUUUAGAGCUAUGCUGUUUUG
2953	CR011657	mA*mC*mA*CA*AAUACCAGU*CCAG*C*G*GUUUUAGAGCUAUGCUGUUUUG
2954	CR011658	mA*mC*mA*CAAA*U*A*CCA*GUCC*AGCGGUUUUAGAGCUAUGCUGUUUUG
2955	CR011659	mA*mC*mA*CAA*A*UA*CCAG*UCCAGCG*GUUUUAGAGCUAUGCUGUUUUG
2956	CR011660	mA*mC*mA*CAA*A*U*ACCAG*UCCA*G*CGGUUUUAGAGCUAUGCUGUUUUG
2957	CR011661	mA*mC*mA*CA*AAUA*C*CA*GU*CC*AGCGGUUUUAGAGCUAUGCUGUUUUG
2958	CR011662	mA*mC*mA*C*AAAUACC*AGU*C*CAGC*G*GUUUUAGAGCUAUGCUGUUUUG
2959	CR011663	mA*mC*mA*C*AA*AU*A*CCA*GUC*CAGCGGUUUUAGAGCUAUGCUGUUUUG
2960	CR011664	mA*mC*mA*CA*AAUAC*CAGUCCA*G*C*G*GUUUUAGAGCUAUGCUGUUUUG
2961	CR011665	mA*mC*mA*CAAA*UA*CC*AG*UCC*AGCG*GUUUUAGAGCUAUGCUGUUUUG
2962	CR011666	mA*mC*mA*CA*AA*UACC*A*GUC*CAG*CGGUUUUAGAGCUAUGCUGUUUUG
2963	CR011667	mA*mC*mA*C*AAAU*ACCAG*UCC*A*GC*GGUUUUAGAGCUAUGCUGUUUUG
2964	CR011668	mA*mC*mA*CAAA*U*A*CCAG*U*CCAG*CG*GUUUUAGAGCUAUGCUGUUUUG
2965	CR011669	mA*mC*mA*C*AAAUAC*C*A*GUC*C*AGC*GGUUUUAGAGCUAUGCUGUUUUG
2966	CR011670	mA*mC*mA*CA*A*AU*AC*CAGU*CC*A*GCGGUUUUAGAGCUAUGCUGUUUUG
2967	CR011671	mA*mC*mA*C*A*A*AUACCA*GUCCA*G*CG*GUUUUAGAGCUAUGCUGUUUUG
2968	CR011672	mA*mC*mA*CA*AA*UA*CC*AG*UC*CAGC*GGUUUUAGAGCUAUGCUGUUUUG
2969	CR011673	mA*mC*mA*CAAAUA*C*CA*GU*CCA*G*C*GGUUUUAGAGCUAUGCUGUUUUG
2970	CR011674	mA*mC*mA*C*AA*AU*ACC*AG*UC*CAGCG*GUUUUAGAGCUAUGCUGUUUUG

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2971	CR011675	mA*mC*mA*CAA*A*UACCA*GUC*C*A*G*CGGUUUUAGAGCUAUGCUGUUUUG
2972	CR011676	mA*mC*mA*C*A*AA*UA*CC*AGU*CC*AGCGGUUUUAGAGCUAUGCUGUUUUG
2973	CR011677	mA*mC*mA*C*A*AAUA*C*C*AG*UCCAGC*G*GUUUUAGAGCUAUGCUGUUUUG
2974	CR011678	mA*mC*mA*CAA*A*U*ACCA*GU*CC*A*G*CGGUUUUAGAGCUAUGCUGUUUUG
2975	CR011679	mA*mC*mA*CAAA*UAC*CA*G*UC*C*AG*C*GGUUUUAGAGCUAUGCUGUUUUG
2976	CR011680	mA*mC*mA*C*A*A*AU*ACC*AGUC*CA*GCG*GUUUUAGAGCUAUGCUGUUUUG
2977	CR011681	mA*mC*mA*CAA*AU*A*C*CAG*U*CC*AGCG*GUUUUAGAGCUAUGCUGUUUUG
2978	CR011682	mA*mC*mA*CA*AA*UA*CC*AGU*CCA*G*C*GGUUUUAGAGCUAUGCUGUUUUG
2979	CR011683	mA*mC*mA*C*AA*A*UACC*A*G*U*C*CAGCGGUUUUAGAGCUAUGCUGUUUUG
2980	CR011684	mA*mC*mA*C*AAAU*A*C*CA*GUC*CA*G*CGGUUUUAGAGCUAUGCUGUUUUG
2981	CR011685	mA*mC*mA*CA*AA*U*ACC*A*GUCC*AGC*G*GUUUUAGAGCUAUGCUGUUUUG
2982	CR011686	mA*mC*mA*CAA*AU*A*CCA*GU*C*C*A*GCG*GUUUUAGAGCUAUGCUGUUUUG
2983	CR011687	mA*mC*mA*C*A*AA*U*AC*C*AG*UCCAG*C*GGUUUUAGAGCUAUGCUGUUUUG
2984	CR011688	mA*mC*mA*CAA*A*UACC*AG*U*C*C*AG*C*GGUUUUAGAGCUAUGCUGUUUUG
2985	CR011689	mA*mC*mA*C*A*AAUA*C*C*A*GUCCA*G*CG*GUUUUAGAGCUAUGCUGUUUUG
2986	CR011690	mA*mC*mA*CA*A*AU*A*C*CAGU*C*C*AG*CG*GUUUUAGAGCUAUGCUGUUUUG
2987	CR011691	mA*mC*mA*C*AAA*UA*CC*A*G*UC*CA*GC*G*GUUUUAGAGCUAUGCUGUUUUG
2988	CR011692	mA*mC*mA*C*A*AAUAC*C*A*G*U*CC*A*G*CGGUUUUAGAGCUAUGCUGUUUUG
2989	CR011693	mA*mC*mA*CAA*A*U*AC*CA*G*UCC*A*G*C*GGUUUUAGAGCUAUGCUGUUUUG
2990	CR011694	mA*mC*mA*C*AA*AU*A*C*C*A*GUCC*A*G*C*GGUUUUAGAGCUAUGCUGUUUUG
2991	CR011695	mA*mC*mA*CA*A*A*U*ACC*AG*U*C*CA*G*CG*GUUUUAGAGCUAUGCUGUUUUG
2992	CR011696	mA*mC*mA*C*A*AA*UA*C*CA*G*U*C*CAGC*G*GUUUUAGAGCUAUGCUGUUUUG
2993	CR011697	mA*mC*mA*CAA*AU*A*CCA*G*U*C*C*A*GC*G*GUUUUAGAGCUAUGCUGUUUUG
2994	CR011698	mA*mC*mA*CAAA*U*A*CC*A*G*UC*C*A*G*C*G*GUUUUAGAGCUAUGCUGUUUUG
2995	CR011699	mA*mC*mA*C*A*A*AUAC*CA*G*U*C*CA*G*C*G*GUUUUAGAGCUAUGCUGUUUUG
2996	CR011700	mA*mC*mA*C*A*A*A*U*A*C*C*AGU*C*C*AGC*GGUUUUAGAGCUAUGCUGUUUUG
2997	CR011701	mA*mC*mA*C*A*A*A*U*ACC*A*G*U*CC*A*GCG*GUUUUAGAGCUAUGCUGUUUUG
2998	CR011702	mA*mC*mA*C*A*AU*ACC*A*GU*C*C*A*G*C*G*GUUUUAGAGCUAUGCUGUUUUG
2999	CR011703	mA*mC*mA*CA*A*A*U*A*C*C*A*G*U*C*C*AGCG*GUUUUAGAGCUAUGCUGUUUUG

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3000	CR011704	mA*mC*mA*C*A*A*A*U*A*C*CA*G*UC*CA*G*C*GGUUUUAGAGCUAUGCUGUUUUG
3001	CR011705	mA*mC*mA*C*AA*A*UA*C*C*AG*U*CC*A*G*C*G*GUUUUAGAGCUAUGCUGUUUUG
3002	CR011706	mA*mC*mA*C*A*AA*U*AC*C*AG*U*C*C*A*G*C*G*GUUUUAGAGCUAUGCUGUUUUG
3003	CR011707	mA*mC*mA*C*AA*AUA*C*C*A*G*U*C*C*A*G*C*G*GUUUUAGAGCUAUGCUGUUUUG
3004	CR011708	mA*mC*mA*CA*A*A*U*A*C*C*CA*G*U*C*CA*G*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
3005	CR011709	mA*mC*mA*C*A*A*A*U*A*CC*C*A*GU*C*C*AG*C*G*GUUUUAGAGCUAUGCUGUUUUG
3006	CR011710	mA*mC*mA*C*A*A*A*UA*C*C*C*A*G*U*C*C*A*GC*G*GUUUUAGAGCUAUGCUGUUUUG
3007	CR011711	mA*mC*mA*CA*A*A*U*A*C*C*C*A*G*U*C*C*A*A*G*C*CG*GUUUUAGAGCUAUGCUGUUUUG
3008	CR011712	mA*mC*mA*C*AA*A*U*A*C*C*C*A*G*UC*C*A*G*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
3009	CR011713	mA*mC*mA*C*A*A*A*U*A*CC*AG*U*C*C*A*G*C*C*G*GUUUUAGAGCUAUGCUGUUUUG
3010	CR011714	ACACA*AAUACCAGUCCA*GCGGUUUUAGAGCUAUGCUGUUUUG
3011	CR011715	ACACAAAU*ACCAG*U*CCAGCGGUUUUAGAGCUAUGCUGUUUUG
3012	CR011716	ACAC*AAA*UA*CCAGUCCAG*CGGUUUUAGAGCUAUGCUGUUUUG
3013	CR011717	ACAC*AAAUACC*AGU*CC*AGCG*GUUUUAGAGCUAUGCUGUUUUG
3014	CR011718	ACAC*AA*AU*A*CCA*GUC*CAGCGGUUUUAGAGCUAUGCUGUUUUG
3015	CR011719	ACAC*AAAUAC*C*A*GUC*C*AGC*GGUUUUAGAGCUAUGCUGUUUUG
3016	CR011720	ACACA*AA*UA*CC*AGU*CCA*G*C*GGUUUUAGAGCUAUGCUGUUUUG
3017	CR011721	ACACAA*A*UACC*AG*U*C*C*AG*C*GGUUUUAGAGCUAUGCUGUUUUG
3018	G014462	mA*mC*mA*mCmAA*A*fU*fA*fC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3019	G014463	mA*mC*mA*mCfAA*A*fU*fA*fC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3020	G014464	mA*mC*mA*mCA*A*A*fU*fA*fC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3021	G014465	mA*mC*mA*mCdAA*A*fU*fA*fC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU

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3022	G014466	mA*mC*mA*mCAA*A*fU*fA*fC*fCmAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3023	G014467	mA*mC*mA*mCAA*A*fU*fA*fC*fCfAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3024	G014468	mA*mC*mA*mCAA*A*fU*fA*fC*fCA*fGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3025	G014469	mA*mC*mA*mCAA*A*fU*fA*fC*fCdAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3026	G014470	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUmCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3027	G014471	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUfCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3028	G014472	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUC*C*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3029	G014473	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUdCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3030	G014474	mA*mC*mA*mCAA*A*fUfA*fC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3031	G014475	mA*mC*mA*mCAA*A*fU*fAfC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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3032	G014476	mA*mC*mA*mCAA*A*fU*fA*fCfCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3033	G014477	mA*mC*mA*mCAA*A*fU*fAfCfCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3034	G014478	mA*mC*mA*mCAA*A*fU*fAfCfCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3035	G014479	mA*mC*mA*mCAA*A*fUfA*fCfCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3036	G014480	mA*mC*mA*mCAA*A*fUfAfCfCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3037	G014481	mA*mC*mA*mCAfAA*fU*fA*fC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3038	G014482	mA*mC*mA*mCAA*fAfU*fA*fC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3039	G014483	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUCfCfAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3040	G014484	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUCC*fAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3041	G014485	mA*mC*mA*mCAfAfAfU*fA*fC*fCAfGfUCC*fAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
3042	G014486	mA*mC*mA*mCAfAfAfU*fA*fC*fCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3043	G014487	mA*mC*mA*mCAfAA*fU*fA*fC*fCAfGfUCC*fAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3044	G014488	mA*mC*mA*mCAA*fAfU*fA*fC*fCAfGfUCC*fAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3045	G014489	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCfCfAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCmA mAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3046	G014490	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCfCfAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCmA mAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3047	G014491	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCfCfAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCmAmAG UfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmG mGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3048	G014492	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCfCfAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCmAmA GUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUm GmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3049	G014493	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCmA mAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3050	G014494	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCC*fAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3051	G014495	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCmAmAG UfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmG mGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
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3053	G014497	mA*mC*mA*fCfAfAfAfUfAfCfCfAfGfUCC*fAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3054	G014498	fA*fC*fA*fCfAfAfAfUfAfCfCfAfGfUCC*fAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAm AGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmAmGmU mGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3055	G014499	mA*mC*mA*mA*fCAfGfUCC*fAfGfCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3056	G014500	mA*mC*mA*mC*mA*mA*U*mAC*mCAmGmUCC*AGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAmGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
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3058	G014502	mA*mC*mA*mCAA*A*fUAfCfCAfGfUCC*fAfGCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmA mAGUfUmAfAmAfAmUAmAmGmGmCmUmAmGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
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3061	G014505	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUmCmCfAfGmCGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmA mGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAmGUmCmCGUfUAmUmCAmAmCmUmUmGmGmAmAmAm AmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
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3063	G014507	mA*mC*mA*mCmAA*A*fU*fA*fC*fCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3064	G014508	mA*mC*mA*mCfAA*A*fU*fA*fC*fCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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3069	G014513	mA*mC*mA*mCAA*A*fU*fA*fC*fCA*fGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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3071	G014515	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUmCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
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3073	G014517	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUC*C*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3074	G014518	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUdCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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3076	G014520	mA*mC*mA*mCAA*A*fU*fAfC*fCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
3077	G014521	mA*mC*mA*mCAA*A*fU*fA*fCfCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
3078	G014522	mA*mC*mA*mCAA*A*fUfAfC*fCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
3079	G014523	mA*mC*mA*mCAA*A*fU*fAfCfCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
3080	G014524	mA*mC*mA*mCAA*A*fUfA*fCfCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
3081	G014525	mA*mC*mA*mCAA*A*fUfAfCfCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU

SEQ ID NO	Name	Sequence
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3091	G014535	mA*mC*mA*mCAfAfAfUfAfCfCfAfGfUCfCfAfGfCAmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmA mAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmGmCmU*mU*mU*mU

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3093	G014537	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCfCfAfGfCAmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmAG UfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUmG mGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3094	G014538	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmG mUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3095	G014539	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCC*fAfGfCAmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmG mUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3096	G014540	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmA GUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUm GmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3097	G014541	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCC*fAfGfCAmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmA GUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUm GmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3098	G014542	mA*mC*mA*fCfAfAfAfUfAfCfCfAfGfUCC*fAfGfCAmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmG mUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3099	G014543	fA*fC*fA*fCfAfAfAfUfAfCfCfAfGfUCC*fAfGfCAmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAm AGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmU mGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
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3101	G014545	mA*mC*mA*mCAA*A*U*mAC*mCAmGmUCC*AGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU

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3103	G014547	mA*mC*mA*mCAA*A*fUAfCfCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmGmCmU*mU*mU*mU
3104	G014548	mA*mC*mA*mCAA*A*fUfACfCAfGfUCC*fAfGC*AmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmGmCmU*mU*mU*mU
3105	G014549	fA*fC*fA*fCfAfAfAfUfAfCfCfAfGfCAmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAm AGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmU mGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmGmCmU*mU*mU*mU
3106	G014550	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUmCmCfAfGmCAmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmA mGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm AmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmGmCmU*mU*mU*mU
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3110	G014556	mU*mG*mU*mUG*G*A*fC*fU*fG*fGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3111	G014557	mU*mG*mU*mUdGG*A*fC*fU*fG*fGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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3113	G014559	mU*mG*mU*mUGG*A*fC*fU*fG*fGfUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAmGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3114	G014560	mU*mG*mU*mUGG*A*fC*fU*fG*fGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAmGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
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3116	G014562	mU*mG*mU*mUGG*A*fC*fU*fG*fGfUfGfUfGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAmGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
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3121	G014567	mU*mG*mU*mUGG*A*fC*fUfG*fGfUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAmGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU

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3123	G014569	mU*mG*mU*mUGG*A*fC*fUfGfGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3124	G014570	mU*mG*mU*mUGG*A*fC*fUfGfGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3125	G014571	mU*mG*mU*mUGG*A*fCfUfGfGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3126	G014572	mU*mG*mU*mUGfGA*fC*fU*fG*fGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3127	G014573	mU*mG*mU*mUGG*fAfC*fU*fG*fGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3128	G014574	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUGfCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3129	G014575	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUGCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3130	G014576	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUGCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3131	G014577	mU*mG*mU*mUGfGfAfC*fU*fG*fGUfGfUGCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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3133	G014579	mU*mG*mU*mUGfGA*fC*fU*fG*fGUfGfUGCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3134	G014580	mU*mG*mU*mUGG*fAfC*fU*fG*fGUfGfUGCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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3137	G014583	fU*fG*fU*fUGfGfAfCfUfGfGUfGfUGfCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAmA GUfUmAfAmAfAmUAmAmGmGmCmUmAmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmUm GmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3138	G014584	fU*fG*fU*fUGfGfAfCfUfGfGUfGfUGfCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AGUfUmAfAmAfAmUAmAmGmGmCmUmAmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmU mGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
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3143	G014589	mU*mG*mU*fUfGfGfAfCfUfGfGfUfGfUGCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3144	G014590	fU*fG*fU*fUfGfGfAfCfUfGfGfUfGfUGCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmAm AGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmAmGmU mGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3145	G014591	mU*mG*mU*mUGG*A*fC*fUfG*fGUfGfUGCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3146	G014592	mU*mG*mU*mUGG*A*C*mUG*mGUmGmUGCCAGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3147	G014593	mU*mG*mU*mUGG*A*fCUGfGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmA mAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3148	G014594	mU*mG*mU*mUGG*A*fCUfGfGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3149	G014595	mU*mG*mU*mUGG*A*fCfUGfGUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3150	G014596	fU*fG*fU*fUfGfGfAfCfUfGfGfUfGfUfGfCfCfAfGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmA mAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU
3151	G014597	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUmGmCfCfAmGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUm AmGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmAmGmUmGmGmCmAmCmCmGmAmGmUmUmCmGmGmUmGmCmU*mU*mU*mU

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3152	G014598	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUfGfCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3153	G014644	mA*mC*mA*mCmAA*A*fU*fA*fC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3154	G014645	mA*mC*mA*mCfAA*A*fU*fA*fC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3155	G014646	mA*mC*mA*mCA*A*A*fU*fA*fC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3156	G014647	mA*mC*mA*mCdAA*A*fU*fA*fC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3157	G014648	mA*mC*mA*mCAA*A*fU*fA*fC*fCmAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3158	G014649	mA*mC*mA*mCAA*A*fU*fA*fC*fCfAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3159	G014650	mA*mC*mA*mCAA*A*fU*fA*fC*fCA*fGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3160	G014651	mA*mC*mA*mCAA*A*fU*fA*fC*fCdAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3161	G014652	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUmCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3162	G014653	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUfCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3163	G014654	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUC*C*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3164	G014655	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUdCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3165	G014656	mA*mC*mA*mCAA*A*fUfA*fC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3166	G014657	mA*mC*mA*mCAA*A*fU*fAfC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3167	G014658	mA*mC*mA*mCAA*A*fU*fA*fCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3168	G014659	mA*mC*mA*mCAA*A*fUfAfC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3169	G014660	mA*mC*mA*mCAA*A*fU*fAfCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3170	G014661	mA*mC*mA*mCAA*A*fUfA*fCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3171	G014662	mA*mC*mA*mCAA*A*fUfAfCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3172	G014663	mA*mC*mA*mCAfAA*fU*fA*fC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3173	G014664	mA*mC*mA*mCAA*fAfU*fA*fC*fCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3174	G014665	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUCfCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3175	G014666	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3176	G014667	mA*mC*mA*mCAfAfAfU*fA*fC*fCAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3177	G014668	mA*mC*mA*mCAfAfAfU*fA*fC*fCAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3178	G014669	mA*mC*mA*mCAfAA*fU*fA*fC*fCAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3179	G014670	mA*mC*mA*mCAA*fAfU*fA*fC*fCAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3180	G014671	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCfCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3181	G014672	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCfCfAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3182	G014673	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCfCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3183	G014674	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCfCfAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3184	G014675	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3185	G014676	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3186	G014677	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAA UAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3187	G014678	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3188	G014679	mA*mC*mA*fCfAfAfAfUfAfCfCfAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3189	G014680	fA*fC*fA*fCfAfAfAfUfAfCfCfAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3190	G014681	mA*mC*mA*mCAA*A*fU*fAfC*fCAfGfUCC*fAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3191	G014682	mA*mC*mA*mCAA*A*U*mAC*mCAmGmUCC*AGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3192	G014683	mA*mC*mA*mCAA*A*fUAfCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3193	G014684	mA*mC*mA*mCAA*A*fUAfCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3194	G014685	mA*mC*mA*mCAA*A*fUfAfCfCAfGfUCC*fAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3195	G014686	fA*fC*fA*fCfAfAfUfAfCfCfAfGfUCfCfAfGfCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3196	G014687	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUmCmCfAfGmCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGm CAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3197	G014688	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUfCfCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3198	G014689	mA*mC*mA*mCmAA*A*fU*fA*fC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3199	G014690	mA*mC*mA*mCfAA*A*fU*fA*fC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3200	G014691	mA*mC*mA*mCA*A*A*fU*fA*fC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3201	G014692	mA*mC*mA*mCdAA*A*fU*fA*fC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3202	G014693	mA*mC*mA*mCAA*A*fU*fA*fC*fCmAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3203	G014694	mA*mC*mA*mCAA*A*fU*fA*fC*fCfAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3204	G014695	mA*mC*mA*mCAA*A*fU*fA*fC*fCA*fGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3205	G014696	mA*mC*mA*mCAA*A*fU*fA*fC*fCdAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3206	G014697	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUmCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3207	G014698	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUfCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3208	G014699	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUC*C*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3209	G014700	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUdCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3210	G014701	mA*mC*mA*mCAA*A*fUfA*fC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3211	G014702	mA*mC*mA*mCAA*A*fU*fAfC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3212	G014703	mA*mC*mA*mCAA*A*fU*fA*fCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3213	G014704	mA*mC*mA*mCAA*A*fUfAfC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3214	G014705	mA*mC*mA*mCAA*A*fU*fAfCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3215	G014706	mA*mC*mA*mCAA*A*fUfA*fCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3216	G014707	mA*mC*mA*mCAA*A*fUfAfCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3217	G014708	mA*mC*mA*mCAfAA*fU*fA*fC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3218	G014709	mA*mC*mA*mCAA*fAfU*fA*fC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3219	G014710	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUCfCfAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3220	G014711	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3221	G014712	mA*mC*mA*mCAfAfAfU*fA*fC*fCAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3222	G014713	mA*mC*mA*mCAfAfAfU*fA*fC*fCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3223	G014714	mA*mC*mA*mCAfAA*fU*fA*fC*fCAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3224	G014715	mA*mC*mA*mCAA*fAfU*fA*fC*fCAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3225	G014716	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCfCfAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3226	G014717	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCfCfAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3227	G014718	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCfCfAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3228	G014719	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCfCfAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3229	G014720	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3230	G014721	mA*mC*mA*mCAfAfAfUfAfCfCAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3231	G014722	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmCmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3232	G014723	fA*fC*fA*fCAfAfAfUfAfCfCAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3233	G014724	mA*mC*mA*fCfAfAfAfUfAfCfCfAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3234	G014725	fA*fC*fA*fCfAfAfAfUfAfCfCfAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3235	G014726	mA*mC*mA*mCAA*A*fU*fAfC*fCAfGfUCC*fAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3236	G014727	mA*mC*mA*mCAA*A*U*mAC*mCAmGmUCC*AGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3237	G014728	mA*mC*mA*mCAA*A*fUAfCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3238	G014729	mA*mC*mA*mCAA*A*fUAfCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3239	G014730	mA*mC*mA*mCAA*A*fUfAfCfCAfGfUCC*fAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3240	G014731	fA*fC*fA*fCfAfAfUfAfCfCfAfGfUfCfCfAfGfCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3241	G014732	mA*mC*mA*mCAA*A*fU*fA*fC*fCAfGfUmCmCfAfGmCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGm CAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3242	G014733	mA*mC*mA*mCAA*A*fU*fA*fC*fCfAfGfUfCfCfAfGC*AGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3243	G014734	mU*mG*mU*mUmGG*A*fC*fU*fG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3244	G014735	mU*mG*mU*mUfGG*A*fC*fU*fG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3245	G014736	mU*mG*mU*mUG*G*A*fC*fU*fG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3246	G014737	mU*mG*mU*mUdGG*A*fC*fU*fG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3247	G014738	mU*mG*mU*mUGG*A*fC*fU*fG*fGmUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3248	G014739	mU*mG*mU*mUGG*A*fC*fU*fG*fGfUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3249	G014740	mU*mG*mU*mUGG*A*fC*fU*fG*fGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3250	G014741	mU*mG*mU*mUGG*A*fC*fU*fG*fGdUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3251	G014742	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUmGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3252	G014743	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUfGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3253	G014744	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUG*CfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3254	G014745	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUdGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3255	G014746	mU*mG*mU*mUGG*A*fCfU*fG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3256	G014747	mU*mG*mU*mUGG*A*fC*fUfG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3257	G014748	mU*mG*mU*mUGG*A*fC*fU*fGfGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3258	G014749	mU*mG*mU*mUGG*A*fCfUfG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3259	G014750	mU*mG*mU*mUGG*A*fC*fUfGfGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3260	G014751	mU*mG*mU*mUGG*A*fCfU*fGfGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3261	G014752	mU*mG*mU*mUGG*A*fCfUfGfGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3262	G014753	mU*mG*mU*mUGfGA*fC*fU*fG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3263	G014754	mU*mG*mU*mUGG*fAfC*fU*fG*fGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3264	G014755	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUGfCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3265	G014756	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3266	G014757	mU*mG*mU*mUGfGfAfC*fU*fG*fGUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3267	G014758	mU*mG*mU*mUGfGfAfC*fU*fG*fGUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3268	G014759	mU*mG*mU*mUGfGA*fC*fU*fG*fGUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3269	G014760	mU*mG*mU*mUGG*fAfC*fU*fG*fGUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3270	G014761	mU*mG*mU*mUGfGfAfCfUfGfGUfGfUGfCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3271	G014762	mU*mG*mU*mUGfGfAfCfUfGfGUfGfUGfCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3272	G014763	fU*fG*fU*fUGfGfAfCfUfGfGfUfGfUGfCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3273	G014764	fU*fG*fU*fUGfGfAfCfUfGfGfUfGfCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3274	G014765	mU*mG*mU*mUGfGfAfCfUfGfGfUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3275	G014766	mU*mG*mU*mUGfGfAfCfUfGfGfUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3276	G014767	fU*fG*fU*fUGfGfAfCfUfGfGfUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3277	G014768	fU*fG*fU*fUGfGfAfCfUfGfGfUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAA AUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3278	G014769	mU*mG*mU*fUfGfGfAfCfUfGfGfUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3279	G014770	fU*fG*fU*fUfGfGfAfCfUfGfGfUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3280	G014771	mU*mG*mU*mUGG*A*fC*fUfG*fGUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3281	G014772	mU*mG*mU*mUGG*A*C*mUG*mGUmGmUGCCAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3282	G014773	mU*mG*mU*mUGG*A*fCUGfGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3283	G014774	mU*mG*mU*mUGG*A*fCUfGfGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3284	G014775	mU*mG*mU*mUGG*A*fCfUGfGUfGfUGCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3285	G014776	fU*fG*fU*fUfGfGfAfCfUfGfGfUfGfUGCfCfAfGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUA AAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3286	G014777	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUmGmCfCfAmGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmG mCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

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3287	G014778	mU*mG*mU*mUGG*A*fC*fU*fG*fGUfGfUfGfCfCfAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3288	G000407	mA*mG*mC*CAGCUCCAGCUGACCACGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
3289	G000408	mG*mC*mU*GAGGAACAGGCCAUUGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
3290	G000409	mA*mC*mU*CACGAUGAAAUCCUGGAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
3291	G000412	mG*mA*mU*CUGUUUCUUGGCCUCUUGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
3292	G000413	mG*mA*mA*GGCGAACUCAGCCAGGUGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
3293	G000414	mC*mA*mA*CCUCACGGAGAUUCCGGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmG mUmGmCmU*mU*mU*mU
3294	G000415	mU*mG*mU*UGGACUGGUGUGCCAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUA AGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGm GmUmGmCmU*mU*mU*mU
3295	G013954	mA*mG*mC*mCAG*C*fU*fC*fC*fAGfCfUGAfCfCACmGUUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3296	G013955	mA*mC*mU*mCAC*G*fA*fU*fG*fAAfAfUCCfUfGGAmGUUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU
3297	G013956	mG*mA*mU*mCUG*U*fU*fU*fC*fUUfGfGCCfUfCUUmGUUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU

SEQ ID NO	Name	Sequence
3298	G013957	mC*mA*mA*mCCU*C*fA*fC*fG*fGAfGfAUUfCfCGGmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3299	G013958	mU*mG*mU*mUGG*A*fC*fU*fG*fGfUfGfUGCfCfAGCmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3300	G013959	mA*mG*mC*CAGCUCCAGCUGACCACGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3301	G013960	mA*mC*mU*CACGAUGAAAUCCUGGAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3302	G013961	mG*mA*mU*CUGUUUCUUGGCCUCUUGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUAAAAUA AGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3303	G013962	mC*mA*mA*CCUCACGGAGAUUCCGGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3304	G013963	mU*mG*mU*UGGACUGGUGUGCCAGCGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGUUAAAAUA AGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3305	G012452	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGmCACCGAGUCGG*mU*mG*mC
3306	G012453	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGU UAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAACUUGGCACCGAGUCGG*mU*mG*mC
3307	G012454	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGU UAAAAUAAGGCmUAGUCCGUUAUmCAACUUGGCACCGAGUCGG*mU*mG*mC
3308	G012455	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGU mUAAAAmUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3309	G012456	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGU mUAAAAmUAAGGCmUAGUCCGUUAUmCAACUUGGCACCGAGUCGG*mU*mG*mC
3310	G012457	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGU mUAAAAmUAmAmGmGmCmUmAGUmCmCGUUAmUmCAACUUGGCACCGAGUCGG*mU*mG*mC
3311	G012458	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCmAAGU mUAAAAmUAAGGCmUAGUCCGUUAUmCAACUUGGmCACCGAGUCGG*mU*mG*mC

SEQ ID NO	Name	Sequence
3312	G012459	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU UAAAAUAAGGCmUAGUCCGUUAUmCAACUUGGmCACCGAGUCGG*mU*mG*mC
3313	G012460	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU mUAAAAAmUAAGGCmUAGUCCGUfUAUmCAACUUGGmCACCGAGUCGG*mU*mG*mC
3314	G012461	mA*mC*mA*CAA*A*fU*fA*fC*fCAfGfUCCfAfGCGGUUUUfUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU mUAAAAAmUAAGGCmUAGUCCGUUAUmCAACUUGGmCACCGAGUCGG*mU*mG*mC
3315	G012728	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGmCACCGAGUCGG*mU*mG*mC
3316	G012729	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU UAAAAUAmGmGmCmUmAGUmCmCGUUAmUmCAACUUGGCACCGAGUCGG*mU*mG*mC
3317	G012730	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU UAAAAUAAGGCmUAGUCCGUUAUmCAACUUGGCACCGAGUCGG*mU*mG*mC
3318	G012731	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU mUAAAAAmUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3319	G012732	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU mUAAAAAmUAAGGCmUAGUCCGUUAUmCAACUUGGCACCGAGUCGG*mU*mG*mC
3320	G012733	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU mUAAAAAmUAmAmGmGmCmUmAGUmCmCGUUAmUmCAACUUGGCACCGAGUCGG*mU*mG*mC
3321	G012734	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU mUAAAAAmUAAGGCmUAGUCCGUUAUmCAACUUGGmCACCGAGUCGG*mU*mG*mC
3322	G012735	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU UAAAAUAAGGCmUAGUCCGUUAUmCAACUUGGmCACCGAGUCGG*mU*mG*mC
3323	G012736	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU mUAAAAAmUAAGGCmUAGUCCGUfUAUmCAACUUGGmCACCGAGUCGG*mU*mG*mC
3324	G012737	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUfUAGAmGmCmUmAmGmAmAmUmAmGmCAAG UmUAAAAAmUAAGGCmUAGUCCGUUAUmCAACUUGGmCACCGAGUCGG*mU*mG*mC
3325	G012741	mU*mU*mA*CAG*C*fC*fA*fC*fGUfCfUACfAfGCAGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC
3326	G012421	mA*mC*mA*fCAAAfUACfCAGUCfCAGCGGUUUUAGAmGmCmUmAmGmAmAmUmAmGmCAAGUUAAAAU AAGGCUAGUCCGUUAUCAmAmCmUmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
3327	G012422	mA*mC*mA*fCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3328	G012423	mA*mC*AfCAAAfUACfCAGUCfCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3329	G012424	mA*mC*AfCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3330	G012426	mA*mC*mA*CAAAfUfAfCfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGUCCGUUAUCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmG mGmUmGmCmU*mU*mU*mU
3331	G012443	mA*mC*mA*fCAAAfUACfCAGUCfCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3332	G012448	mA*mC*mA*mCAAAfUACfCAGUCCAGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAmAmGmGmCmUmAGUmCmCGUUAmUmCAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3333	G012973	mA*mC*mA*mCmAmAmAmUmAmCfCfAfGfUfCfCfAfGfCmGmGfUfUfUfUfAmGmAmGmCmUmAmGmAmAmAmUmAmGmGfUfUmAfAmAmAfUmAmAmGmGfCfUmAfGfUfCmCfGfUfUmAmUmCmAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3334	G012974	mA*mC*mA*mCmAmAmAmUmAmCfCfAfGfUfCfCfAfGfCmGmGfUfUfUfUfAmGmAmGmCmUmAmGmAmAmAmUmAmGmGmCmAmAmAmUmAmGmGC*U*U*mAG*U*C*mCG*U*U*mAmUmCmAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3335	G012975	mA*mC*mA*mCmAmAmAmUmAmCfCfAfGfUfCfCfAfGfCmGmGfUfUfUfUfAmGmAmGmCmUmAmGmAmAmAmUmAmGmGCUmAGUCmCGUUmAmUmCmAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3336	G012976	mA*mC*mA*mCmAmAmAmUmAmCfCfAfGfUC*C*fAfGC*mGmGU*U*U*fUfAmGmAmGmCmUmAmGmAmAmAmUmAmGmGfUfUmAfAmAmAfUmAmAmGmGfCfUmAfGfUfCmCfGfUfUmAmUmCmAmAmCmUmUmGmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

SEQ ID NO	Name	Sequence
3337	G012977	mA*mC*mA*mCmAmAmAmUmAmCfCfAfGfUC*C*fAfGC*mGmGU*U*U*fUfAmGmAmGmCmUmAmGmAmA mAmUmAmGmCmAmAmGU*U*mAA*mAmAU*mAmAmGmGC*U*mAG*U*C*mCG*U*U*mAmUmCmCmAmAm CmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3338	G012978	mA*mC*mA*mCmAmAmAmUmAmCfCfAfGfUC*C*fAfGC*mGmGU*U*U*fUfAmGmAmGmCmUmAmGmAmA mAmUmAmGmCmAmAmGUUmAAmAmAUmAmAmGmGCUmAGUCmCGUUmAmUmCmAmAmCmUmUmGmGm AmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3339	G012979	mA*mC*mA*mCmAmAmAmUmAmCfCfAfGfUC*C*fAfGC*mGmGU*U*U*mUmAmGmAmGmCmUmAmGmAm AmAmUmAmGmCmAmAmGU*U*mAA*mAmAU*mAmAmGmGC*U*mAG*U*C*mCG*U*U*mAmUmCmCmAmA mCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*m U
3340	G011771	mU*mU*mA*CAGCCACGUCUACAGCAGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAA GGCUAGUCCGUUAUCAACUUGGCACCGAGUCGGmUmGmC
3341	CR012980	mA*mC*mA*mCmAmAmAmUmAmCfCfAfGfUfCfCfAfGfCmGmGfUfUfUfUfAmGmAmGmCmUmAmU*mG*mC* mU
3342	TR012982	mA*mG*mC*mAmUmAmGmCmAmAmGfUfUmAfAmAmAfUmAmAmGmGfCfUmAfGfUfCmCfGfUfUmAmUmC mAmAmCmUmUmGmAmAmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmC*mU*mU* mU
3343	N20-G014462	mN*mN*mN*mNmNN*N*fN*fN*fNNfNfNNNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmA mGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm AmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3344	N20-G014463	mN*mN*mN*mNfNN*N*fN*fN*fN*fNNfNfNNNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3345	N20-G014464	mN*mN*mN*mNN*N*N*fN*fN*fN*fNNfNfNNNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3346	N20-G014465	mN*mN*mN*mNdNN*N*fN*fN*fN*fNNfNfNNNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3347	N20-G014466	mN*mN*mN*mNNN*N*fN*fN*fN*fNmNfNfNNNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmA mGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm AmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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3348	N20-G014467	mN*mN*mN*mNNN*N*fN*fN*fN*fNfNfNfNNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3349	N20-G014468	mN*mN*mN*mNNN*N*fN*fN*fN*fNfNNNfNfNNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3350	N20-G014469	mN*mN*mN*mNNN*N*fN*fN*fN*fNdNfNfNNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3351	N20-G014470	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmA mGmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm AmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3352	N20-G014471	mN*mN*mN*mNNN*N*fN*fN*fN*fNfNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3353	N20-G014472	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNN*NfNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3354	N20-G014473	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNdNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3355	N20-G014474	mN*mN*mN*mNNN*N*fN*fN*fNfNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3356	N20-G014475	mN*mN*mN*mNNN*N*fN*fN*fNfNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3357	N20-G014476	mN*mN*mN*mNNN*N*fN*fN*fNfNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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3358	N20-G014477	mN*mN*mN*mNNN*N*fNfNfN*fNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3359	N20-G014478	mN*mN*mN*mNNN*N*fN*fNfNfNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3360	N20-G014479	mN*mN*mN*mNNN*N*fNfN*fNfNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGm CmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3361	N20-G014480	mN*mN*mN*mNNN*N*fNfNfNfNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3362	N20-G014481	mN*mN*mN*mNNfNN*fN*fN*fNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3363	N20-G014482	mN*mN*mN*mNNN*fNfN*fN*fN*fNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3364	N20-G014483	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3365	N20-G014484	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3366	N20-G014485	mN*mN*mN*mNNfNfNfN*fN*fN*fNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3367	N20-G014486	mN*mN*mN*mNNfNfNfN*fN*fN*fNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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3368	N20-G014487	mN*mN*mN*mNNfNN*fN*fN*fNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3369	N20-G014488	mN*mN*mN*mNNN*fNfN*fN*fNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3370	N20-G014489	mN*mN*mN*mNNfNfNfNfNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmGmUmAmAmAmAm mAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3371	N20-G014490	mN*mN*mN*mNNfNfNfNfNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmGmUmAmAmAmAm mAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3372	N20-G014491	fN*fN*fN*fNNfNfNfNfNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmGmUmAmAmAmAm AGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmU mGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3373	N20-G014492	fN*fN*fN*fNNfNfNfNfNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmGmUmAmAmAmAm mAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3374	N20-G014493	mN*mN*mN*mNNfNfNfNfNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmGmUmAmAmAmAm mAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3375	N20-G014494	mN*mN*mN*mNNfNfNfNfNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmGmUmAmAmAmAm mAmAGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3376	N20-G014495	fN*fN*fN*fNNfNfNfNfNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmGmUmAmAmAmAm AGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmU mGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3377	N20-G014496	fN*fN*fN*fNNfNfNfNfNNfNfNfNNmGUUUfUAGmAmGmCmUmAmGmAmGmUmAmAmAmAm AGUfUmAfAmAfAmUAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGmU mGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU

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3378	N20-G014497	mN*mN*mN*fNfNfNfNfNfNfNfNfNNNfNfNfNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3379	N20-G014498	fN*fN*fN*fNfNfNfNfNfNfNfNfNNNfNfNfNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCmA mAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmGm UmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3380	N20-G014499	mN*mN*mN*mNNN*N*fN*fNfN*fNNfNfNNNfNfNfNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmG mCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm AmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3381	N20-G014500	mN*mN*mN*mNNN*N*N*mNN*mNNmNmNNNNNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3382	N20-G014501	mN*mN*mN*mNNN*N*fNNNfNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3383	N20-G014502	mN*mN*mN*mNNN*N*fNNfNfNNfNfNNNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3384	N20-G014503	mN*mN*mN*mNNN*N*fNfNNfNfNfNfNfNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmC mAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAm GmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3385	N20-G014504	fN*fN*fN*fNfNfNfNfNfNfNfNfNfNfNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAmGmCm AmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmAmG mUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3386	N20-G014505	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNmNmNfNfNmNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm mAmGmCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAm AmAmAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3387	N20-G014506	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNfNfNfNfNNNmGUUUfUAGmAmGmCmUmAmGmAmAmAmUmAm GmCmAmAGUfUmAfAmAfAmUAmAmAmGmGmCmUmAGUmCmCGUfUAmUmCAmAmCmUmUmGmAmAmAmA mAmGmUmGmGmCmAmCmCmGmAmGmUmCmGmGmUmGmCmU*mU*mU*mU
3388	N20-G014644	mN*mN*mN*mNmNN*N*fN*fN*fNNfNfNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGm CAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU

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3389	N20-G014645	mN*mN*mN*mNfNN*N*fN*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3390	N20-G014646	mN*mN*mN*mNN*N*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3391	N20-G014647	mN*mN*mN*mNdNN*N*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3392	N20-G014648	mN*mN*mN*mNNN*N*fN*fN*fNmNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGm CAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3393	N20-G014649	mN*mN*mN*mNNN*N*fN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3394	N20-G014650	mN*mN*mN*mNNN*N*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3395	N20-G014651	mN*mN*mN*mNNN*N*fN*fN*fNdNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3396	N20-G014652	mN*mN*mN*mNNN*N*fN*fN*fNNfNfNmNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGm CAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3397	N20-G014653	mN*mN*mN*mNNN*N*fN*fN*fNNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3398	N20-G014654	mN*mN*mN*mNNN*N*fN*fN*fNNfNfNN*NfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3399	N20-G014655	mN*mN*mN*mNNN*N*fN*fN*fNNfNfNdNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3400	N20-G014656	mN*mN*mN*mNNN*N*fNfN*fN*fNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3401	N20-G014657	mN*mN*mN*mNNN*N*fN*fNfN*fNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3402	N20-G014658	mN*mN*mN*mNNN*N*fN*fN*fNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3403	N20-G014659	mN*mN*mN*mNNN*N*fNfNfN*fNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU

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3404	N20-G014660	mN*mN*mN*mNNN*N*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3405	N20-G014661	mN*mN*mN*mNNN*N*fNfN*fNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAA GUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3406	N20-G014662	mN*mN*mN*mNNN*N*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3407	N20-G014663	mN*mN*mN*mNNfNfNfN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3408	N20-G014664	mN*mN*mN*mNNN*fNfN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3409	N20-G014665	mN*mN*mN*mNNN*N*fN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3410	N20-G014666	mN*mN*mN*mNNN*N*fN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3411	N20-G014667	mN*mN*mN*mNNfNfNfN*fN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3412	N20-G014668	mN*mN*mN*mNNfNfNfN*fN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3413	N20-G014669	mN*mN*mN*mNNfNN*fN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3414	N20-G014670	mN*mN*mN*mNNN*fNfN*fN*fNfNfNNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3415	N20-G014671	mN*mN*mN*mNNfNfNfNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3416	N20-G014672	mN*mN*mN*mNNfNfNfNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3417	N20-G014673	fN*fN*fN*fNNfNfNfNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUA AAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3418	N20-G014674	fN*fN*fN*fNNfNfNfNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUA AAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU

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3419	N20-G014675	mN*mN*mN*mNNfNfNfNfNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3420	N20-G014676	mN*mN*mN*mNNfNfNfNfNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3421	N20-G014677	fN*fN*fN*fNNfNfNfNfNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAA AAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3422	N20-G014678	fN*fN*fN*fNNfNfNfNfNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUA AAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3423	N20-G014679	mN*mN*mN*fNfNfNfNfNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAG UUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3424	N20-G014680	fN*fN*fN*fNfNfNfNfNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUU AAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3425	N20-G014681	mN*mN*mN*mNNN*N*fN*fNfNfNNNfNfNfNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCA AGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3426	N20-G014682	mN*mN*mN*mNNN*N*fN*mNNmNmNNNNNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
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3428	N20-G014684	mN*mN*mN*mNNN*N*fNNfNfNfNfNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3429	N20-G014685	mN*mN*mN*mNNN*N*fNfNfNfNfNfNNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
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3432	N20-G014688	mN*mN*mN*mNNN*N*fN*fN*fN*fNNfNfNfNfNfNNNGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmC AAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mCmU
3433-3498		Not Used
3499	Cas9 mRNA sequence	GGGUCCCGCAGUCGGCGUCCAGCGGCUCUGCUUGUUCGUGUGUGUCGUUGCAGGCCUUAUUCGGAUCCGCCA CCAUGGACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUA

SEQ ID NO	Name	Sequence
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SEQ ID NO	Name	Sequence
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		GAGCGAACUGGACAAGGCAGGAUUUCAUCAAGAGACAGCUGGUCGAAACAAGACAGAUCACACAAAGCACGUCGCACAG
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3500	Cas9 mRNA sequence	GGGUCCCGCAGUCGGCGUCCAGCGGCUCUGCUUGUUCGUGUGUGUCGUUGCAGGCCUUAUUCGGAUCCAUGG
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SEQ ID NO	Name	Sequence
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SEQ ID NO	Name	Sequence
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3501	Cas9 transcript with 5' UTR of HSD, ORF corresponding to SEQ ID NO: 3504, Kozak sequence, and 3' UTR of ALB	GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTCGTTGCAGGCCTTATTCGGATCCGCCACCATGG
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SEQ ID NO	Name	Sequence
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SEQ ID NO	Name	Sequence
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3502	Cas9 DNA coding sequence	ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCAGTCATCACAGACGAATACAAG
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		GAACAGAGAAGACCTGCTGAGAAAGCAGAGAACATTCGACAACGGAAGCATCCCGCACCAGATCCACCTGGGAGAACT
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		AGCGTCGAAATCAGCGGAGTCGAAGACAGATTCAACGCAAGCCTGGGAACATACCACGACCTGCTGAAGATCATCAAGG
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3503	Cas9 DNA coding sequence 1	ATGGATAAGAAGTACTCAATCGGGCTGGATATCGGAACTAATTCCGTGGGTTGGGCAGTGATCACGGATGAATACAAAG
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3504	Cas9 mRNA open reading frame (ORF) 2	AUGGACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUAC
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3505	Cas9 mRNA ORF 1	AUGGAUAAGAAGUACUCAAUCGGGCUGGAUAUCGGAACUAAUUCCGUGGGUUGGGCAGUGAUCACGGAUGAAUA
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		AAGGUGAUUACCCUGAAAGCAAACUUGUGUCGGACUUUCGGAAGGACUUUUCAGUUUUACAAAGUGAGAGAAAU
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		UUGAAUCGGAGUUUGUGUACGGAGACUACAAGGUCUACGACGUGAGGAAGAUGAUAAGCCAAGUCCGAACAGGAA
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		GACUUCGCAACUGUUCGCAAAGUGCUCUCUAUGCCGCAAGUCAAUAUUGUGAAGAAAACCGAAGUGCAAACCGGC
		GGAUUUUCAAAGGAAUCGAUCCUCCCAAAGAGAAAUAGCGACAAGCUCAUUGCACGCAAGAAAGACUGGGACCCGA
		AGAAGUACGGAGGAUUCGAUUCGCCGACUGUCGCAUACUCCGUCCUCGUGGUGGCCAAGGUGGAGAAGGGAAAG
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3506	Cas9 nickase (D10A) mRNA ORF	AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUAC
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		CCUGAAGAGCGACGGAUUCGCAAACAGAAACUUCAUGCAGCUGAUCCACGACACAGCCUGACACAUUCAAGGAAGAC
		AUCCAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAACCUGGCAGGAAGCCCGGCAA
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		UCCUGAGCAUGCCGCAGGUCAACAUCGUCAAGAAGACAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCU
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		GAGAAUGCUGGCAAGCGCAGGAGAACUGCAGAAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUCCU
		GUACCUGGCAAGCCACUACGAAAAGCUGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCUGUUCGUCGAACAG
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		UGCUGUUCGACAGCGGAGAAACAGCAGAAGCAACAAGAGUGAAGAGAACAGCAAGAAGAAGAUACACAAGAAGAAA
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		ACUGAUCUACCUGGCACUGGCACACAUGAUCAAGUUCAGAGGACACUUCCUGAUCGAAGGAGACCUGAACCCGGAC
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		GAGCAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGCUGAGCAAGGACACAUACGACGACGACCUGGACAACCUG
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		GCAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUUCUACAAGUUCAUCAAGCCGAUCCU
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3508	Cas9 bare coding sequence	GACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUACAAG
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		CAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAAUGGCAAAGGUCGACGACAGCUUCUUCCACAGACUGGAA
		GAAAGCUUCCUGGUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAAACAUCGUCGACGAAGUCGCAU
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SEQ ID NO	Name	Sequence
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		CAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUUCUACAAGUUCAUCAAGCCGAUCCUG
		GAAAAGAUGGACGGAACAGAAGAACUGCUGGUCAAGCUGAACAGAGAAGACCUGCUGAGAAAGCAGAGAACAUUC
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SEQ ID NO	Name	Sequence
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3509	Cas9 nickase bare coding sequence	GACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUACAAG
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		CAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAAUGGCAAAGGUCGACGACAGCUUCUUCCACAGACUGGAA
		GAAAGCUUCCUGGUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAAACAUCGUCGACGAAGUCGCAU
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3510	dCas9 bare coding sequence	GACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUACAAG
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3511	Cas9 mRNA ORF using minimal uridine codons, with start and stop codons	AUGGACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUAC
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3512	Cas9 coding sequence using minimal uridine codons (no start or stop codons; suitable for inclusion in fusion protein coding sequence)	GACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUACAAG
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		CAGCUGGGAGGAGAC
3515	dCas9 mRNA ORF using minimal uridine codons, with start and stop codons	AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUAC
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		ACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAGAAGCUGGUCGACAGCACAGACAAGGCAGACCUGAGACU
		GAUCUACCUGGCACUGGCACACAUGAUCAAGUUCAGAGGACACUUCCUGAUCGAAGGAGACCUGAACCCGGACAAC
		AGCGACGUCGACAAGCUGUUCAUCCAGCUGGUCCAGACAUACAACCAGCUGUUCGAAGAAAACCCGAUCAACGCAA
		GCGGAGUCGACGCAAAGGCAAUCCUGAGCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCU
		GCCGGGAGAAAAGAAGAACGGACUGUUCGGAAACCUGAUCGCACUGAGCCUGGGACUGACACCGAACUUCAAGAG
		CAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGCUGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUG
		GCACAGAUCGGAGACCAGUACGCAGACCUGUUCCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGAGCGACA
		UCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGCAUGAUCAAGAGAUACGACGAACACCACCA
		GGACCUGACACUGCUGAAGGCACUGGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCAGAG
		CAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUUCUACAAGUUCAUCAAGCCGAUCCUG
		GAAAAGAUGGACGGAACAGAAGAACUGCUGGUCAAGCUGAACAGAGAAGACCUGCUGAGAAAGCAGAGAACAUUC

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		AAGAGGAAACAGCAGAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAACAAUCACACCGUGGAACUUCGAAGAAGU
		CGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAACUUCGACACAAGAACCUGCCGAACGAAAAG
		GUCCUGCCGAAGCACAGCCUGCUGUACGAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG
		AAGGAAUGAGAAAGCCGGCAUUCCUGAGCGGAGAACAGAAGAAGGCAAUCGUCGACCUGCUGUUCAAGACAAACA
		GAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUACUUCAAGAAGAUCGAAUGCUUCGACAGCGUCGAAAUCAGCG
		GAGUCGAAGACAGAUUCAACGCAAGCCUGGGAACAUACCACGACCUGCUGAAGAUCAUCAAGGACAAGGACUUCCU
		GGACAACGAAGAAAACGAAGACAUCCUGGAAGACAUCGUCCUGACACUGACGUUUCGAAGACAGAGAAAUGAUC
		GAAGAAAGACUGAAGACAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACACA
		GGAUGGGGAAGACUGAGCAGAAAGCUGAAUCAACGGAAUCAGAGACAAGCAGAGCGGAAAGACAAUCCUGGACUUC
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		ACAGCUGCUGAACGCAAAGCUGAUCACACAGAGAAAGUUCGACAACCUGACAAAGGCAGAGAAGGGAGGAGACUGAGC
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		CAAGCACUACCUGGACGAAAUCAUCGAACAGAUCAGCGAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACCUG
		GACAAGGUCCUGAGCGCAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCAUCCACCUGU
		UCACACUGACAAACCUGGGAGCACCGGCAGCAUUCAAGUACUUCGACACAACAAUCGACAGAAAGAGAUACACAAG
		CACAAAGGAAGUCCUGGACGCAACACUGAUCCACCAGAGCAUCACACAGGACUGUACGAAACAAGAAUCGACCUGAGC
		CAGCUGGGAGGAGACGGAGGAGGAAGC
3517	Cas9 mRNA ORF using minimal uridine codons, with start and stop codons	AUGGACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUAC
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		ACAUCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGCAUGAUCAAGAGAUACGACGAACACCAC
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		GCAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUUCUACAAGUUCAUCAAGCCGAUCCU
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		GGAGUCGAAGACAGAUUCAACGCAAGCCUGGGAACAUACCACGACCUGCUGAAGAUCAUCAAGGACAAGGACUUCC
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		AUCCAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAACCUGGCAGGAAGCCCGGCAA
		UCAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGACGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGGAAA
		ACAUCGUCAUCGAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAGAAUGAAGAG
		AAUCGAAGAAGGAAUCAAGGAACUGGGAAGCCAGAUCCUGAAGGAACACCCGGUCGAAAACACACAGCUGCAGAAC
		GAAAAGCUGUACCUGUACUACCUGCAGAACGGAAGAGACAUGUACGUCGACCAGGAACUGGACAUCAACAGACUG
		AGCGACUACGACGUCGACCACACAUCGUCCCGCAGAGCUUCCUGAAGGACGACAGCAUCGACAACAAGGUCCUGACAA
		GAAGCGACAAGAACAGAGGAAAGAGCGACAACGUCCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGA
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		GCGAACUGGACAAGGCAGGAUUCAUCAAGAGACAGCUGGUCGAAACAAGACAGAUCACACAAAGCACGUCGCACAGAU
		CCUGGACAGCAGAAUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCAUCACACUGAAG
		AGCAAGCUGGUCAGCGACUUCAGAAAGGACUUCCAGUUCUACAAGGUCAGAGAAAUCAACAACUACCACCACGCAC
		ACGACGCAUACCUGAACGCAGUCGUCGGAACAGCACUGAUCAAGAAGUACCCGAAGCUGGAAAGCGAAUUCGUCUA
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		UCCUGAGCAUGCCGCAGGUCAACAUCGUCAAGAAGACAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCU
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		GUACCUGGCAAGCCACUACGAAAAGCUGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCUGUUCGUCGAACAG
		CACAAGCACUACCUGGACGAAAUCAUCGAACAGAUCAGCGAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACC
		UGGACAAGGUCCUGAGCGCAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCAUCCACCU
		GUUCACACUGACAAACCUGGGAGCACCGGCAGCAUUCAAGUACUUCGACACAACAAUCGACAGAAAGAGAUACACA
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		AGGUCGACAGCGGAUAG

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3518	Cas9 coding sequence using minimal uridine codons (no start or stop codons; suitable for inclusion in fusion protein coding sequence)	GACAAGAAGUACAGCAUCGGACUGGACAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUACAAG GUCCCGAGCAAGAAGUUCAAGGUCCUGGGAAACACAGACGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGC UGUUCGACAGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAGAUACACAAGAAAGAA CAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAAUGGCAAAGGUCGACGACAGCUUCUUCCACAGACUGGAA GAAAGCUUCCUGGUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAAACAUCGUCGACGAAGUCGCAU ACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAGAAGCUGGUCGACAGCACACAGACAAGGCAGACCUGAGACU GAUCUACCUGGCACUGGCACACAUGAUCAAGUUCAGAGGACACUUCCUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACACAAGCUGUUCAUCCAGCUGGUCCAGACAUACAACCAGCUGUUCGAAGAAAACCCGAUCAACGCAA GCGGAGUCGACGCAAAGGCAAUCCUGAGCGCAAGACUGAGACAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCU GCCGGGAGAAAAGAAGAACGGACUGUUCGGAAACCUGAUCGCACUGAGCCUGGGACUGACACCGAACUUCAAGAG CAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGCUGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUG GCACAGAUCGGAGACCAGUACGCAGACCUGUUCCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGAGCGACA UCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGCAUGAUCAAGAGAUACGACGAACACCACCA GGACCUGACACUGCUGAAGGCACUGGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCAGAG CAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUUCUACAAGUUCAUCAAGCCGAUCCUG GAAAAGAUGGACGGAACAGAAGAACUGCUGGUCAAGCUGAACAGAGAAGACCUGCUGAGAAAGCAGAGAACAUUC GACAACGGAAGCAUCCCGCACCAGAUCCACCUGGGAGAACUGCACGCAAUCCUGAGAAGACAGGAAGACUUCUACC CGUUCCUGAAGGACAACAGAGAAAAGAUCGAAAAGAUCCUGACAUUCAGAAUCCCGUACUACGUCGGACCGCUGGC AAGAGGAAACAGCAGAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAACAAUCACACCGUGGAACUUCGAAGAAGU CGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAACUUCGACAAGAACCUGCCGAACGAAAAG GUCCUGCCGAAGCACAGCCUGCUGUACGAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAGCCGGCAUUCCUGAGCGGAGAACAGAAGAAGGGCAAUCGUCGACCUGCUGUUCAAGACAAACA GAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUACUUCAAGAAGAUCGAAUGCUUCGACAGCGUCGAAAUCAGCG GAGUCGAAGACAGAUUCAACGCAAGCCUGGGAAACAUACCACGACCUGCUGAAGAUCAUCAAGGACAAGGACUUCCU GGACAACGAAGAAAACGAAGACAUCCUGGAAGACAUCGUCCUGACACUGACGCUGUUCGAAGACAGAGAAAUGAUC GAAGAAAGACUGAAGACAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGGAUACACA GGAUGGGGAAGACUGAGCAGAAAGCUGAUCAACGGAAUCAGAGACAAGCAGAGCGGAAAGACAAUCCUGGACUUC CUGAAGAGCGACGGAUUUCGCAAACAGAAACUUCAUGCAGCUGAUCCACGACAGCCUGACAUUCAAGGAAGACA UCCAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAACCUGGCAGGAAGCCCGGCAAU CAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGUCGACGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGGAAAA CAUCGUCAUCGAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAGAAUGAAGAGA AUCGAAGAAGGAAUCAAGGAACUGGGAAGCCAGAUCCUGAAGGAACACCCGGUCGAAAACACACAGGCUGCAGAACG

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		AAGCGACAAGAACAGAGGAAAGAGCGACAACGUCCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAG
		ACAGCUGCUGAACGCAAAGCUGAUCACACAGAGAAAGUUCGACAACCUGACAAAGGCAGAGAGAGGAGACUGAGC
		GAACUGGACAAGGCAGGAUUCAUCAAGAGACAGCUGGUCGAAACAAGACAGAUCACACAAAGCACGUCGCACAGAUCC
		UGGACAGCAGAAUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCACUCACACUGAAGAG
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		CACAAAGGAAGUCCUGGACGCAACACUGAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUGAGC
		CAGCUGGGAGGAGACGGAAGCGGAAGCCCGAAGAAGAAGAGAAAGGUCGACGGAAGCCCGAAGAAGAAGAGAAAG
		GUCGACAGCGGA
3519	Cas9 nickase mRNA ORF using minimal uridine codons, with start and stop codons	AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUAC
		AAGGUCCCGAGCAAGAAGUUCAAGGUCCUGGGAAACACAGACACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCAC
		UGCUGUUCGACAGCGGAGAAACAGCAGAAGCAACAAGAGCUGAAGAGAGAACAGCAAGAAGAAGAUACACAAGAAGAAA
		GAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAAUGGCAAAGGUCGACGACAGCUUCUUCCACAGACUG
		GAAGAAAGCUUCCUGGUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAAACAUCGUCGACGAAGUCG
		CAUACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAGAAGCUGGUCGACAGCACAGACAAGGCAGACCUGAG
		ACUGAUCUACCUGGCACUGGCACACAUGAUCAAGUUCAGAGGACACUUCCUGAUCGAAGGAGACCUGAACCCGGAC
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		GGAAAAGAUGGACGGAACAGAAGAACUGCUGGUCAAGCUGAACAGAGAAGACCUGCUGAGAAAGCAGAGAACAUU
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		CAAGAGGAAACAGCAGAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAACAAUCACACCGUGGAACUUCGAAGAAG
		UCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACACAAACUUCGACAAGAACCUGCCGAACGAAAA
		GGUCCUGCCGAAGCACAGCCUGCUGUACGAAUACUUCACAGUCUACACAACGAACUGACAAAGGUCAAGUACGUCACA
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		AGAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUACUUCAAGAAGAUCGAAUGCUUCGACAGCGUCGAAAUCAGC
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		AGCGACUACGACGUCGACCACACAUCGUCCCGCAGAGCUUCCUGAAGGACGACAGCAUCGACAACAAGGUCCUGACAA
		GAAGCGACAAGAACAGAGGAAAGAGCGACAACGUCCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGA
		GACAGCUGCUGAACGCAAAGCUGAUCACACAGAGAAAGUUCGACAACCUGACAAAGGCAGAGAGAGGAGGACUGA
		GCGAACUGGACAAGGCAGGAUUCAUCAAGAGACAGCUGGUCGAAACAAGACAGAUCACACAAAGCACGUCGCACAGAU
		CCUGGACAGCAGAAUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCACAUCACACUGAAG
		AGCAAGCUGGUCAGCGACUUCAGAAAGGACUUCCAGUUCUACAAGGUCAGAGAAAUCAACAACUACCACGCCCAC
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SEQ ID NO	Name	Sequence
		CGGAGACUACAAGGUCUACGACGUCAGAAAGAUGAUCGCAAAGAGCGAACAGGAAAUCGGAAAGGCAACAGCAAAG
		UACUUCUUCUACAGCAACAUCAUGAACUUCUUCAAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAGAGAC
		CGCUGAUCGAAACAAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAACAGUCAGAAAGG
		UCCUGAGCAUGCCGCAGGUCAACAUCGUCAAGAAGACAGAAGUCCAGACAGGAGGAUUCAGCAAGGAAAGCAUCCU
		GCCGAAGAGAAACAGCGACAAGCUGAUCGCAAAGAAAGGACUGGGACCCGAAGAAGUACGGAGGAUUCGACAG
		CCCGACAGUCGCAUACAGCGUCCUGGUCGUCGCAAAGGUCGAAAAGGGAAAGAGCAAGAAGCUGAAGAGCGUCAA
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		AUACAAGGAAGUCAAGAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUUCGAACUGGAAAACGGAAGAAA
		GAGAAUGCUGGCAAGCGCAGGAGAACUGCAGAAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUUCCU
		GUACCUGGCAAGCCACUACGAAAAGCUGAAGGGAAGCCCGGAAGACAACGAAGCAGCUGUUCGUCGAACAG
		CACAAGCACUACCUGGACGAAAUCAUCGAACAGAUCAGCGAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACC
		UGGACAAGGUCCUGAGCGCAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCAUCCACCU
		GUUCACACUGACAAACCUGGGAGCACCGGCAGCAUUCAAGUACUUCGACACAACAAUCGACAGAAAGAGAUACACA
		AGCACAAAGGAAGUCCUGGACGCAACACUGAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUGA
		GCCAGCUGGGAGGAGACGGAAGCGGAAGCCCGAAGAAGAGAAAGGUCGACGGAAGCCCGAAGAAGAAGAGAA
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3520	Cas9 nickase coding sequence using minimal uridine codons (no start or stop codons; suitable for inclusion in fusion protein coding sequence)	GACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUACAAG
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		UGUUCGACAGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAUACACAAGAAGAAAGAA
		CAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAAUGGCAAAGGUCGACGACAGCUUCUUCCACAGACUGGAA
		GAAAGCUUCCUGGUCGAAGAAGACAAGAAGCACGAAAGAACACCCGAUCUUCGGAAACAUCGUCGACGAAGUCGCAU
		ACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAGAAGCUGGUCGACAGCACAGACAAGGCAGACCUGAGACU
		GAUCUACCUGGCACUGGCACACAUGAUCAAGUUCAGAGGACACUUCCUGAUCGAAGGAGACCUGAACCCGGACAAC
		AGCGACGUCGACAAGCUGUUCAUCCAGCUGGUCCAGACAUACAACCAGCUGUUCGAAGAAAACCCGAUCAACGCAA
		GCGGAGUCGACGCAAAGGCAAUCCUGAGCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCU
		GCCGGGAGAAAAGAAGAACGGACUGUUCGGAAACCUGAUCGCACUGAGCCUGGGACUGACACCGAACUUCAAGAG
		CAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGCUGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUG
		GCACAGAUCGGAGACCAGUACGCAGACCUGUUUCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGAGCGACA
		UCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGCAUGAUCAAGAGAUACGACGAACACCACCA
		GGACCUGACACUGCUGAAGGCACUGGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCAGAG
		CAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUUCUACAAGUUCAUCAAGCCGAUCCUG
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		AAGAGGAAACAGCAGAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAACAAUCACACCGUGGAACUUCGAAGAAGU
		CGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAACUUCGACACAAGAACCUGCCGAACGAAAAG
		GUCCUGCCGAAGCACAGCCUGCUGUACGAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG
		AAGGAAUGAGAAAGCCGGCAUUCCUGAGCGGAGAACAGAAGAAGGCAAUCGUCGACCUGCUGUUCAAGACAAACA
		GAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUACUUCAAGAAGAUCGAAUGCUUCGACAGCGUCGAAAUCAGCG
		GAGUCGAAGACAGAUUCAACGCAAGCCUGGGAACAUACCACGACCUGCUGAAGAUCAUCAAGGACAAGGACUUCCU
		GGACAACGAAGAAAACGAAGACAUCCUGGAAGACAUCGUCCUGACACUGACGUUUCGAAGACAGAGAAAUGAUC
		GAAGAAAGACUGAAGACAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGAUACACA
		GGAUGGGGAAGACUGAGCAGAAAGCUGAAUCAACGGAAUCAGAGACAAGCAGAGCGGAAAGACAAUCCUGGACUUC
		CUGAAGAGCGACGGAUUUCGCAAACAGAAACUUCAUGCAGCUGAUCCCACGACGCAGCCUGACAUUCAAGGAAGACA
		UCCAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAACCUGGCAGGAAGCCCGGCAAU
		CAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGUCGACGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGGAAAA
		CAUCGUCAUCGAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAGAAUGAAGAGA
		AUCGAAGAAGGAAUCAAGGAACUGGGAAGCCAGAUCCUGAAGGAACACCCGGUCGAAAACACACAGCUGCAGAACG
		AAAAGCUGUACCUGUACUACCUGCAGAACGGAAGAGACAUGUACGUCGACCAGGAACUGGACAUCAACAGACUGA
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		AAGCGACAAGAACAGAGGAAAGAGCGACAACGUCCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAG
		ACAGCUGCUGAACGCAAAGCUGAUCACACAGAGAAAGUUCGACAACCUGACAAAGGCAGAGAAGGGAGGAGACUGAGC
		GAACUGGACAAGGCAGGAUUCAUCAUCAAGAGACAGCUGGUCGAAACAAGACAGAUCACACAAAGCACGUCGCACAGAUCC
		UGGACAGCAGAAUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCAUCACACACUGAAGAG
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		ACUUCUUCUACAGCAACAUCAUGAACUUCUUCAAGACAGAAAUCACACUGGCAAACGGAGAAAUCAGAAAGAGACC
		GCUGAUCGAAACAAACGGAGAAACAGGAGAAAUCGUCUGGGACAAGGGAAGAGACUUCGCAACAGUCAGAAAGGU
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		AACUGCUGGGAAUCACAAUCAUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCCUGGAAGCAAAGGGAU
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		ACCUGGCAAGCCACUACGAAAAGCUGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCUGUUCGUCGAACAGCA
		CAAGCACUACCUGGACGAAAUCAUCGAACAGAUCAGCGAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACCUG
		GACAAGGUCCUGAGCGCAUACAACAAGCACAGAGACAAGCCGAUCAGAGAACAGGCAGAAAACAUCAUCCACCUGU
		UCACACUGACAAACCUGGGAGCACCGGCAGCAUUCAAGUACUUCGACACAACAAUCGACAGAAAGAGAUACACAAG
		CACAAAGGAAGUCCUGGACGCAACACUGAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUGAGC
		CAGCUGGGAGGAGAC
		GGAAGCGGAAGCCCGAAGAAGAAGAAAGGUCGACGGAAGCCCGAAGAAGAAAGGUCGACAGCGGA
3521	dCas9 mRNA ORF using minimal uridine codons, with start and stop codons	AUGGACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUAC
		AAGGUCCCGAGCAAGAAGUUCAAGGUCCUGGGAAACACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCAC
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		GAACAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAAUGGCAAAGGUCGACGACAGCUUCUUCCACAGACUG
		GAAGAAAGCUUCCUGGUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAAACAUCGUCGACGAAGUCG
		CAUACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAGAAGCUGGUCGACAGCACAGACAAGGCAGACCUGAG
		ACUGAUCUACCUGGCACUGGCACACAUGAUCAAGUUCAGAGGACACUUCCUGAUCGAAGGAGACCUGAACCCGGAC
		AACAGCGACGUCGACAAGCUGUUCAUCCAGCUGGUCCAGACAUACAACCAGCUGUUCGAAGAAAACCCGAUCAACG
		CAAGCGGAGUCGACGCAAAGGCAAUCCUGAGCGCAAGACUGAGCAAGAGCAGAAGACUGGAAAACCUGAUCGCACA
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		GAGCAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGCUGAGCAAGGACACAUACGACGACGACCUGGACAACCUG
		CUGGCACAGAUCGGAGACCAGUACGCAGACCUGUUCCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGAGCG
		ACAUCCUGAGAGUCAACACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGCAUGAUCAAGAGAUACGACGAACACCAC
		CAGGACCUGACACUGCUGAAGGCACUGGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCAGA
		GCAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUUCUACAAGUUCAUCAAGCCGAUCCU
		GGAAAAGAUGGACGGAACAGAAGAACUGCUGGUCAAGCUGAACAGAGAAGACCUGCUGAGAAAGCAGAGAACAUU
		CGACAACGGAAGCAUCCCGCACCAGAUCCACCUGGGAGAACUGCACGCAAUCCUGAGAAGACAGGAAGACUUCUAC
		CCGUUCCUGAAGGACAACAGAGAAAAGAUCGAAAAGAUCCUGACAUUCAGAAUCCCGUACUACGUCGGACCGCUGG
		CAAGAGGAAACAGCAGAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAACAAUCACACCGUGGAACUUCGAAGAAG
		UCGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAACUUCGACAAGAACCUGCCGAACGAAAA
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		GAAGGAAUGAGAAAGCCGGCAUUCCUGAGCGGAGAACAGAAGAAGGCAAUCGUCGACCUGCUGUUCAAGACAAAC
		AGAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUACUUCAAGAAGAUCGAAUGCUUCGACAGCGUCGAAAUCAGC
		GGAGUCGAAGACAGAUUCAACGCAAGCCUGGGAACAUACCACGACCUGCUGAAGAUCAUCAAGGACAAGGACUUCC

SEQ ID NO	Name	Sequence
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		ACAUCGUCAUCGAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAGAAUGAAGAG
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		AUACAAGGAAGUCAAGAAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUCGAACUGGAAAACGGAAGAAA
		GAGAAUGCUGGCAAGCGCAGGAGAACUGCAGAAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUCCU
		GUACCUGGCAAGCCACUACGAAAAGCUGAAGGGAAGCCCGGAAGACAACGAACAGAAGCAGCUGUUCGUCGAACAG
		CACAAGCACUACCUGGACGAAAUCAUCGAACAGAUCAGCGAAUUCAGCAAGAGAGUCAUCCUGGCAGACGCAAACC
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SEQ ID NO	Name	Sequence
3522	dCas9 coding sequence using minimal uridine codons (no start or stop codons; suitable for inclusion in fusion protein coding sequence)	GACAAGAAGUACAGCAUCGGACUGGCAAUCGGAACAAACAGCGUCGGAUGGGCAGUCAUCACAGACGAAUACAAG GUCCCGAGCAAGAAGUUCAAGGUCCUGGGAAACACAGACAGACACAGCAUCAAGAAGAACCUGAUCGGAGCACUGC UGUUCGACAGCGGAGAAACAGCAGAAGCAACAAGACUGAAGAGAACAGCAAGAAGAAGAUACACAAGAAAGAA CAGAAUCUGCUACCUGCAGGAAAUCUUCAGCAACGAAAUGGCAAAGGUCGACGACAGCUUCUUCCACAGACUGGAA GAAAGCUUCCUGGUCGAAGAAGACAAGAAGCACGAAAGACACCCGAUCUUCGGAAACAUCGUCGACGAAGUCGCAU ACCACGAAAAGUACCCGACAAUCUACCACCUGAGAAAGAAGCUGGUCGACAGCACACAGACAAGGCAGACCUGAGACU GAUCUACCUGGCACUGGCACACAUGAUCAAGUUCAGAGGACACUUCCUGAUCGAAGGAGACCUGAACCCGGACAAC AGCGACGUCGACACAAGCUGUUCAUCCAGCUGGUCCAGACAUACAACCAGCUGUUCGAAGAAAACCCGAUCAACGCAA GCGGAGUCGACGCAAAGGCAAUCCUGAGCGCAAGACUGAGACAAGAGCAGAAGACUGGAAAACCUGAUCGCACAGCU GCCGGGAGAAAAGAAGAACGGACUGUUCGGAAACCUGAUCGCACUGAGCCUGGGACUGACACCGAACUUCAAGAG CAACUUCGACCUGGCAGAAGACGCAAAGCUGCAGCUGAGCAAGGACACAUACGACGACGACCUGGACAACCUGCUG GCACAGAUCGGAGACCAGUACGCAGACCUGUUCCUGGCAGCAAAGAACCUGAGCGACGCAAUCCUGCUGAGCGACA UCCUGAGAGUCAACACAGAAAUCACAAAGGCACCGCUGAGCGCAAGCAUGAUCAAGAGAUACGACGAACACCACCA GGACCUGACACUGCUGAAGGCACUGGUCAGACAGCAGCUGCCGGAAAAGUACAAGGAAAUCUUCUUCGACCAGAG CAAGAACGGAUACGCAGGAUACAUCGACGGAGGAGCAAGCCAGGAAGAAUUCUACAAGUUCAUCAAGCCGAUCCUG GAAAAGAUGGACGGAACAGAAGAACUGCUGGUCAAGCUGAACAGAGAAGACCUGCUGAGAAAGCAGAGAACAUUC GACAACGGAAGCAUCCCGCACCAGAUCCACCUGGGAGAACUGCACGCAAUCCUGAGAAGACAGGAAGACUUCUACC CGUUCCUGAAGGACAACAGAGAAAAGAUCGAAAAGAUCCUGACAUUCAGAAUCCCGUACUACGUCGGACCGCUGGC AAGAGGAAACAGCAGAUUCGCAUGGAUGACAAGAAAGAGCGAAGAAACAAUCACACCGUGGAACUUCGAAGAAGU CGUCGACAAGGGAGCAAGCGCACAGAGCUUCAUCGAAAGAAUGACAAACUUCGACAAGAACCUGCCGAACGAAAAG GUCCUGCCGAAGCACAGCCUGCUGUACGAAUACUUCACAGUCUACAACGAACUGACAAAGGUCAAGUACGUCACAG AAGGAAUGAGAAAGCCGGCAUUCCUGAGCGGAGAACAGAAGAAGGGCAAUCGUCGACCUGCUGUUCAAGACAAACA GAAAGGUCACAGUCAAGCAGCUGAAGGAAGACUACUUCAAGAAGAUCGAAUGCUUCGACAGCGUCGAAAUCAGCG GAGUCGAAGACAGAUUCAACGCAAGCCUGGGAAACAUACCACGACCUGCUGAAGAUCAUCAAGGACAAGGACUUCCU GGACAACGAAGAAAACGAAGACAUCCUGGAAGACAUCGUCCUGACACUGACCUGAAGACAGAGAAAUGAUC GAAGAAAGACUGAAGACAUACGCACACCUGUUCGACGACAAGGUCAUGAAGCAGCUGAAGAGAAGAAGGAUACACA GGAUGGGGAAGACUGAGCAGAAAGCUGAUCAACGGAAUCAGAGACAAGCAGAGCGGAAAGACAAUCCUGGACUUC CUGAAGAGCGACGGAUUUCGCAAACAGAAACUUCAUGCAGCUGAUCCACGACAGCCUGACAUUCAAGGAAGACA UCCAGAAGGCACAGGUCAGCGGACAGGGAGACAGCCUGCACGAACACAUCGCAAACCUGGCAGGAAGCCCGGCAAU CAAGAAGGGAAUCCUGCAGACAGUCAAGGUCGUCGACGAACUGGUCAAGGUCAUGGGAAGACACAAGCCGGAAAA CAUCGUCAUCGAAAUGGCAAGAGAAAACCAGACAACACAGAAGGGACAGAAGAACAGCAGAGAAAGAAUGAAGAGA AUCGAAGAAGGAAUCAAGGAACUGGGAAGCCAGAUCCUGAAGGAACACCCGGUCGAAAACACACAGCUGCAGAACG

SEQ ID NO	Name	Sequence
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		AAGCGACAAGAACAGAGGAAAGAGCGACAACGUCCCGAGCGAAGAAGUCGUCAAGAAGAUGAAGAACUACUGGAG
		ACAGCUGCUGAACGCAAAGCUGAUCACACAGAGAAAGUUCGACACAACCUGACAAAGGCAGAGAGAGGAGGACUGAGC
		GAACUGGACAAGGCAGGAUUCAUCAAGAGACAGCUGGUCGAAACAAGACAGAUCACACAAAGCACGUCGCACAGAUCC
		UGGACAGCAGAAUGAACACAAAGUACGACGAAAACGACAAGCUGAUCAGAGAAGUCAAGGUCACUCACACUGAAGAG
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		CGACAGUCGCAUACAGCGCUCCUGGUCGUCGCAAAGGUCGAAAAGGGAAAGAGCAAGAAGCUGAAGAGCGUCAAGG
		AACUGCUGGGAAUCACAAUCAUGGAAAGAAGCAGCUUCGAAAAGAACCCGAUCGACUUCCUGGAAGCAAAGGGAU
		ACAAGGAAGUCAAGAAAGGACCUGAUCAUCAAGCUGCCGAAGUACAGCCUGUUCGAACUGGAAAACGGAAGAAAGA
		GAAUGCUGGGCAAGCGCAGGAGAACUGCAGAAGGGAAACGAACUGGCACUGCCGAGCAAGUACGUCAACUUCCUGU
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		CACAAAGGAAGUCCUGGACGCAACACUGAUCCACCAGAGCAUCACAGGACUGUACGAAACAAGAAUCGACCUGAGC
		CAGCUGGGAGGAGAC
		GGAAGCGGAAGCCCGAAGAAGAAGAGGUCGACGGAAGCCCGAAGAAGAAGAGAAAGGUCGACAGCGGA
3523	Cas9 transcript with 5' UTR of HSD, ORF corresponding to SEQ ID NO: 3502, Kozak sequence, and 3' UTR of ALB	GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTCGTTGCAGGCCTTATTCGGATCCGCCACCATGG
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SEQ ID NO	Name	Sequence
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3524	Cas9 transcript with 5' UTR of HSD, ORF corresponding to SEQ ID NO: 3502, and 3' UTR of ALB	GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTCGTTGCAGGCCTTATTCGGATCCATGGACAAGA
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SEQ ID NO	Name	Sequence
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3525	Cas9 ORF with splice junctions removed; 12.75% U content	ATGGACAAGAAGTACAGCATCGGACTGGACATCGGAACAAACAGCGTCGGATGGGCAGTCATCACAGACGAATACAAG
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SEQ ID NO	Name	Sequence
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SEQ ID NO	Name	Sequence
3526	Cas9 ORF with minimal uridine codons frequently used in humans in general; 12.75% U content	ATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACACAGACATCAAGAAGAACCTGATCGGCGCCCTGCTGT TCGACAGCGGCGAGACCGCCGAGGCCACCAGACTGAAGAGAACCGCCAGAAGAAGATACACCAGAAGAACAGA ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACAGACTGGAGGAGAGCT TCCTGGTGGAGGAGGACAAGAAGCACGAGAGACACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA AGTACCCCACCATCTACCACCTGAGAAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGAGACTGATCTACCTGGC CCTGGCCCACATGATCAAGTTCAGAGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG CTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCCAAGG CCATCCTGAGCGCCAGACTGAGCAAGAGCAGAAGACTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACG GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGAGAGTGAACACCGAGATCACCAAGGC CCCCCTGAGCGCCAGCATGATCAAGAGATACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGAGACAG CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA ACAGAGAGGACCTGCTGAGAAAGCAGAGAACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCA CGCCATCCTGAGAAGACAGGAGGACTTCTACCCCTTCCTGAAGGACAACAGAGAGAAGATCGAGAAGATCCTGACCTTC AGAATCCCCTACTACGTGGGCCCCCTGGCCAGAGGCAACAGCAGATTCGCCTGGATGACCAGAAAGAGCGAGGAGACC ATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGAGAATGACCAACTTCG ACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGAC CAAGGTGAAGTACGTGACCGAGGGCATGAGAAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACCT GCTGTTCAAGACCAACAGAAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAG CGTGGAGATCAGCGGCGTGGAGGACAGATTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGA CAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACAG AGAGATGATCGAGGAGAGACTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGAGAAGAAG ATACACCGGCTGGGGCAGACTGAGCAGAAAGCTGATCAACGGCATCAGAGACAAGCAGAGCGGCAAGACCATCCTGGA CTTCCTGAAGAGCGACGGCTTCGCCAACAGAAACTTCATGCAGCTGATCCACGACGACAGCCTGACCTTCAAGGAGGAC ATCCAGAAGGCCCAGGTGAGCGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCAGACACAAGCCCGAGAACAT CGTGATCGAGATGGCCAGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCAGAGAGAGAATGAAGAGAATCG AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG CTGTACCTGTACTACCTGCAGAACGGGCAGAGACATGTACGTGGACCAGGAGCTGGACATCAACAGACTGAGCGACTACG

SEQ ID NO	Name	Sequence
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		GACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGAGAAACAGCGACAAGCTGATCGCCAGAAA
		GAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGT
		GGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGAGAAGCAGCTTCG
		AGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGT
		ACAGCCTGTTCGAGCTGGAGAACGGCAGAAAGAGAATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTG
		GCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACG
		AGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGA
		GAGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACAGAGACAAGCCCATCAGAGAGC
		AGGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCG
		ACAGAAAGAGATACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGAC
		CAGAATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCAGCCCCAAGAAGAAGAGAAAGGTGTGA
3527	Cas9 transcript with 5' UTR of HSD, ORF corresponding to SEQ ID NO: 3526, Kozak sequence, and 3' UTR of ALB	GGGTCCCGCAGTCGGCGTCCAGCGGCTCTGCTTGTTCGTGTGTGTCGTTGCAGGCCTTATTCGGATCCGCCACCATGG
		ACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGGTGC
		CCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACAGACACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTCGA
		CAGCGGCGAGACCGCCGAGGCCACCAGACTGAAGAGAACCGCCAGAAGAAGATACACCAGAAGAAAGAACAGAATCT
		GCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACAGACTGGAGGAGAGCTTCCT
		GGTGGAGGAGGACAAGAAGCACGAGAGACACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGTA
		CCCCACCATCTACCACCTGAGAAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGAGACTGATCTACCTGGCCCTG
		GCCCACATGATCAAGTTCAGAGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAGCTGT
		TCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCCAAGGCCAT
		CCTGAGCGCCAGACTGAGCAAGAGCAGAAGACTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCT
		GTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCCAAG

SEQ ID NO	Name	Sequence
		CTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGT
		TCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGAGAGTGAACACCGAGATCACCAAGGCCCC
		CCTGAGCGCCAGCATGATCAAGAGATACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGAGACAGCA
		GCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCAG
		CCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAA
		CAGAGAGGACCTGCTGAGAAAGCAGAGAACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGCAC
		GCCATCCTGAGAAGACAGGAGGACTTCTACCCCTTCCTGAAGGACAACAGAGAGAAGATCGAGAAGATCCTGACCTTCA
		GAATCCCCTACTACGTGGGCCCCCTGGCCAGAGGCAACAGCAGATTCGCCTGGATGACCAGAAAGAGCGAGGAGACCA
		TCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGAGAATGACCAACTTCGA
		CAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACC
		AAGGTGAAGTACGTGACCGAGGGCATGAGAAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACCTG
		CTGTTCAAGACCAACAGAAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACAGC
		GTGGAGATCAGCGGCGTGGAGGACAGATTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGAC
		AAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACAGA
		GAGATGATCGAGGAGAGACTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGAGAAGAAGA
		TACACCGGCTGGGGCAGACTGAGCAGAAAGCTGATCAACGGCATCAGAGACAAGCAGAGCGGCAAGACCATCCTGGAC
		TTCCTGAAGAGCGACGGCTTCGCCAACAGAAACTTCATGCAGCTGATCCACGACGACAGCCTGACCTTCAAGGAGGACA
		TCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATCA
		AGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCAGACACAAGCCCGAGAACATC
		GTGATCGAGATGGCCAGAGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCAGAGAGAGAATGAAGAGAATCGA
		GGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGC
		TGTACCTGTACTACCTGCAGAACGGCAGAGACATGTACGTGGACCAGGAGCTGGACATCAACAGACTGAGCGACTACGA
		CGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCAGAAGCGACAAGAAC
		AGAGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGAGACAGCTGCTGAACGC
		CAAGCTGATCACCCAGAGAAAGTTCGACAACCTGACCAAGGCCGAGAGAGGCGGCCTGAGCGAGCTGGACAAGGCCGG
		CTTCATCAAGAGACAGCTGGTGGAGACCAGACAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCAGAATGAACACC
		AAGTACGACGAGAACGACAAGCTGATCAGAGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTCAGA
		AAGGACTTCCAGTTCTACAAGGTGAGAGAGATCAACAACTACCACCACGACGCCCACGACGCCTACCTGAACGCCGTGGTGG
		GCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGAGAA
		AGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTTCTTC
		AAGACCGAGATCACCCTGGCCAACGGCGAGATCAGAAAGAGACCCCTGATCGAGACCAACGGCGAGACCGGCGAGATC
		GTGTGGGACAAGGGCAGAGACTTCGCCACCGTGAGAAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAGACC

SEQ ID NO	Name	Sequence
		GAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGAGAAACAGCGACAAGCTGATCGCCAGAAAGAAG
		GACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGTGGAG
		AAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGAAGCAGCTTCGAGAA
		GAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACAGC
		CTGTTCGAGCTGGAGAACGGCAGAAGAGAATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCT
		GCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGAGCA
		GAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGAGAGT
		GATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACAGAGACAAGCCCATCAGAGAGGCAGGC
		CGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCGCCTTCAAGTACTTCGACACCACCATCGACAG
		AAAGAGATACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACCAGA
		ATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCAGCCCCAAGAAGAAGAAAGGTGTGACTAGCCATCACATTT
		AAAAGCATCTCAGCCTACCATGAGAATAAGAGAAAGAAAATGAAGATCAATAGCTTATTCATCTCTTTTTCTTTTTCGTTG
		GTGTAAAGCCAACACCCTGTCTAAAAAACATAAATTTCTTTAATCATTTTGCCTCTTTTCTCTGTGCTTCAATTAATAAAAAA
		TGGAAAGAACCTCGAG
3528		Not Used
3529	Cas9 ORF using long half life codons of Table 4, with start and stop codons	ATGGACAAGAAGTACTCTATCGGTTTGGACATCGGTACCAACTCTGTCGGTTGGGCCGTCATCACCGACGAATACAAGGT
		CCCATCTAAGAAGTTCAAGGTCTTGGGTAACACCGACAGACACTCTATCAAGAAGAACTTGATCGGTGCCTTGTTGTTCG
		ACTCTGGTGAAACCGCCGAAGCCACCAGATTGAAGAGAACCGCCAGAAGAAGATACACCAGAAGAAAGAACAGAATCT
		GCTACTTGCAAGAAATCTTCTCTAACGAAATGGCCAAGGTCGACGACTCTTTCTTCCACAGATTGGAAGAATCTTTCTTGG
		TCGAAGAAGACAAGAAGCACGAAAGACACCCAATCTTCGGTAACATCGTCGACGAAGTCGCCTACCACGAAAAGTACCC
		AACCATCTACCACTTGAGAAAGAAGTTGGTCGACTCTACCGACAAGGCCGACTTGAGATTGATCTACTTGGCCTTGGCCC
		ACATGATCAAGTTCAGAGGTCACTTCTTGATCGAAGGTGACTTGAACCCAGACAACTCTGACGTCGACAAGTTGTTCATC
		CAATTGGTCCAAACCTACAACCAATTGTTCGAAGAAAACCCAATCAACGCCTCTGGTGTCGACGCCAAGGCCATCTTGTCT
		GCCAGATTGTCTAAGAGCAGAAGATTGGAAAACTTGATCGCCCAATTGCCAGGTGAAAAGAAGAACGGTTTGTTCGGTA
		ACTTGATCGCCTTGTCTTTGGGTTTGACCCCAAACTTCAAGTCTAACTTCGACTTGGCCGAAGACGCCAAGTTGCAATTGT
		CTAAGGACACCTACGACGACGACTTGGACAACTTGTTGGCCCAAATCGGTGACCAATACGCCGACTTGTTCTTGGCCGCC
		AAGAACTTGTCTGACGCCATCTTGTTGTCTGACATCTTGAGAGTCAACACCGAAATCACCAAGGCCCCATTGTCTGCCTCT
		ATGATCAAGAGATACGACGAACACCACCAAGACTTGACCTTGTTGAAGGCCTTGGTCAGACACAACAATTGCCAGAAAAGT
		ACAAGGAAATCTTCTTCGACCAATCTAAGAACGGTTACGCCGGTTACATCGACGGTGGTGCCTCTCAAGAAGAATTCTAC
		AAGTTCATCAAGCCAATCTTGGAAAAGATGGACGGTACCGAAGAATTGTTGGTCAAGTTGAACAGAGAAGACTTGTTGA
		GAAAGCAAAGAACCTTCGACAACGGTTCTATCCCACACCAAATCCACTTGGGTGAATTGCACGCCATCTTGAGAAGACAA
		GAAGACTTCTACCCATTCTTGAAGGACAACAGAGAAAAGATCGAAAAGATCTTGACCTTCAGAATCCCATACTACGTCGG

SEQ ID NO	Name	Sequence
		TCCATTGGCCAGAGGTAACAGCAGATTCGCCTGGATGACCAGAAAGTCTGAAGAAACCATCACCCCATGGAACTTCGAA
		GAAGTCGTCGACAAGGGTGCCTCTGCCCAATCTTTCATCGAAAGAATGACCAACTTCGACAAGAACTTGCCAAACGAAAA
		GGTCTTGCCAAAGCACTCTTTGTTGTACGAATACTTCACCGTCTACAACGAATTGACCAAGGTCAAGTACGTCACCGAAG
		GTATGAGAAAGCCAGCCTTCTTGTCTGGTGAACAAAAGAAGGCCATCGTCGACTTGTTGTTCAAGACCAACAGAAAGGT
		CACCGTCAAGCAATTGAAGGAAGACTACTTCAAGAAGATCGAATGCTTCGACTCTGTCGAAATCTCTGGTGTCGAAGACA
		GATTCAACGCCTCCTTTGGGTACCTACCACGACTTGTTGAAGATCATCAAGGACAAGGACTTCTTGGACAACGAAGAAAAC
		GAAGACATCTTGGAAGACATCGTCTTGACCTTGACCTTGTTCGAAGACAGAGAAATGATCGAAGAAAGATTGAAGACCT
		ACGCCCACTTGTTCGACGACAAGGTCATGAAGCAATTGAAGAGAAGAAGATACACCGGTTGGGGTAGATTGAGCAGAA
		AGTTGATCAACGGTATCAGAGACAAGCAATCTGGTAAGACCATCTTGGACTTCTTGAAGTCTGACGGTTTCGCCAACAGA
		AACTTCATGCAATTGATCCACGACGACTCTTTGACCTTCAAGGAAGACATCCAAAAGGCCCAAGTCTCTGGTCAAGGTGA
		CTCTTTGCACGAACACATCGCCAACTTGGCCGGTTCTCCAGCCATCAAGAAGGGTATCTTGCAAACCGTCAAGGTCGTCG
		ACGAATTGGTCAAGGTCATGGGTAGACACAAGCCAGAAAACATCGTCATCGAAATGGCCAGAGAAAACCAAACCACCCA
		AAAGGGTCAAAAGAACAGCAGAGAAAGAATGAAGAGAATCGAAGAAGGTATCAAGGAATTGGGTTCTCAAATCTTGAA
		GGAACACCCAGTCGAAAAACACCCAATTGCAAAACGAAAAGTTGTACTTGTACTACTTGCAAAACGGTAGAGACATGTAC
		GTCGACCAAGAATTGGACATCAACAGATTGTCTGACTACGACGTCGACCACATCGTCCCACAATCTTTCTTGAAGGACGA
		CTCTATCGACAACAAGGTCTTGACCAGATCTGACAAGAACAGAGGTAAGTCTGACAACGTCCCATCTGAAGAAGTCGTCA
		AGAAGATGAAGAACTACTGGAGACAATTGTTGAACGCCAAGTTGATCACCCAAAGAAAGTTCGACAACTTGACCAAGGC
		CGAAAGAGGTGGTTTGTCTGAATTGGACAAGGCCGGTTTCATCAAGAGACAATTGGTCGAAACCAGACAAATCACCAAG
		CACGTCGCCCAAATCTTGGACAGCAGAATGAACACCAAGTACGACGAAAACGACAAGTTGATCAGAGAAGTCAAGGTCA
		TCACCTTGAAGTCTAAGTTGGTCTCTGACTTCAGAAAGGACTTCCAATTCTACAAGGTCAGAGAAATCAACAACTACCACC
		ACGCCCACGACGCCTACTTGAACGCCGTCGTCGGTACCGCCTTGATCAAGAAGTACCCAAAGTTGGAATCTGAATTCGTC
		TACGGTGACTACAAGGTCTACGACGTCAGAAAGATGATCGCCAAGTCTGAACAAGAAATCGGTAAGGCCACCGCCAAGT
		ACTTCTTCTACTCTAACATCATGAACTTCTTCAAGACCGAAATCACCTTGGCCAACGGTGAAATCAGAAAGAGACCATTGA
		TCGAAACCAACGGTGAAACCGGTGAAATCGTCTGGGACAAGGGTAGAGACTTCGCCACCGTCAGAAAGGTCTTGTCTAT
		GCCACAAGTCAACATCGTCAAGAAGACCGAAGTCCAAACCGGTGGTTTCTCTAAGGAATCTATCTTGCCAAAGAGAAACT
		CTGACAAGTTGATCGCCAGAAAGAAGGACTGGGACCCAAAGAAGTACGGTGGTTTCGACTCTCCAACCGTCGCCTACTCT
		GTCTTGGTCGTCGCCAAGGTCGAAAAGGGTAAGTCTAAGAAGTTGAAGTCTGTCAAGGAATTGTTGGGTATCACCATCAT
		GGAAAGATCTTCTTTCGAAAAGAACCCAATCGACTTCTTGGAAGCCAAGGGTTACAAGGAAGTCAAGAAGGACTTGATC
		ATCAAGTTGCCAAAGTACTCTTTGTTCGAATTGGAAAACGGTAGAAAGAGAATGTTGGCCTCTGCCGGTGAATTGCAAAA
		GGGTAACGAATTGGCCTTGCCATCTAAGTACGTCAACTTCTTGTACTTGGCCTCTCACTACGAAAAGTTGAAGGGTTCTCC
		AGAAGACAACGAACAAAAGCAATTGTTCGTCGAACAACACAAGCACTACTTGGACGAAATCATCGAACAAATCTCTGAAT
		TCTCTAAGAGAGTCATCTTGGCCGACGCCAACTTGGACAAGGTCTTGTCTGCCTACAACAAGCACAGAGACAAGCCAATC

SEQ ID NO	Name	Sequence
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		ACCATCGACAGAAAGAGATACACCTCTACCAAGGAAGTCTTGGACGCCACCCTTGATCCACCAATCTATCACCGGTTTGTA
		CGAAACCAGAATCGACTTGTCTCAATTGGGTGGTGACGGTGGTGGTTCTCCAAAGAAGAAGAGAAAGGTCTAA
		ATGGACAAGAAGTACTCCATCGGCCTGGACATCGGCACCAACTCCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGG
		TGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGTTC
		GACTCCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGGAT
		CTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACTCCTTCTTCCACCGGCTGGAGGAGTCCTTCC
		TGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGT
		ACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGCCCTG
		GCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCCGACGTGGACAAGCTGTT
		CATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGGCCATC
		CTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGT
		TCGGCAACCTGATCGCCCTGTCCCTGGGCCTGACCCCCAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCCAAGCTG
		CAGCTGTCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGTTCCT
		GGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCCTGT
		CCGCCTCCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAGCTGCC
3530	Cas9 ORF using low A codons of Table 4, with start and stop codons	CGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCTCCCAGGAG
		GAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG
		GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCT
		GCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCC
		TACTACGTGGGCCCCCTGGCCCGGGGCAACTCCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCCCT
		GGAACTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCCAGTCCTTCATCGAGCGGATGACCAACTTCGACAAGAACCT
		GCCCAACGAGAAGGTGCTGCCCAAGCACTCCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAG
		TACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCTGCTGTTCAAGA
		CCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTC
		CGGCGTGGAGGACCGGTTCAACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTG
		GACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCGGGAGATGATCGAG
		GAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG
		GGCCGGCTGTCCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGTCCG
		ACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACTCCCTGACCTTCAAGGAGGACATCCAGAAGGCCCA
		GGTGTCCGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCCGGCTCCCCCGCCATCAAGAAGGGCATCCTG
		CAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAGATGGC

SEQ ID NO	Name	Sequence
		CCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGG
		AGCTGGGCTCCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCT
		GCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGTCCGACTACGACGTGGACCACATCGT
		GCCCCAGTCCTTCCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCGGGGCAAGTCCGAC
		AACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAG
		CGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAG
		CTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAAC
		GACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCT
		ACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAA
		GAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCCAAGTCC
		GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACCCT
		GGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCC
		GGGACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCG
		GCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACTCCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAA
		GTACGGCGGCTTCGACTCCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCCAAGAA
		GCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTCCTTCGAGAAGAACCCCATCGACTTCCTG
		GAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACTCCCTGTTCGAGCTGGAGAAC
		GGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCTCCAAGTACGTGAAC
		TTCCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCCCCCGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGC
		AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAACCT
		GGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTC
		ACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAA
		GGAGGTGCTGGACGCCACCCTGATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACCTGTCCCAGCTGGGC
		GGCGACGGCGGCGGCTCCCCCAAGAAGAAGCGGAAGGTGTGA
3531	Cas9 ORF using low A/U codons of Table 4, with start and stop codons	ATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG
		GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT
		TCGACAGCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGG
		ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT
		TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA
		AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC
		CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG
		CTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCCAAGG

SEQ ID NO	Name	Sequence
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		GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC
		AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC
		TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC
		CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG
		CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA
		GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA
		ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC
		ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT
		CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC
		CATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC
		GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA
		CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC
		TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA
		GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG
		ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG
		GGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCG
		GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA
		CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACAGCCTGACCTTCAAGGAGGAC
		ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC
		AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACAT
		CGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCCGCGAGCGGATGAAGCGGATCG
		AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG
		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGA
		ACCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAAC
		GCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCC
		GGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCCGGATGAAC
		ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTC
		CGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGG
		TGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGC
		GGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTT

SEQ ID NO	Name	Sequence
		CTTCAAGACCGAGATCACCCTGGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGA
		GATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCGGAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAA
		GACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAA
		GAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGT
		GGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGAGCAGCTTCG
		AGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGT
		ACAGCCTGTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTG
		GCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACG
		AGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGC
		GGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC
		AGGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCGCCTTCAAGTACTTCGACACCACCATCG
		ACCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGAC
		CCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCAGCCCCAAGAAGAAGCGGAAGGTGTGA
3532	Cas9 ORF using low A codons of Table 4, with two C-terminal NLS sequences and start and stop codons	ATGGACAAGAAGTACTCCATCGGCCTGGACATCGGCACCAACTCCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGG
		TGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTC
		GACTCCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGGAT
		CTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACTCCTTCTTCCACCGGCTGGAGGAGTCCTTCC
		TGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGT
		ACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGCCCTG
		GCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCCGACGTGGACAAGCTGTT
		CATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGGCCATC
		CTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGT
		TCGGCAACCTGATCGCCCTGTCCCTGGGCCTGACCCCCAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCCAAGCTG
		CAGCTGTCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGTTCCT
		GGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCCTGT
		CCGCCTCCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAGCTGCC
		CGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCTCCCAGGAG
		GAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG
		GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCT
		GCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCC
		TACTACGTGGGCCCCCTGGCCCGGGGCAACTCCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCCCT
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SEQ ID NO	Name	Sequence
		GCCCAACGAGAAGGTGCTGCCCAAGCACTCCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAG
		TACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCTGCTGTTCAAGA
		CCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTC
		CGGCGTGGAGGACCGGTTCAACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTG
		GACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCGGGAGATGATCGAG
		GAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG
		GGCCGGCTGTCCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGTCCG
		ACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACTCCCTGACCTTCAAGGAGGACATCCAGAAGGCCCA
		GGTGTCCGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCCGGCTCCCCCGCCATCAAGAAGGGCATCCTG
		CAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAGATGGC
		CCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGG
		AGCTGGGCTCCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCT
		GCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGTCCGACTACGACGTGGACCACATCGT
		GCCCCAGTCCTTCCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCGGGGCAAGTCCGAC
		AACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAG
		CGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAG
		CTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAAC
		GACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCT
		ACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAA
		GAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCCAAGTCC
		GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACCCT
		GGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCC
		GGGACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCG
		GCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACTCCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAA
		GTACGGCGGCTTCGACTCCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCCAAGAA
		GCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTCCTTCGAGAAGAACCCCATCGACTTCCTG
		GAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACTCCCTGTTCGAGCTGGAGAAC
		GGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCTCCAAGTACGTGAAC
		TTCCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCCCCCGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGC
		AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAACCT
		GGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTC
		ACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAA

SEQ ID NO	Name	Sequence
		GGAGGTGCTGGACGCCACCCTGATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACCTGTCCCAGCTGGGC GGCGACGGCTCCGGCTCCCCCAAGAAGAAGCGGAAGGTGGACGGCTCCCCCAAGAAGAAGCGGAAGGTGGACTCCGG CTGA
3533	Cas9 nickase ORF using low A codons of Table 4, with start and stop codons	ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGG TGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGTTC GACTCCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGGAT CTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACTCCTTCTTCCACCGGCTGGAGGAGTCCTTCC TGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGT ACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGCCCTG GCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCCGACGTGGACAAGCTGTT CATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGGCCATC CTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGT TCGGCAACCTGATCGCCCTGTCCCTGGGCCTGACCCCCAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCCAAGCTG CAGCTGTCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGTTCCT GGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCCTGT CCGCCTCCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAGCTGCC CGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCTCCCAGGAG GAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCT GCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCC TACTACGTGGGCCCCCTGGCCCGGGGCAACTCCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCCT GGAACTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCCAGTCCTTCATCGAGCGGATGACCAACTTCGACAAGAACCT GCCCAACGAGAAGGTGCTGCCCAAGCACTCCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCTGCTGTTCAAGA CCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTC CGGCGTGGAGGACCGGTTCAACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTG GACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCGGGAGATGATCGAG GAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG GGCCGGCTGTCCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGTCCG ACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACTCCCTGACCTTCAAGGAGGACATCCAGAAGGCCCA GGTGTCCGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCCGGCTCCCCCGCCATCAAGAAGGGCATCCTG CAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAGATGGC

SEQ ID NO	Name	Sequence
		CCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGG
		AGCTGGGCTCCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCT
		GCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGTCCGACTACGACGTGGACCACATCGT
		GCCCCAGTCCTTCCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCGGGGCAAGTCCGAC
		AACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAG
		CGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAG
		CTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAAC
		GACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCT
		ACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAA
		GAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCCAAGTCC
		GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACCCT
		GGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCC
		GGGACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCG
		GCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACTCCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAA
		GTACGGCGGCTTCGACTCCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCCAAGAA
		GCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTCCTTCGAGAAGAACCCCATCGACTTCCTG
		GAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACTCCCTGTTCGAGCTGGAGAAC
		GGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCTCCAAGTACGTGAAC
		TTCCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCCCCCGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGC
		AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAACCT
		GGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTC
		ACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAA
		GGAGGTGCTGGACGCCACCCTGATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACCTGTCCCAGCTGGGC
		GGCGACGGCGGCGGCTCCCCCAAGAAGAAGCGGAAGGTGTGA
3534	Cas9 nickase ORF using low A codons of Table 4, with start and stop codons and no NLS	ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGG
		TGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTC
		GACTCCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGGAT
		CTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACTCCTTCTTCCACCGGCTGGAGGAGTCCTTCC
		TGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGT
		ACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGCCCTG
		GCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCCGACGTGGACAAGCTGTT
		CATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGGCCATC

SEQ ID NO	Name	Sequence
		CTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAACGGCCTGT
		TCGGCAACCTGATCGCCCTGTCCCTGGGCCTGACCCCCAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCCAAGCTG
		CAGCTGTCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGTTCCT
		GGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCCTGT
		CCGCCTCCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAGCTGCC
		CGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCTCCCAGGAG
		GAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG
		GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCT
		GCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCC
		TACTACGTGGGCCCCCTGGCCCGGGGCAACTCCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCCT
		GGAACTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCCAGTCCTTCATCGAGCGGATGACCAACTTCGACAAGAACCT
		GCCCAACGAGAAGGTGCTGCCCAAGCACTCCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAG
		TACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCTGCTGTTCAAGA
		CCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTC
		CGGCGTGGAGGACCGGTTCAACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTG
		GACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCGGGAGATGATCGAG
		GAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG
		GGCCGGCTGTCCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGTCCG
		ACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACTCCCTGACCTTCAAGGAGGACATCCAGAAGGCCCA
		GGTGTCCGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCCGGCTCCCCCGCCATCAAGAAGGGCATCCTG
		CAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAGATGGC
		CCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGG
		AGCTGGGCTCCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCT
		GCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGTCCGACTACGACGTGGACCACATCGT
		GCCCCAGTCCTTCCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCGGGGCAAGTCCGAC
		AACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAG
		CGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAG
		CTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAAC
		GACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCT
		ACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAA
		GAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCCAAGTCC
		GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACCCT

SEQ ID NO	Name	Sequence
		GGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCC
		GGGACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCG
		GCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACTCCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAA
		GTACGGCGGCTTCGACTCCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCCAAGAA
		GCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTCCTTCGAGAAGAACCCCATCGACTTCCTG
		GAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACTCCCTGTTCGAGCTGGAGAAC
		GGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCTCCAAGTACGTGAAC
		TTCCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCCCCCGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGC
		AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAACCT
		GGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTC
		ACCCTGACCAACCTGGGCGCCCCCGCCGCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAA
		GGAGGTGCTGGACGCCACCCTGATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACCTGTCCCAGCTGGGC
		GGCGACTGA
3535	Cas9 nickase ORF using low A codons of Table 4, with two C-terminal NLS sequences and start and stop codons	ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGG
		TGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTC
		GACTCCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGGAT
		CTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACTCCTTCTTCCACCGGCTGGAGGAGTCCTTCC
		TGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGT
		ACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGCCCTG
		GCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCCGACGTGGACAAGCTGTT
		CATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGGCCATC
		CTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGT
		TCGGCAACCTGATCGCCCTGTCCCTGGGCCTGACCCCCAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCCAAGCTG
		CAGCTGTCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGTTCCT
		GGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCCTGT
		CCGCCTCCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAGCTGCC
		CGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCTCCCAGGAG
		GAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG
		GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCT
		GCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCC
		TACTACGTGGGCCCCCTGGCCCGGGGCAACTCCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCCCT
		GGAACTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCCAGTCCTTCATCGAGCGGATGACCAACTTCGACAAGAACCT

SEQ ID NO	Name	Sequence
		GCCCAACGAGAAGGTGCTGCCCAAGCACTCCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAG
		TACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCTGCTGTTCAAGA
		CCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTC
		CGGCGTGGAGGACCGGTTCAACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTG
		GACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCGGGAGATGATCGAG
		GAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG
		GGCCGGCTGTCCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGTCCG
		ACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACTCCCTGACCTTCAAGGAGGACATCCAGAAGGCCCA
		GGTGTCCGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCCGGCTCCCCCGCCATCAAGAAGGGCATCCTG
		CAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAGATGGC
		CCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGG
		AGCTGGGCTCCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCT
		GCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGTCCGACTACGACGTGGACCACATCGT
		GCCCCAGTCCTTCCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCGGGGCAAGTCCGAC
		AACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAG
		CGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAG
		CTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAAC
		GACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCT
		ACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAA
		GAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCCAAGTCC
		GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACCCT
		GGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCC
		GGGACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCG
		GCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACTCCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAA
		GTACGGCGGCTTCGACTCCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCCAAGAA
		GCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTCCTTCGAGAAGAACCCCATCGACTTCCTG
		GAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACTCCCTGTTCGAGCTGGAGAAC
		GGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCTCCAAGTACGTGAAC
		TTCCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCCCCCGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGC
		AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAACCT
		GGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTC
		ACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAA

SEQ ID NO	Name	Sequence
		GGAGGTGCTGGACGCCACCCTGATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACCTGTCCCAGCTGGGC GGCGACGGCTCCGGCTCCCCCAAGAAGAAGCGGAAGGTGGACGGCTCCCCCAAGAAGAAGCGGAAGGTGGACTCCGG CTGA
3536	dCas9 ORF using low A codons of Table 4, with start and stop codons	ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGG TGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTC GACTCCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGGAT CTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACTCCTTCTTCCACCGGCTGGAGGAGTCCTTCC TGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGT ACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGCCCTG GCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCCGACGTGGACAAGCTGTT CATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGGCCATC CTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGT TCGGCAACCTGATCGCCCTGTCCCTGGGCCTGACCCCCAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCCAAGCTG CAGCTGTCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGTTCCT GGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCCTGT CCGCCTCCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAGCTGCC CGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCTCCCAGGAG GAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCT GCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCC TACTACGTGGGCCCCCTGGCCCGGGGCAACTCCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCCT GGAACTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCCAGTCCTTCATCGAGCGGATGACCAACTTCGACAAGAACCT GCCCAACGAGAAGGTGCTGCCCAAGCACTCCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAG TACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCTGCTGTTCAAGA CCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTC CGGCGTGGAGGACCGGTTCAACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTG GACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCGGGAGATGATCGAG GAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG GGCCGGCTGTCCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGTCCG ACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACTCCCTGACCTTCAAGGAGGACATCCAGAAGGCCCA GGTGTCCGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCCGGCTCCCCCGCCATCAAGAAGGGCATCCTG CAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAGATGGC

SEQ ID NO	Name	Sequence
		CCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGG
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		GCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGTCCGACTACGACGTGGACGCCATCGT
		GCCCCAGTCCTTCCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCGGGGCAAGTCCGAC
		AACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAG
		CGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAG
		CTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAAC
		GACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCT
		ACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAA
		GAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCCAAGTCC
		GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACCCT
		GGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCC
		GGGACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCG
		GCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACTCCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAA
		GTACGGCGGCTTCGACTCCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCCAAGAA
		GCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTCCTTCGAGAAGAACCCCATCGACTTCCTG
		GAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACTCCCTGTTCGAGCTGGAGAAC
		GGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCTCCAAGTACGTGAAC
		TTCCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCCCCCGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGC
		AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAACCT
		GGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTC
		ACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAA
		GGAGGTGCTGGACGCCACCCTGATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACCTGTCCCAGCTGGGC
		GGCGACGGCGGCGGCTCCCCCAAGAAGAAGCGGAAGGTGTGA
3537	dCas9 ORF using low A codons of Table 4, with start and stop codons and no NLS	ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGG
		TGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTC
		GACTCCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGGAT
		CTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACTCCTTCTTCCACCGGCTGGAGGAGTCCTTCC
		TGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGT
		ACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGCCCTG
		GCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCCGACGTGGACAAGCTGTT
		CATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGGCCATC

SEQ ID NO	Name	Sequence
		CTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAACGGCCTGT
		TCGGCAACCTGATCGCCCTGTCCCTGGGCCTGACCCCCAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCCAAGCTG
		CAGCTGTCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGTTCCT
		GGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCCTGT
		CCGCCTCCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAGCTGCC
		CGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCTCCCAGGAG
		GAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG
		GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCT
		GCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCC
		TACTACGTGGGCCCCCTGGCCCGGGGCAACTCCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCCT
		GGAACTTCGAGGAGGTGGTGGACAAGGGCGCCTCCGCCCAGTCCTTCATCGAGCGGATGACCAACTTCGACAAGAACCT
		GCCCAACGAGAAGGTGCTGCCCAAGCACTCCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGACCAAGGTGAAG
		TACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGTCCGGCGAGCAGAAGAAGGCCATCGTGGACCTGCTGTTCAAGA
		CCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTC
		CGGCGTGGAGGACCGGTTCAACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTG
		GACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCGGGAGATGATCGAG
		GAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG
		GGCCGGCTGTCCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGTCCG
		ACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACTCCCTGACCTTCAAGGAGGACATCCAGAAGGCCCA
		GGTGTCCGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCCGGCTCCCCCGCCATCAAGAAGGGCATCCTG
		CAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAGATGGC
		CCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGG
		AGCTGGGCTCCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCT
		GCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGTCCGACTACGACGTGGACGCCATCGT
		GCCCCAGTCCTTCCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCGGGGCAAGTCCGAC
		AACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAG
		CGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGTCCGAGCTGGACAAGGCCGGCTTCATCAAGCGGCAG
		CTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAAC
		GACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCT
		ACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAA
		GAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCCAAGTCC
		GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACCCT

SEQ ID NO	Name	Sequence
		GGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCC
		GGGACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCG
		GCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACTCCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAA
		GTACGGCGGCTTCGACTCCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCCAAGAA
		GCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTCCTTCGAGAAGAACCCCATCGACTTCCTG
		GAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACTCCCTGTTCGAGCTGGAGAAC
		GGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCTCCAAGTACGTGAAC
		TTCCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCCCCCGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGC
		AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAACCT
		GGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTC
		ACCCTGACCAACCTGGGCGCCCCCGCCGCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAA
		GGAGGTGCTGGACGCCACCCTGATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACCTGTCCCAGCTGGGC
		GGCGACTGA
3538	dCas9 ORF using low A codons of Table 4, with two C-terminal NLS sequences and start and stop codons	ATGGACAAGAAGTACTCCATCGGCCTGGCCATCGGCACCAACTCCGTGGGCTGGGCCGTGATCACCGACGAGTACAAGG
		TGCCCTCCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACTCCATCAAGAAGAACCTGATCGGCGCCCTGCTGTTC
		GACTCCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGGAT
		CTGCTACCTGCAGGAGATCTTCTCCAACGAGATGGCCAAGGTGGACGACTCCTTCTTCCACCGGCTGGAGGAGTCCTTCC
		TGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGAAGT
		ACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACTCCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGCCCTG
		GCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACTCCGACGTGGACAAGCTGTT
		CATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCTCCGGCGTGGACGCCAAGGCCATC
		CTGTCCGCCCGGCTGTCCAAGTCCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACGGCCTGT
		TCGGCAACCTGATCGCCCTGTCCCTGGGCCTGACCCCCAACTTCAAGTCCAACTTCGACCTGGCCGAGGACGCCAAGCTG
		CAGCTGTCCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACCTGTTCCT
		GGCCGCCAAGAACCTGTCCGACGCCATCCTGCTGTCCGACATCCTGCGGGTGAACACCGAGATCACCAAGGCCCCCCTGT
		CCGCCTCCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAGCAGCTGCC
		CGAGAAGTACAAGGAGATCTTCTTCGACCAGTCCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCTCCCAGGAG
		GAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGAACCGGGAG
		GACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCTCCATCCCCCACCAGATCCACCTGGGCGAGCTGCACGCCATCCT
		GCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTTCCGGATCCCC
		TACTACGTGGGCCCCCTGGCCCGGGGCAACTCCCGGTTCGCCTGGATGACCCGGAAGTCCGAGGAGACCATCACCCCCT
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SEQ ID NO	Name	Sequence
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		CCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACTCCGTGGAGATCTC
		CGGCGTGGAGGACCGGTTCAACGCCTCCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGGACAAGGACTTCCTG
		GACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCGGGAGATGATCGAG
		GAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCGGTACACCGGCTGG
		GGCCGGCTGTCCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGTCCGGCAAGACCATCCTGGACTTCCTGAAGTCCG
		ACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACTCCCTGACCTTCAAGGAGGACATCCAGAAGGCCCA
		GGTGTCCGGCCAGGGCGACTCCCTGCACGAGCACATCGCCAACCTGGCCGGCTCCCCCGCCATCAAGAAGGGCATCCTG
		CAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACATCGTGATCGAGATGGC
		CCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACTCCCGGGAGCGGATGAAGCGGATCGAGGAGGGCATCAAGG
		AGCTGGGCTCCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAGCTGTACCTGTACTACCT
		GCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGTCCGACTACGACGTGGACGCCATCGT
		GCCCCAGTCCTTCCTGAAGGACGACTCCATCGACAACAAGGTGCTGACCCGGTCCGACAAGAACCGGGGCAAGTCCGAC
		AACGTGCCCTCCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACGCCAAGCTGATCACCCAG
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		CTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACTCCCGGATGAACACCAAGTACGACGAGAAC
		GACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGTCCAAGCTGGTGTCCGACTTCCGGAAGGACTTCCAGTTCT
		ACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGTGGGCACCGCCCTGATCAA
		GAAGTACCCCAAGCTGGAGTCCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCGGAAGATGATCGCCAAGTCC
		GAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACTCCAACATCATGAACTTCTTCAAGACCGAGATCACCCT
		GGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAGATCGTGTGGGACAAGGGCC
		GGGACTTCGCCACCGTGCGGAAGGTGCTGTCCATGCCCCAGGTGAACATCGTGAAGAAGACCGAGGTGCAGACCGGCG
		GCTTCTCCAAGGAGTCCATCCTGCCCAAGCGGAACTCCGACAAGCTGATCGCCCGGAAGAAGGACTGGGACCCCAAGAA
		GTACGGCGGCTTCGACTCCCCCACCGTGGCCTACTCCGTGCTGGTGGTGGCCAAGGTGGAGAAGGGCAAGTCCAAGAA
		GCTGAAGTCCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGTCCTCCTTCGAGAAGAACCCCATCGACTTCCTG
		GAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTACTCCCTGTTCGAGCTGGAGAAC
		GGCCGGAAGCGGATGCTGGCCTCCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGGCCCTGCCCTCCAAGTACGTGAAC
		TTCCTGTACCTGGCCTCCCACTACGAGAAGCTGAAGGGCTCCCCCGAGGACAACGAGCAGAAGCAGCTGTTCGTGGAGC
		AGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCTCCGAGTTCTCCAAGCGGGTGATCCTGGCCGACGCCAACCT
		GGACAAGGTGCTGTCCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCAGGCCGAGAACATCATCCACCTGTTC
		ACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCGACCGGAAGCGGTACACCTCCACCAA

SEQ ID NO	Name	Sequence
		GGAGGTGCTGGACGCCACCCTGATCCACCAGTCCATCACCGGCCTGTACGAGACCCGGATCGACCTGTCCCAGCTGGGC GGCGACGGCTCCGGCTCCCCCAAGAAGAAGCGGAAGGTGGACGGCTCCCCCAAGAAGAAGCGGAAGGTGGACTCCGG CTGA
3539	Cas9 ORF using low A/U codons of Table 4, with two C-terminal NLS sequences and start and stop codons	ATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT TCGACAGCGGCGAAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGG ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG CTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCCAAGG CCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACG GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC CATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG GGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGCCGG GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACAGCCTGACCTTCAAGGAGGAC ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACAT

SEQ ID NO	Name	Sequence
		CGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCG
		AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG
		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGA
		ACCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAAC
		GCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCC
		GGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCCGGATGAAC
		ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTC
		CGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGG
		TGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGC
		GGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTT
		CTTCAAGACCGAGATCACCCTGGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGA
		GATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCGGAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAA
		GACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAA
		GAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGT
		GGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGAGCAGCTTCG
		AGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGT
		ACAGCCTGTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTG
		GCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACG
		AGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGC
		GGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC
		AGGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCG
		ACCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGAC
		CCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCAGCCCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCCA
		AGAAGAAGCGGAAGGTGGACAGCGGCTGA
3540	Cas9 ORF using low A/U codons of Table 4, with start and stop codons and no NLS	ATGGACAAGAAGTACAGCATCGGCCTGGACATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG
		GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT
		TCGACAGCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCTACACCCGGCGGAAGAACCGG
		ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT
		TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA
		AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC
		CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG

SEQ ID NO	Name	Sequence
		CTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCCAAGG
		CCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACG
		GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC
		AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC
		TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC
		CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG
		CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA
		GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA
		ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC
		ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT
		CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC
		CATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC
		GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA
		CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC
		TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA
		GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG
		ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG
		GGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCG
		GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA
		CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACAGCCTGACCTTCAAGGAGGAC
		ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC
		AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACAT
		CGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCCGCGAGCGGATGAAGCGGATCG
		AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG
		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGA
		ACCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAAC
		GCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCC
		GGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCCGGATGAAC
		ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTC
		CGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACCACGACGCCCACGACGCCTACCTGAACGCCGTGG
		TGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGC

SEQ ID NO	Name	Sequence
		GGAAGATGATCGCCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTT
		CTTCAAGACCGAGATCACCCTGGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGA
		GATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCGGAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAA
		GACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAA
		GAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGT
		GGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGAGCAGCTTCG
		AGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGT
		ACAGCCTGTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTG
		GCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACG
		AGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGC
		GGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC
		AGGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCG
		ACCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGAC
		CCGGATCGACCTGAGCCAGCTGGGCGGCGACTGA
3541	Cas9 nickase ORF using low A/U codons of Table 4, with start and stop codons	ATGGACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG
		GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT
		TCGACAGCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGG
		ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT
		TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA
		AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC
		CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG
		CTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCCAAGG
		CCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACG
		GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC
		AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC
		TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC
		CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG
		CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA
		GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA
		ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC
		ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT
		CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC

SEQ ID NO	Name	Sequence
		CATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC
		GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA
		CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC
		TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA
		GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG
		ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG
		GGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCG
		GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA
		CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACAGCCTGACCTTCAAGGAGGAC
		ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC
		AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACAT
		CGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCG
		AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG
		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACATCGACAACAAGGTGCTGACCCGGAGCGACAAGA
		ACCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAAC
		GCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCC
		GGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCCGGATGAAC
		ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTC
		CGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGG
		TGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGC
		GGAAGATGATCGCCAAGAGCGAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTT
		CTTCAAGACCGAGATCACCCTGGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGA
		GATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCGGAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAA
		GACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAA
		GAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGT
		GGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGAGCAGCTTCG
		AGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGT
		ACAGCCTGTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTG
		GCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACG
		AGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGC
		GGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC

SEQ ID NO	Name	Sequence
		AGGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCGCCTTCAAGTACTTCGACACCACCATCG
		ACCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGAC
		CCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCGCAGCCCCAAGAAGAAGCGGAAGGTGTGA
3542	Cas9 nickase ORF using low A/U codons of Table 4, with two C-terminal NLS sequences and start and stop codons	ATGGACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG
		GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT
		TCGACAGCGGCGAAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGG
		ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT
		TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA
		AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC
		CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG
		CTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCCAAGG
		CCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACG
		GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC
		AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC
		TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC
		CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG
		CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA
		GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA
		ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC
		ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT
		CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC
		CATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC
		GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA
		CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC
		TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA
		GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG
		ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG
		GGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGCGG
		GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA
		CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACAGCCTGACCTTCAAGGAGGAC
		ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC
		AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACAT

SEQ ID NO	Name	Sequence
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		AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG
		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGA
		ACCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAAC
		GCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCC
		GGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCCGGATGAAC
		ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTC
		CGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGG
		TGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGC
		GGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTT
		CTTCAAGACCGAGATCACCCTGGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGA
		GATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCGGAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAA
		GACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAA
		GAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGT
		GGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGAGCAGCTTCG
		AGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGT
		ACAGCCTGTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTG
		GCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACG
		AGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGC
		GGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC
		AGGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCG
		ACCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGAC
		CCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCAGCCCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCCA
		AGAAGAAGCGGAAGGTGGACAGCGGCTGA
3543	Cas9 nickase ORF using low A/U codons of Table 4, with start and stop codons and no NLS	ATGGACAAGAAGTACAGCATCGGCCTGGcCATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG
		GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT
		TCGACAGCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCTACACCCGGCGGAAGAACCGG
		ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT
		TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA
		AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC
		CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG

SEQ ID NO	Name	Sequence
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		CCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACG
		GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC
		AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC
		TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC
		CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG
		CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA
		GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA
		ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC
		ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT
		CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC
		CATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC
		GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA
		CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC
		TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA
		GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG
		ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG
		GGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCG
		GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA
		CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACAGCCTGACCTTCAAGGAGGAC
		ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC
		AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACAT
		CGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCCGGGAGCGGATGAAGCGGATCG
		AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG
		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACCACATCGTGCCCCAGAGCTTCCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGA
		ACCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAAC
		GCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCC
		GGCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCCGGATGAAC
		ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTC
		CGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACCACGACGCCCACGACGCCTACCTGAACGCCGTGG
		TGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGC

SEQ ID NO	Name	Sequence
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		GATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCGGAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAA
		GACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAA
		GAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGT
		GGAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGAGCAGCTTCG
		AGAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGT
		ACAGCCTGTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTG
		GCCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACG
		AGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGC
		GGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC
		AGGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCG
		ACCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGAC
		CCGGATCGACCTGAGCCAGCTGGGCGGCGACTGA
3544	dCas9 ORF using low A/U codons of Table 4, with start and stop codons	ATGGACAAGAAGTACAGCATCGGCCTGGcCATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG
		GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT
		TCGACAGCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGG
		ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT
		TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA
		AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC
		CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG
		CTGTTCATCCAGCTGGTGCAGACCTACAACCAGCTGTTCGAGGAGAACCCCATCAACGCCAGCGGCGTGGACGCCAAGG
		CCATCCTGAGCGCCCGGCTGAGCAAGAGCCGGCTGGAGAACCTGATCGCCCAGCTGCCCGGCGAGAAGAAGAACG
		GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC
		AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC
		TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC
		CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG
		CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA
		GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA
		ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC
		ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT
		CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC

SEQ ID NO	Name	Sequence
		CATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC
		GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA
		CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC
		TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA
		GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG
		ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG
		GGAGATGATCGAGGAGCGCCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGCCG
		GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA
		CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACGACAGCCTGACCTTCAAGGAGGAC
		ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC
		AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACAT
		CGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCCGCGGGAGCGGATGAAGCGGATCG
		AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG
		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACgcCATCGTGCCCCAGAGCTTCCTGAAGGACGACATCGACAACAAGGTGCTGACCCGGAGCGACAAGAA
		CCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACG
		CCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCCG
		GCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCCGGATGAACA
		CCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTCC
		GGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGGT
		GGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCG
		GAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTTC
		TTCAAGACCGAGATCACCCTGGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAG
		ATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCGGAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAG
		ACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAG
		AAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGTG
		GAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAAGCGGAAGCAGCTTCGA
		GAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTA
		CAGCCTGTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGG
		CCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGA
		GCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGCG
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SEQ ID NO	Name	Sequence
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		CCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACC
		CGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCAGCCCCAAGAAGAAGCGGAAGGTGTGA
3545	dCas9 ORF using low A/U codons of Table 4, with two C-terminal NLS sequences and start and stop codons	ATGGACAAGAAGTACAGCATCGGCCTGGCCATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG
		GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT
		TCGACAGCGGCGAAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCGGTACACCCGGCGGAAGAACCGG
		ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT
		TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA
		AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC
		CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG
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		GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC
		AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC
		TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC
		CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG
		CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA
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		ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC
		ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT
		CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC
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		GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA
		CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC
		TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA
		GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG
		ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG
		GGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCG
		GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA
		CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACAGCCTGACCTTCAAGGAGGAC
		ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC
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SEQ ID NO	Name	Sequence
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		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACGCCATCGTGCCCCAGAGCTTCCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGA
		ACCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAAC
		GCCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCC
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		ACCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTC
		CGGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACGCCCACGACGCCTACCTGAACGCCGTGG
		TGGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGC
		GGAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTT
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		GACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAA
		GAAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGT
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		AGCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGC
		GGGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGC
		AGGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCTTCAAGTACTTCGACACCACCATCG
		ACCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGAC
		CCGGATCGACCTGAGCCAGCTGGGCGGCGACGGCGGCAGCCCCAAGAAGAAGCGGAAGGTGGACGGCAGCCCCA
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3546	dCas9 ORF using low A/U codons of Table 4, with start and stop codons and no NLS	ATGGACAAGAAGTACAGCATCGGCCTGGcCATCGGCACCAACAGCGTGGGCTGGGCCGTGATCACCGACGAGTACAAG
		GTGCCCAGCAAGAAGTTCAAGGTGCTGGGCAACACCGACCGGCACAGCATCAAGAAGAACCTGATCGGCGCCCTGCTGT
		TCGACAGCGGCGAGACCGCCGAGGCCACCCGGCTGAAGCGGACCGCCCGGCGGCTACACCCGGCGGAAGAACCGG
		ATCTGCTACCTGCAGGAGATCTTCAGCAACGAGATGGCCAAGGTGGACGACAGCTTCTTCCACCGGCTGGAGGAGAGCT
		TCCTGGTGGAGGAGGACAAGAAGCACGAGCGGCACCCCATCTTCGGCAACATCGTGGACGAGGTGGCCTACCACGAGA
		AGTACCCCACCATCTACCACCTGCGGAAGAAGCTGGTGGACAGCACCGACAAGGCCGACCTGCGGCTGATCTACCTGGC
		CCTGGCCCACATGATCAAGTTCCGGGGCCACTTCCTGATCGAGGGCGACCTGAACCCCGACAACAGCGACGTGGACAAG

SEQ ID NO	Name	Sequence
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		GCCTGTTCGGCAACCTGATCGCCCTGAGCCTGGGCCTGACCCCCAACTTCAAGAGCAACTTCGACCTGGCCGAGGACGCC
		AAGCTGCAGCTGAGCAAGGACACCTACGACGACGACCTGGACAACCTGCTGGCCCAGATCGGCGACCAGTACGCCGACC
		TGTTCCTGGCCGCCAAGAACCTGAGCGACGCCATCCTGCTGAGCGACATCCTGCGGGTGAACACCGAGATCACCAAGGC
		CCCCCTGAGCGCCAGCATGATCAAGCGGTACGACGAGCACCACCAGGACCTGACCCTGCTGAAGGCCCTGGTGCGGCAG
		CAGCTGCCCGAGAAGTACAAGGAGATCTTCTTCGACCAGAGCAAGAACGGCTACGCCGGCTACATCGACGGCGGCGCCA
		GCCAGGAGGAGTTCTACAAGTTCATCAAGCCCATCCTGGAGAAGATGGACGGCACCGAGGAGCTGCTGGTGAAGCTGA
		ACCGGGAGGACCTGCTGCGGAAGCAGCGGACCTTCGACAACGGCAGCATCCCCCACCAGATCCACCTGGGCGAGCTGC
		ACGCCATCCTGCGGCGGCAGGAGGACTTCTACCCCTTCCTGAAGGACAACCGGGAGAAGATCGAGAAGATCCTGACCTT
		CCGGATCCCCTACTACGTGGGCCCCCTGGCCCGGGGCAACAGCCGGTTCGCCTGGATGACCCGGAAGAGCGAGGAGAC
		CATCACCCCCTGGAACTTCGAGGAGGTGGTGGACAAGGGCGCCAGCGCCCAGAGCTTCATCGAGCGGATGACCAACTTC
		GACAAGAACCTGCCCAACGAGAAGGTGCTGCCCAAGCACAGCCTGCTGTACGAGTACTTCACCGTGTACAACGAGCTGA
		CCAAGGTGAAGTACGTGACCGAGGGCATGCGGAAGCCCGCCTTCCTGAGCGGCGAGCAGAAGAAGGCCATCGTGGACC
		TGCTGTTCAAGACCAACCGGAAGGTGACCGTGAAGCAGCTGAAGGAGGACTACTTCAAGAAGATCGAGTGCTTCGACA
		GCGTGGAGATCAGCGGCGTGGAGGACCGGTTCAACGCCAGCCTGGGCACCTACCACGACCTGCTGAAGATCATCAAGG
		ACAAGGACTTCCTGGACAACGAGGAGAACGAGGACATCCTGGAGGACATCGTGCTGACCCTGACCCTGTTCGAGGACCG
		GGAGATGATCGAGGAGCGGCTGAAGACCTACGCCCACCTGTTCGACGACAAGGTGATGAAGCAGCTGAAGCGGCGGCG
		GTACACCGGCTGGGGCCGGCTGAGCCGGAAGCTGATCAACGGCATCCGGGACAAGCAGAGCGGCAAGACCATCCTGGA
		CTTCCTGAAGAGCGACGGCTTCGCCAACCGGAACTTCATGCAGCTGATCCACGACAGCCTGACCTTCAAGGAGGAC
		ATCCAGAAGGCCCAGGTGAGCGGCCAGGGCGACAGCCTGCACGAGCACATCGCCAACCTGGCCGGCAGCCCCGCCATC
		AAGAAGGGCATCCTGCAGACCGTGAAGGTGGTGGACGAGCTGGTGAAGGTGATGGGCCGGCACAAGCCCGAGAACAT
		CGTGATCGAGATGGCCCGGGAGAACCAGACCACCCAGAAGGGCCAGAAGAACAGCCGCGAGCGGATGAAGCGGATCG
		AGGAGGGCATCAAGGAGCTGGGCAGCCAGATCCTGAAGGAGCACCCCGTGGAGAACACCCAGCTGCAGAACGAGAAG
		CTGTACCTGTACTACCTGCAGAACGGCCGGGACATGTACGTGGACCAGGAGCTGGACATCAACCGGCTGAGCGACTACG
		ACGTGGACgcCATCGTGCCCCAGAGCTTCCTGAAGGACGACAGCATCGACAACAAGGTGCTGACCCGGAGCGACAAGAA
		CCGGGGCAAGAGCGACAACGTGCCCAGCGAGGAGGTGGTGAAGAAGATGAAGAACTACTGGCGGCAGCTGCTGAACG
		CCAAGCTGATCACCCAGCGGAAGTTCGACAACCTGACCAAGGCCGAGCGGGGCGGCCTGAGCGAGCTGGACAAGGCCG
		GCTTCATCAAGCGGCAGCTGGTGGAGACCCGGCAGATCACCAAGCACGTGGCCCAGATCCTGGACAGCCGGATGAACA
		CCAAGTACGACGAGAACGACAAGCTGATCCGGGAGGTGAAGGTGATCACCCTGAAGAGCAAGCTGGTGAGCGACTTCC
		GGAAGGACTTCCAGTTCTACAAGGTGCGGGAGATCAACAACTACCACCACGCCCACGACGCCTACCTGAACGCCGTGGT
		GGGCACCGCCCTGATCAAGAAGTACCCCAAGCTGGAGAGCGAGTTCGTGTACGGCGACTACAAGGTGTACGACGTGCG

SEQ ID NO	Name	Sequence
		GAAGATGATCGCCAAGAGCGAGCAGGAGATCGGCAAGGCCACCGCCAAGTACTTCTTCTACAGCAACATCATGAACTTC TTCAAGACCGAGATCACCCTGGCCAACGGCGAGATCCGGAAGCGGCCCCTGATCGAGACCAACGGCGAGACCGGCGAG ATCGTGTGGGACAAGGGCCGGGACTTCGCCACCGTGCGGAAGGTGCTGAGCATGCCCCAGGTGAACATCGTGAAGAAG ACCGAGGTGCAGACCGGCGGCTTCAGCAAGGAGAGCATCCTGCCCAAGCGGAACAGCGACAAGCTGATCGCCCGGAAG AAGGACTGGGACCCCAAGAAGTACGGCGGCTTCGACAGCCCCACCGTGGCCTACAGCGTGCTGGTGGTGGCCAAGGTG GAGAAGGGCAAGAGCAAGAAGCTGAAGAGCGTGAAGGAGCTGCTGGGCATCACCATCATGGAGCGGAGCAGCTTCGA GAAGAACCCCATCGACTTCCTGGAGGCCAAGGGCTACAAGGAGGTGAAGAAGGACCTGATCATCAAGCTGCCCAAGTA CAGCCTGTTCGAGCTGGAGAACGGCCGGAAGCGGATGCTGGCCAGCGCCGGCGAGCTGCAGAAGGGCAACGAGCTGG CCCTGCCCAGCAAGTACGTGAACTTCCTGTACCTGGCCAGCCACTACGAGAAGCTGAAGGGCAGCCCCGAGGACAACGA GCAGAAGCAGCTGTTCGTGGAGCAGCACAAGCACTACCTGGACGAGATCATCGAGCAGATCAGCGAGTTCAGCAAGCG GGTGATCCTGGCCGACGCCAACCTGGACAAGGTGCTGAGCGCCTACAACAAGCACCGGGACAAGCCCATCCGGGAGCA GGCCGAGAACATCATCCACCTGTTCACCCTGACCAACCTGGGCGCCCCCGCCGCCTTCAAGTACTTCGACACCACCATCGA CCGGAAGCGGTACACCAGCACCAAGGAGGTGCTGGACGCCACCCTGATCCACCAGAGCATCACCGGCCTGTACGAGACC CGGATCGACCTGAGCCAGCTGGGCGGCGACTGA
3547	CR003353	AAAGGCUGCUGAUGACACCUGUUUUAGAGCUAUGCUGUUUUG
3548	CR003366	AAAUAGACACCAAAUCUUACGUUUUAGAGCUAUGCUGUUUUG
3549	CR009660	mA*mC*mA*CAAAUACCAGUCCfAfGCGGUUUUAGAGCUAUGCUGUUUUG
3550	CR009753	mA*mA*mA*GGCUGCUGAUGACfAfCCUGUUUUAGAGCUAUGCUGUUUUG
3551	CR010158	mA*mA*mA*GUUCUAGAUGCUGfUfCCGGUUUUAGAGCUAUGCUGUUUUG
3552	G013498	mA*mC*mG*CAA*A*fU*fA*fU*fCAfGfUCCfAfGCGGUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGU UAAAAUAAGGCUAGUCCGUUAUCAACUUGGCACCGAGUCGG*mU*mG*mC

[0052] In Table 1, $(N)_x$ represents x contiguous nucleotides, where x is 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25.

[0053] Nucleotide modifications are indicated in Table 1 as follows: m: 2'-OMe; *: PS linkage; f: 2'-fluoro; (invd): inverted abasic; moe: 2'-moe; e: ENA; d: deoxyribonucleotide (also note that T is always a deoxyribonucleotide); x: UNA. Thus, for example, mA represents 2'-O-methyl adenosine; xA represents a UNA nucleotide with an adenine nucleobase; eA represents an ENA nucleotide with an adenine nucleobase; and dA represents an adenosine deoxyribonucleotide.

[0054] sgRNA designations are sometimes provided with one or more leading zeroes immediately following the G. This does not affect the meaning of the designation. Thus, for example, G000282, G0282, G00282, and G282 refer to the same sgRNA. Similarly, crRNA and or trRNA designations are sometimes provided with one or more leading zeroes immediately following the CR or TR, respectively, which does not affect the meaning of the designation. Thus, for example, CR000100, CR00100, CR0100, and CR100 refer to the same crRNA, and TR000200, TR00200, TR0200, and TR200 refer to the same trRNA.

[0055] For SEQ ID NOs: 401-535, 1001, and 1007-1032, positions correspond to sgRNA regions as follows: 1-20, guide region; 21-26 and 45-50, lower stem; 27-28 and 41-44, bulge; 29-40, upper stem (of which 33-36 are a tetraloop); 51-68, nexus; 69-80, hairpin 1; 82-96, hairpin 2 (position 81 is a nucleotide between hairpin 1 and hairpin 2); 97-100, 3' terminus region.

[0056] For SEQ ID NOs 601 and 607-732, no guide region is shown and the positions corresponding to the remaining regions are each decremented by 20 relative to those given for SEQ ID NOs: 401-532. For SEQ ID NOs 801 and 807-932, the spacer is the length of x and the positions corresponding to the remaining regions are each decremented by 20 and incremented by x relative to those given for SEQ ID NOs: 401-532.

Definitions

[0057] "Editing efficiency" or "editing percentage" or "percent editing" as used herein is the total number of sequence reads with insertions or deletions of nucleotides into the target region of interest over the total number of sequence reads following cleavage by a Cas RNP.

[0058] "Regions" as used herein describes conserved groups of nucleic acids. Regions may also be referred to as "modules" or "domains." Regions of an sgRNA may perform particular functions, e.g., in directing endonuclease activity of the RNP, for example as described in Briner AE et al., *Molecular Cell* 56:333–339 (2014). Exemplary regions of an sgRNA are described in Table 3.

[0059] "Hairpin" as used herein describes a duplex of nucleic acids that is created when a nucleic acid strand folds and forms base pairs with another section of the same strand. A hairpin may form a structure that comprises a loop or a U-shape. In some embodiments, a hairpin may be comprised of an RNA loop. Hairpins can be formed with two complementary sequences in a single nucleic acid molecule bind together, with a folding or wrinkling of the molecule. In some embodiments, hairpins comprise stem or stem loop structures. As used

herein, a "hairpin region" refers to hairpin 1 and hairpin 2 and the "n" between hairpin 1 and hairpin 2 of a conserved portion of an sgRNA.

[0060] "Ribonucleoprotein" (RNP) or "RNP complex" as used herein describes an sgRNA, for example, together with a nuclease, such as a Cas protein. In some embodiments, the RNP comprises Cas9 and gRNA (e.g., sgRNA, short-sgRNA, dgRNA, or crRNA).

[0061] "Stem loop" as used herein describes a secondary structure of nucleotides that form a base-paired "stem" that ends in a loop of unpaired nucleic acids. A stem may be formed when two regions of the same nucleic acid strand are at least partially complementary in sequence when read in opposite directions. "Loop" as used herein describes a region of nucleotides that do not base pair (i.e., are not complementary) that may cap a stem. A "tetraloop" describes a loop of 4 nucleotides. As used herein, the upper stem of an sgRNA may comprise a tetraloop.

[0062] "Guide RNA", "gRNA", and "guide" are used herein interchangeably to refer to either a crRNA (also known as CRISPR RNA), or the combination of a crRNA and a trRNA (also known as tracrRNA). The crRNA and trRNA may be associated as a single RNA molecule (single guide RNA, sgRNA) or in two separate RNA molecules (dual guide RNA, dgRNA). "Guide RNA" or "gRNA" refers to each type. The trRNA may be a naturally-occurring sequence, or a trRNA sequence with modifications or variations compared to naturally-occurring sequences. Guide RNAs can include modified RNAs as described herein.

[0063] In some embodiments, the gRNA (e.g., sgRNA) comprises a "guide region", which is sometimes referred to as a "spacer" or "spacer region," for example, in Briner AE et al., *Molecular Cell* 56:333–339 (2014) for sgRNA (but applicable herein to all guide RNAs). The guide region or spacer region is also sometimes referred to as a "variable region," "guide domain" or "targeting domain." In some embodiments, a "guide region" immediately precedes a "conserved portion of an sgRNA" at its 5' end, and in some embodiments the sgRNA is a short-sgRNA. An exemplary "conserved portion of an sgRNA" is shown in Table 2. In some embodiments, a "guide region" comprises a series of nucleotides at the 5' end of a crRNA. In some embodiments, the guide region comprises one or more YA sites ("guide region YA sites"). In some embodiments, the guide region comprises one or more YA sites located at positions from a given nucleotide relative to the 5' end to the end of the guide region. Such ranges of positions are referred to as, e.g., "5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus" where the "end" in "5-end", etc., refers to most 3' nucleotide in the guide region. (Similarly, expressions such as "nucleotides 21-end of the gRNA" refer to the range from nucleotide 21 from the 5' end of the 5' terminus of the gRNA

to the final nucleotide at the 3' end of the gRNA.) Furthermore, a nucleotide that is, for example, 6 nucleotides from the 5' end of a particular sgRNA segment is the sixth nucleotide of that segment, or "nucleotide 6" from the 5' end, e.g., XXXXXN, where N is the 6th nucleotide from the 5' end. A range of nucleotides that is located "at or after" 6 nucleotides from the 5' end begins with the 6th nucleotide and continues down the chain toward the 3' end. Similarly, a nucleotide that is, for example, 5 nucleotides from the 3' end of the chain is the 5th nucleotide when counting from the 3' end of the chain, e.g. NXXXX. A numeric position or range in the guide region refers to the position as determined from the 5' end unless another point of reference is specified; for example, "nucleotide 5" in a guide region is the 5th nucleotide from the 5' end.

[0064] In some embodiments, a gRNA comprises nucleotides that "match the modification pattern" at corresponding or specified nucleotides of a gRNA described herein. This means that the nucleotides matching the modification pattern have the same modifications (e.g., phosphorothioate, 2'-fluoro, 2'-OMe, etc.) as the nucleotides at the corresponding positions of the gRNA described herein, regardless of whether the nucleobases at those positions match. For example, if in a first gRNA, nucleotides 5 and 6, respectively, have 2'-OMe and phosphorothioate modifications, then this gRNA has the same modification pattern at nucleotides 5 and 6 as a second gRNA that also has 2'-OMe and phosphorothioate modifications at nucleotides 5 and 6, respectively, regardless of whether the nucleobases at positions 5 and 6 are the same or different in the first and second gRNAs. However, a 2'-OMe modification at nucleotide 6 but not nucleotide 7 is not the same modification pattern at nucleotides 6 and 7 as a 2'-OMe modification at nucleotide 7 but not nucleotide 6. Similarly, a modification pattern that matches at least 75% of the modification pattern of a gRNA described herein means that at least 75% of the nucleotides have the same modifications as the corresponding positions of the gRNA described herein. Corresponding positions may be determined by pairwise or structural alignment.

[0065] A "conserved region" of a *S. pyogenes* Cas9 ("spyCas9" (also referred to as "spCas9")) sgRNA" is shown in Table 2. The first row shows the numbering of the nucleotides; the second row shows the sequence (e.g., SEQ ID NO: 400); and the third row shows the regions.

[0066] As used herein, a "short-single guide RNA" ("short-sgRNA") is an sgRNA comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 or 6-10 nucleotides. In some embodiments, a short-sgRNA lacks at least nucleotides 54-58 (AAAAA) of the conserved portion of a *S. pyogenes* Cas9

("spyCas9") sgRNA, as shown in Table 2. In some embodiments, a short-sgRNA is a non-spyCas9 sgRNA that lacks nucleotides corresponding to nucleotides 54-58 (AAAAA) of the conserved portion of a spyCas9 as determined, for example, by pairwise or structural alignment. In some embodiments, a short-sgRNA lacks at least nucleotides 54-61 (AAAAAGUG) of the conserved portion of a spyCas9 sgRNA. In some embodiments, a short-sgRNA lacks at least nucleotides 53-60 (GAAAAAGU) of the conserved portion of a spyCas9 sgRNA. In some embodiments, a short-sgRNA lacks 4, 5, 6, 7, or 8 nucleotides of nucleotides 53-60 (GAAAAAGU) or nucleotides 54-61 (AAAAAGUG) of the conserved portion of a spyCas9 sgRNA, or the corresponding nucleotides of the conserved portion of a non-spyCas9 sgRNA as determined, for example, by pairwise or structural alignment.

[0067] As used herein, a "YA site" refers to a 5'-pyrimidine-adenine-3' dinucleotide. For clarification, a "YA site" in an original sequence that is altered by modifying a base is still considered a (modified) YA site in the resulting sequence, regardless of the absence of a literal YA dinucleotide. A "conserved region YA site" is present in the conserved region of an sgRNA. A "guide region YA site" is present in the guide region of an sgRNA. An unmodified YA site in an sgRNA may be susceptible to cleavage by RNase-A like endonucleases, e.g., RNase A. In some embodiments, a short-sgRNA comprises about 10 YA sites in its conserved region. In some embodiments, an sgRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 YA sites in its conserved region. Exemplary conserved region YA sites are indicated in Fig. 10B. Exemplary guide region YA sites are not shown in Fig. 10B, as the guide region may be any sequence, including any number of YA sites. In some embodiments, an sgRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of the YA sites indicated in Fig. 10B. In some embodiments, an sgRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 YA sites at the following positions or a subset thereof: LS5-LS6; US3-US4; US9-US10; US12-B3; LS7-LS8; LS12-N1; N6-N7; N14-N15; N17-N18; and H2-2 to H2-3. In some embodiments, a YA site comprises a modification, meaning that at least one nucleotide of the YA site is modified. In some embodiments, the pyrimidine (also called the pyrimidine position) of the YA site comprises a modification (which includes a modification altering the internucleoside linkage immediately 3' of the sugar of the pyrimidine). In some embodiments, the adenine (also called the adenine position) of the YA site comprises a modification (which includes a modification altering the internucleoside linkage immediately 3' of the sugar of the adenine). In some embodiments, the pyrimidine position and the adenine position of the YA site comprise modifications. In some embodiments, a short-sgRNA guide region or short-sgRNA conserved region described herein comprises one or more YA sites ("guide region YA sites"

or "conserved region YA sites"). In some embodiments, a crRNA or a trRNA described herein comprises one or more YA sites.

[0068] As discussed herein, positions of nucleotides corresponding to those described with respect to spyCas9 gRNA can be identified in another gRNA with sequence and/or structural similarity by pairwise or structural alignment. Structural alignment is useful where molecules share similar structures despite considerable sequence variation. For example, spyCas9 and *Staphylococcus aureus* Cas9 ("SaCas9") have divergent sequences, but significant structural alignment. *See*, e.g., Figure 2(F) from Nishimasu et al., *Cell* 162(5): 1113-1126 (2015). Structural alignment can be used to identify nucleotides in a saCas9 or other sgRNA that correspond to particular positions, such as nucleotides 54-58 (AAAAA) of the conserved portion of a spyCas9 sgRNA.

[0069] Structural alignment involves identifying corresponding residues across two (or more) sequences by (i) modeling the structure of a first sequence using the known structure of the second sequence or (ii) comparing the structures of the first and second sequences where both are known, and identifying the residue in the first sequence most similarly positioned to a residue of interest in the second sequence. Corresponding residues are identified in some algorithms based on distance minimization given position (e.g., nucleobase position 1 or the 1' carbon of the pentose ring for polynucleotides, or alpha carbons for polypeptides) in the overlaid structures (e.g., what set of paired positions provides a minimized root-mean-square deviation for the alignment). When identifying positions in a non-spyCas9 gRNA corresponding to positions described with respect to spyCas9 gRNA, spyCas9 gRNA can be the "second" sequence. Where a non-spyCas9 gRNA of interest does not have an available known structure, but is more closely related to another non-spyCas9 gRNA that does have a known structure, it may be most effective to model the non-spyCas9 gRNA of interest using the known structure of the closely related non-spyCas9 gRNA, and then compare that model to the spyCas9 gRNA structure to identify the desired corresponding residue in the non-spyCas9 gRNA of interest. There is an extensive literature on structural modeling and alignment for proteins; representative disclosures include US 6859736; US 8738343; and those cited in Aslam et al., Electronic Journal of Biotechnology 20 (2016) 9–13. For discussion of modeling a structure based on a known related structure or structures, *see, e.g.*, Bordoli et al., *Nature Protocols* 4 (2009) 1–13, and references cited therein. *See also* Figure 2(F) from Nishimasu et al., *Cell* 162(5): 1113-1126 (2015) for alignment of nucleic acid.

[0070] A "target sequence" as used herein refers to a sequence of nucleic acid to which the guide region directs a nuclease for cleavage. In some embodiments, a spyCas9 protein may be directed by a guide region to a target sequence by the nucleotides present in the guide region. In some embodiments, the sgRNA does not comprise a spacer region.

[0071] As used herein, the "5' end" refers to the first nucleotide of the gRNA (including a dgRNA (typically the 5' end of the crRNA of the dgRNA), sgRNA or a short-sgRNA), in which the 5' position is not linked to another nucleotide.

[0072] As used herein, a "5' end modification" refers to a gRNA comprising a guide region having modifications in one or more of the one (1) to about seven (7) nucleotides at its 5' end, optionally wherein the first nucleotide (from the 5' end) of the gRNA is modified.

[0073] As used herein, the "3' end" refers to the end or terminal nucleotide of a gRNA, in which the 3' position is not linked to another nucleotide. In some embodiment, the 3' end is in the 3' tail. In some embodiments, the 3' end is in the conserved portion of an gRNA.

[0074] As used herein, a "3' end modification" refers to a gRNA having modifications in one or more of the one (1) to about seven (7) nucleotides at its 3' end, optionally wherein the last nucleotide (i.e., the 3' most nucleotide) of the gRNA is modified. If a 3' tail is present, the 1 to about 7 nucleotides may be within the 3' tail. If a 3' tail is not present, the 1 to about 7 nucleotides may be within the conserved portion of a sgRNA.

[0075] The "last," "second to last," "third to last," etc., nucleotide refers to the 3' most, second 3' most, third 3' most, etc., nucleotide, respectively in a given sequence. For example, in the sequence 5'-AAACTG-3', the last, second to last, and third to last nucleotides are G, T, and C, respectively. The phrase "last 3 nucleotides" refers to the last, second to last, and third to last nucleotides; more generally, "last N nucleotides" refers to the last to the Nth to last nucleotides, inclusive. "Third nucleotide from the 3' end of the 3' terminus" is equivalent to "third to last nucleotide." Similarly, "third nucleotide from the 5' end of the 5' terminus" is equivalent to "third nucleotide at the 5' terminus."

[0076] As used herein, a "protective end modification" (such as a protective 5' end modification or protective 3' end modification) refers to a modification of one or more nucleotides within seven nucleotides of the end of an sgRNA that reduces degradation of the sgRNA, such as exonucleolytic degradation. In some embodiments, a protective end modification comprises modifications of at least two or at least three nucleotides within seven nucleotides of the end of the sgRNA. In some embodiments, the modifications comprise phosphorothioate linkages, 2' modifications such as 2'-OMe or 2'-fluoro, 2'-H (DNA), ENA,

UNA, or a combination thereof. In some embodiments, the modifications comprise phosphorothioate linkages and 2'-OMe modifications. In some embodiments, at least three terminal nucleotides are modified, e.g., with phosphorothioate linkages or with a combination of phosphorothioate linkages and 2'-OMe modifications. Modifications known to those of skill in the art to reduce exonucleolytic degradation are encompassed.

[0077] In some embodiments, a "3' tail" comprising between 1 and about 20 nucleotides follows the conserved portion of a sgRNA at its 3' end.

[0078] As used herein, an "RNA-guided DNA binding agent" means a polypeptide or complex of polypeptides having RNA and DNA binding activity, or a DNA-binding subunit of such a complex, wherein the DNA binding activity is sequence-specific and depends on the sequence of the RNA. Exemplary RNA-guided DNA binding agents include Cas cleavases/nickases and inactivated forms thereof ("dCas DNA binding agents"). "Cas nuclease", also called "Cas protein", as used herein, encompasses Cas cleavases, Cas nickases, and dCas DNA binding agents. Cas cleavases/nickases and dCas DNA binding agents include a Csm or Cmr complex of a type III CRISPR system, the Cas10, Csm1, or Cmr2 subunit thereof, a Cascade complex of a type I CRISPR system, the Cas3 subunit thereof, and Class 2 Cas nucleases. As used herein, a "Class 2 Cas nuclease" is a single-chain polypeptide with RNA-guided DNA binding activity, such as a Cas9 nuclease or a Cpf1 nuclease. Class 2 Cas nucleases include Class 2 Cas cleavases and Class 2 Cas nickases (e.g., H840A, D10A, or N863A variants), which further have RNA-guided DNA cleavases or nickase activity, and Class 2 dCas DNA binding agents, in which cleavase/nickase activity is inactivated. Class 2 Cas nucleases include, for example, Cas9, Cpf1, C2c1, C2c2, C2c3, HF Cas9 (e.g., N497A, R661A, Q695A, Q926A variants), HypaCas9 (e.g., N692A, M694A, Q695A, H698A variants), eSPCas9(1.0) (e.g, K810A, K1003A, R1060A variants), and eSPCas9(1.1) (e.g., K848A, K1003A, R1060A variants) proteins and modifications thereof. Cpf1 protein, Zetsche et al., *Cell*, 163: 1-13 (2015), is homologous to Cas9, and contains a RuvC-like nuclease domain. Cpf1 sequences of Zetsche are incorporated by reference in their entirety. *See, e.g.*, Zetsche, Tables S1 and S3. "Cas9" encompasses Spy Cas9, the variants of Cas9 listed herein, and equivalents thereof. See, *e.g.*, Makarova et al., *Nat Rev Microbiol*, 13(11): 722-36 (2015); Shmakov et al., *Molecular Cell,* 60:385-397 (2015).

[0079] As used herein, a first sequence is considered to "comprise a sequence with at least X% identity to" a second sequence if an alignment of the first sequence to the second sequence shows that X% or more of the positions of the second sequence in its entirety are matched by the first sequence. For example, the sequence AAGA comprises a sequence with

100% identity to the sequence AAG because an alignment would give 100% identity in that there are matches to all three positions of the second sequence. The differences between RNA and DNA (generally the exchange of uridine for thymidine or vice versa) and the presence of nucleoside analogs such as modified uridines do not contribute to differences in identity or complementarity among polynucleotides as long as the relevant nucleotides (such as thymidine, uridine, or modified uridine) have the same complement (e.g., adenosine for all of thymidine, uridine, or modified uridine; another example is cytosine and 5-methylcytosine, both of which have guanosine or modified guanosine as a complement). Thus, for example, the sequence 5'-AXG where X is any modified uridine, such as pseudouridine, N1-methyl pseudouridine, or 5-methoxyuridine, is considered 100% identical to AUG in that both are perfectly complementary to the same sequence (5'-CAU). Exemplary alignment algorithms are the Smith-Waterman and Needleman-Wunsch algorithms, which are well-known in the art. One skilled in the art will understand what choice of algorithm and parameter settings are appropriate for a given pair of sequences to be aligned; for sequences of generally similar length and expected identity >50% for amino acids or >75% for nucleotides, the Needleman-Wunsch algorithm with default settings of the Needleman-Wunsch algorithm interface provided by the EBI at the www.ebi.ac.uk web server is generally appropriate.

[0080] "mRNA" is used herein to refer to a polynucleotide that is RNA or modified RNA and comprises an open reading frame that can be translated into a polypeptide (i.e., can serve as a substrate for translation by a ribosome and amino-acylated tRNAs). mRNA can comprise a phosphate-sugar backbone including ribose residues or analogs thereof, e.g., 2'-methoxy ribose residues. In some embodiments, the sugars of a nucleic acid phosphate-sugar backbone consist essentially of ribose residues, 2'-methoxy ribose residues, or a combination thereof. In general, mRNAs do not contain a substantial quantity of thymidine residues (e.g., 0 residues or fewer than 30, 20, 10, 5, 4, 3, or 2 thymidine residues; or less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 4%, 3%, 2%, 1%, 0.5%, 0.2%, or 0.1% thymidine content). An mRNA can contain modified uridines at some or all of its uridine positions.

[0081] As used herein, the "minimum uridine content" of a given ORF is the uridine content of an ORF that (a) uses a minimal uridine codon at every position and (b) encodes the same amino acid sequence as the given ORF. The minimal uridine codon(s) for a given amino acid is the codon(s) with the fewest uridines (usually 0 or 1 except for a codon for phenylalanine, where the minimal uridine codon has 2 uridines). Modified uridine residues are considered equivalent to uridines for the purpose of evaluating minimum uridine content.

[0082] As used herein, the "minimum uridine dinucleotide content" of a given ORF is the lowest possible uridine dinucleotide (UU) content of an ORF that (a) uses a minimal uridine codon (as discussed above) at every position and (b) encodes the same amino acid sequence as the given ORF. The uridine dinucleotide (UU) content can be expressed in absolute terms as the enumeration of UU dinucleotides in an ORF or on a rate basis as the percentage of positions occupied by the uridines of uridine dinucleotides (for example, AUUAU would have a uridine dinucleotide content of 40% because 2 of 5 positions are occupied by the uridines of a uridine dinucleotide). Modified uridine residues are considered equivalent to uridines for the purpose of evaluating minimum uridine dinucleotide content.

[0083] As used herein, the "minimum adenine content" of a given open reading frame (ORF) is the adenine content of an ORF that (a) uses a minimal adenine codon at every position and (b) encodes the same amino acid sequence as the given ORF. The minimal adenine codon(s) for a given amino acid is the codon(s) with the fewest adenines (usually 0 or 1 except for a codon for lysine and asparagine, where the minimal adenine codon has 2 adenines). Modified adenine residues are considered equivalent to adenines for the purpose of evaluating minimum adenine content.

[0084] As used herein, the "minimum adenine dinucleotide content" of a given open reading frame (ORF) is the lowest possible adenine dinucleotide (AA) content of an ORF that (a) uses a minimal adenine codon (as discussed above) at every position and (b) encodes the same amino acid sequence as the given ORF. The adenine dinucleotide (AA) content can be expressed in absolute terms as the enumeration of AA dinucleotides in an ORF or on a rate basis as the percentage of positions occupied by the adenines of adenine dinucleotides (for example, UAAUA would have an adenine dinucleotide content of 40% because 2 of 5 positions are occupied by the adenines of an adenine dinucleotide). Modified adenine residues are considered equivalent to adenines for the purpose of evaluating minimum adenine dinucleotide content.

[0085] As used herein, a "subject" refers to any member of the animal kingdom. In some embodiments, "subject" refers to humans. In some embodiments, "subject" refers to non-human animals. In some embodiments, "subject" refers to primates. In some embodiments, subjects include, but are not limited to, mammals, birds, reptiles, amphibians, fish, insects, and/or worms. In certain embodiments, the non-human subject is a mammal (e.g., a rodent, a mouse, a rat, a rabbit, a monkey, a dog, a cat, a sheep, cattle, a primate, and/or a pig). In some embodiments, a subject may be a transgenic animal, genetically-engineered animal, and/or a clone. In certain embodiments of the present invention the

subject is an adult, an adolescent or an infant. In some embodiments, terms "individual" or "patient" are used and are intended to be interchangeable with "subject".

Types of modifications described herein

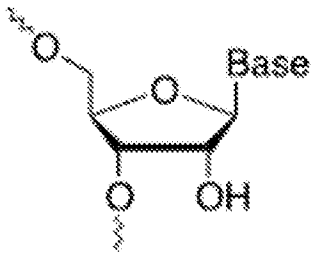
[0086] Guide RNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, and crRNAs) comprising modifications at various positions are disclosed herein. In some embodiments, a position of a gRNA that comprises a modification is modified with any one or more of the following types of modifications.

2'-O-methyl modifications

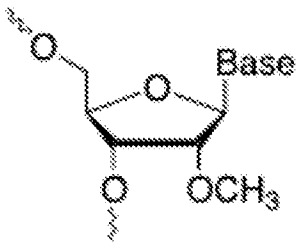
[0087] Modified sugars are believed to control the puckering of nucleotide sugar rings, a physical property that influences oligonucleotide binding affinity for complementary strands, duplex formation, and interaction with nucleases. Substitutions on sugar rings can therefore alter the conformation and puckering of these sugars. For example, 2'-O-methyl (2'-OMe) modifications can increase binding affinity and nuclease stability of oligonucleotides, though as shown in the Examples, the effect of any modification at a given position in an oligonucleotide needs to be empirically determined.

[0088] The terms "mA," "mC," "mU," or "mG" may be used to denote a nucleotide that has been modified with 2'-OMe.

[0089] A ribonucleotide and a modified 2'-O-methyl ribonucleotide can be depicted as follows:



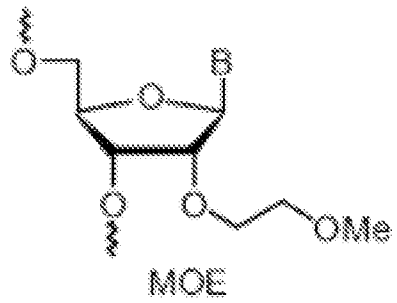
RNA



2'-O-Me

2'-O-(2-methoxyethyl) modifications

[0090] In some embodiments, the modification may be 2'-O-(2-methoxyethyl) (2'-O-moe). A modified 2'-O-moe ribonucleotide can be depicted as follows:



MOE

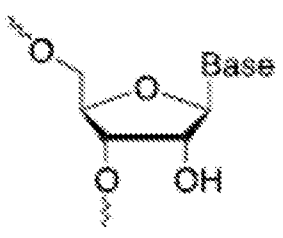
[0091] The terms "moeA," "moeC," "moeU," or "moeG" may be used to denote a nucleotide that has been modified with 2'-O-moe.

2'-fluoro modifications

[0092] Another chemical modification that has been shown to influence nucleotide sugar rings is halogen substitution. For example, 2'-fluoro (2'-F) substitution on nucleotide sugar rings can increase oligonucleotide binding affinity and nuclease stability.

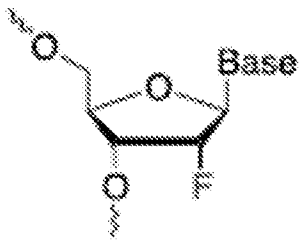
[0093] In this application, the terms "fA," "fC," "fU," or "fG" may be used to denote a nucleotide that has been substituted with 2'-F.

[0094] A ribonucleotide without and with a 2'-F substitution can be depicted as follows:



RNA

Natural composition of RNA



2'F-RNA

2'F substitution

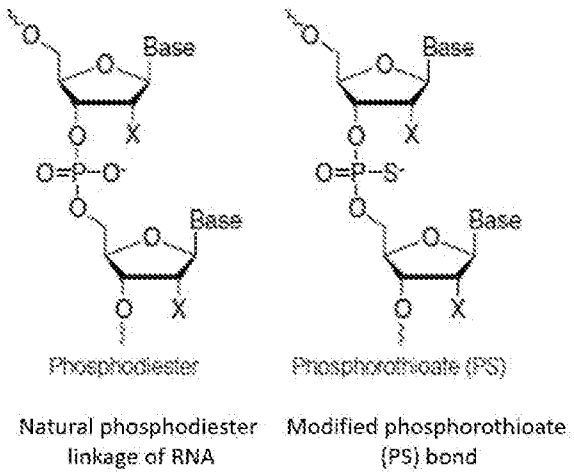
Phosphorothioate modifications

[0095] A phosphorothioate (PS) linkage or bond refers to a bond where a sulfur is substituted for one nonbridging phosphate oxygen in a phosphodiester linkage, for example between nucleotides. When phosphorothioates are used to generate oligonucleotides, the modified oligonucleotides may also be referred to as S-oligos.

[0096] A "*" may be used to depict a PS modification. In this application, the terms A*, C*, U*, or G* may be used to denote a nucleotide that is linked to the next (e.g., 3') nucleotide with a PS bond. Throughout this application, PS modifications are grouped with the nucleotide whose 3' carbon is bonded to the phosphorothioate; thus, indicating that a PS modification is at position 1 means that the phosphorothioate is bonded to the 3' carbon of nucleotide 1 and the 5' carbon of nucleotide 2. Thus, where a YA site is indicated as being "PS modified" or the like, the PS linkage is between the Y and A or between the A and the next nucleotide.

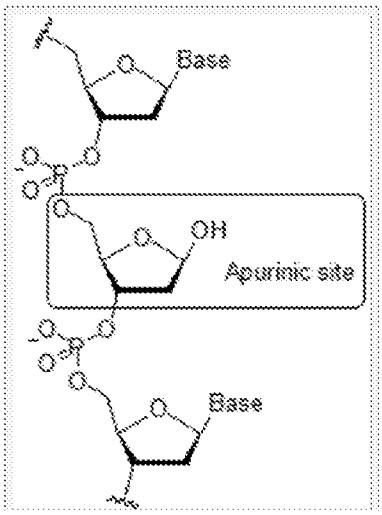
[0097] In this application, the terms "mA*," "mC*," "mU*," or "mG*" may be used to denote a nucleotide that has been substituted with 2'-OMe and that is linked to the next (e.g., 3') nucleotide with a PS linkage, which may sometimes be referred to as a "PS bond." Similarly, the terms "fA*," "fC*," "fU*," or "fG*" may be used to denote a nucleotide that has been substituted with 2'-F and that is linked to the next (e.g., 3') nucleotide with a PS linkage. Equivalents of a PS linkage or bond are encompassed by embodiments described herein.

[0098] The diagram below shows the substitution of S- for a nonbridging phosphate oxygen, generating a PS linkage in lieu of a phosphodiester linkage:

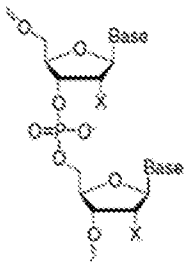


Inverted abasic modifications

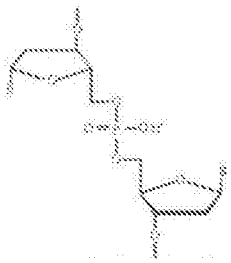
[0099] Abasic nucleotides refer to those which lack nitrogenous bases. The figure below depicts an oligonucleotide with an abasic (in this case, shown as apurinic; an abasic site could also be an apyrimidinic site, wherein the description of the abasic site is typically in reference to Watson-Crick base pairing—e.g., an apurinic site refers to a site that lacks a nitrogenous base and would typically base pair with a pyrimidinic site) site that lacks a base, wherein the base may be substituted by another moiety at the 1' position of the furan ring (e.g., a hydroxyl group, as shown below, to form a ribose or deoxyribose site, as shown below, or a hydrogen):



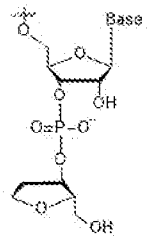
[00100] Inverted bases refer to those with linkages that are inverted from the normal 5' to 3' linkage (i.e., either a 5' to 5' linkage or a 3' to 3' linkage). For example:



Normal oligonucleotide linkage



5'-inverted oligonucleotide linkage



3'-inverted linkage with H-substituted 3'inverted abasic site

[00101] An abasic nucleotide can be attached with an inverted linkage. For example, an abasic nucleotide may be attached to the terminal 5' nucleotide via a 5' to 5' linkage, or an

abasic nucleotide may be attached to the terminal 3' nucleotide via a 3' to 3' linkage. An inverted abasic nucleotide at either the terminal 5' or 3' nucleotide may also be called an inverted abasic end cap. In this application, the terms "invd" indicates an inverted abasic nucleotide linkage.

Deoxyribonucleotides

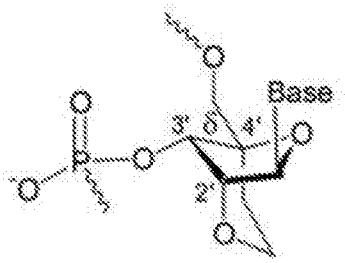
[00102] A deoxyribonucleotide (in which the sugar comprises a 2'-deoxy position) is considered a modification in the context of a gRNA, in that the nucleotide is modified relative to standard RNA by the substitution of a proton for a hydroxyl at the 2' position. Unless otherwise indicated, a deoxyribonucleotide modification at a position that is U in an unmodified RNA can also comprise replacement of the U nucleobase with a T.

Bicyclic ribose analog

[00103] Exemplary bicyclic ribose analogs include locked nucleic acid (LNA), ENA, bridged nucleic acid (BNA), or another LNA-like modifications. In some instances, a bicyclic ribose analog has 2' and 4' positions connected through a linker. The linker can be of the formula -X-$(CH_2)_n$- where n is 1 or 2; X is O, NR, or S; and R is H or C_{1-3} alkyl, e.g., methyl. Examples of bicyclic ribose analogs include LNAs comprising a 2′-O-CH_2-4′ bicyclic structure (oxy-LNA) (see WO 98/39352 and WO 99/14226); 2′-NH-CH_2-4′ or 2′-N(CH_3)-CH_2-4′ (amino-LNAs) (Singh et al., *J. Org. Chem.* 63:10035-10039 (1998); Singh et al., *J. Org. Chem.* 63:6078-6079 (1998)); and 2′-S-CH_2-4′ (thio-LNA) (Singh et al., *J. Org. Chem.* 63:6078-6079 (1998); Kumar et al., *Biorg. Med. Chem. Lett.* 8:2219-2222 (1998)).

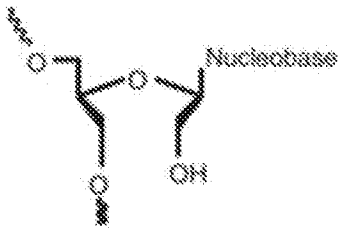
ENA

[00104] An ENA modification refers to a nucleotide comprising a 2′-*O*,4′-*C*-ethylene modification. An exemplary structure of an ENA nucleotide is shown below, in which wavy lines indicate connections to the adjacent nucleotides (or terminal positions as the case may be, with the understanding that if the 3' terminal nucleotide is an ENA nucleotide, the 3' position may comprise a hydroxyl rather than phosphate). For further discussion of ENA nucleotides, *see, e.g.*, Koizumi et al., *Nucleic Acids Res.* 31: 3267–3273 (2003).



UNA

[00105] A UNA or unlocked nucleic acid modification refers to a nucleotide comprising a 2′,3′-seco-RNA modification, in which the 2' and 3' carbons are not bonded directly to each other. An exemplary structure of a UNA nucleotide is shown below, in which wavy lines indicate connections to the adjacent phosphates or modifications replacing phosphates (or terminal positions as the case may be). For further discussion of UNA nucleotides, *see, e.g.*, Snead et al., *Molecular Therapy* 2: e103, doi:10.1038/mtna.2013.36 (2013).



Base modifications

[00106] A base modification is any modification that alters the structure of a nucleobase or its bond to the backbone, including isomerization (as in pseudouridine). In some embodiments, a base modification includes inosine. In some embodiments, a modification comprises a base modification that reduces RNA endonuclease activity, e.g., by interfering with recognition of a cleavage site by an RNase and/or by stabilizing an RNA structure (e.g., secondary structure) that decreases accessibility of a cleavage site to an RNase. Exemplary base modifications that can stabilize RNA structures are pseudouridine and 5-methylcytosine. *See* Peacock et al., *J Org Chem*. 76: 7295–7300 (2011). In some embodiments, a base modification can increase or decrease the melting temperature (Tm) of a nucleic acid, e.g., by increasing the hydrogen bonding in a Watson-Crick base pair, forming non-canonical base pair, or creating a mismatched base pair.

[00107] The above modifications and their equivalents are included within the scope of the embodiments described herein.

YA modifications

[00108] A modification at a YA site (also referred to as a YA modification) can be a modification of the internucleoside linkage, a modification of the base (pyrimidine or adenine), e.g. by chemical modification, substitution, or otherwise, and/or a modification of the sugar (e.g. at the 2' position, such as 2'-O-alkyl, 2'-F, 2'-moe, 2'-F arabinose, 2'-H (deoxyribose), and the like). In some embodiments, a "YA modification" is any modification that alters the structure of the dinucleotide motif to reduce RNA endonuclease activity, e.g., by interfering with recognition or cleavage of a YA site by an RNase and/or by stabilizing an RNA structure (e.g., secondary structure) that decreases accessibility of a cleavage site to an RNase. *See* Peacock et al., *J Org Chem.* 76: 7295–7300 (2011); Behlke, *Oligonucleotides* 18:305-320 (2008); Ku et al., *Adv. Drug Delivery Reviews* 104: 16-28 (2016); Ghidini et al., *Chem. Commun.,* 2013, 49, 9036. Peacock et al., Belhke, Ku, and Ghidini provide exemplary modifications suitable as YA modifications. Modifications known to those of skill in the art to reduce endonucleolytic degradation are encompassed. Exemplary 2' ribose modifications that affect the 2' hydroxyl group involved in RNase cleavage are 2'-H and 2'-O-alkyl, including 2'-O-Me. Modifications such as bicyclic ribose analogs, UNA, and modified internucleoside linkages of the residues at the YA site can be YA modifications. Exemplary base modifications that can stabilize RNA structures are pseudouridine and 5-methylcytosine. In some embodiments, at least one nucleotide of the YA site is modified. In some embodiments, the pyrimidine (also called "pyrimidine position") of the YA site comprises a modification (which includes a modification altering the internucleoside linkage immediately 3' of the sugar of the pyrimidine, a modification of the pyrimidine base, and a modification of the ribose, e.g. at its 2' position). In some embodiments, the adenine (also called "adenine position") of the YA site comprises a modification (which includes a modification altering the internucleoside linkage immediately 3' of the sugar of the pyrimidine, a modification of the pyrimidine base, and a modification of the ribose, e.g. at its 2' position). In some embodiments, the pyrimidine and the adenine of the YA site comprise modifications. In some embodiments, the YA modification reduces RNA endonuclease activity.

[00109] The above modifications and their equivalents are included within the scope of the embodiments described herein.

Domains/regions of sgRNAs

[00110] *Briner AE et al., Molecular Cell* 56:333–339 (2014) describes functional domains of sgRNAs, referred to herein as "domains", including the "spacer" domain responsible for targeting, the "lower stem", the "bulge", "upper stem" (which may include a tetraloop), the "nexus", and the "hairpin 1" and "hairpin 2" domains. See, Briner et al. at page 334, Figure 1A.

[00111] **Table 3** provides a schematic of the domains of an sgRNA as used herein. In Table 3, the "n" between regions represents a variable number of nucleotides, for example, from 0 to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more. In some embodiments, n equals 0. In some embodiments, n equals 1.

5' terminus region

[00112] In some embodiments, the sgRNA or short-sgRNA comprises nucleotides at the 5' terminus as shown in Table 3. In some embodiments, the 5' terminus of the sgRNA or short-sgRNA comprises a spacer or guide region that functions to direct a Cas protein, e.g., a Cas9 protein, to a target nucleotide sequence. In some embodiments, the 5' terminus does not comprise a guide region. In some embodiments, the 5' terminus comprises a spacer and additional nucleotides that do not function to direct a Cas protein to a target nucleotide region.

Lower stem

[00113] In some embodiments, the sgRNA or short-sgRNA comprises a lower stem (LS) region that when viewed linearly, is separated by a bulge and upper stem regions. See Table 3.

[00114] In some embodiments, the lower stem regions comprise 1-12 nucleotides, e.g. in one embodiment the lower stem regions comprise LS1-LS12. In some embodiments, the lower stem region comprises fewer nucleotides than shown in Table 3. In some embodiments, the lower stem region comprises more nucleotides than shown in Table 3. When the lower stem region comprises fewer or more nucleotides than shown in the schematic of Table 3, the modification pattern, as will be apparent to the skilled artisan, should be maintained.

[00115] In some embodiments, the lower stem region has nucleotides that are complementary in nucleic acid sequence when read in opposite directions. In some embodiments, the complementarity in nucleic acid sequence of lower stem leads to a secondary structure of a stem in the sgRNA or short-sgRNA (e.g., the regions may base pair

with one another). In some embodiments, the lower stem regions may not be perfectly complimentary to each other when read in opposite directions.

Bulge

[00116] In some embodiments, the sgRNA or short-sgRNA comprises a bulge region comprising six nucleotides, B1-B6. When viewed linearly, the bulge region is separated into two regions. See Table 3. In some embodiments, the bulge region comprises six nucleotides, wherein the first two nucleotides are followed by an upper stem region, followed by the last four nucleotides of the bulge. In some embodiments, the bulge region comprises fewer nucleotides than shown in Table 3. In some embodiments, the bulge region comprises more nucleotides than shown in Table 3. When the bulge region comprises fewer or more nucleotides than shown in the schematic of Table 3, the modification pattern, as will be apparent to the skilled artisan, should be maintained.

[00117] In some embodiments, the presence of a bulge results in a directional kink between the upper and lower stem modules in an sgRNA or short-sgRNA.

Upper stem

[00118] In some embodiments, the sgRNA or short-sgRNA comprises an upper stem region comprising 12 nucleotides. In some embodiments, the upper stem region comprises a loop sequence. In some instances, the loop is a tetraloop (loop consisting of four nucleotides).

[00119] In some embodiments, the upper stem region comprises fewer nucleotides than shown in Table 3. In some embodiments, the upper stem region comprises more nucleotides than shown in Table 3. When the upper stem region comprises fewer or more nucleotides than shown in the schematic of Table 3, the modification pattern, as will be apparent to the skilled artisan, should be maintained.

[00120] In some embodiments, the upper stem region has nucleotides that are complementary in nucleic acid sequence when read in opposite directions. In some embodiments, the complementarity in nucleic acid sequence of upper stem leads to a secondary structure of a stem in the sgRNA or short-sgRNA (e.g., the regions may base pair with one another). In some embodiments, the upper stem regions may not be perfectly complimentary to each other when read in opposite directions.

Nexus

[00121] In some embodiments, the sgRNA or short-sgRNA comprises a nexus region that is located between the lower stem region and the hairpin 1 region. In some embodiments, the nexus comprises 18 nucleotides. In some embodiments, the nexus region comprises nucleotides N1 through N18 as shown in Table 3.

[00122] In some embodiments, the nexus region comprises fewer nucleotides than shown in Table 3. In some embodiments, the nexus region comprises more nucleotides than shown in Table 3. When the nexus region comprises fewer or more nucleotides than shown in the schematic of Table 3, the modification pattern, as will be apparent to the skilled artisan, should be maintained.

[00123] In some embodiments, the nexus region has nucleotides that are complementary in nucleic acid sequence when read in opposite directions. In some embodiments, the complementarity in nucleic acid sequence leads to a secondary structure of a stem and/or stem loop in the sgRNA or short-sgRNA (e.g., certain nucleotides in the nexus region may base pair with one another). In some embodiments, the nexus regions may not be perfectly complimentary to each other when read in opposite directions.

Hairpin

[00124] In some embodiments, the sgRNA or short-sgRNA comprises one or more hairpin regions. In some embodiments, the hairpin region is downstream of (e.g., 3' to) the nexus region. In some embodiments, the region of nucleotides immediately downstream of the nexus region is termed "hairpin 1" or "H1". In some embodiments, the region of nucleotides 3' to hairpin 1 is termed "hairpin 2" or "H2". In some embodiments, the hairpin region comprises both hairpin 1 and hairpin 2. In some embodiments, the sgRNA or short-sgRNA comprises hairpin 1 or hairpin 2.

[00125] In some embodiments, the hairpin 1 region comprises 12 nucleic acids immediately downstream of the nexus region. In some embodiments, the hairpin 1 region comprises nucleotides H1-1 through H1-12 as shown in Table 3.

[00126] In some embodiments, the hairpin 2 region comprises 15 nucleic acids downstream of the hairpin 1 region. In some embodiments, the hairpin 2 region comprises nucleotides H2-1 through H2-15 as shown in Table 3.

[00127] In some embodiments, one or more nucleotides is present between the hairpin 1 and the hairpin 2 regions. The one or more nucleotides between the hairpin 1 and hairpin 2

region may be modified or unmodified. In some embodiments, hairpin 1 and hairpin 2 are separated by one nucleotide. In some embodiments, the hairpin regions comprise fewer nucleotides than shown in Table 3. In some embodiments, the hairpin regions comprise more nucleotides than shown in Table 3. When a hairpin region comprises fewer or more nucleotides than shown in the schematic of Table 3, the modification pattern, as will be apparent to the skilled artisan, should be maintained.

[00128] In some embodiments, a hairpin region has nucleotides that are complementary in nucleic acid sequence when read in opposite directions. In some embodiments, the hairpin regions may not be perfectly complimentary to each other when read in opposite directions (e.g., the top or loop of the hairpin comprises unpaired nucleotides).

[00129] In some embodiments, the sgRNA or short-sgRNA comprises replacement of hairpin 1 with nucleotides "n", wherein "n" is an integer between 1 and 50, 40, 30, 20, 15, 10, 5, 4, 3, and 2. In some embodiments, the hairpin 1 region of an sgRNA is replaced by 2 nucleotides.

3' terminus

[00130] The sgRNA or short-sgRNA has a 3' end, which is the last nucleotide of the sgRNA. The 3' terminus region includes the last 1-7 nucleotides from the 3' end. In some embodiments, the 3' end is the end of hairpin 2. In some embodiments, the sgRNA comprises nucleotides after the hairpin region(s). In some embodiments, the sgRNA includes a 3' tail region, in which case the last nucleotide of the 3' tail is the 3' terminus. In some embodiments, the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15 or 20 or more nucleotides, e.g. that are not associated with the secondary structure of a hairpin. In some embodiments, the 3' tail region comprises 1, 2, 3, or 4 nucleotides that are not associated with the secondary structure of a hairpin. In some embodiments, the 3' tail region comprises 4 nucleotides that are not associated with the secondary structure of a hairpin. In some embodiments, the 3' tail region comprises 1, 2, or 3 nucleotides that are not associated with the secondary structure of a hairpin.

Table 2 (Conserved Portion of a spyCas9 sgRNA; SEQ ID NO:400)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
G	U	U	U	U	A	G	A	G	C	U	A	G	A	A	A	U	A	G	C	A	A	G	U	U	A	A	A	A	U
LS1-LS6						B1-B2		US1-US12												B2-B6				LS7-LS12					

31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
A	A	G	G	C	U	A	G	U	C	C	G	U	U	A	U	C	A	A	C	U	U	G	A	A	A	A	A	G	U
Nexus																		H1-1 through H1-12											

61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76
G	G	C	A	C	C	G	A	G	U	C	G	G	U	G	C
N	H2-1 through H2-15														

Table 3 (Regions of sgRNA (linear view, 5' to 3')

	LS1-6		B1 -2		US1-12		B3-6	
5' terminus (n)	lower stem	n	bulge	n	upper stem	n	bulge	n

LS7-12		N1-18		H1-1 thru H1-12		H2-1 thru H2-15	
lower stem	n	nexus	n	hairpin 1	n	hairpin 2	3' terminus

gRNAs comprising modifications, including modifications of YA sites

[00131] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, dgRNA, or crRNA) described herein comprises modifications at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more YA sites (e.g., in the conserved region and/or the guide region) and/or a modification, such as a YA modification, at one or more nucleotides located at or after nucleotide 6 from the 5' end of the 5' terminus. In some embodiments, the pyrimidine of the YA site comprises a modification (which includes a modification altering the internucleoside linkage immediately 3' of the sugar of the pyrimidine). In some embodiments, the adenine of the YA site comprises a modification (which includes a modification altering the internucleoside linkage immediately 3' of the sugar of the adenine). In some embodiments, the pyrimidine and the adenine of the YA site comprise modifications, such as sugar, base, or internucleoside linkage modifications. The YA modifications can be any of the types of modifications set forth herein. In some embodiments, the YA modifications comprise one or more of phosphorothioate, 2'-OMe, or 2'-fluoro. In some embodiments, the YA modifications comprise pyrimidine modifications comprising one or more of phosphorothioate, 2'-OMe, or 2'-fluoro. In some embodiments, the YA modification comprises a bicyclic ribose analog (e.g., an LNA, BNA, or ENA) within an RNA duplex region that contains one or more YA sites. In some embodiments, the YA modification comprises a bicyclic ribose analog (e.g., an LNA, BNA, or ENA) within an RNA duplex region that contains a YA site, wherein the YA modification is distal to the YA site.

[00132] Any of the embodiments described above may be combined with the following: (i) at least one of nucleotides 8-11, 13, 14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification, and/or (ii) at least one of nucleotides 6-10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage; *and* (i) at least one of nucleotides 7-10 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification, (ii) nucleotide 20 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification, and/or (iii) or the guide RNA comprises a 2'-fluoro modification at any one or more of nucleotides 1-20 from the 5' end of the 5' terminus and at least one of nucleotides 11, 12, 13, 14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification, optionally wherein nucleotide 12 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification. Such embodiments may be further, or alternatively, combined with any other one or more embodiments described herein to the extent feasible.

Guide region modifications including YA site modifications

[00133] In some embodiments, the guide region comprises one or more modifications, optionally including YA site modifications. In some embodiments, the guide region comprises 1, 2, 3, 4, 5, or more YA sites ("guide region YA sites") that may comprise YA modifications. In some embodiments, one or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus (where "5-end", etc., refers to position 5 to the 3' end of the guide region, i.e., the most 3' nucleotide in the guide region) comprise YA modifications. In some embodiments, two or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus comprise YA modifications. In some embodiments, three or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus comprise YA modifications. In some embodiments, four or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus comprise YA modifications. In some embodiments, five or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus comprise YA modifications. A modified guide region YA site comprises a YA modification.

[00134] In some embodiments, a modified guide region YA site is within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region. For example, if a modified guide region YA site is within 10 nucleotides of the 3' terminal nucleotide of the guide region and the guide region is 20 nucleotides long, then the modified nucleotide of the modified guide region YA site is located at any of positions 11-20. In some embodiments, a YA modification is located within a YA site 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 nucleotides from the 3' terminal nucleotide of the guide region. In some embodiments, a YA modification is located 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 nucleotides from the 3' terminal nucleotide of the guide region.

[00135] In some embodiments, a modified guide region YA site is at or after nucleotide 4, 5, 6, 7, 8, 9, 10, or 11 from the 5' end of the 5' terminus.

[00136] In some embodiments, a modified guide region YA site is other than a 5' end modification. For example, a gRNAcan comprise a 5' end modification as described herein and further comprise a modified guide region YA site. Alternatively, a gRNAcan comprise an unmodified 5' end and a modified guide region YA site. Alternatively, a gRNA can comprise a modified 5' end and an unmodified guide region YA site.

[00137] In some embodiments, a modified guide region YA site comprises a modification that at least one nucleotide located 5' of the guide region YA site does not comprise. For example, if nucleotides 1-3 comprise phosphorothioates, nucleotide 4 comprises only a 2'-OMe modification, and nucleotide 5 is the pyrimidine of a YA site and comprises a phosphorothioate, then the modified guide region YA site comprises a modification (phosphorothioate) that at least one nucleotide located 5' of the guide region YA site (nucleotide 4) does not comprise. In another example, if nucleotides 1-3 comprise phosphorothioates, and nucleotide 4 is the pyrimidine of a YA site and comprises a 2'-OMe, then the modified guide region YA site comprises a modification (2'-OMe) that at least one nucleotide located 5' of the guide region YA site (any of nucleotides 1-3) does not comprise. This condition is also always satisfied if an unmodified nucleotide is located 5' of the modified guide region YA site.

[00138] In some embodiments, the guide region comprises modifications at 1-14 of nucleotides 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18 of the guide region. Such modifications may be 2'-OMe, 2'-fluoro, 2'-H, inosine, or phosphorothioate modifications, or a combination thereof. For example, 2'-OMe modifications may be included at any or all of nucleotides 1-4 and 12; phosphorothioate modifications may be included at any or all of nucleotides 1-3 and 6-10; and/or 2'-fluoro modifications may be included at any or all of nucleotides 8-11, 13, 14, 17, and 18. In negative terms, 2'-OMe modifications may be excluded from nucleotides 6-11 and 13-end; 2'-fluoro modifications may be excluded from nucleotides 1-7, 15, 16, and 20 (if present); and/or phosphorothioate modifications may be excluded from nucleotides 4, 5, 11-14, 17, and 18. In some embodiments, nucleotides are modified in a YA-site dependent manner, e.g., if a YA site is present at any of nucleotides 5-6, 12-13, 15-16, 16-17, or 19-20, then at least one nucleotide of the YA site is modified, e.g., at least the pyrimidine of the YA site is modified, optionally wherein the nucleotides at positions 5, 12, 15, 16, and 19 are unmodified if they are not the pyrimidine of a YA site. In some embodiments, the modification at nucleotide 5 when it is the pyrimidine of a YA site is 2'-OMe; the modification at nucleotide 12 when it is the pyrimidine of a YA site is 2'-OMe; the modification at nucleotide 15 when it is the pyrimidine of a YA site is phosphorothioate; the modification at nucleotide 16 when it is the pyrimidine of a YA site is phosphorothioate; and/or the modification at nucleotide 19 when it is the pyrimidine of a YA site is phosphorothioate. Recognizing that YA sites cannot be present at both positions 15-16 and 16-17, it is thus possible for there to be up to four modifications contingent on the presence of YA sites. In an alternative embodiment, the modification at nucleotide 19 may instead be a

2'-fluoro. This can be present in a YA site-dependent manner or it can be present regardless of whether there is a YA site at positions 19-20. In some embodiments, nucleotide 15 and 16 are unmodified or modified only with a phosphorothioate, e.g., only at a nucleotide which is the pyrimidine of a YA site located at nucleotides 15-16 or 16-17. In some embodiments, nucleotides 15 and 16 comprise unmodified riboses and/or unmodified nucleobases. In some embodiments, nucleotide 5 is unmodified or is modified only with 2'-OMe if it is the pyrimidine of a YA site. In some embodiments, nucleotide 12 is unmodified or is modified only with 2'-OMe if it is the pyrimidine of a YA site. In some embodiments, nucleotide 20 (or the 3'-terminal nucleotide of the guide region) is unmodified. In any of the foregoing embodiments, the guide region may consist of 20 nucleotides.

[00139] In some embodiments, a gRNA comprises a guide region that comprises a modification at one or more of nucleotide 5 and/or 12. The modifications at nucleotide 5 and/or 12 may be independently selected from modifications described herein, e.g., 2'-OMe, 2'-F, phosphorothioate, and 2'-H (a deoxyribonucleotide). Such modifications may be combined with another modification pattern or nucleotide modifications described herein, e.g., as shown in a gRNA described herein. Particular examples of such embodiments are described herein, e.g., in certain numbered embodiments set forth above and in modification patterns represented by sequences in the Table of Sequences. In some embodiments, such a modification is combined with one or more, or all, of 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

[00140] In some embodiments, a gRNA comprises a guide region that comprises modifications at any one, two, or all of nucleotides 8-10. Such modifications may be combined with another modification pattern or nucleotide modifications described herein, e.g., as shown in a gRNA described herein. The modifications may be independently selected from modifications described herein, e.g., 2'-F modifications and phosphorothioate modifications, or a combination thereof. In some embodiments, any one, two, or all of nucleotides 8-10 comprise 2'-F modifications. In some embodiments, any one, two, or all of nucleotides 8-10 comprise 2'-F modifications but not phosphorothioate modifications. In some embodiments, any one, two, or all of nucleotides 8-10 comprise 2'-F modifications and phosphorothioate modifications. Particular examples of such embodiments are described herein, e.g., in certain numbered embodiments set forth above and in modification patterns represented by sequences in the Table of Sequences. In some embodiments, such a modification is combined with one or more, or all, of 2'-OMe modifications at nucleotides 1-

4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

[00141] In some embodiments, a gRNA comprises a guide region that comprises modifications at any one or both of nucleotides 5 and 6. The modifications may be independently selected from modifications described herein, e.g., 2'-F modifications and phosphorothioate modifications, or a combination thereof. In some embodiments, any one or both of nucleotides 5 and 6 comprise 2'-F modifications. In some embodiments, any one or both of nucleotides 5 and 6 comprise 2'-F modifications but not phosphorothioate modifications. In some embodiments, any one or both of nucleotides 5 and 6 comprise 2'-F modifications and phosphorothioate modifications. Particular examples of such embodiments are described herein, e.g., in certain numbered embodiments set forth above and in modification patterns represented by sequences in the Table of Sequences. In some embodiments, such a modification is combined with one or more, or all, of 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 7-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

[00142] In some embodiments, a gRNA comprises a guide region that comprises modifications at at least 1, 2, 3, 4, 5, or 6 of nucleotides 6-11. The modifications may be independently selected from modifications described herein, e.g., 2'-F modifications. In some embodiments, 2'-F modifications at 1, 2, 3, 4, 5, or 6 of nucleotides 6-11 are combined with another compatible modification, such as a phosphorothioate modification, at one or more of the positions comprising a 2'-F modification. Particular examples of such embodiments are described herein, e.g., in certain numbered embodiments set forth above and in modification patterns represented by sequences in the Table of Sequences. In some embodiments, such a modification is combined with one or more, or all, of 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3, and/or 2'-F modifications at nucleotides 13, 14, 17, and 18.

[00143] In some embodiments, a gRNA comprises a guide region that comprises modifications at at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of nucleotides 1-4 and 6-11. The modifications may be independently selected from modifications described herein, e.g., 2'-F modifications. In some embodiments, 2'-F modifications at 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of nucleotides 1-4 and 6-11 are combined with another compatible modification, such as a phosphorothioate modification, at one or more of the positions comprising a 2'-F modification. Particular examples of such embodiments are described herein, e.g., in certain numbered embodiments set forth above and in modification patterns represented by

sequences in the Table of Sequences. In some embodiments, such a modification is combined with one or more, or all, of phosphorothioate modifications at nucleotides 1-3 and/or 2'-F modifications at nucleotides 13, 14, 17, and 18.

[00144] In some embodiments, a gRNA comprises a guide region that comprises 2'-OMe modifications at at least 1, 2, 3, or 4 of nucleotides 9, 11, 13, and 14. In some embodiments, 2'-OMe modifications at at least 1, 2, 3, or 4 of nucleotides 9, 11, 13, and 14 are combined with another compatible modification, such as a phosphorothioate modification, at one or more of the positions comprising a 2'-OMe modification. Particular examples of such embodiments are described herein, e.g., in certain numbered embodiments set forth above and in modification patterns represented by sequences in the Table of Sequences. In some embodiments, such a modification is combined with one or more, or all, of 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

[00145] In some embodiments, the modified guide region YA sites comprise modifications as described for YA sites above.

[00146] Additional embodiments of guide region YA site modifications are set forth in the summary above. Any embodiments set forth elsewhere in this disclosure may be combined to the extent feasible with any of the foregoing embodiments.

Conserved region YA site modifications

[00147] Conserved region YA sites 1-10 are illustrated in Fig. 1B. In some embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 conserved region YA sites comprise modifications.

[00148] In some embodiments, conserved region YA sites 1, 8, or 1 and 8 comprise YA modifications. In some embodiments, conserved region YA sites 1, 2, 3, 4, and 10 comprise YA modifications. In some embodiments, YA sites 2, 3, 4, 8, and 10 comprise YA modifications. In some embodiments, conserved region YA sites 1, 2, 3, and 10 comprise YA modifications. In some embodiments, YA sites 2, 3, 8, and 10 comprise YA modifications. In some embodiments, YA sites 1, 2, 3, 4, 8, and 10 comprise YA modifications. In some embodiments, 1, 2, 3, 4, 5, 6, 7, or 8 additional conserved region YA sites comprise YA modifications.

[00149] In some embodiments, 1, 2, 3, or 4 of conserved region YA sites 2, 3, 4, and 10 comprise YA modifications. In some embodiments, 1, 2, 3, 4, 5, 6, 7, or 8 additional conserved region YA sites comprise YA modifications.

[00150] In some embodiments, the modified conserved region YA sites comprise modifications as described for YA sites above.

[00151] Additional embodiments of conserved region YA site modifications are set forth in the summary above. Any embodiments set forth elsewhere in this disclosure may be combined to the extent feasible with any of the foregoing embodiments.

Modifications to terminal nucleotides

[00152] In some embodiments, the 5' and/or 3' terminus regions of a gRNA (e.g., sgRNA, short-sgRNA, dgRNA, or crRNA) are modified.

3' terminus region modifications

[00153] In some embodiments, the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region are modified. Throughout, this modification may be referred to as a "3' end modification". In some embodiments, the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region comprise more than one modification. In some embodiments, at least one of the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region are modified. In some embodiments, at least two of the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region are modified. In some embodiments, at least three of the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region are modified. In some embodiments, the modification comprises a PS linkage. In some embodiments, the modification to the 3' terminus region is a 3' protective end modification. In some embodiments, the 3' end modification comprises a 3' protective end modification.

[00154] In some embodiments, the 3' end modification comprises a modified nucleotide selected from 2'-O-methyl (2'-O-Me) modified nucleotide, 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, an inverted abasic modified nucleotide, an ENA, a UNA, a 2'-H (DNA), or combinations thereof.

[00155] In some embodiments, the 3' end modification comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

[00156] In some embodiments, the 3' end modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

[00157] In some embodiments, the 3' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides.

[00158] In some embodiments, the 3' end modification comprises or further comprises an inverted abasic modified nucleotide.

[00159] In some embodiments, the 3' end modification comprises or further comprises an ENA.

[00160] In some embodiments, the 3' end modification comprises or further comprises a UNA.

[00161] In some embodiments, the 3' end modification comprises or further comprises a 2'-H (DNA).

[00162] In some embodiments, the 3' end modification comprises or further comprises a modification of any one or more of the last 7, 6, 5, 4, 3, 2, or 1 nucleotides. In some embodiments, the 3' end modification comprises or further comprises one modified nucleotide. In some embodiments, the 3' end modification comprises or further comprises two modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises three modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises four modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises five modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises six modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises seven modified nucleotides.

[00163] In some embodiments, the 3' end modification comprises or further comprises a modification of between 1 and 7 or between 1 and 5 nucleotides.

[00164] In some embodiments, the 3' end modification comprises or further comprises modifications of 1, 2, 3, 4, 5, 6, or 7 nucleotides at the 3' terminus of the gRNA.

[00165] In some embodiments, the 3' end modification comprises or further comprises modifications of about 1-3, 1-5, 1-6, or 1-7 nucleotides at the 3' terminus of the gRNA.

[00166] In some embodiments, the 3' end modification comprises or further comprises any one or more of the following: a phosphorothioate (PS) linkage between nucleotides, a 2'-O-Me modified nucleotide, a 2'-O-moe modified nucleotide, a 2'-F modified nucleotide, an inverted abasic modified nucleotide, an ENA, a UNA, and a combination thereof.

[00167] In some embodiments, the 3' end modification comprises or further comprises 1, 2, 3, 4, 5, 6, or 7 PS linkages between nucleotides.

[00168] In some embodiments, the 3' end modification comprises or further comprises at least one 2'-O-Me, 2'-O-moe, inverted abasic, or 2'-F modified nucleotide.

[00169] In some embodiments, the 3' end modification comprises or further comprises one PS linkage, wherein the linkage is between the last and second to last nucleotide. In some embodiments, the 3' end modification comprises or further comprises two PS linkages between the last three nucleotides. In some embodiments, the 3' end modification comprises or further comprises four PS linkages between the last four nucleotides.

[00170] In some embodiments, the 3' end modification comprises or further comprises PS linkages between any one or more of the last four nucleotides. In some embodiments, the 3' end modification comprises or further comprises PS linkages between any one or more of the last five nucleotides. In some embodiments, the 3' end modification comprises or further comprises PS linkages between any one or more of the last 2, 3, 4, 5, 6, or 7 nucleotides.

[00171] In some embodiments, the 3' end modification comprises or further comprises a modification of one or more of the last 1-7 nucleotides, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof.

[00172] In some embodiments, the 3' end modification comprises or further comprises a modification to the last nucleotide with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and an optionally one or two PS linkages to the next nucleotide and/or the first nucleotide of the 3' tail.

[00173] In some embodiments, the 3' end modification comprises or further comprises a modification to the last and/or second to last nucleotide with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

[00174] In some embodiments, the 3' end modification comprises or further comprises a modification to the last, second to last, and/or third to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

[00175] In some embodiments, the 3' end modification comprises or further comprises a modification to the last, second to last, third to last, and/or fourth to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

[00176] In some embodiments, the 3' end modification comprises or further comprises a modification to the last, second to last, third to last, fourth to last, and/or fifth to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

[00177] In some embodiments, an sgRNA or short-sgRNA comprising a 3' end modification comprises or further comprises a 3' tail, wherein the 3' tail comprises a modification of any one or more of the nucleotides present in the 3' tail. In some embodiments, the 3' tail is fully modified. In some embodiments, the 3' tail comprises 1, 2, 3,

4, 5, 6, 7, 8, 9, 10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, or 1-10 nucleotides, optionally where any one or more of these nucleotides are modified.

[00178] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises the 3' end modification as shown in any one of SEQ ID Nos: 1-132. In some embodiments, an sgRNA is provided comprising a 3' protective end modification.

[00179] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) a 2'-OMe modified nucleotide at the last nucleotide of the conserved region of an sgRNA or sgRNA (ii) three consecutive 2'O-moe modified nucleotides immediately 5' to the 2'-OMe modified nucleotide, and (iii) three consecutive PS linkages between the last three nucleotides.

[00180] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) five consecutive 2'-OMe modified nucleotides from the last nucleotide of the conserved region of an sgRNA or sgRNA, and (ii) three PS linkages between the last three nucleotides.

[00181] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or sgRNA.

[00182] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, and (ii) three consecutive 2'-OMe modified nucleotides at the last three nucleotides of the conserved region of an sgRNA or short-sgRNA.

[00183] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) 15 consecutive 2'-OMe modified nucleotides from the last nucleotide of the conserved region of an sgRNA, (ii) five consecutive 2'-F modified nucleotides immediately 5' to the 2'-OMe modified nucleotides, and (iii) three PS linkages between the last three nucleotides.

[00184] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) alternating 2'-OMe modified nucleotides and 2'-F modified nucleotides at the last 20 nucleotides of the conserved region of an sgRNA or sgRNA, and (ii) three PS linkages between the last three nucleotides.

[00185] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) two or three consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

[00186] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises one PS linkage between the last and next to last nucleotides.

[00187] In some embodiments, the sgRNA or short-sgRNA comprises a 5' end modification and a 3' end modification.

3' tail

[00188] In some embodiments, the sgRNA comprises a 3' terminus comprising a 3' tail, which follows the 3' end of the conserved portion of an sgRNA. In some embodiments, the 3' tail comprises between 1 and about 20 nucleotides, between 1 and about 15 nucleotides, between 1 and about 10 nucleotides, between 1 and about 5 nucleotides, between 1 and about 4 nucleotides, between 1 and about 3 nucleotides, and between 1 and about 2 nucleotides. In some embodiments, the 3' tail comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides. In some embodiments, the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides. In some embodiments, the 3' tail comprises 1 nucleotide. In some embodiments, the 3' tail comprises 2 nucleotides. In some embodiments, the 3' tail comprises 3 nucleotides. In some embodiments, the 3' tail comprises 4 nucleotides. In some embodiments, the 3' tail comprises about 1-2, 1-3, 1-4, 1-5, 1-7, 1-10, at least 1-5, at least 1-3, at least 1-4, at least 1-5, at least 1-5, at least 1-7, or at least 1-10 nucleotides.

[00189] In some embodiments, the 3' tail comprising between 1 and 20 nucleotides and follows the 3' end of the conserved portion of an sgRNA.

[00190] In some embodiments, the 3' tail comprises or further comprises one or more of a protective end modification, a phosphorothioate (PS) linkage between nucleotides, a 2'-O-Me modified nucleotide, a 2'-O-moe modified nucleotide, a 2'-F modified nucleotide, an inverted abasic modified nucleotide, and a combination thereof.

[00191] In some embodiments, the 3' tail comprises or further comprises one or more phosphorothioate (PS) linkages between nucleotides. In some embodiments, the 3' tail comprises or further comprises one or more 2'-O-Me modified nucleotides. In some embodiments, the 3' tail comprises or further comprises one or more 2'-O-moe modified nucleotides. In some embodiments, the 3' tail comprises or further comprises one or more 2'-F modified nucleotide. In some embodiments, the 3' tail comprises or further comprises one

or more an inverted abasic modified nucleotides. In some embodiments, the 3' tail comprises or further comprises one or more protective end modifications. In some embodiments, the 3' tail comprises or further comprises a combination of one or more of a phosphorothioate (PS) linkage between nucleotides, a 2'-O-Me modified nucleotide, a 2'-O-moe modified nucleotide, a 2'-F modified nucleotide, and an inverted abasic modified nucleotide.

[00192] In some embodiments, the sgRNA does not comprise a 3' tail.

5' terminus region modifications

[00193] In some embodiments, the 5' terminus region is modified, for example, the first 1, 2, 3, 4, 5, 6, or 7 nucleotides of the gRNA (e.g., sgRNA, short-sgRNA, or crRNA) are modified. Throughout, this modification may be referred to as a "5' end modification". In some embodiments, the first 1, 2, 3, 4, 5, 6, or 7 nucleotides of the 5' terminus region (i.e., the first 1, 2, 3, 4, 5, 6, or 7 nucleotides from the 5' end of the 5' terminus) comprise more than one modification. In some embodiments, at least one of the terminal (i.e., first) 1, 2, 3, 4, 5, 6, or 7 nucleotides from the 5' end of the 5' terminus are modified. In some embodiments, at least two of the terminal 1, 2, 3, 4, 5, 6, or 7 nucleotides from the 5' end of the 5' terminus are modified. In some embodiments, at least three of the terminal 1, 2, 3, 4, 5, 6, or 7 nucleotides from the 5' end of the 5' terminus are modified. In some embodiments, the modification comprises a PS linkage. In some embodiments, the modification to the 5' terminus region is a 5' protective end modification. In some embodiments, the 5' end modification comprises a 5' protective end modification.

[00194] In some embodiments, both the 5' and 3' terminus regions of the sgRNA or short-sgRNA are modified (e.g., including the first and last nucleotides of the gRNA). In some embodiments, only the 5' terminus region of the sgRNA or short-sgRNA is modified. In some embodiments, only the 3' terminus region (plus or minus a 3' tail) of the conserved portion of an sgRNA or short-sgRNA is modified.

[00195] In some embodiments, the gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises modifications at 1, 2, 3, 4, 5, 6, or 7 of the first 7 nucleotides from the 5' end of the 5' terminus of the gRNA. In some embodiments, the gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises modifications at 1, 2, 3, 4, 5, 6, or 7 of the 7 terminal nucleotides from the 3' end of the 3' terminus. In some embodiments, 2, 3, or 4 of the first 4 nucleotides from the 5' end of the 5' terminus, and/or 2, 3, or 4 of the terminal 4 nucleotides from the 3' end of the 3' terminus are modified. In some embodiments, 2, 3, or 4 of the first 4 nucleotides from the 5' end of the 5' terminus are linked with phosphorothioate (PS) bonds.

[00196] In some embodiments, the modification to the 5' terminus and/or 3' terminus comprises a 2'-O-methyl (2'-O-Me) or 2'-O-(2-methoxyethyl) (2'-O-moe) modification. In some embodiments, the modification comprises a 2'-fluoro (2'-F) modification to a nucleotide. In some embodiments, the modification comprises a phosphorothioate (PS) linkage between nucleotides. In some embodiments, the modification comprises an inverted abasic nucleotide. In some embodiments, the modification comprises a protective end modification. In some embodiments, the modification comprises a more than one modification selected from protective end modification, 2'-O-Me, 2'-O-moe, 2'-fluoro (2'-F), a phosphorothioate (PS) linkage between nucleotides, 2'-H (DNA), an ENA, a UNA, and an inverted abasic nucleotide. In some embodiments, an equivalent modification is encompassed.

[00197] In some embodiments, the gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises one or more phosphorothioate (PS) linkages between the first one, two, three, four, five, six, or seven nucleotides at the 5' terminus. In some embodiments, the sgRNA comprises one or more PS linkages between the last one, two, three, four, five, six, or seven nucleotides at the 3' terminus. In some embodiments, the sgRNA or short-sgRNA comprises one or more PS linkages between both the last one, two, three, four, five, six, or seven nucleotides at the 3' terminus and the first 1, 2, 3, 4, 5, 6, or 7 nucleotides from the 5' end of the 5' terminus. In some embodiments, in addition to PS linkages, the 5' and 3' terminal nucleotides may comprise 2'-O-Me, 2'-O-moe, or 2'-F modified nucleotides.

[00198] In some embodiments, the sgRNA comprises a 5' end modification, e.g., wherein the first nucleotide of the guide region is modified. In some embodiments, the sgRNA comprises a 5' end modification, wherein the first nucleotide of the guide region comprises a 5' protective end modification.

[00199] In some embodiments, the 5' end modification comprises a modified nucleotide selected from 2'-O-methyl (2'-O-Me) modified nucleotide, 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, an inverted abasic modified nucleotide, an ENA, a UNA, a 2'H (DNA), or combinations thereof.

[00200] In some embodiments, the 5' end modification comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

[00201] In some embodiments, the 5' end modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

[00202] In some embodiments, the 5' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides.

[00203] In some embodiments, the 5' end modification comprises or further comprises an inverted abasic modified nucleotide.

[00204] In some embodiments, the 5' end modification comprises or further comprises an ENA.

[00205] In some embodiments, the 5' end modification comprises or further comprises a UNA.

[00206] In some embodiments, the 5' end modification comprises or further comprises a 2'-H (DNA).

[00207] In some embodiments, the 5' end modification comprises or further comprises a modification of any one or more of nucleotides 1-7 of the guide region of an gRNA (e.g., sgRNA, short-sgRNA, or crRNA). In some embodiments, the 5' end modification comprises or further comprises one modified nucleotide. In some embodiments, the 5' end modification comprises or further comprises two modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises three modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises four modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises five modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises six modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises seven modified nucleotides.

[00208] In some embodiments, the 5' end modification comprises or further comprises a modification of between 1 and 7, between 1 and 5, between 1 and 4, between 1 and 3, or between 1 and 2 nucleotides.

[00209] In some embodiments, the 5' end modification comprises or further comprises modifications of 1, 2, 3, 4, 5, 6, or 7 nucleotides from the 5' end. In some embodiments, the 5' end modification comprises or further comprises modifications of about 1-3, 1-4, 1-5, 1-6, or 1-7 nucleotides from the 5' end.

[00210] In some embodiments, the 5' end modification comprises or further comprises modifications at the first nucleotide from the 5' end of the gRNA (e.g., sgRNA, short-sgRNA, or crRNA). In some embodiments, the 5' end modification comprises or further comprises modifications at the first and second nucleotide from the 5' end of the gRNA (e.g., sgRNA, short-sgRNA, or crRNA). In some embodiments, the 5' end modification comprises or further comprises modifications from the first, second, and third nucleotide at the 5' end of

the gRNA (e.g., sgRNA, short-sgRNA, or crRNA). In some embodiments, the 5' end modification comprises or further comprises modifications at the first, second, third, and fourth nucleotide from the 5' end of the gRNA (e.g., sgRNA, short-sgRNA, or crRNA). In some embodiments, the 5' end modification comprises or further comprises modifications at the first, second, third, fourth, and fifth nucleotide from the 5' end of the gRNA (e.g., sgRNA, short-sgRNA, or crRNA). In some embodiments, the 5' end modification comprises or further comprises modifications at the first, second, third, fourth, fifth, and sixth nucleotide from the 5' end of the gRNA (e.g., sgRNA, short-sgRNA, or crRNA). In some embodiments, the 5' end modification comprises or further comprises modifications from the first, second, third, fourth, fifth, sixth, and seventh nucleotide at the 5' end of the gRNA (e.g., sgRNA, short-sgRNA, or crRNA).

[00211] In some embodiments, the 5' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides, and/or a 2'-O-Me modified nucleotide, and/or a 2'-O-moe modified nucleotide, and/or a 2'-F modified nucleotide, and/or an inverted abasic modified nucleotide, and/or combinations thereof.

[00212] In some embodiments, the 5' end modification comprises or further comprises 1, 2, 3, 4, 5, 6, and/or 7 PS linkages between nucleotides. In some embodiments, the 5' end modification comprises or further comprises about 1-2, 1-3, 1-4, 1-5, 1-6, or 1-7 PS linkages between nucleotides.

[00213] In some embodiments, the 5' end modification comprises or further comprises at least one PS linkage, wherein if there is one PS linkage, the linkage is between nucleotides 1 and 2 of the guide region.

[00214] In some embodiments, the 5' end modification comprises or further comprises at least two PS linkages, and the linkages are between nucleotides 1 and 2, and 2 and 3 of the guide region.

[00215] In some embodiments, the 5' end modification comprises or further comprises PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region.

[00216] In some embodiments, the 5' end modification comprises or further comprises PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, and 4 and 5 of the guide region.

[00217] In some embodiments, the 5' end modification comprises or further comprises PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region.

[00218] In some embodiments, the 5' end modification comprises or further comprises PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, 5 and 6, and 7 and 8 of the guide region.

[00219] In some embodiments, the 5' end modification comprises or further comprises a modification of one or more of nucleotides 1-7 of the guide region, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-O-Me, 2'-O-moe, 2'-F, and/or combinations thereof.

[00220] In some embodiments, the 5' end modification comprises or further comprises a modification to the first nucleotide of the guide region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and an optional PS linkage to the next nucleotide;

[00221] In some embodiments, the 5' end modification comprises or further comprises a modification to the first and/or second nucleotide of the guide region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages between the first and second nucleotide and/or between the second and third nucleotide.

[00222] In some embodiments, the 5' end modification comprises or further comprises a modification to the first, second, and/or third nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages between the first and second nucleotide, between the second and third nucleotide, and/or between the third and the fourth nucleotide.

[00223] In some embodiments, the 5' end modification comprises or further comprises a modification to the first, second, third, and/or fourth nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages between the first and second nucleotide, between the second and third nucleotide, between the third and the fourth nucleotide, and/or between the fourth and the fifth nucleotide.

[00224] In some embodiments, the 5' end modification comprises or further comprises a modification to the first, second, third, fourth, and/or fifth nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages between the first and second nucleotide, between the second and third nucleotide, between the third and the fourth nucleotide, between the fourth and the fifth nucleotide, and/or between the fifth and the sixth nucleotide.

[00225] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises a 5' end modification as shown in any one of SEQ ID Nos: 401-532, 1001, or 1007-1132. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5'

end modification, wherein the 5' end modification comprises a 5' end modification as shown in nucleotides 1-3 of any one of SEQ ID Nos: 401-532, 1001, or 1007-1132. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises a 5' end modification as shown in nucleotides 1-4 of any one of SEQ ID Nos: 401-532, 1001, or 1007-1132. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises a 5' end modification as shown in nucleotides 1-5 of any one of SEQ ID Nos: 401-532, 1001, or 1007-1132. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises a 5' end modification as shown in nucleotides 1-6 of any one of SEQ ID Nos: 401-532, 1001, or 1007-1132. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises a 5' end modification as shown in nucleotides 1-7 of any one of SEQ ID Nos: 401-532, 1001, or 1007-1132.

[00226] In some embodiments, the gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises a 5' end modification comprising a 5' protective end modification. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region.

[00227] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region.

[00228] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region.

[00229] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region.

[00230] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region.

[00231] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region.

[00232] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises an inverted abasic modified nucleotide at nucleotide 1 of the guide region.

[00233] In some embodiments, agRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises an inverted abasic modified nucleotide at nucleotide 1 of the guide region and 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region.

[00234] In some embodiments, agRNA (e.g., sgRNA, short-sgRNA, or crRNA) is provided comprising a 5' end modification, wherein the 5' end modification comprises an inverted abasic modified nucleotide at nucleotide 1 of the guide region, 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region, and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region.

[00235] In some embodiments, an sgRNA or short-sgRNA is provided comprising a 5' end modification and a 3' end modification. Any of the 5' end modifications discussed above and/or otherwise disclosed herein can be combined with a 3' end modification, such as a 3' end modification represented in the Table of Sequences and/or discussed below.

[00236] In some embodiments, the sgRNA or short-sgRNA comprises modified nucleotides at the 5' and 3' terminus, and modified nucleotides in one or more other regions described in Table 3.

[00237] In some embodiments, the sgRNA or short-sgRNA comprises modified nucleotides that are not at the 5' or 3' ends. Exemplary patterns of modifications are described below and in Table 1.

Modifications to stabilize secondary structures

[00238] In some embodiments, an gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises a modification that stabilizes a secondary structure, e.g. a duplex region. Increased stability of a secondary structure can be determined empirically, e.g., by a melting temperature analysis. To simplify the analysis, the secondary structure element sought to be stabilized can be tested in isolation from the rest of the sgRNA structure. Increased stability of a secondary structure can also be determined by a reduction in accessibility of an

endonucleolytic cleavage site (e.g., YA site) wherein the modification does not alter the endonucleolytic cleavage site primary structure but does occur in or affect a secondary structure comprising the endonucleolytic cleavage site. This is referred to as having a distal effect on the endonucleolytic cleavage site. In some embodiments, the endonucleolytic cleavage site is in the lower stem. In some embodiments, the endonucleolytic cleavage site is conserved region YA site 1. In some embodiments, the endonucleolytic cleavage site is conserved region YA site 2. In some embodiments, the endonucleolytic cleavage site is conserved region YA site 3. In some embodiments, the endonucleolytic cleavage site is conserved region YA site 10. In some embodiments, the modification is a bicyclic ribose analog modification, such as, a locked nucleic acid (LNA) or LNA-like modification. In some embodiments, the modification is an ENA modification. In some embodiments, nucleotide LS8 comprises a modification that stabilizes a secondary structure. In some embodiments, nucleotide LS11 comprises a modification that stabilizes a secondary structure. In some embodiments, one or both of nucleotides LS8 and LS11 collectively comprise one or more modifications (e.g., 2 modifications), such as ENA modifications, that stabilize a secondary structure. See discussion of G10008 and G10038 in the examples.

Additional modifications

[00239] In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises modifications and/or unmodified nucleotides at at least 15 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises modifications and/or unmodified nucleotides at at least 16 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises modifications and/or unmodified nucleotides at at least 17 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises modifications and/or unmodified nucleotides at at least 18 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises modifications and/or unmodified nucleotides at at least 19 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at

nucleotides 1-20 of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA (e.g., sgRNA, short-sgRNA, or crRNA) comprises modifications and/or unmodified nucleotides at nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA comprises a modification pattern that matches at least 75% of the modification pattern of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA comprises a modification pattern that matches at least 80% of the modification pattern of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA comprises a modification pattern that matches at least 85% of the modification pattern of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA comprises a modification pattern that matches at least 90% of the modification pattern of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA comprises a modification pattern that matches at least 95% of the modification pattern of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA comprises a modification pattern that matches at least 98% of the modification pattern of a gRNA described herein, e.g., in Table 1. In some embodiments, a gRNA comprises a modification pattern that matches the modification pattern of a gRNA described herein, e.g., in Table 1. In some embodiments, an sgRNA or short-sgRNA comprises modifications in any one or more of the regions shown as modified in Table 1. In some embodiments, an sgRNA or short-sgRNA comprises modifications at any of the positions shown as modified in Table 1. In some embodiments, an sgRNA or short-sgRNA comprises any of the modifications shown in Table 1. Additional modifications are set forth in the summary section above, which may be combined to the extent feasible with modifications disclosed elsewhere herein, such as YA site modifications.

[00240] In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a modification to any one or more of US1-US12 in the upper stem region.

[00241] In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a modification of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all 12 nucleotides in the upper stem region.

[00242] In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a modification of about 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, or 1-12 nucleotides in the upper stem region.

[00243] In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises 1, 2, 3, 4, or 5 YA

modifications in a YA site. In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises at least 1, 2, 3, 4, or 5 YA modifications. In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises one YA modification. In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises 2 YA modifications. In some embodiments, the upper stem modification comprises 3 YA modifications. In some embodiments, one or more YA modifications are in a YA site. In some embodiments, one or more YA modifications are distal to a YA site.

[00244] In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a 2'-O-Me modified nucleotide. In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a 2'-O-moe modified nucleotide. In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a 2'-F modified nucleotide.

[00245] In some embodiments, an sgRNA or short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a 2'-O-Me modified nucleotide, a 2'-O-moe modified nucleotide, a 2'-F modified nucleotide, and/or combinations thereof.

[00246] In some embodiments, the sgRNA or short-sgRNA comprises an upper stem modification as shown in any one of the sequences in Table 1. In some embodiments, such an upper stem modification is combined with a 5' protective end modification, e.g. as shown for the corresponding sequence in Table 1. In some embodiments, such an upper stem modification is combined with a 3' protective end modification, e.g. as shown for the corresponding sequence in Table 1. In some embodiments, such an upper stem modification is combined with 5' and 3' end modifications as shown for the corresponding sequence in Table 1.

[00247] In some embodiments, the sgRNA or short-sgRNA comprises a 5' end modification and an upper stem modification. In some embodiments, the sgRNA or short-sgRNA comprises a 3' end modification and an upper stem modification. In some embodiments, the sgRNA or short-sgRNA comprises a 5' end modification, a 3' end modification and an upper stem modification.

[00248] In some embodiments, the sgRNA or short-sgRNA comprises a modification in the hairpin region. In some embodiments, the hairpin region modification is in hairpin 1. In some embodiments, the hairpin region modification is in hairpin 2. In some embodiments, modifications are within hairpin 1 and 2, optionally wherein the "n" between hairpin 1 and 2 is also modified. In some embodiments, the hairpin region modification comprises at least one modified nucleotide selected from a 2'H modified nucleotide (DNA), PS modified nucleotide, a YA modification, a 2'-O-methyl (2'-O-Me) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, and/or combinations thereof.

[00249] In some embodiments, an sgRNA or short-sgRNA is provided comprising a hairpin modification, wherein the hairpin modification comprises 1, 2, or 3 YA modifications in a YA site. In some embodiments, an sgRNA or short-sgRNA is provided comprising a hairpin modification, wherein the hairpin modification comprises at least 1, 2, 3, 4, 5, or 6 YA modifications. In some embodiments, an sgRNA or short-sgRNA is provided comprising a hairpin modification, wherein the hairpin modification comprises one YA modification. In some embodiments, an sgRNA or short-sgRNA is provided comprising a hairpin modification, wherein hairpin modification comprises 2 YA modifications. In some embodiments, the hairpin modification comprises 3 YA modifications. In some embodiments, one or more YA modifications are in a YA site. In some embodiments, one or more YA modifications are distal to a YA site.

[00250] In some embodiments, the hairpin modification comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

[00251] In some embodiments, the hairpin modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

[00252] In some embodiments, the sgRNA or short-sgRNA comprises a 3' end modification, and a modification in the hairpin region.

[00253] In some embodiments, the sgRNA or short-sgRNA comprises a 5' end modification, and a modification in the hairpin region.

[00254] In some embodiments, the sgRNA or short-sgRNA comprises an upper stem modification, and a modification in the hairpin region.

[00255] In some embodiments, the sgRNA or short-sgRNA comprises a hairpin modification as shown in any one of the sequences in Table 1. In some embodiments, such a hairpin modification is combined with a 5' end modification as shown for the corresponding sequence in Table 1. In some embodiments, such a hairpin modification is combined with a 3' end modification as shown for the corresponding sequence in Table 1. In some

embodiments, such an hairpin modification is combined with 5' and 3' end modifications as shown for the corresponding sequence in Table 1.

[00256] In some embodiments, the sgRNA or short-sgRNA comprises a 3' end modification, a modification in the hairpin region, an upper stem modification, and a 5' end modification.

[00257] In some embodiments, the sgRNA or short-sgRNA comprising one or more modifications of YA sites is a short-sgRNA as described herein, e.g., comprising a hairpin region that lacks at least 5-10 nucleotides, e.g., as defined herein or relative to the hairpin region shown in Table 2. Such an sgRNA may have any of the features set forth herein with respect to an sgRNA, e.g., in the summary and in the detailed description section regarding short-sgRNAs above.

Exemplary modified sgRNAs

[00258] In some embodiments, the sgRNAs described herein comprise or consist of any of the sequences shown in Table 1. Further, sgRNAs are encompassed that comprise the modifications of any of the sequences shown in Table 1, and identified therein by SEQ ID No. That is, the nucleotides may be the same or different, but the modification pattern shown may be the same or similar to a modification pattern of a guide sequence of Table 1. A modification pattern includes the relative position and identity of modifications of the sgRNA (e.g. 5' terminus region, lower stem region, bulge region, upper stem region, nexus region, hairpin 1 region, hairpin 2 region, 3' tail region).

[00259] In some embodiments, the modification pattern contains at least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% of the modifications of any one of the sequences shown in the sequence column of Table 1, or over one or more regions of the sequence. In some embodiments, the modification pattern is at least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical to the modification pattern of any one of the sequences shown in the sequence column of Table 1. In some embodiments, the modification pattern is at least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over 1, 2, 3, 4, 5, 6, 7, or 8 regions of the sequence shown in Table 1, e.g., a 5' terminus region, lower stem region, bulge region, upper stem region, nexus region, hairpin 1 region, hairpin 2 region, and/or 3' terminus region.

[00260] For example, in some embodiments, an sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical to the modification pattern of a sequence over the 5' terminus region.

In some embodiments, an sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the lower stem. In some embodiments, an sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the bulge. In some embodiments, an sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the upper stem. In some embodiments, an sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the nexus. In some embodiments, an sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the hairpin 1. In some embodiments, an sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the hairpin 2. In some embodiments, an sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the 3' terminus. In some embodiments, the modification pattern differs from the modification pattern of a sequence of Table 1, or a region (e.g. 5' terminus, lower stem, bulge, upper stem, nexus, hairpin 1, hairpin 2, 3' terminus) of such a sequence, at 0, 1, 2, 3, 4, 5, or 6 nucleotides. In some embodiments, the sgRNA comprises modifications that differ from the modifications of a sequence of Table 1, at 0, 1, 2, 3, 4, 5, or 6 nucleotides. In some embodiments, the sgRNA comprises modifications that differ from modifications of a region (e.g. 5' terminus, lower stem, bulge, upper stem, nexus, hairpin 1, hairpin 2, 3' terminus) of a sequence of Table 1, at 0, 1, 2, 3, 4, 5, or 6 nucleotides.

[00261] In some embodiments, the sgRNA comprises a 2'-O-methyl (2'-O-Me) modified nucleotide. In some embodiments, the sgRNA comprises a 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide. In some embodiments, the sgRNA comprises a 2'-fluoro (2'-F) modified nucleotide. In some embodiments, the sgRNA comprises a phosphorothioate (PS) bond between nucleotides. In some embodiments, the sgRNA comprises a YA modification.

[00262] In some embodiments, the sgRNA comprises a 5' end modification, a 3' end modification, or 5' and 3' end modification and further comprises a YA modification. In some embodiments, the 5' end modification comprises a protective end modification. In some embodiments, the 5' end modification comprises a phosphorothioate (PS) bond between nucleotides. In some embodiments, the 5' end modification comprises a 2'-O-

methyl (2'-O-Me), 2'-O-(2-methoxyethyl) (2'-O-moe), and/or 2'-fluoro (2'-F) modified nucleotide. In some embodiments, the 5' end modification comprises at least one phosphorothioate (PS) bond and one or more of a 2'-O-methyl (2'-O-Me), 2'-O-(2-methoxyethyl) (2'-O-moe), and/or 2'-fluoro (2'-F) modified nucleotide. The end modification may comprise a phosphorothioate (PS), 2'-O-methyl (2'-O-Me), 2'-O-(2-methoxyethyl) (2'-O-moe), and/or 2'-fluoro (2'-F) modification. Equivalent end modifications are also encompassed by embodiments described herein. In some embodiments, the sgRNA comprises an end modification in combination with a modification of one or more regions of the sgRNA.

[00263] Modified sgRNAs comprising combinations of 5' end modifications, 3' end modifications, upper stem modifications, hairpin modifications, and 3' terminus modifications, as described above, are encompassed. Exemplary modified sgRNAs are described below.

[00264] In some embodiments, an sgRNA is provided comprising or consisting of any one of the sequences described in SEQ ID Nos: 401-535, 601, 607-732, 801, 807-932, 1001, or 1007-1132.

[00265] In some embodiments, an sgRNA is provided comprising any one of the modified sequences of SEQ ID Nos: 601 or 607-732, wherein the sgRNA further comprises a guide region that is complementary to a target sequence, and directs a Cas9 to its target for cleavage. In some instances, an sgRNA is provided comprising nucleic acids having at least 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% identity to the nucleic acids of any one of SEQ ID Nos: 401-535, 601, 607-732, 801, 807-932, 1001, or 1007-1132, wherein the modification pattern is identical to the modification pattern shown in the reference sequence identifier in Table 1. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00266] In some embodiments, the sgRNA comprises modifications at 1, 2, 3, or 4 of the first 4 nucleotides at its 5' end. In some embodiments, the first three or four nucleotides at the 5' terminus, and the last three or four nucleotides at the 3' terminus are modified. In some embodiments, the first four nucleotides at the 5' end, and the last four nucleotides at the 3' terminus are linked with phosphorothioate (PS) bonds. In some embodiments, the modification comprises 2'-O-Me. In some embodiments, the modification comprises 2'-F. In some embodiments, the modification comprises 2'-O-moe.

[00267] In some embodiments, the sgRNA comprises, if the nucleotide mentioned is present in the sgRNA, modifications at 1, 2, 3, or 4 of the first 4 nucleotides at the 5' end. In some embodiments, the sgRNA comprises modifications at 1, 2, 3, or 4 of the last 4 nucleotides at the 3' end (3' tail or conserved portion of an sgRNA). In some embodiments, the first four nucleotides at the 5' terminus and the last four nucleotides at the 3' terminus are linked with a PS bond, and the first three nucleotides at the 5' terminus and the last three nucleotides at the 3' terminus comprise 2'-O-Me or 2'-O-moe modifications.

[00268] In some embodiments, the first four nucleotides at the 5' terminus and the last four nucleotides at the 3' terminus are linked with a PS bond, and the first three nucleotides at the 5' terminus and the last three nucleotides at the 3' terminus comprise 2'-F modifications.

[00269] In some embodiments, an sgRNA is provided, if the nucleotide mentioned is present in the sgRNA, wherein LS1, LS6, LS7, LS8, LS11, and LS12 are modified with 2'-O-Me. In some embodiments, each of the nucleotides in the bulge region of the sgRNA are modified with 2'-O-Me. In some embodiments, each of the nucleotides in the upper stem region of the sgRNA are modified with 2'-O-Me. In some embodiments, N16, N17, and N18 in the nexus region of the sgRNA are modified with 2'-O-Me. In some embodiments, each of the nucleotides in the hairpin 1 region of the sgRNA are modified with 2'-O-Me. In some embodiments, each of the nucleotides in the hairpin 2 region of the sgRNA are modified with 2'-O-Me.

[00270] In some embodiments, the sgRNA comprises 2'-O-Me modified nucleotides at the following nucleotides: the first three nucleotides at the 5' terminus; LS1, LS6, LS7, LS8, LS11, and LS12; B1 and B2 in the bulge region; each of the nucleotides in the upper stem region of the sgRNA; N16, N17, and N18 in the nexus region; each of the nucleotides in the hairpin 1 region; each of the nucleotides in the hairpin 2 region; and last four nucleotides at the 3' terminus.

[00271] In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises 2'-O-Me or 2'-F modified nucleic acids at the first three nucleotides at the 5' terminus, and 2'-O-Me or 2'-F modified nucleic acids at the last four nucleotides at the 3' terminus. In some embodiments, LS9 and LS10 are modified with 2'-F. In some embodiments, N15, N16, N17, and N18 are modified with 2'-F. In some embodiments, H2-9, H2-10, H2-11, H2-12, H2-13, HS-14, and H2-15 are modified with 2'-F. In some embodiments, the second to last, third to last, and fourth to last nucleotides at the 3' terminus are modified with 2'-F.

[00272] In some embodiments, sgRNA is provided comprising 2'-F modified nucleic acids at the following nucleotides: LS9 and LS10 in the lower stem region; N15, N16, N17, and N18 in the nexus region; and H2-9, H2-10, H2-11, H2-12, H2-13, HS-14, and H2-15 in the hairpin 2 region. In some embodiments, the sgRNA further comprises 2'-F modified nucleotides at the second to last, third to last, and fourth to last nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises 2'-O-Me or 2'-F modified nucleic acids at the first three nucleotides at the 5' terminus, and 2'-O-Me or 2'-F modified nucleic acids at three of the last four nucleotides at the 3' terminus.

[00273] In some embodiments, an sgRNA is provided comprising: 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-O-Me modified nucleotides at LS1 and LS6; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at H1-1 – H1-12; a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2; 2'-O-Me modified nucleotides at H2-1 – H2-15; and 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00274] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-F modified nucleotides at LS1-LS6; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at H1-1 – H1-12; a 2'-O-Me modified nucleotide at "n" between Hairpin 1 and Hairpin 2; 2'-O-Me modified nucleotides at H2-1 – H2-15; and 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00275] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-F modified nucleotides at LS2-LS5; 2'-O-Me modified nucleotides at LS1 and LS6; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at H1-1 – H1-12; a 2'-O-Me modified nucleotide at "n" between Hairpin 1 and Hairpin 2; 2'-O-Me modified nucleotides at H2-1 – H2-15; and 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the

first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00276] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at LS7, LS8, LS11, and LS12; 2'-O-Me modified nucleotides at H1-1 – H1-12; a 2'-O-Me modified nucleotide at "n" between Hairpin 1 and Hairpin 2; 2'-O-Me modified nucleotides at H2-1 – H2-15; and 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00277] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at LS8, LS10, and LS12; 2'-O-F modified nucleotides at LS7, LS9, and LS11; 2'-O-Me modified nucleotides at H1-1 – H1-12; a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2; 2'-O-Me modified nucleotides at H2-1 – H2-15; and 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00278] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-O-Me modified nucleotides at LS1, LS6, LS7, LS8, LS11, and LS12; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at H1-1 – H1-12; a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2; 2'-O-Me modified nucleotides at H2-1 – H2-15; and 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00279] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-O-Me modified nucleotides at LS1, LS6, LS7, LS8, LS11, and LS12; 2'-F modified nucleotides at LS9 and LS10; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at H1-1 – H1-12; a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2; 2'-O-Me modified nucleotides at H2-1 – H2-15; and 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS)

bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00280] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at H1-1 – H1-12; a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2; 2'-O-Me modified nucleotides at H2-1 – H2-8; 2'-F modified nucleotides at H2-9 – H2-15; 2'-F modified nucleotides at the second from last, third from last, and fourth from last nucleotide at the 3' terminus; and a 2'-O-Me modified nucleotide at the last nucleotide at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00281] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus; 2'-O-Me modified nucleotides at US1-US12; 2'-O-Me modified nucleotides at H1-2, H1-4, H1-6, H1-8, H1-10, and H1-12; 2'-F modified nucleotides at H1-1, H1-3, H1-5, H1-7, H1-9, and H1-11; a 2'-F modified nucleotide between Hairpin 1 and Hairpin 2; 2'-F modified nucleotides at H2-2, H2-4, H2-6, H2-8, H2-10, H2-12; and H2-14; 2'-O-Me modified nucleotides at H2-1, H2-3, H2-5, H2-7, H2-9, H2-11; H2-13, and H2-15; 2'-F modified nucleotides at the second from last, and fourth from last nucleotide at the 3' terminus; and 2'-O-Me modified nucleotide at the third from last, and last nucleotide at the 3' terminus. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00282] Disclosed herein, in some embodiments, is an sgRNA comprising 2'-O-Me modifications at nucleotides LS8, LS10, LS12, H1-2, H1-4, H1-6, H1-8, H1-10, H1-12, H2-1, H2-3, H2-5, H2-7, H2-9, H2-11, H2-13, and H2-15; and 2'-F modifications at LS7, LS9, LS11; H1-1, H1-3, H1-5, H1-7, H1-9, H1-11, H1-13, H2-2, H2-4, H2-6, H2-8, H2-10, H2-12, and H2-14. In some embodiments, the sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises 2'-O-Me modified nucleotides at the last and third to last nucleotide at the 3' terminus; and 2'-F modified nucleotides at the second to last and third to last nucleotide at the 3' terminus.

[00283] In some embodiments, an sgRNA comprising a 5' end modification and one or more modifications in one or more of: the upper stem region; the hairpin 1 region; and the

hairpin 2 region is provided, wherein the 5' end modification comprises at least two phosphorothioate linkages within the first seven nucleotides of the 5' terminus.

[00284] In some embodiments, an sgRNA comprising a 5' end modification and one or more modifications in one or more of: the upper stem region; the hairpin 1 region; and the hairpin 2 region is provided, wherein the 5' end modification comprises one or more phosphorothioate linkages at the 5' end. In some embodiments, one or more phosphorothioate bonds link the 5' terminal nucleotides.

[00285] In some embodiments, an sgRNA is provided, comprising a 5' end modification and one or more modifications in one or more of: the upper stem region; the hairpin 1 region; and the hairpin 2 region is provided, wherein the 5' end modification comprises one or more phosphorothioate linkages within the first seven nucleotides of the 5' terminus.

[00286] In some embodiments, an sgRNA comprising any one of the modified sequences of SEQ ID Nos: 601 or 607-732 is provided, wherein the sgRNA further comprises a 5' guide region that is at least partially complementary to a target sequence, and optionally directs a Cas9 to its target for cleavage.

[00287] In some embodiments, an sgRNA comprising nucleotides having at least 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% identity to the nucleotides of any one of SEQ ID Nos: 401-532, 601, 607-732, 801, 807-932, 1001, or 1007-1132, is provided, wherein the modification pattern is identical to the modification pattern shown in the reference sequence identifier. That is, the nucleotides A, U (and/or T in the case of deoxyribonucleotide modifications), C, and G may differ by 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% compared to what is shown in in the sequences, but the modification remains unchanged.

[00288] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at: the first three nucleotides in the 5' terminus; LS1, LS6, LS7, LS8, LS11, and LS12 in the lower stem; B1 and B2 in the bulge region; each of the nucleotides in the upper stem region; N16, N17, and N18 in the nexus region; each of the nucleotides in the hairpin 1 region; one nucleotide between hairpin 1 and hairpin 2; each of the nucleotides in the hairpin 2 region; and the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three PS bonds between the first four nucleotides at the 5' terminus and three PS bonds between the last four nucleotides at the 3' terminus.

[00289] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at: the first three nucleotides in the 5' terminus; LS1, LS6, LS7, LS8, LS11, and

LS12 in the lower stem; B1-B6 in the bulge region; each of the nucleotides in the upper stem region; N16, N17, and N18 in the nexus region; each of the nucleotides in the hairpin 1 region; one nucleotide between hairpin 1 and hairpin 2; each of the nucleotides in the hairpin 2 region; and the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three PS bonds between the first four nucleotides at the 5' terminus and three PS bonds between the last four nucleotides in the 3' terminus region.

[00290] In some embodiments, an sgRNA is provided comprising 2'-F modified nucleotides at: LS9 and LS10 in the lower stem; 15-N18 in the nexus region; H2-9-HS-15 in the hairpin 2 region; and the second to last, third to last, and fourth to last nucleotide in the 3' terminus region.

[00291] In some embodiments, an sgRNA is provided comprising 2'-F modified nucleotides at: each nucleotide in the lower stem; 15-N18 in the nexus region; H2-9-HS-15 in the hairpin 2 region; and the second to last, third to last, and fourth to last nucleotide in the 3' terminus region.

[00292] In some embodiments, an sgRNA is provided comprising 2'-O-Me modified nucleotides at LS8, LS10, LS12, H1-2, H1-4, H1-6, H1-8, H1-10, H1-12, H2-1, H2-3, H2-5, H2-7, H2-9, H2-11, H2-13, H2-15, and the last and third to last nucleotides in the 3' terminus region; and 2'-F modifications at LS7, LS9, LS11; H1-1, H1-3, H1-5, H1-7, H1-9, H1-11, H1-13, H2-2, H2-4, H2-6, H2-8, H2-10, H2-12, H2-14, and the second to last and fourth to last nucleotide in the 3' terminus region.

[00293] In some embodiments, a single guide RNA (sgRNA) comprises one or more guide region YA site modifications or conserved region YA modifications, a 5' end modification and one or more modification in one or more of: the upper stem region; the hairpin 1 region; and the hairpin 2 region, wherein the 5' end modification comprises at least two phosphorothioate linkages within the first seven nucleotides at the 5' end of the 5' terminus. In some instances, the modification is a 2'-O-methyl (2'-O-Me) modified nucleotide. In some embodiments, the modification is a 2'-fluoro (2'-F) modified nucleotide.

[00294] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications, modifications at US1 to US12 and/or a modification at H1-1 and/or a modification in H2-1. In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and modifications at H1-1 to H1-12 and/or H2-1 to H2-15. In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and one or more modifications in each of the upper stem

region, the hairpin 1 region, and the hairpin 2 region. In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and a modified nucleotide between hairpin 1 and hairpin 2 regions. In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and a modification in the lower stem region.

[00295] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and a modification in the bulge region. In some embodiments, 50% of the nucleotides in the bulge region are modified, wherein the modification is 2'-O-Me or 2'-F.

[00296] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and a modification in the nexus region. In some embodiments, the sgRNA comprises modifications at N15, N16, N17, and/or N18 in the nexus region, wherein the modification is 2'-O-Me or 2'-F. In some instances, N16, N17, and N18 are linked with PS bonds.

[00297] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and modifications at the first four nucleotides at the 5' end of the 5' terminus and the last four nucleotides at the 3' end of the 3'terminus. In some instances, these modifications are linking PS bond (i.e., PS bonds that link the first four and last four nucleotides). In some embodiments, the sgRNA further comprises 2'-O-Me modifications at the first three nucleotides at the 5' end of the 5' terminus and the last three nucleotides at the 3' end of the 3' terminus.

[00298] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and modifications LS1, LS6, LS7, LS8, LS11, and LS12, wherein the modification is 2'-O-Me or 2'-F.

[00299] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and modifications at each of the nucleotides in the bulge region, wherein the modification is 2'-O-Me or 2'-F.

[00300] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and modifications at each of the nucleotides in the upper stem region, wherein the modification is 2'-O-Me or 2'-F.

[00301] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and modifications at each of the nucleotides in the hairpin 1 region, wherein the modification is 2'-O-Me or 2'-F.

[00302] In some embodiments, the sgRNA comprises one or more guide region YA site modifications or conserved region YA modifications and modifications at each of the nucleotides in the hairpin 2 region, wherein the modification is 2'-O-Me or 2'-F.

[00303] In some embodiments, an sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising 2'-O-Me modified nucleotides at the following positions:

a. LS1, LS6, LS7, LS8, LS11, and/or LS12 in the lower stem region;
b. B1 and/or B2 in the bulge region;
c. each nucleotide in the upper stem region;
d. N16, N17, and/or N18 in the nexus region;
e. each nucleotide in the hairpin 1 region; and
f. each nucleotide in the hairpin 2 region.

In some embodiments, B3-B6 are modified with 2'-O-Me. In some instances, the sgRNA further comprising a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification. In some embodiments, the sgRNA comprises 2'-F modifications at LS9 and LS10. In some embodiments, the sgRNA comprises 2'F modifications at N15, N16, N17, and N18. In some embodiments, the sgRNA comprises 2'F modifications at H2-9, H2-10, H2-11, H2-12, H2-13, H2-14, and H2-15. In some embodiments, the sgRNA comprises 2'F modifications at the second to last, third to last, and fourth to last nucleotides at the 3' end of the 3' terminus.

[00304] In some embodiments, an sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and 2'-F modified nucleotides at the following positions:

a. LS9 and LS10 in the lower stem region;
b. N15, N16, N17, and N18 in the nexus region; and
c. H2-9, H2-10, H2-11, H2-12, H2-13, H2-14, and H2-15 in the hairpin 2 region.

In some embodiments, the sgRNA comprises 2'-F modified nucleotides at the second to last, third to last, and fourth to last nucleotides at the 3' terminus. In some embodiments, the sgRNA comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' end of the 5' terminus and three PS bonds linking the last four nucleotides at the 3' end of the 3' terminus. In some embodiments, the sgRNA comprises 2'-O-Me or 2'-F modified nucleotides at the first three nucleotides at the 5' end of the 5' terminus, and 2'-O-Me or 2'-F modified nucleotides at three of the last four nucleotides at the 3' end of the 3' terminus.

[00305] In some embodiments, an sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' end of the 5' terminus;
b. Optional 2'-O-Me modified nucleotides at LS1 and/or LS6;
c. 2'-O-Me modified nucleotides at US1-US12;
d. 2'-O-Me modified nucleotides at H1-1 – H1-12;
e. Optional 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
f. 2'-O-Me modified nucleotides at H2-1 – H2-15; and
g. 2'-O-Me modified nucleotides at the last four nucleotides at the 3' end of the 3' terminus; and optionally

a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00306] In some embodiments, an sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' end of the 5' terminus;
b. 2'-F modified nucleotides at LS1-LS6;
c. 2'-O-Me modified nucleotides at US1-US12;
d. 2'-O-Me modified nucleotides at H1-1 – H1-12;
e. a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
f. 2'-O-Me modified nucleotides at H2-1 – H2-15; and
g. 2'-O-Me modified nucleotides at the last four nucleotides at the 3' end of the 3' terminus; and optionally

a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00307] In some embodiments, an sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus;
b. 2'-F modified nucleotides at LS2-LS5;
c. 2'-O-Me modified nucleotides at LS1 and LS6;
d. 2'-O-Me modified nucleotides at US1-US12;

e. 2'-O-Me modified nucleotides at H1-1 – H1-12;
f. a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
g. 2'-O-Me modified nucleotides at H2-1 – H2-15; and
h. 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus and optionally

a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00308] In some embodiments, a sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus;
b. 2'-O-Me modified nucleotides at US1-US12;
c. 2'-O-Me modified nucleotides at LS7, LS8, LS11, and LS12;
d. 2'-O-Me modified nucleotides at H1-1 – H1-12;
e. a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
f. 2'-O-Me modified nucleotides at H2-1 – H2-15; and
g. 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus,

and optionally a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00309] In some embodiments, a sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus;
b. 2'-O-Me modified nucleotides at US1-US12;
c. 2'-O-Me modified nucleotides at LS7, LS8, LS11, and LS12;
d. 2'-F modified nucleotides at LS9 and LS10;
e. 2'-O-Me modified nucleotides at H1-1 – H1-12;
f. a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
g. 2'-O-Me modified nucleotides at H2-1 – H2-15; and
h. 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus,

and optionally a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00310] In some embodiments, an sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus;
b. 2'-O-Me modified nucleotides at US1-US12;
c. 2'-O-Me modified nucleotides at LS8, LS10, and LS12;
d. 2'-O-F modified nucleotides at LS7, LS9, and LS11;
e. 2'-O-Me modified nucleotides at H1-1 – H1-12;
f. a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
g. 2'-O-Me modified nucleotides at H2-1 – H2-15; and
h. 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus, and optionally

a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00311] In some embodiments, a sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus;
b. 2'-O-Me modified nucleotides at LS1, LS6, LS7, LS8, LS11, and LS12
c. 2'-O-Me modified nucleotides at US1-US12;
d. 2'-O-Me modified nucleotides at H1-1 – H1-12;
e. a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
f. 2'-O-Me modified nucleotides at H2-1 – H2-15; and
g. 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus, and optionally

a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00312] In some embodiments, a sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' terminus;
b. 2'-O-Me modified nucleotides at LS1, LS6, LS7, LS8, LS11, and LS12;
c. 2'-F modified nucleotides at LS9 and LS10;
d. 2'-O-Me modified nucleotides at US1-US12;

e. 2'-O-Me modified nucleotides at H1-1 – H1-12;
f. a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
g. 2'-O-Me modified nucleotides at H2-1 – H2-15; and
h. 2'-O-Me modified nucleotides at the last four nucleotides at the 3' terminus, and optionally

a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00313] In some embodiments, a sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' end of the 5' terminus;
b. 2'-O-Me modified nucleotides at US1-US12;
c. 2'-O-Me modified nucleotides at H1-1 – H1-12;
d. a 2'-O-Me modified nucleotide between Hairpin 1 and Hairpin 2;
e. 2'-O-Me modified nucleotides at H2-1 – H2-8;
f. 2'-F modified nucleotides at H2-9 – H2-15;
g. 2'-F modified nucleotides at the second from last, third from last, and fourth from last nucleotide at the 3' terminus; and
h. a 2'-O-Me modified nucleotide at the last nucleotide at the 3' terminus, and optionally

a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00314] In some embodiments, a sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides at the first three nucleotides at the 5' end of the 5' terminus;
b. 2'-O-Me modified nucleotides at US1-US12;
c. 2'-O-Me modified nucleotides at H1-2, H1-4, H1-6, H1-8, H1-10, and H1-12;
d. 2'-F modified nucleotides at H1-1, H1-3, H1-5, H1-7, H1-9, and H1-11;
e. a 2'-F modified nucleotide between Hairpin 1 and Hairpin 2;
f. 2'-F modified nucleotides at H2-2, H2-4, H2-6, H2-8, H2-10, H2-12; and H2-14;

g. 2'-O-Me modified nucleotides at H2-1, H2-3, H2-5, H2-7, H2-9, H2-11; H2-13, and H2-15;
h. 2'-F modified nucleotides at the second from last, and fourth from last nucleotide at the 3' terminus; and
i. 2'-O-Me modified nucleotide at the third from last and last nucleotide at the 3' end of the 3' terminus,

and optionally a 5' protective end modification, a 3' protective end modification, or both a 3' and a 5' protective end modification.

[00315] In some embodiments, a sgRNA is encompassed comprising one or more guide region YA site modifications or conserved region YA modifications and further comprising:

a. 2'-O-Me modified nucleotides LS8, LS10, LS12, H1-2, H1-4, H1-6, H1-8, H1-10, H1-12, H2-1, H2-3, H2-5, H2-7, H2-9, H2-11, H2-13, and H2-15; and
b. 2'-F modified nucleotides at LS7, LS9, LS11; H1-1, H1-3, H1-5, H1-7, H1-9, H1-11, H1-13, H2-2, H2-4, H2-6, H2-8, H2-10, H2-12, and H2-14, and optionally

further comprising three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' end of the 5' terminus and three PS bonds linking the last four nucleotides at the 3' end of the 3' terminus; and optionally further comprising:

c. 2'-O-Me modified nucleotides at the last and third to last nucleotide at the 3' end of the 3' terminus; and/or
d. 2'-F modified nucleotides at the second to last, fourth to last, and/or last nucleotide at the 3' end of the 3' terminus.

[00316] Any of the foregoing modification patterns can be combined with a modification pattern set forth in the embodiments described above, e.g., in the summary section or Table 1, to the extent that they are non-overlapping. In the event that combining a foregoing modification pattern with a modification pattern set forth in the summary section or Table 1 would result in incompatible modifications (e.g., the same position would be both 2'-OMe and 2'-fluoro), the modification set forth in the summary section or Table 1 controls.

Short-single guide RNA (short-sgRNA)

[00317] In some embodiments, an sgRNA provided herein is a short-single guide RNAs (short-sgRNAs), e.g., comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides or 6-10 nucleotides. In some embodiments, the sgRNA is from *S. pyogenes* Cas9 ("spyCas9") or a spyCas9

equivalent. In some embodiments, the sgRNA is not from *S. pyogenes* Cas9 ("non-spyCas9"). In some embodiments, the 5-10 nucleotides or 6-10 nucleotides are consecutive.

[00318] In some embodiments, a short-sgRNA lacks at least nucleotides 54-58 (AAAAA) of the conserved portion of a spyCas9 sgRNA, as shown in Table 2. In some embodiments, a short-sgRNA is a non-spyCas9 sgRNA that lacks nucleotides corresponding to nucleotides 54-58 (AAAAA) of the conserved portion of a spyCas9 as determined, for example, by pairwise or structural alignment. In some embodiments, the non-spyCas9 sgRNA is *Staphylococcus aureus* Cas9 ("saCas9") sgRNA.

[00319] In some embodiments, the hairpin regions lacks 5, 6, 7, 8, 9, 10, 11, or 12 nucleotides. In some embodiments, the hairpin 1 portion lacks 5, 6, 7, 8, 9, 10, 11, or 12 nucleotides. In some embodiments, the hairpin 2 portion lacks 5, 6, 7, 8, 9, 10, 11, or 12 nucleotides. In some embodiments, the hairpin regions lacks 5, 6, 7, 8, 9, 10, 11, or 12 consecutive nucleotides. In some embodiments, the hairpin 1 portion lacks 5, 6, 7, 8, 9, 10, 11, or 12 consecutive nucleotides. In some embodiments, the hairpin 2 portion lacks 5, 6, 7, 8, 9, 10, 11, or 12 consecutive nucleotides. In some embodiments, the 5-10 lacking nucleotides or 6-10 lacking nucleotides are within hairpin 1. In some embodiments, the 5-10 lacking nucleotides or 6-10 lacking nucleotides are within hairpin 2. In some embodiments, the 5-10 lacking nucleotides or 6-10 lacking nucleotides are within hairpin 1 and hairpin 2. In some embodiments, the 5-10 lacking nucleotides or 6-10 lacking nucleotides are within hairpin 1 or hairpin 2. In some embodiments, the 5-10 lacking nucleotides or 6-10 lacking nucleotides are consecutive and include the "N" between hairpin 1 and hairpin 2. In some embodiments, the 5-10 or 6-10 lacking nucleotides include the "N" between hairpin 1 and hairpin 2. In some embodiments, the 5-10 or 6-10 lacking nucleotides are consecutive and span at least a portion of hairpin 1. In some embodiments, the 5-10 or 6-10 lacking nucleotides are consecutive and span at least a portion of hairpin 2. In some embodiments, the 5-10 lacking nucleotides or 6-10 lacking nucleotides are consecutive and span at least a portion of hairpin 1 and a portion of hairpin 2. In some embodiments, the 5-10 lacking nucleotides or 6-10 lacking nucleotides are consecutive and span at least a portion of hairpin 1 and the "N" between hairpin 1 and hairpin 2. In some embodiments, the 5-10 lacking nucleotides comprise or consist of nucleotides 54-58, 54-61, or 53-60 of SEQ ID NO: 400.

[00320] In some embodiments, the short-sgRNA described herein further comprises a nexus region, wherein the nexus region lacks at least one nucleotide. In some embodiments, the short-sgRNA lacks at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides in the nexus region. In some embodiments, the short-sgRNA lacks at least 1-2, 1-3, 1-4 nucleotides, 1-5 nucleotides,

1-6 nucleotides, 1-10 nucleotides, or 1-15 nucleotides in the nexus region. In some embodiments, the short-sgRNA lacks each nucleotide in the nexus region.

[00321] In some embodiments, the short-sgRNA further comprises a guide region. In some embodiments, the guide region comprises the first 1-10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides at the 5' end of the short-sgRNA. In some embodiments, the guide region comprises 20 nucleotides. In some embodiments, the guide region comprises 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more nucleotides. In some embodiments, the guide region comprises 17 nucleotides. In some embodiments, the guide region comprises 18 nucleotides. In some embodiments, the guide region comprises 19 nucleotides.

[00322] In some embodiments, the selection of the guide region is determined based on target sequences within the gene of interest for editing. For example, in some embodiments, the short-sgRNA comprises a guide region that is complementary to target sequences of a gene of interest.

[00323] In some embodiments, the target sequence in the gene of interest may be complementary to the guide region of the short-sgRNA. In some embodiments, the degree of complementarity or identity between a guide region of a short-sgRNA and its corresponding target sequence in the gene of interest may be about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%. In some embodiments, the guide region of a short-sgRNA and the target region of a gene of interest may be 100% complementary or identical. In other embodiments, the guide region of a short-sgRNA and the target region of a gene of interest may contain at least one mismatch. For example, the guide region of a short-sgRNA and the target sequence of a gene of interest may contain 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mismatches, where the total length of the target sequence is at least about 17, 18, 19, 20 or more base pairs. In some embodiments, the guide region of a short-sgRNA and the target region of a gene of interest may contain 1-6 mismatches where the guide sequence comprises at least about 17, 18, 19, 20 or more nucleotides. In some embodiments, the guide region of a short-sgRNA and the target region of a gene of interest may contain 1, 2, 3, 4, 5, or 6 mismatches where the guide sequence comprises about 20 nucleotides. The 5' terminus may comprise nucleotides that are not considered guide regions (i.e., do not function to direct a Cas9 protein to a target nucleic acid).

Modified short-single guide RNA (short-sgRNA)

[00324] In some embodiments, the short-sgRNA is modified. The term "modified" or "modification" in the context of a short-sgRNA described herein includes, the modifications described above, including, for example, (a) end modifications, e.g., 5′ end modifications or 3′ end modifications, including 5' or 3' protective end modifications, (b) nucleobase (or "base") modifications, including replacement or removal of bases, (c) sugar modifications, including modifications at the 2′, 3′, and/or 4′ positions, (d) internucleoside linkage modifications, and (e) backbone modifications, which can include modification or replacement of the phosphodiester linkages and/or the ribose sugar. A modification of a nucleotide at a given position includes a modification or replacement of the phosphodiester linkage immediately 3' of the sugar of the nucleotide. Thus, for example, a nucleic acid comprising a phosphorothioate between the first and second sugars from the 5' end is considered to comprise a modification at position 1. The term "modified short-sgRNA" generally refers to a short-sgRNA having a modification to the chemical structure of one or more of the base, the sugar, and the phosphodiester linkage or backbone portions, including nucleotide phosphates, all as detailed and exemplified herein.

[00325] Exemplary patterns of modifications are shown in Table 1. Additional exemplary patterns are discussed below.

Modifications of guide regions and/or YA sites

[00326] In some embodiments, a short-sgRNA comprises modifications at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more YA sites. In some embodiments, the pyrimidine of the YA site comprises a modification (which includes a modification altering the internucleoside linkage immediately 3' of the sugar of the pyrimidine). In some embodiments, the adenine of the YA site comprises a modification (which includes a modification altering the internucleoside linkage immediately 3' of the sugar of the adenine). In some embodiments, the pyrimidine and the adenine of the YA site comprise modifications, such as sugar, base, or internucleoside linkage modifications. The YA modifications can be any of the types of modifications set forth herein. In some embodiments, the YA modifications comprise one or more of phosphorothioate, 2'-OMe, or 2'-fluoro. In some embodiments, the YA modifications comprise pyrimidine modifications comprising one or more of phosphorothioate, 2'-OMe, 2'-H, inosine, or 2'-fluoro. In some embodiments, the YA modification comprises a bicyclic ribose analog (e.g., an LNA, BNA, or ENA) within an RNA duplex region that contains one or more YA sites. In some embodiments, the YA

modification comprises a bicyclic ribose analog (e.g., an LNA, BNA, or ENA) within an RNA duplex region that contains a YA site, wherein the YA modification is distal to the YA site.

Guide region modifications, including YA site modifications

[00327] In some embodiments, the guide region comprises 1, 2, 3, 4, 5, or more YA sites ("guide region YA sites") that may comprise YA modifications. In some embodiments, one or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus (where "5-end", etc., refers to position 5 to the 3' end of the guide region, i.e., the most 3' nucleotide in the guide region) comprise YA modifications. In some embodiments, two or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus comprise YA modifications. In some embodiments, three or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus comprise YA modifications. In some embodiments, four or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus comprise YA modifications. In some embodiments, five or more YA sites located at 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus comprise YA modifications. A modified guide region YA site comprises a YA modification.

[00328] In some embodiments, a modified guide region YA site is within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region. For example, if a modified guide region YA site is within 10 nucleotides of the 3' terminal nucleotide of the guide region and the guide region is 20 nucleotides long, then the modified nucleotide of the modified guide region YA site is located at any of positions 11-20. In some embodiments, a YA modification is located within a YA site 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 nucleotides from the 3' terminal nucleotide of the guide region. In some embodiments, a YA modification is located 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 nucleotides from the 3' terminal nucleotide of the guide region.

[00329] In some embodiments, a modified guide region YA site is at or after nucleotide 4, 5, 6, 7, 8, 9, 10, or 11 from the 5' end of the 5' terminus.

[00330] In some embodiments, a modified guide region YA site is other than a 5' end modification. For example, a short-sgRNA can comprise a 5' end modification as described herein and further comprise a modified guide region YA site. Alternatively, a short-sgRNA

can comprise an unmodified 5' end and a modified guide region YA site. Alternatively, a short-sgRNA can comprise a modified 5' end and an unmodified guide region YA site.

[00331] In some embodiments, a modified guide region YA site comprises a modification that at least one nucleotide located 5' of the guide region YA site does not comprise. For example, if nucleotides 1-3 comprise phosphorothioates, nucleotide 4 comprises only a 2'-OMe modification, and nucleotide 5 is the pyrimidine of a YA site and comprises a phosphorothioate, then the modified guide region YA site comprises a modification (phosphorothioate) that at least one nucleotide located 5' of the guide region YA site (nucleotide 4) does not comprise. In another example, if nucleotides 1-3 comprise phosphorothioates, and nucleotide 4 is the pyrimidine of a YA site and comprises a 2'-OMe, then the modified guide region YA site comprises a modification (2'-OMe) that at least one nucleotide located 5' of the guide region YA site (any of nucleotides 1-3) does not comprise. This condition is also always satisfied if an unmodified nucleotide is located 5' of the modified guide region YA site.

[00332] In some embodiments, the modified guide region YA sites comprise modifications as described for YA sites above.

[00333] Additional embodiments of guide region modifications, including guide region YA site modifications, are set forth elsewhere herein, including in the summary above and in the discussion of gRNAs comprising modifications, including modifications at YA sites above, and elsewhere herein. The guide region of a short-sgRNA may be modified according to any embodiment comprising a modified guide region set forth herein. Any embodiments set forth elsewhere in this disclosure may be combined to the extent feasible with any of the foregoing embodiments.

Conserved region YA site modifications

[00334] Conserved region YA sites 1-10 are illustrated in Fig. 1B. In some embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 conserved region YA sites comprise modifications.

[00335] In some embodiments, conserved region YA sites 1, 8, or 1 and 8 comprise YA modifications. In some embodiments, conserved region YA sites 1, 2, 3, 4, and 10 comprise YA modifications. In some embodiments, YA sites 2, 3, 4, 8, and 10 comprise YA modifications. In some embodiments, conserved region YA sites 1, 2, 3, and 10 comprise YA modifications. In some embodiments, YA sites 2, 3, 8, and 10 comprise YA modifications. In some embodiments, YA sites 1, 2, 3, 4, 8, and 10 comprise YA

modifications. In some embodiments, 1, 2, 3, 4, 5, 6, 7, or 8 additional conserved region YA sites comprise YA modifications.

[00336] In some embodiments, 1, 2, 3, or 4 of conserved region YA sites 2, 3, 4, and 10 comprise YA modifications. In some embodiments, 1, 2, 3, 4, 5, 6, 7, or 8 additional conserved region YA sites comprise YA modifications.

[00337] In some embodiments, the modified conserved region YA sites comprise modifications as described for YA sites above.

[00338] Additional embodiments of conserved region YA site modifications are set forth in the summary above. Any embodiments set forth elsewhere in this disclosure may be combined to the extent feasible with any of the foregoing embodiments.

Modifications to terminal nucleotides

[00339] In some embodiments, the 5' and/or 3' terminus regions of a short-sgRNA are modified.

3' terminus region modifications

[00340] In some embodiments, the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region are modified. Throughout, this modification may be referred to as a "3' end modification". In some embodiments, the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region comprise more than one modification. In some embodiments, at least one of the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region are modified. In some embodiments, at least two of the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region are modified. In some embodiments, at least three of the terminal (i.e., last) 1, 2, 3, 4, 5, 6, or 7 nucleotides in the 3' terminus region are modified. In some embodiments, the modification comprises a PS linkage. In some embodiments, the modification to the 3' terminus region is a 3' protective end modification. In some embodiments, the 3' end modification comprises a 3' protective end modification.

[00341] In some embodiments, the 3' end modification comprises a modified nucleotide selected from 2'-O-methyl (2'-O-Me) modified nucleotide, 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, an inverted abasic modified nucleotide, or combinations thereof.

[00342] In some embodiments, the 3' end modification comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

[00343] In some embodiments, the 3' end modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

[00344] In some embodiments, the 3' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides.

[00345] In some embodiments, the 3' end modification comprises or further comprises an inverted abasic modified nucleotide.

[00346] In some embodiments, the 3' end modification comprises or further comprises a modification of any one or more of the last 7, 6, 5, 4, 3, 2, or 1 nucleotides. In some embodiments, the 3' end modification comprises or further comprises one modified nucleotide. In some embodiments, the 3' end modification comprises or further comprises two modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises three modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises four modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises five modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises six modified nucleotides. In some embodiments, the 3' end modification comprises or further comprises seven modified nucleotides.

[00347] In some embodiments, the 3' end modification comprises or further comprises a modification of between 1 and 7 or between 1 and 5 nucleotides.

[00348] In some embodiments, the 3' end modification comprises or further comprises modifications of 1, 2, 3, 4, 5, 6, or 7 nucleotides at the 3' end of the gRNA.

[00349] In some embodiments, the 3' end modification comprises or further comprises modifications of about 1-3, 1-5, 1-6, or 1-7 nucleotides at the 3' end of the gRNA.

[00350] In some embodiments, the 3' end modification comprises or further comprises any one or more of the following: a phosphorothioate (PS) linkage between nucleotides, a 2'-O-Me modified nucleotide, a 2'-O-moe modified nucleotide, a 2'-F modified nucleotide, an inverted abasic modified nucleotide, and a combination thereof.

[00351] In some embodiments, the 3' end modification comprises or further comprises 1, 2, 3, 4, 5, 6, or 7 PS linkages between nucleotides.

[00352] In some embodiments, the 3' end modification comprises or further comprises at least one 2'-O-Me, 2'-O-moe, inverted abasic, or 2'-F modified nucleotide.

In some embodiments, the 3' end modification comprises or further comprises one PS linkage, wherein the linkage is between the last and second to last nucleotide. In some embodiments, the 3' end modification comprises or further comprises two PS linkages between the last three nucleotides. In some embodiments, the 3' end modification comprises or further comprises four PS linkages between the last four nucleotides.

[00353] In some embodiments, the 3' end modification comprises or further comprises PS linkages between any one or more of the last four nucleotides. In some embodiments, the 3' end modification comprises or further comprises PS linkages between any one or more of the last five nucleotides. In some embodiments, the 3' end modification comprises or further comprises PS linkages between any one or more of the last 2, 3, 4, 5, 6, or 7 nucleotides.

[00354] In some embodiments, the 3' end modification comprises or further comprises a modification of one or more of the last 1-7 nucleotides, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof.

[00355] In some embodiments, the 3' end modification comprises or further comprises a modification to the last nucleotide with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and an optionally one or two PS linkages to the next nucleotide and/or the first nucleotide of the 3' tail.

[00356] In some embodiments, the 3' end modification comprises or further comprises a modification to the last and/or second to last nucleotide with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

[00357] In some embodiments, the 3' end modification comprises or further comprises a modification to the last, second to last, and/or third to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

[00358] In some embodiments, the 3' end modification comprises or further comprises a modification to the last, second to last, third to last, and/or fourth to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

[00359] In some embodiments, the 3' end modification comprises or further comprises a modification to the last, second to last, third to last, fourth to last, and/or fifth to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

[00360] In some embodiments, the gRNA comprising a 3' end modification comprises or further comprises a 3' tail, wherein the 3' tail comprises a modification of any one or more of the nucleotides present in the 3' tail. In some embodiments, the 3' tail is fully modified. In some embodiments, the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-

7, 1-8, 1-9, or 1-10 nucleotides, optionally where any one or more of these nucleotides are modified.

[00361] In some embodiments, a gRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises the 3' end modification as shown in any one of SEQ ID Nos: 1-54. In some embodiments, a gRNA is provided comprising a 3' protective end modification.

[00362] In some embodiments, agRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) a 2'-OMe modified nucleotide at the last nucleotide of the conserved region of an gRNA or short-sgRNA (ii) three consecutive 2'O-moe modified nucleotides immediately 5' to the 2'-OMe modified nucleotide, and (iii) three consecutive PS linkages between the last three nucleotides.

[00363] In some embodiments, a gRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) five consecutive 2'-OMe modified nucleotides from the last nucleotide of the conserved region of an sgRNA or the conserved region of a short-sgRNA, and (ii) three PS linkages between the last three nucleotides.

[00364] In some embodiments, a gRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or the conserved region of a short-sgRNA.

[00365] In some embodiments, a gRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, and (ii) three consecutive 2'-OMe modified nucleotides at the last three nucleotides of the conserved region of an sgRNA or the conserved region of a short-sgRNA.

[00366] In some embodiments, a gRNA is provided comprising (i) 15 consecutive 2'-OMe modified nucleotides from the last nucleotide of the conserved region of an sgRNA or short-sgRNA, (ii) five consecutive 2'-F modified nucleotides immediately 5' to the 2'-OMe modified nucleotides, and (iii) three PS linkages between the last three nucleotides.

[00367] In some embodiments, a short-sgRNA is provided comprising (i) alternating 2'-OMe modified nucleotides and 2'-F modified nucleotides at the last 20 nucleotides of the conserved region of an sgRNA or short-sgRNA, and (ii) three PS linkages between the last three nucleotides.

[00368] In some embodiments, a short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises (i) two or three consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

[00369] In some embodiments, a short-sgRNA is provided comprising a 3' end modification, wherein the 3' end modification comprises one PS linkage between the last and next to last nucleotides.

[00370] In some embodiments, a short-sgRNA is provided comprising (i) 15 or 20 consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

[00371] In some embodiments, the short-sgRNA comprises a 5' end modification and a 3' end modification.

3' tail

[00372] In some embodiments, the short-sgRNA comprises a 3' terminus comprising a 3' tail, which follows and is 3' of the conserved portion of a short-sgRNA. In some embodiments, the 3' tail comprises between 1 and about 20 nucleotides, between 1 and about 15 nucleotides, between 1 and about 10 nucleotides, between 1 and about 5 nucleotides, between 1 and about 4 nucleotides, between 1 and about 3 nucleotides, and between 1 and about 2 nucleotides. In some embodiments, the 3' tail comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides. In some embodiments, the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides. In some embodiments, the 3' tail comprises 1 nucleotide. In some embodiments, the 3' tail comprises 2 nucleotides. In some embodiments, the 3' tail comprises 3 nucleotides. In some embodiments, the 3' tail comprises 4 nucleotides. In some embodiments, the 3' tail comprises about 1-2, 1-3, 1-4, 1-5, 1-7, 1-10, at least 1-5, at least 1-3, at least 1-4, at least 1-5, at least 1-5, at least 1-7, or at least 1-10 nucleotides.

[00373] In some embodiments, the 3' tail comprising between 1 and 20 nucleotides and follows the 3' end of the conserved portion of a short-sgRNA.

[00374] In some embodiments, the 3' tail comprises or further comprises one or more of a protective end modification, a phosphorothioate (PS) linkage between nucleotides, a 2'-OMe modified nucleotide, a 2'-O-moe modified nucleotide, a 2'-F modified nucleotide, an inverted abasic modified nucleotide, and a combination thereof.

[00375] In some embodiments, the 3' tail comprises or further comprises one or more phosphorothioate (PS) linkages between nucleotides. In some embodiments, the 3' tail comprises or further comprises one or more 2'-OMe modified nucleotides. In some embodiments, the 3' tail comprises or further comprises one or more 2'-O-moe modified nucleotides. In some embodiments, the 3' tail comprises or further comprises one or more 2'-F modified nucleotide. In some embodiments, the 3' tail comprises or further comprises one

or more an inverted abasic modified nucleotides. In some embodiments, the 3' tail comprises or further comprises one or more protective end modifications. In some embodiments, the 3' tail comprises or further comprises a combination of one or more of a phosphorothioate (PS) linkage between nucleotides, a 2'-OMe modified nucleotide, a 2'-O-moe modified nucleotide, a 2'-F modified nucleotide, and an inverted abasic modified nucleotide.

[00376] In some embodiments, the short-sgRNA does not comprise a 3' tail.

5' terminus region modifications

[00377] In some embodiments, the 5' terminus region is modified, for example, the first 1, 2, 3, 4, 5, 6, or 7 nucleotides of the short-sgRNA are modified. Throughout, this modification may be referred to as a "5' end modification". In some embodiments, the first 1, 2, 3, 4, 5, 6, or 7 nucleotides of the 5' terminus region comprise more than one modification. In some embodiments, at least one of the terminal (i.e., first) 1, 2, 3, 4, 5, 6, or 7 nucleotides at the 5' end are modified. In some embodiments, at least two of the terminal 1, 2, 3, 4, 5, 6, or 7 nucleotides at the 5' terminus region are modified. In some embodiments, at least three of the terminal 1, 2, 3, 4, 5, 6, or 7 nucleotides at the 5' terminus region are modified. In some embodiments, the 5' end modification is a 5' protective end modification.

[00378] In some embodiments, both the 5' and 3' terminus regions (e.g., ends) of the short-sgRNA are modified. In some embodiments, only the 5' terminus region of the short-sgRNA is modified. In some embodiments, only the 3' terminus region (plus or minus a 3' tail) of the conserved portion of a short sgRNA is modified.

[00379] In some embodiments, the short-sgRNA comprises modifications at 1, 2, 3, 4, 5, 6, or 7 of the first 7 nucleotides at a 5' terminus region of the short-sgRNA. In some embodiments, the short-sgRNA comprises modifications at 1, 2, 3, 4, 5, 6, or 7 of the 7 terminal nucleotides at a 3' terminus region. In some embodiments, 2, 3, or 4 of the first 4 nucleotides at the 5' terminus region, and/or 2, 3, or 4 of the terminal 4 nucleotides at the 3' terminus region are modified. In some embodiments, 2, 3, or 4 of the first 4 nucleotides at the 5' terminus region are linked with phosphorothioate (PS) bonds.

[00380] In some embodiments, the modification to the 5' terminus and/or 3' terminus comprises a 2'-O-methyl (2'-O-Me) or 2'-O-(2-methoxyethyl) (2'-O-moe) modification. In some embodiments, the modification comprises a 2'-fluoro (2'-F) modification to a nucleotide. In some embodiments, the modification comprises a phosphorothioate (PS) linkage between nucleotides. In some embodiments, the modification comprises an inverted abasic nucleotide. In some embodiments, the modification comprises a protective end

modification. In some embodiments, the modification comprises a more than one modification selected from protective end modification, 2'-O-Me, 2'-O-moe, 2'-fluoro (2'-F), a phosphorothioate (PS) linkage between nucleotides, and an inverted abasic nucleotide. In some embodiments, an equivalent modification is encompassed.

[00381] In some embodiments, the short-sgRNA comprises one or more phosphorothioate (PS) linkages between the first one, two, three, four, five, six, or seven nucleotides at the 5' terminus. In some embodiments, the short-sgRNA comprises one or more PS linkages between the last one, two, three, four, five, six, or seven nucleotides at the 3' terminus. In some embodiments, the short-sgRNA comprises one or more PS linkages between both the last one, two, three, four, five, six, or seven nucleotides at the 3' terminus and the first one, two, three, four, five, six, or seven nucleotides from the 5' end of the 5' terminus. In some embodiments, in addition to PS linkages, the 5' and 3' terminal nucleotides may comprise 2'-O-Me, 2'-O-moe, or 2'-F modified nucleotides.

[00382] In some embodiments, the short-sgRNA comprises a 5' end modification, e.g., wherein the first nucleotide of the guide region is modified. In some embodiments, the short-sgRNA comprises a 5' end modification, wherein the first nucleotide of the guide region comprises a 5' protective end modification.

[00383] In some embodiments, the 5' end modification comprises a modified nucleotide selected from 2'-O-methyl (2'-O-Me) modified nucleotide, 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, an inverted abasic modified nucleotide, or combinations thereof.

[00384] In some embodiments, the 5' end modification comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

[00385] In some embodiments, the 5' end modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

[00386] In some embodiments, the 5' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides.

[00387] In some embodiments, the 5' end modification comprises or further comprises an inverted abasic modified nucleotide.

[00388] In some embodiments, the 5' end modification comprises or further comprises a modification of any one or more of nucleotides 1-7 of the guide region of a short-sgRNA. In some embodiments, the 5' end modification comprises or further comprises one modified nucleotide. In some embodiments, the 5' end modification comprises or further comprises

two modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises three modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises four modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises five modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises six modified nucleotides. In some embodiments, the 5' end modification comprises or further comprises seven modified nucleotides.

[00389] In some embodiments, the 5' end modification comprises or further comprises a modification of between 1 and 7, between 1 and 5, between 1 and 4, between 1 and 3, or between 1 and 2 nucleotides.

[00390] In some embodiments, the 5' end modification comprises or further comprises modifications of 1, 2, 3, 4, 5, 6, or 7 nucleotides from the 5' end. In some embodiments, the 5' end modification comprises or further comprises modifications of about 1-3, 1-4, 1-5, 1-6, or 1-7 nucleotides from the 5' end.

[00391] In some embodiments, the 5' end modification comprises or further comprises modifications at the first nucleotide at the 5' end of the short-sgRNA. In some embodiments, the 5' end modification comprises or further comprises modifications at the first and second nucleotide from the 5' end of the short-sgRNA. In some embodiments, the 5' end modification comprises or further comprises modifications at the first, second, and third nucleotide from the 5' end of the short-sgRNA. In some embodiments, the 5' end modification comprises or further comprises modifications at the first, second, third, and fourth nucleotide from the 5' end of the short-sgRNA. In some embodiments, the 5' end modification comprises or further comprises modifications at the first, second, third, fourth, and fifth nucleotide from the 5' end of the short-sgRNA. In some embodiments, the 5' end modification comprises or further comprises modifications at the first, second, third, fourth, fifth, and sixth nucleotide from the 5' end of the short-sgRNA. In some embodiments, the 5' end modification comprises or further comprises modifications at the first, second, third, fourth, fifth, sixth, and seventh nucleotide from the 5' end of the short-sgRNA.

[00392] In some embodiments, the 5' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides, and/or a 2'-O-Me modified nucleotide, and/or a 2'-O-moe modified nucleotide, and/or a 2'-F modified nucleotide, and/or an inverted abasic modified nucleotide, and/or combinations thereof.

[00393] In some embodiments, the 5' end modification comprises or further comprises 1, 2, 3, 4, 5, 6, and/or 7 PS linkages between nucleotides. In some embodiments, the 5' end

modification comprises or further comprises about 1-2, 1-3, 1-4, 1-5, 1-6, or 1-7 PS linkages between nucleotides.

[00394] In some embodiments, the 5' end modification comprises or further comprises at least one PS linkage, wherein if there is one PS linkage, the linkage is between nucleotides 1 and 2 of the guide region.

[00395] In some embodiments, the 5' end modification comprises or further comprises at least two PS linkages, and the linkages are between nucleotides 1 and 2, and 2 and 3 of the guide region.

[00396] In some embodiments, the 5' end modification comprises or further comprises PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region.

[00397] In some embodiments, the 5' end modification comprises or further comprises PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, and 4 and 5 of the guide region.

[00398] In some embodiments, the 5' end modification comprises or further comprises PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region.

[00399] In some embodiments, the 5' end modification comprises or further comprises PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, 5 and 6, and 7 and 8 of the guide region.

[00400] In some embodiments, the 5' end modification comprises or further comprises a modification of one or more of nucleotides 1-7 of the guide region, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-O-Me, 2'-O-moe, 2'-F, and/or combinations thereof.

[00401] In some embodiments, the 5' end modification comprises or further comprises a modification to the first nucleotide of the guide region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and an optional PS linkage to the next nucleotide;

[00402] In some embodiments, the 5' end modification comprises or further comprises a modification to the first and/or second nucleotide of the guide region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages between the first and second nucleotide and/or between the second and third nucleotide.

[00403] In some embodiments, the 5' end modification comprises or further comprises a modification to the first, second, and/or third nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages

between the first and second nucleotide, between the second and third nucleotide, and/or between the third and the fourth nucleotide.

[00404] In some embodiments, the 5' end modification comprises or further comprises a modification to the first, second, third, and/or fourth nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages between the first and second nucleotide, between the second and third nucleotide, between the third and the fourth nucleotide, and/or between the fourth and the fifth nucleotide.

[00405] In some embodiments, the 5' end modification comprises or further comprises a modification to the first, second, third, fourth, and/or fifth nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages between the first and second nucleotide, between the second and third nucleotide, between the third and the fourth nucleotide, between the fourth and the fifth nucleotide, and/or between the fifth and the sixth nucleotide.

[00406] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises a 5' end modification as shown in any one of SEQ ID Nos: 1-54.

[00407] In some embodiments, the sgRNA comprises a 5' end modification comprising a 5' protective end modification. In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region.

[00408] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region.

[00409] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region.

[00410] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region.

[00411] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region.

[00412] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region.

[00413] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises an inverted abasic modified nucleotide at nucleotide 1 of the guide region.

[00414] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises an inverted abasic modified nucleotide at nucleotide 1 of the guide region and 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region.

[00415] In some embodiments, a short-sgRNA is provided comprising a 5' end modification, wherein the 5' end modification comprises an inverted abasic modified nucleotide at nucleotide 1 of the guide region, 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region, and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region.

[00416] In some embodiments, a short-sgRNA is provided comprising a 5' end modification and a 3' end modification. In some embodiments, the sgRNA comprises modified nucleotides at the 5' and 3' terminus, and modified nucleotides in one or more other regions described in Table 3.

[00417] In some embodiments, the sgRNA comprises modified nucleotides that are not at the 5' or 3' ends. Exemplary patterns of modifications are described below and in Table 1.

Upper stem modifications

[00418] In some embodiments, a short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a modification to any one or more of US1-US12 in the upper stem region.

[00419] In some embodiments, a short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a modification of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all 12 nucleotides in the upper stem region.

[00420] In some embodiments, a short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a modification of about 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, or 1-12 nucleotides in the upper stem region.

[00421] In some embodiments, an sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises 1, 2, 3, 4, or 5 YA modifications in a YA site. In some embodiments, an sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises at least 1, 2, 3, 4, or 5 YA modifications. In some embodiments, an sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises one YA modification. In some embodiments, an sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises 2 YA modifications. In some embodiments, the upper stem modification comprises 3 YA modifications. In some embodiments, one or more YA modifications are in a YA site. In some embodiments, one or more YA modifications are distal to a YA site.

[00422] In some embodiments, a short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a 2'-OMe modified nucleotide. In some embodiments, a short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a 2'-O-moe modified nucleotide. In some embodiments, a short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a 2'-F modified nucleotide.

[00423] In some embodiments, a short-sgRNA is provided comprising an upper stem modification, wherein the upper stem modification comprises a 2'-OMe modified nucleotide, a 2'-O-moe modified nucleotide, a 2'-F modified nucleotide, and/or combinations thereof.

[00424] In some embodiments, the sgRNA comprises an upper stem modification as shown in any one of the sequences in Table 1. In some embodiments, such an upper stem modification is combined with a 5' protective end modification, e.g. as shown for the corresponding sequence in Table 1. In some embodiments, such an upper stem modification is combined with a 3' protective end modification, e.g. as shown for the corresponding sequence in Table 1. In some embodiments, such an upper stem modification is combined with 5' and 3' end modifications as shown for the corresponding sequence in Table 1.

[00425] In some embodiments, the short-sgRNA comprises a 5' end modification and an upper stem modification. In some embodiments, the short-sgRNA comprises a 3' end modification and an upper stem modification. In some embodiments, the short-sgRNA comprises a 5' end modification, a 3' end modification and an upper stem modification.

Hairpin modifications

[00426] In some embodiments, the short-sgRNA comprises a modification in the hairpin region. In some embodiments, the hairpin region modification comprises at least one modified nucleotide selected from a 2'-O-methyl (2'-OMe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, and/or combinations thereof.

[00427] In some embodiments, the hairpin region modification is in the hairpin 1 region. In some embodiments, the hairpin region modification is in the hairpin 2 region. In some embodiments, modifications are within the hairpin 1 and hairpin 2 regions, optionally wherein the "n" between hairpin 1 and 2 is also modified.

[00428] In some embodiments, a short-sgRNA is provided comprising a hairpin modification, wherein the hairpin modification comprises 1, 2, or 3 YA modifications in a YA site. In some embodiments, a short-sgRNA is provided comprising a hairpin modification, wherein the hairpin modification comprises at least 1, 2, 3, 4, 5, or 6 YA modifications. In some embodiments, a short-sgRNA is provided comprising a hairpin modification, wherein the hairpin modification comprises one YA modification. In some embodiments, a short-sgRNA is provided comprising a hairpin modification, wherein hairpin modification comprises 2 YA modifications. In some embodiments, the hairpin modification comprises 3 YA modifications. In some embodiments, one or more YA modifications are in a YA site. In some embodiments, one or more YA modifications are distal to a YA site.

[00429] In some embodiments, the hairpin modification comprises or further comprises a 2'-O-methyl (2'-OMe) modified nucleotide.

[00430] In some embodiments, the hairpin modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

[00431] In some embodiments, the hairpin region modification comprises at least one modified nucleotide selected from a 2'H modified nucleotide (DNA), PS modified nucleotide, a YA modification, a 2'-O-methyl (2'-O-Me) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, and/or combinations thereof.

[00432] In some embodiments, the short-sgRNA comprises a 3' end modification, and a modification in the hairpin region.

[00433] In some embodiments, the short-sgRNA comprises a 5' end modification, and a modification in the hairpin region.

[00434] In some embodiments, the short-sgRNA comprises an upper stem modification, and a modification in the hairpin region.

[00435] In some embodiments, the short-sgRNA comprises a hairpin modification as shown in any one of the sequences in Table 1. In some embodiments, such a hairpin modification is combined with a 5' end modification as shown for the corresponding sequence in Table 1. In some embodiments, such a hairpin modification is combined with a 3' end modification as shown for the corresponding sequence in Table 1. In some embodiments, such a hairpin modification is combined with 5' and 3' end modifications as shown for the corresponding sequence in Table 1.

[00436] In some embodiments, the short-sgRNA comprises a 3' end modification, a modification in the hairpin region, an upper stem modification, and a 5' end modification.

Exemplary modified short-sgRNAs

[00437] In some embodiments, the short-sgRNAs described herein comprise or consist of any of the sequences shown in Table 1. Further, short-sgRNAs are encompassed that comprise the modifications of any of the sequences shown in Table 1, and identified therein by SEQ ID No. That is, the nucleotides may be the same or different, but the modification pattern shown may be the same or similar to a modification pattern of a guide sequence of Table 1. A modification pattern includes the relative position and identity of modifications of the short-sgRNA (e.g. 5' terminus region, lower stem region, bulge region, upper stem region, nexus region, hairpin 1 region, hairpin 2 region, 3' tail region).

[00438] In some embodiments, the modification pattern contains at least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% of the modifications of any one of the sequences shown in the sequence column of Table 1, or over one or more regions of the sequence. In some embodiments, the modification pattern is at least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical to the modification pattern of any one of the sequences shown in the sequence column of Table 1. In some embodiments, the modification pattern is at least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over one or more (e.g., 1, 2, 3, 4, 5, 6, 7, or 8) regions of the sequence shown in Table 1, e.g., a 5' terminus region, lower stem region, bulge region, upper stem region, nexus region, hairpin 1 region, hairpin 2 region, and/or 3' terminus region.

[00439] For example, in some embodiments, a short-sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical to the modification pattern of a sequence over the 5' terminus region. In some embodiments, a short-sgRNA is encompassed wherein the modification

pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the lower stem. In some embodiments, a short-sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the bulge. In some embodiments, a short-sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the upper stem. In some embodiments, a short-sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the nexus. In some embodiments, a short-sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the hairpin 1. In some embodiments, a short-sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the hairpin 2. In some embodiments, a short-sgRNA is encompassed wherein the modification pattern is least 50%, 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, and 99% identical over the 3' terminus. In some embodiments, the modification pattern differs from the modification pattern of a sequence of Table 1, or a region (e.g. 5' terminus, lower stem, bulge, upper stem, nexus, hairpin 1, hairpin 2, 3' terminus) of such a sequence, at 0, 1, 2, 3, 4, 5, or 6 nucleotides. In some embodiments, the short-sgRNA comprises modifications that differ from the modifications of a sequence of Table 1, at 0, 1, 2, 3, 4, 5, or 6 nucleotides. In some embodiments, the short-sgRNA comprises modifications that differ from modifications of a region (e.g. 5' terminus, lower stem, bulge, upper stem, nexus, hairpin 1, hairpin 2, 3' terminus) of a sequence of Table 1, at 0, 1, 2, 3, 4, 5, or 6 nucleotides.

[00440] In some embodiments, the short-sgRNA comprises a 2'-O-methyl (2'-O-Me) modified nucleotide. In some embodiments, the short-sgRNA comprises a 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide. In some embodiments, the short-sgRNA comprises a 2'-fluoro (2'-F) modified nucleotide. In some embodiments, the short-sgRNA comprises a phosphorothioate (PS) bond between nucleotides. In some embodiments, the sgRNA comprises a YA modification.

[00441] In some embodiments, the short-sgRNA comprises a 5' end modification, a 3' end modification, or 5' and 3' end modification, such as a protective end modification. In some embodiments, the 5' end modification comprises a phosphorothioate (PS) bond between nucleotides. In some embodiments, the 5' end modification comprises a 2'-O-methyl (2'-O-Me), 2'-O-(2-methoxyethyl) (2'-O-moe), and/or 2'-fluoro (2'-F) modified

nucleotide. In some embodiments, the 5' end modification comprises at least one phosphorothioate (PS) bond and one or more of a 2'-O-methyl (2'-O-Me), 2'-O-(2-methoxyethyl) (2'-O-moe), and/or 2'-fluoro (2'-F) modified nucleotide. The end modification may comprise a phosphorothioate (PS), 2'-O-methyl (2'-O-Me), 2'-O-(2-methoxyethyl) (2'-O-moe), and/or 2'-fluoro (2'-F) modification. Equivalent end modifications are also encompassed by embodiments described herein. In some embodiments, the short-sgRNA comprises an end modification in combination with a modification of one or more regions of the short-sgRNA.

[00442] Modified short-sgRNAs comprising combinations of 5' end modifications, 3' end modifications, upper stem modifications, hairpin modifications, and 3' terminus modifications, as described above, are encompassed. Exemplary modified short-sgRNAs are described below.

[00443] In some embodiments, the invention comprises a short-sgRNA comprising or consisting of any one of the sequences described in SEQ ID Nos: 1-54, 201-254, and 301-354.

[00444] In some embodiments, a short-sgRNA is provided comprising any one of the modified sequences of SEQ ID Nos: 201-254, and 301-354, wherein the short-sgRNA further comprises a guide region that is complementary to a target sequence, and directs a Cas9 to its target for cleavage. In some instances, the invention comprises short-sgRNA comprising nucleic acids having at least 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% identity to the nucleic acids of any one of SEQ ID Nos: 1-54, 201-254, and 301-354, wherein the modification pattern is identical to the modification pattern shown in the reference sequence identifier in Table 1. In some embodiments, the short-sgRNA further comprises three phosphorothioate (PS) bonds linking the first four nucleotides at the 5' terminus and three PS bonds linking the last four nucleotides at the 3' terminus.

[00445] In some embodiments, the short-sgRNA comprises modifications at 1, 2, 3, or 4 of the first 4 nucleotides at its 5' end. In some embodiments, the first three or four nucleotides at the 5' terminus, and the last three or four nucleotides at the 3' terminus are modified. In some embodiments, the first four nucleotides at the 5' end, and the last four nucleotides at the 3' terminus are linked with phosphorothioate (PS) bonds. In some embodiments, the modification comprises 2'-O-Me. In some embodiments, the modification comprises 2'-F. In some embodiments, the modification comprises 2'-O-moe.

[00446] In some embodiments, the short-sgRNA comprises, if the nucleotide mentioned is present in the short-sgRNA, modifications at 1, 2, 3, or 4 of the first 4

nucleotides at the 5' end. In some embodiments, the short-sgRNA comprises modifications at 1, 2, 3, or 4 of the last 4 nucleotides at the 3' end (3' tail or conserved portion of an sgRNA). In some embodiments, the first four nucleotides at the 5' terminus and the last four nucleotides at the 3' terminus are linked with a PS bond, and the first three nucleotides at the 5' terminus and the last three nucleotides at the 3' terminus comprise 2'-O-Me or 2'-O-moe modifications.

[00447] In some embodiments, the first four nucleotides at the 5' terminus and the last four nucleotides at the 3' terminus are linked with a PS bond, and the first three nucleotides at the 5' terminus and the last three nucleotides at the 3' terminus comprise 2'-F modifications.

[00448] In some embodiments, a short-sgRNA is provided, if the nucleotide mentioned is present in the short-sgRNA, wherein LS1, LS6, LS7, LS8, LS11, and LS12 are modified with 2'-O-Me. In some embodiments, each of the nucleotides in the bulge region of the short-sgRNA are modified with 2'-O-Me. In some embodiments, each of the nucleotides in the upper stem region of the short-sgRNA are modified with 2'-O-Me. In some embodiments, N16, N17, and N18 in the nexus region of the short-sgRNA are modified with 2'-O-Me. In some embodiments, each of the nucleotides remaining in the hairpin 1 region of the short-sgRNA are modified with 2'-O-Me. In some embodiments, each of the nucleotides remaining in the hairpin 2 region of the short-sgRNA are modified with 2'-O-Me.

[00449] In some embodiments, a short-sgRNA comprising a 5' end modification and one or more modifications in one or more of: the upper stem region; the hairpin 1 region; and the hairpin 2 region is provided, wherein the 5' end modification comprises at least two phosphorothioate linkages within the first seven nucleotides of the 5' terminus.

[00450] In some embodiments, a short-sgRNA comprising a 5' end modification and one or more modifications in one or more of: the upper stem region; the hairpin 1 region; and the hairpin 2 region is provided, wherein the 5' end modification comprises one or more phosphorothioate linkages at the 5' end. In some embodiments, one or more phorphorothioate bonds link the 5' terminal nucleotides.

[00451] In some embodiments, a short-sgRNA comprising a 5' end modification and one or more modifications in one or more of: the upper stem region; the hairpin 1 region; and the hairpin 2 region is provided, wherein the 5' end modification comprises one or more phosphorothioate linkages within the first seven nucleotides of the 5' terminus.

[00452] In some embodiments, the invention comprises a short-sgRNA comprising any one of the modified sequences of SEQ ID Nos: 201-254, and 301-354, wherein the short-

sgRNA further comprises a 5' guide region that is at least partially complementary to a target sequence, and optionally directs a Cas9 to its target for cleavage.

[00453] In some embodiments, the invention comprises a short-sgRNA comprising nucleotides having at least 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% identity to the nucleotides of any one of SEQ ID Nos: 1-54, 201-254, and 301-354, wherein the modification pattern is identical to the modification pattern shown in the reference sequence identifier. That is, the nucleotides A, U, C, and G may differ by 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% compared to what is shown in in the sequences, but the modification remains unchanged.

[00454] In some embodiments, a short-sgRNA is provided comprising, if the nucleotide mentioned is present in the short guide, 2'-O-Me modified nucleotides at: the first three nucleotides in the 5' terminus; LS1, LS6, LS7, LS8, LS11, and LS12 in the lower stem; B1 and B2 in the bulge region; each of the nucleotides in the upper stem region; N16, N17, and N18 in the nexus region; each of the nucleotides in the hairpin 1 region; one nucleotide between hairpin 1 and hairpin 2; each of the nucleotides in the hairpin 2 region; and the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three PS bonds between the first four nucleotides at the 5' terminus and three PS bonds between the last four nucleotides at the 3' terminus.

[00455] In some embodiments, a short-sgRNA is provided comprising, if the nucleotide mentioned is present in the short guide, 2'-O-Me modified nucleotides at: the first three nucleotides in the 5' terminus; LS1, LS6, LS7, LS8, LS11, and LS12 in the lower stem; B1-B6 in the bulge region; each of the nucleotides in the upper stem region; N16, N17, and N18 in the nexus region; each of the nucleotides in the hairpin 1 region; one nucleotide between hairpin 1 and hairpin 2; each of the nucleotides in the hairpin 2 region; and the last four nucleotides at the 3' terminus. In some embodiments, the sgRNA further comprises three PS bonds between the first four nucleotides at the 5' terminus and three PS bonds between the last four nucleotides at the 3' terminus.

[00456] In some embodiments, a short-sgRNA is provided comprising 2'-F modified nucleotides at: LS9 and LS10 in the lower stem; 15-N18 in the nexus region; H2-9-HS-15 in the hairpin 2 region; and the second to last, third to last, and fourth to last nucleotide in the 3' terminus region.

[00457] In some embodiments, a short-sgRNA is provided comprising 2'-F modified nucleotides at: each nucleotide in the lower stem; 15-N18 in the nexus region; H2-9-HS-15 in

the hairpin 2 region; and the second to last, third to last, and fourth to last nucleotide in the 3' terminus region.

[00458] In some embodiments, a short-sgRNA is provided comprising, if the nucleotide mentioned is present in the short guide, 2'-OMe modified nucleotides at LS8, LS10, LS12, H1-2, H1-4, H1-6, H1-8, H1-10, H1-12, H2-1, H2-3, H2-5, H2-7, H2-9, H2-11, H2-13, H2-15, and the last and third to last nucleotides at the 3' terminus; and 2'-F modifications at LS7, LS9, LS11; H1-1, H1-3, H1-5, H1-7, H1-9, H1-11, H1-13, H2-2, H2-4, H2-6, H2-8, H2-10, H2-12, H2-14, and the second to last and fourth to last nucleotide at the 3' terminus.

[00459] Any of the foregoing modification patterns can be combined with a modification pattern set forth in the embodiments described above, e.g., in the summary section or Table 1, to the extent that they are non-overlapping. In the event that combining a foregoing modification pattern with a modification pattern set forth in the summary section or Table 1 would result in incompatible modifications (e.g., the same position would be both 2'-OMe and 2'-fluoro), the modification set forth in the summary section or Table 1 controls.

Compositions and kits

[00460] Compositions comprising any of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs) described herein and a carrier, excipient, diluent, or the like are encompassed. In some instances, the excipient or diluent is inert. In some instances, the excipient or diluent is not inert. In some embodiments, a pharmaceutical formulation is provided comprising any of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs) described herein and a pharmaceutically acceptable carrier, excipient, diluent, or the like. In some embodiments, the pharmaceutical formulation further comprises an LNP. In some embodiments, the pharmaceutical formulation further comprises a Cas9 protein or an mRNA encoding a Cas9 protein. In some embodiments, the pharmaceutical formulation comprises any one or more of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs), an LNP, and a Cas9 protein or mRNA encoding a Cas9 protein.

[00461] Also provided are kits comprising one or more gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs), compositions, or pharmaceutical formulations described herein. In some embodiments, a kit further comprises one or more of a solvent, solution, buffer, each separate from the composition or pharmaceutical formulation, instructions, or desiccant.

Compositions comprising an RNA-guided DNA Binding Agent or mRNA encoding RNA-guided DNA Binding Agent

[00462] In some embodiments, compositions or pharmaceutical formulations are provided comprising at least one gRNA (e.g., sgRNA, short-sgRNA, dgRNA, or crRNA) described herein and a nuclease or a nucleic acid (e.g., an mRNA) encoding a nuclease. In some embodiments, the nuclease is an RNA-guided DNA binding agent, such as a Cas protein. In some embodiments, the short-sgRNA together with a Cas protein or nucleic acid (e.g., mRNA) encoding Cas protein is called a Cas RNP. In some embodiments, the RNA-guided DNA binding agent is one that functions with the short-sgRNA to direct a RNA-guided DNA binding agent to a target nucleic acid sequence. In some embodiments, the RNA-guided DNA binding agent is a Cas protein from the Type-II CRISPR/Cas system. In some embodiments, the Cas protein is Cas9. In some embodiments, the Cas9 protein is a wild type Cas9. In some embodiments, the Cas9 protein is derived from the *Streptococcus pyogenes* Cas9 protein, e.g., a S. *pyogenes* Cas9 (sypCas9). In some embodiments, compositions are provided comprising at least one short-sgRNA and a nuclease or an mRNA encoding a spyCas9. In some embodiments, the Cas9 protein is not derived from S. *pyogenes*, but functions in the same way as S. *pyogenes* Cas9 such that short-sgRNA that is specific to S. *pyogenes* Cas9 will direct the non-S. *pyogenes* Cas9 to its target site. In some embodiments, the Cas9 protein is derived from the *Staphylococcus aureus* Cas9 protein, e.g., a SaCas9. In some embodiments, compositions are provided comprising at least one short-sgRNA and a nuclease or an mRNA encoding a saCas9. In some embodiments, the Cas induces a double strand break in target DNA. Equivalents of spyCas9 and saCas9 protein are encompassed by the embodiments described herein.

[00463] RNA-guided DNA binding agents, including Cas9, encompass modified and variants thereof. Modified versions having one catalytic domain, either RuvC or HNH, that is inactive are termed "nickases." Nickases cut only one strand on the target DNA, thus creating a single-strand break. A single-strand break may also be known as a "nick." In some embodiments, the compositions and methods comprise nickases. In some embodiments, the compositions and methods comprise a nickase RNA-guided DNA binding agent, such as a nickase Cas9, that induces a nick rather than a double strand break in the target DNA.

[00464] In some embodiments, the RNA-guided DNA binding agent may be modified to contain only one functional nuclease domain. For example, the RNA-guided DNA binding agent may be modified such that one of the nuclease domains is mutated or fully or partially deleted to reduce its nucleic acid cleavage activity. In some embodiments, a nickase Cas is

used having a RuvC domain with reduced activity. In some embodiments, a nickase Cas is used having an inactive RuvC domain. In some embodiments, a nickase Cas is used having an HNH domain with reduced activity. In some embodiments, a nickase Cas is used having an inactive HNH domain.

[00465] In some embodiments, a conserved amino acid within an RNA-guided DNA binding agent nuclease domain is substituted to reduce or alter nuclease activity. In some embodiments, a Cas protein may comprise an amino acid substitution in the RuvC or RuvC-like nuclease domain. Exemplary amino acid substitutions in the RuvC or RuvC-like nuclease domain include D10A (based on the S. *pyogenes* Cas9 protein). In some embodiments, the Cas protein may comprise an amino acid substitution in the HNH or HNH-like nuclease domain. Exemplary amino acid substitutions in the HNH or HNH-like nuclease domain include E762A, H840A, N863A, H983A, and D986A (based on the spyCas9 protein).

[00466] In some embodiments, the RNP complex described herein comprises a nickase or an mRNA encoding a nickase and a pair of gRNAs (one or both of which may be sgRNAs and/or short-sgRNAs) that are complementary to the sense and antisense strands of the target sequence, respectively. In this embodiment, the gRNAs (e.g., sgRNAs and/or short-sgRNAs) direct the nickase to a target sequence and introduce a double stranded break (DSB) by generating a nick on opposite strands of the target sequence (i.e., double nicking). In some embodiments, use of double nicking may improve specificity and reduce off-target effects. In some embodiments, a nickase RNA-guided DNA binding agent is used together with two separate short-sgRNAs targeting opposite strands of DNA to produce a double nick in the target DNA. In some embodiments, a nickase RNA-guided DNA binding agent is used together with two separate gRNAs (e.g., sgRNAs or short-sgRNAs) that are selected to be in close proximity to produce a double nick in the target DNA.

[00467] In some embodiments, chimeric Cas proteins are used, where one domain or region of the protein is replaced by a portion of a different protein. In some embodiments, a Cas nuclease domain may be replaced with a domain from a different nuclease such as Fok1. In some embodiments, a Cas protein may be a modified nuclease.

[00468] In some embodiments, the Cas protein comprises a fusion protein comprising a catalytically inactive Cas (e.g., Cas9) linked to a heterologous functional domain (see, e.g., WO2014152432). In some embodiments, the catalytically inactive Cas9 is from *S. pyogenes*. In some embodiments, the catalytically inactive Cas comprises mutations that inactivate the Cas. In some embodiments, the heterologous functional domain is a domain that modifies

gene expression, histones, or DNA. In some embodiments, the heterologous functional domain is a transcriptional activation domain or a transcriptional repressor domain.

[00469] In some embodiments, the target sequence may be adjacent to a PAM. In some embodiments, the PAM may be adjacent to or within 1, 2, 3, or 4, nucleotides of the 3' end of the target sequence. The length and the sequence of the PAM may depend on the Cas protein used. For example, the PAM may be selected from a consensus or a particular PAM sequence for a specific Cas9 protein or Cas9 ortholog, including those disclosed in Figure 1 of Ran et al., Nature 520:186-191 (2015). In some embodiments, the PAM may comprise 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides in length. Non-limiting exemplary PAM sequences include NGG, NAG, NGA, NGAG, NGCG, NNGRRT, TTN, NGGNG, NG, NAAAAN, NNAAAAW, NNNNACA, GNNNCNNA, and NNNNGATT (wherein N is defined as any nucleotide, and W is defined as either A or T, and R is defined as either A or G). In some embodiments, the PAM sequence may be NGG. In some embodiments, the PAM sequence may be NGGNG. In some embodiments, the PAM sequence may be NNAAAAW.

[00470] In some embodiments, an nucleic acid (e.g., mRNA) comprising an ORF encoding an RNA-guided DNA binding agent is used which has one or more of the following features. In some embodiments, the ORF encoding the RNA-guided DNA-binding agent, e.g. a Cas9 nuclease such as an *S. pyogenes* Cas9, has an adenine content ranging from its minimum adenine content to about 150% of its minimum adenine content. In some embodiments, the adenine content of the ORF is less than or equal to about 145%, 140%, 135%, 130%, 125%, 120%, 115%, 110%, 105%, 104%, 103%, 102%, or 101% of its minimum adenine content. In some embodiments, the ORF has an adenine content equal to its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 150% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 145% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 140% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 135% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 130% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 125% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 120% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 115% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 110% of its

minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 105% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 104% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 103% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 102% of its minimum adenine content. In some embodiments, the ORF has an adenine content less than or equal to about 101% of its minimum adenine content.

[00471] In some embodiments, the ORF has an adenine dinucleotide content ranging from its minimum adenine dinucleotide content to 200% of its minimum adenine dinucleotide content. In some embodiments, the adenine dinucleotide content of the ORF is less than or equal to about 195%, 190%, 185%, 180%, 175%, 170%, 165%, 160%, 155%, 150%, 145%, 140%, 135%, 130%, 125%, 120%, 115%, 110%, 105%, 104%, 103%, 102%, or 101% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content equal to its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 200% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 195% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 190% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 185% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 180% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 175% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 170% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 165% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 160% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 155% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content equal to its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 150% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine

dinucleotide content less than or equal to about 145% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 140% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 135% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 130% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 125% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 120% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 115% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 110% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 105% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 104% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 103% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 102% of its minimum adenine dinucleotide content. In some embodiments, the ORF has an adenine dinucleotide content less than or equal to about 101% of its minimum adenine dinucleotide content.

[00472] In some embodiments, the ORF has an adenine dinucleotide content ranging from its minimum adenine dinucleotide content to the adenine dinucleotide content that is 90% or lower of the maximum adenine dinucleotide content of a reference sequence that encodes the same protein as the mRNA in question. In some embodiments, the adenine dinucleotide content of the ORF is less than or equal to about 85%, 80%, 75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, or 5% of the maximum adenine dinucleotide content of a reference sequence that encodes the same protein as the mRNA in question.

[00473] In some embodiments, the ORF has an adenine trinucleotide content ranging from 0 adenine trinucleotides to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, or 50 adenine trinucleotides (where a longer run of adenines counts as the number of unique three-adenine segments within it, e.g., an adenine tetranucleotide contains two adenine trinucleotides, an

adenine pentanucleotide contains three adenine trinucleotides, etc.). In some embodiments, the ORF has an adenine trinucleotide content ranging from 0% adenine trinucleotides to 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 1.5%, or 2% adenine trinucleotides, where the percentage content of adenine trinucleotides is calculated as the percentage of positions in a sequence that are occupied by adenines that form part of an adenine trinucleotide (or longer run of adenines), such that the sequences UUUAAA and UUUUAAAA would each have an adenine trinucleotide content of 50%. For example, in some embodiments, the ORF has an adenine trinucleotide content less than or equal to 2%. For example, in some embodiments, the ORF has an adenine trinucleotide content less than or equal to 1.5%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 1%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.9%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.8%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.7%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.6%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.5%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.4%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.3%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.2%. In some embodiments, the ORF has an adenine trinucleotide content less than or equal to 0.1%. In some embodiments, a nucleic acid is provided that encodes an RNA-guided DNA-binding agent comprising an ORF containing no adenine trinucleotides.

[00474] In some embodiments, the ORF has an adenine trinucleotide content ranging from its minimum adenine trinucleotide content to the adenine trinucleotide content that is 90% or lower of the maximum adenine trinucleotide content of a reference sequence that encodes the same protein as the mRNA in question. In some embodiments, the adenine trinucleotide content of the ORF is less than or equal to about 85%, 80%, 75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, or 5% of the maximum adenine trinucleotide content of a reference sequence that encodes the same protein as the mRNA in question.

[00475] A given ORF can be reduced in adenine content or adenine dinucleotide content or adenine trinucleotide content, for example, by using minimal adenine codons in a sufficient fraction of the ORF. For example, an amino acid sequence for an RNA-guided DNA-binding agent can be back-translated into an ORF sequence by converting

amino acids to codons, wherein some or all of the ORF uses the exemplary minimal adenine codons shown below. In some embodiments, at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98%, 99%, or 100% of the codons in the ORF are codons listed in Table 4.

Table 4. Exemplary minimal adenine codons

	Amino Acid	**Minimal adenine codon**
A	Alanine	GCU or GCC or GCG
G	Glycine	GGU or GGC or GGG
V	Valine	GUC or GUU or GUG
D	Aspartic acid	GAC or GAU
E	Glutamic acid	GAG
I	Isoleucine	AUC or AUU
T	Threonine	ACU or ACC or ACG
N	Asparagine	AAC or AAU
K	Lysine	AAG
S	Serine	UCU or UCC or UCG
R	Arginine	CGU or CGC or CGG
L	Leucine	CUG or CUC or CUU
P	Proline	CCG or CCU or CCC
H	Histidine	CAC or CAU
Q	Glutamine	CAG
F	Phenylalanine	UUC or UUU
Y	Tyrosine	UAC or UAU
C	Cysteine	UGC or UGU
W	Tryptophan	UGG
M	Methionine	AUG

[00476] In some embodiments, a nucleic acid is provided that encodes an RNA-guided DNA-binding agent, e.g. a Cas9 nuclease such as an *S. pyogenes* Cas9, comprising an ORF consisting of a set of codons of which at least about 75%, 80%, 85%, 90%, 95%, 98%, 99%, or 100% of the codons are codons listed in Table 4. In some embodiments, the ORF has minimal nucleotide homopolymers, e.g., repetitive strings of the same nucleotides. For example, in some embodiments, when selecting a minimal uridine codon from the codons listed in Table 4, a nucleic acid is constructed by selecting the minimal adenine codons that reduce the number and length of nucleotide homopolymers, e.g., selecting GCG instead of GCC for alanine or selecting GGC instead of GGG for glycine.

[00477] In any of the foregoing embodiments, the nucleic acid may be an mRNA.

[00478] In some embodiments, at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% of the codons in an ORF are codons from a codon set shown in Table 5 (e.g., the low U, low A, or low A/U codon set). The codons in the low U, low A, and low A/U sets use codons that minimize the indicated nucleotides while also using codons corresponding to highly expressed tRNAs where more than one option is available. In some embodiments, at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% of the codons in an ORF are codons from the low U codon set shown in Table 5. In some embodiments, at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% of the codons in an ORF are codons from the low A codon set shown in Table 5. In some embodiments, at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% of the codons in an ORF are codons from the low A/U codon set shown in Table 5.

Table 5. Exemplary Codon Sets

Amino Acid	Low U	Low A	Low A/U	Long Half Life
Gly	GGC	GGC	GGC	GGT
Glu	GAG	GAG	GAG	GAA
Asp	GAC	GAC	GAC	GAC
Val	GTG	GTG	GTG	GTC
Ala	GCC	GCC	GCC	GCC
Arg	AGA	CGG	CGG	AGA
Ser	AGC	TCC	AGC	TCT
Lys	AAG	AAG	AAG	AAG
Asn	AAC	AAC	AAC	AAC
Met	ATG	ATG	ATG	ATG
Ile	ATC	ATC	ATC	ATC
Thr	ACC	ACC	ACC	ACC
Trp	TGG	TGG	TGG	TGG

Cys	TGC	TGC	TGC	TGC
Tyr	TAC	TAC	TAC	TAC
Leu	CTG	CTG	CTG	TTG
Phe	TTC	TTC	TTC	TTC
Gln	CAG	CAG	CAG	CAA
His	CAC	CAC	CAC	CAC

Exemplary sequences

[00479] In some embodiments, the ORF encoding the RNA-guided DNA binding agent comprises a sequence with at least 90%, 93%, 95%, 96%, 97%, 98%, 99%, 99.5%, or 100% identity to any one of SEQ ID NOs: 3502-3522, 3525, 3526, or 3529-3546; and/or the ORF has at least 90%, 93%, 95%, 96%, 97%, 98%, 99%, 99.5%, or 100% identity to any one of SEQ ID NOs: 3502-3522, 3525, 3526, or 3529-3546 over at least its first 50, 200, 250, or 300 nucleotides, or at least 95% identity to any one of SEQ ID NOs: 3502-3522, 3525, 3526, or 3529-3546 over at least its first 30, 50, 70, 100, 150, 200, 250, or 300 nucleotides; and/or the ORF consists of a set of codons of which at least 95%, 96%, 97%, 98%, 99%, 99.5%, or 100% of the codons are codons listed in Table 4 or 5; and/or the ORF has an adenine content ranging from its minimum adenine content to 123% of the minimum adenine content; and/or the ORF has an adenine dinucleotide content ranging from its minimum adenine dinucleotide content to 150% of the minimum adenine dinucleotide content. In some embodiments, the polynucleotide encoding the RNA-guided DNA binding agent comprises a sequence with at least 95%, 96%, 97%, 98%, 99%, 99.5%, or 100% identity to any one of SEQ ID NOs: 3502-3522, 3525, 3526, or 3529-3546.

[00480] In some embodiments, the mRNA comprises a sequence with at least 90% identity to any one of SEQ ID NOs: 3501, 3523, 3524, or 3527, wherein the sequence comprises an ORF encoding an RNA-guided DNA binding agent. In some embodiments, the mRNA comprises a sequence with at least 90% identity to any one of SEQ ID NOs: 3501, 3523, 3524, or 3527, wherein the sequence comprises an ORF encoding an RNA-guided DNA binding agent, wherein the first three nucleotides of SEQ ID NOs: 3501, 3523, 3524, or 3527 are omitted. In some embodiments, the mRNA comprises a sequence with at least 90% identity to any one of SEQ ID NOs: 3501, 3523, 3524, or 3527, wherein the sequence

comprises an ORF encoding an RNA-guided DNA binding agent, wherein the first three nucleotides of SEQ ID NOs: 3501, 3523, 3524, or 3527 are omitted and/or the ORF coding sequence contained within SEQ ID NO: 3501, 3523, 3524, or 3527 is substituted with the coding sequence of any one of SEQ ID NOs: 3502-3522, 3525, 3526, or 3529-3546. In some embodiments, any of the foregoing levels of identity is at least 95%, at least 98%, at least 99%, or 100%.

Methods of Gene Modulation

[00481] In some embodiments, any one or more of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs), compositions, or pharmaceutical formulations described herein is for use in preparing a medicament for treating or preventing a disease or disorder in a subject.

[00482] In some embodiments, the invention comprises a method of treating or preventing a disease or disorder in subject comprising administering any one or more of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs), compositions, or pharmaceutical formulations described herein.

[00483] In some embodiments, the invention comprises a method or use of modifying a target DNA comprising, administering or delivering any one or more of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs), compositions, or pharmaceutical formulations described herein.

[00484] In some embodiments, the invention comprises a method or use for modulation of a target gene comprising, administering or delivering any one or more of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs), compositions, or pharmaceutical formulations described herein. In some embodiments, the modulation is editing of the target gene. In some embodiments, the modulation is a change in expression of the protein encoded by the target gene.

[00485] In some embodiments, the method or use results in gene editing. In some embodiments, the method or use results in a double-stranded break within the target gene. In some embodiments, the method or use results in formation of indel mutations during non-homologous end joining of the DSB. In some embodiments, the method or use results in an insertion or deletion of nucleotides in a target gene. In some embodiments, the insertion or deletion of nucleotides in a target gene leads to a frameshift mutation or premature stop codon that results in a non-functional protein. In some embodiments, the insertion or deletion of nucleotides in a target gene leads to a knockdown or elimination of target gene expression.

In some embodiments, the method or use comprises homology directed repair of a DSB. In some embodiments, the method or use further comprises delivering to the cell a template, wherein at least a part of the template incorporates into a target DNA at or near a double strand break site induced by the nuclease.

[00486] In some embodiments, the method or use results in gene modulation. In some embodiments, the gene modulation is an increase or decrease in gene expression, a change in methylation state of DNA, or modification of a histone subunit. In some embodiments, the method or use results in increased or decreased expression of the protein encoded by the target gene.

[00487] The efficacy of gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs) can be tested in vitro and in vivo. In some embodiments, the invention comprises one or more of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs), compositions, or pharmaceutical formulations described herein, wherein the short-sgRNA results in gene modulation when provided to a cell together with Cas9 or mRNA encoding Cas9. In some embodiments, the efficacy of short-sgRNA can be measured *in vitro* or *in vivo*.

[00488] In some embodiments, the activity of a Cas RNP comprising a short-sgRNA is compared to the activity of a Cas RNP comprising an unmodified sgRNA or a reference sgRNA lacking modifications present in the sgRNA or short-sgRNA, such as YA site modifications.

[00489] In some embodiments, the efficiency of a sgRNA or short-sgRNA in increasing or decreasing target protein expression is determined by measuring the amount of target protein.

[00490] In some embodiments, the efficiency of editing with specific gRNAs is determined by the editing present at the target location in the genome following delivery of Cas9 and the gRNA. In some embodiments, the efficiency of editing with specific gRNAs is measured by next-generation sequencing. In some embodiments, the editing percentage of the target region of interest is determined. In some embodiments, the total number of sequence reads with insertions or deletions of nucleotides into the target region of interest over the total number of sequence reads is measured following delivery of a gRNA and Cas9.

[00491] In some embodiments, the efficiency of editing with specific gRNAs is measured by the presence of insertions or deletions of nucleotides introduced by successful gene editing. In some embodiments, activity of a Cas9 and gRNAs is tested in biochemical assays. In some embodiments, activity of a Cas9 and gRNAs is tested in a cell-free cleavage assay. In some embodiments, activity of a Cas9 and gRNAs is tested in Neuro2A cells.

[00492] In some embodiments, the activity of modified gRNAs is measured after in vivo dosing of LNPs comprising modified gRNAs and Cas protein or mRNA encoding Cas protein.

[00493] In some embodiments, in vivo efficacy of a gRNA or composition provided herein is determined by editing efficacy measured in DNA extracted from tissue (e.g., liver tissue) after administration of gRNA and Cas9.

[00494] In some embodiments, activation of the subject's immune response is measured by serum concentrations of cytokine(s) following in vivo dosing of sgRNA together with Cas9 mRNA or protein (e.g., formulated in a LNP). In some embodiments, the cytokine is interferon-alpha (IFN-alpha), interleukin 6 (IL-6), monocyte chemotactic protein 1 (MCP-1), and/or tumor necrosis factor alpha (TNF-alpha).

[00495] In some embodiments, administration of Cas RNP or Cas9 mRNA together with the modified gRNA (e.g., sgRNA, short-sgRNA, or dgRNA) produces lower serum concentration(s) of immune cytokines compared to administration of unmodified sgRNA. In some embodiments, the invention comprises a method of reducing a subject's serum concentration of immune cytokines comprising, administering any one of the gRNAs disclosed herein, wherein the gRNA produces a lower concentration of immune cytokines in a subject's serum as compared to a control gRNA that is not similarly modified.

LNP delivery of gRNA

[00496] Lipid nanoparticles (LNPs) are a well-known means for delivery of nucleotide and protein cargo, and may be used for delivery of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs), compositions, or pharmaceutical formulations disclosed herein. In some embodiments, the LNPs deliver nucleic acid, protein, or nucleic acid together with protein.

[00497] In some embodiments, the invention comprises a method for delivering any one of the gRNAs (e.g., sgRNAs, short-sgRNAs, dgRNAs, or crRNAs) disclosed herein to a subject, wherein the gRNA is associated with an LNP. In some embodiments, the gRNA/LNP is also associated with a Cas9 or an mRNA encoding Cas9.

[00498] In some embodiments, the invention comprises a composition comprising any one of the gRNAs disclosed and an LNP. In some embodiments, the composition further comprises a Cas9 or an mRNA encoding Cas9.

[00499] In some embodiments, the LNPs comprise cationic lipids. In some embodiments, the LNPs comprise (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-

(diethylamino)propoxy)carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate, also called 3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,12Z)-octadeca-9,12-dienoate). In some embodiments, the LNPs comprise molar ratios of a cationic lipid amine to RNA phosphate (N:P) of about 4.5.

[00500] In some embodiments, LNPs associated with the gRNAs disclosed herein are for use in preparing a medicament for treating a disease or disorder.

[00501] Electroporation is a well-known means for delivery of cargo, and any electroporation methodology may be used for delivery of any one of the gRNAs disclosed herein. In some embodiments, electroporation may be used to deliver any one of the gRNAs disclosed herein and Cas9 or an mRNA encoding Cas9.

[00502] In some embodiments, the invention comprises a method for delivering any one of the gRNAs disclosed herein to an ex vivo cell, wherein the gRNA is associated with an LNP or not associated with an LNP. In some embodiments, the gRNA/LNP or gRNA is also associated with a Cas9 or an mRNA encoding Cas9.

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[00503] This description and exemplary embodiments should not be taken as limiting. For the purposes of this specification and appended claims, unless otherwise indicated, all numbers expressing quantities, percentages, or proportions, and other numerical values used in the specification and claims, are to be understood as being modified in all instances by the term "about," to the extent they are not already so modified. "About" indicates a degree of variation that does not substantially affect the properties of the described subject matter, e.g., within 10%, 5%, 2%, or 1%. Accordingly, unless indicated to the contrary, the numerical parameters set forth in the following specification and attached claims are approximations that may vary depending upon the desired properties sought to be obtained. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter should at least be construed in light of the number of reported significant digits and by applying ordinary rounding techniques.

[00504] It is noted that, as used in this specification and the appended claims, the singular forms "a," "an," and "the," and any singular use of any word, include plural referents unless expressly and unequivocally limited to one referent. As used herein, the term "include" and its grammatical variants are intended to be non-limiting, such that recitation of items in a list is not to the exclusion of other like items that can be substituted or added to the listed items.

EXAMPLES

[00505] The following examples are provided to illustrate certain disclosed embodiments and are not to be construed as limiting the scope of this disclosure in any way.

Example 1 – Materials and Methods

Synthetic sgRNA and short-single guide RNA (short-sgRNA)

[00506] Single-guide RNA (sgRNA) and short-single guide (short-sgRNA) was chemically synthesized by commercial vendors or using standard in vitro synthesis techniques with modified nucleotides as provided in Table 1.

In vitro transcription ("IVT") of Cas9 mRNA

[00507] Capped and polyadenylated Cas9 mRNA containing N1-methyl pseudouridine was generated by *in vitro* transcription using a linearized plasmid DNA template and T7 RNA polymerase. Plasmid DNA containing a T7 promoter and a sequence for transcription (for producing mRNA comprising an mRNA described herein (see SEQ ID NOs: 3499, 3500, 3501, 3523, 3524, and 3527 for exemplary transcripts and SEQ ID NOs: 3502-3522, 3525, 3526, and 3529-3546 for exemplary ORFs) was linearized by incubating at 37°C to complete digestion with XbaI with the following conditions. The XbaI may be heat inactivated. The linearized plasmid was purified from enzyme and buffer salts and analyzed by agarose gel to confirm linearization. The IVT reaction to generate Cas9 modified mRNA was incubated at 37°C for 2-4 hours in the following conditions: 50 ng/μL linearized plasmid; 2 mM each of GTP, ATP, CTP, and N1-methyl pseudo-UTP (Trilink); 10 mM ARCA (Trilink); 5 U/μL T7 RNA polymerase (NEB); 1 U/μL Murine RNase inhibitor (NEB); 0.004 U/μL inorganic E. coli pyrophosphatase (NEB); and 1x reaction buffer. After the 4-hour incubation, TURBO DNase (ThermoFisher) was added to a final concentration of 0.01 U/μL, and the reaction was incubated for an additional 30 minutes to remove the DNA template. The Cas9 mRNA was purified from enzyme and nucleotides using a MegaClear Transcription Clean-up kit per the manufacturer's protocol (ThermoFisher). Alternatively, the mRNA was purified through a precipitation protocol, which in some cases was followed by HPLC-based purification. Briefly, after the DNase digestion, the mRNA was precipitated by adding 0.21x volume of a 7.5 M LiCl solution and mixing, and the precipitated mRNA was pelleted by centrifugation. Once the supernatant was removed, the mRNA was reconstituted in water. The mRNA was precipitated again using ammonium acetate and ethanol. 5M Ammonium acetate was added to the mRNA solution for a final concentration of 2M along with 2x volume of 100% EtOH.

The solution was mixed and incubated at -20 °C for 15 min. The precipitated mRNA was again pelleted by centrifugation, the supernatant was removed, and the mRNA was reconstituted in water. As a final step, the mRNA was precipitated using sodium acetate and ethanol. 1/10 volume of 3 M sodium acetate (pH 5.5) was added to the solution along with 2x volume of 100% EtOH. The solution was mixed and incubated at -20 °C for 15 min. The precipitated mRNA was again pelleted by centrifugation, the supernatant was removed, the pellet was washed with 70% cold ethanol and allowed to air dry. The mRNA was reconstituted in water. For HPLC purified mRNA, after the LiCl precipitation and reconstitution, the mRNA was purified by RP-IP HPLC (see, e.g., Kariko, et al. *Nucleic Acids Research*, 2011, Vol. 39, No. 21 e142). The fractions chosen for pooling were combined and desalted by sodium acetate/ethanol precipitation as described above. The transcript concentration was determined by measuring the light absorbance at 260 nm (Nanodrop), and the transcript was analyzed by capillary electrophoresis by Bioanalyzer (Agilent).

Cas9 mRNA and gRNA Transfections in Neuro2A Cells

[00508] The mouse cell line Neuro2A was cultured in DMEM media supplemented with 10% fetal bovine serum and was plated at a density of 15,000 cells/well in a 96-well plate 24 hours prior to transfection. On the day of transfection, the media was aspirated from cells and replaced with fresh media. Lipofectamine-2000 (Invitrogen) was diluted 1:50 (v/v) in Opti-MEM (Invitrogen). Cas9 mRNA and guide RNA were diluted separately in Opti-MEM. Both Cas9 mRNA and gRNA were mixed separately 1:1 (v/v) with diluted Lipofectamine-2000, producing two lipoplexes. After 5 minutes of incubation, lipoplexes were added in succession to cells, for a final concentration of 100 ng Cas9 mRNA and 0.4 µL total lipofection reagent per well. Guides were tested at four dose levels, including 3 nM, 0.3 nM, 0.03 nM, and 0.003 nM. Cells were lysed 24 hours post transfection, and lysates were used directly in the PCR reaction that was analyzed for editing by NGS.

Primary hepatocytes

[00509] Primary human liver hepatocytes (PHH), primary cynomolgus liver hepatocytes (PCH), or primary mouse liver hepatocytes (PMH) (Thermo Fisher) were cultured per the manufacturer's protocol (Invitrogen, protocol 11.28.2012). In brief, the cells were thawed and resuspended in hepatocyte thawing medium (Thermo Fisher, Cat. CM7000) followed by centrifugation at 100 g for 10 minutes for PHH, 100g for 4 min for PMH, or 80g for 4

minutes for PCH. The supernatant was discarded and the pelleted cells resuspended in hepatocyte plating medium plus supplement pack (Invitrogen, Cat. A1217601 and CM3000). Cells were counted and plated on Bio-coat collagen I coated 96-well plates (Thermo Fisher, Cat. 877272) at a density of 30,000-35,000 cells/well for PHH, 50,000-60,000 cells/well for PCH, or 15,000-20,000 cells/well for PMH. Plated cells were allowed to settle and adhere for 4 to 6 hours in a tissue culture incubator at 37°C and 5% CO_2 atmosphere. After incubation, cells were checked for monolayer formation. Cells were then washed with hepatocyte maintenance media/culture media with serum-free supplement pack (Invitrogen, Cat. A1217601 and CM4000) and then fresh hepatocyte maintenance media was added on to the cells

[00510] For lipoplex transfection experiments, Lipofectamine RNAiMax (ThermoFisher, Cat. 13778150) based transfections were conducted as per the manufacturer's protocol. Cells were transfected with a single lipoplex containing Spy Cas9 mRNA (100 ng for PMH, 50ng for PHH and 25ng for PCH) and OptiMem sgRNA (25nM for PMH, 12.5nM for PHH and 0.125nM for PCH) and OptiMem and Lipofectamine RNAiMax (1 µL/well for PHH and PCH both and 2uL/well for PMH).

[00511] For experiments involving LNP treatment, after 4-6 hours, the plating media was removed, cells were then washed with hepatocyte maintenance media/culture media with serum-free supplement pack (Invitrogen, Cat. A1217601 and CM4000), and replaced with supplemented hepatocyte culture medium (Invitrogen, Cat. A1217601 and CM4000) containing LNP formulated Cas9 mRNA and guide RNA plus 3% serum. LNPs were diluted from a starting dose level of 100ng Cas9 mRNA and approximately 30nM guide RNA per well, carrying out serial dilutions down to 0.1ng mRNA and 0.03nM guide per well. Cells were incubated for approximately 72 hours at 37°C and 5% CO_2 atmosphere before cell lysis and NGS analysis as described herein.

HepG2

[00512] The human hepatocellular carcinoma cell line HepG2 (American Type Culture Collection, Cat. HB-8065) was cultured in DMEM media containing penstrep supplemented with 10% fetal bovine serum. Cells were counted and plated on Bio-coat collagen I coated 96-well plates (ThermoFisher, Cat. 877272) at a density of 10,000 cells/well in a 96-well plate 24 hours prior to transfection.

[00513] After 4-6 hours, the plating media was removed, cells were then washed with hepatocyte maintenance media/culture media with serum-free supplement pack (Invitrogen,

Cat. A1217601 and CM4000), and replaced with supplemented hepatocyte culture medium (Invitrogen, Cat. A1217601 and CM4000) containing LNP formulated Cas9 mRNA and guide RNA plus 3% serum. LNPs were diluted from a starting dose level of 100ng Cas9 mRNA and approximately 30nM guide RNA per well, carrying out serial dilutions down to 0.1ng mRNA and 0.03nM guide per well. Cells were incubated for approximately 72 hours at 37°C and 5% CO_2 atmosphere before cell lysis and NGS analysis as described herein.

Lipid Nanoparticle ("LNP") Formulation

[00514] LNP Procedure A: LNPs were formulated with a cationic lipid amine to RNA phosphate (N:P) molar ratio of about 4.5. The lipid nanoparticle components were dissolved in 100% ethanol with the following molar ratios: 45 mol-% (12.7 mM) cationic lipid (*e.g.*, (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)-carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate, also called 3-((4,4-bis(octyloxy)-butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,12Z)-octadeca-9,12-dienoate); 44 mol-% (12.4 mM) helper lipid (*e.g.*, cholesterol); 9 mol-% (2.53 mM) neutral lipid (*e.g.*, DSPC); and 2 mol-% (.563 mM) PEG (*e.g.*, PEG2k-DMG).

[00515] The LNPs were formed by microfluidic mixing of the lipid and RNA solutions using a Precision Nanosystems NanoAssemblr™ Benchtop Instrument, according to the manufacturer's protocol. A 2:1 ratio of aqueous to organic solvent was maintained during mixing using differential flow rates.

[00516] The RNA cargo were prepared in 25 mM sodium acetate buffer, pH 4.5, resulting in a concentration of RNA cargo of approximately 0.45 mg/mL, with a ratio of Cas9 mRNA:sgRNA of 1:1 (wt/wt). After mixing, the LNPs were collected, diluted in 50mM Tris at pH 7.5 (approximately 1:1), and then LNPs were exchanged into 50mM Tris at pH 7.5 (100-fold excess of sample volume), overnight at 4°C under gentle stirring using a 10 kDa Slide-a-LyzerTM G2 Dialysis Cassette (ThermoFisher Scientific). The LNPs were concentrated using 10kDa Amicon spin filter (centrifugation at 4000g at 4°C) to achieve twice the desired concentration. These concentrated LNPs were mixed 1:1 with 50mM Tris, 90mM NaCl, 10% sucrose at pH 7.5 (2X TSS). The resulting mixture was then filtered using a 0.2 μM sterile filter. The resulting filtrate was stored at 2-8 °C.

[00517] LNP Procedure B: LNPs were formulated with a cationic lipid amine to RNA phosphate (N:P) molar ratio of about 4.5. The lipid nanoparticle components were dissolved in 100% ethanol with the following molar ratios: 45 mol-% (12.7 mM) cationic lipid (*e.g.*, (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)-

carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate, also called 3-((4,4-bis(octyloxy)-butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,12Z)-octadeca-9,12-dienoate); 44 mol-% (12.4 mM) helper lipid (*e.g.*, cholesterol); 9 mol-% (2.53 mM) neutral lipid (*e.g.*, DSPC); and 2 mol-% (.563 mM) PEG (*e.g.*, PEG2k-DMG).

[00518] The LNPs were formed by microfluidic mixing of the lipid and RNA solutions using a Precision Nanosystems NanoAssemblr™ Benchtop Instrument, according to the manufacturer's protocol. A 2:1 ratio of aqueous to organic solvent was maintained during mixing using differential flow rates.

[00519] The RNA cargo were prepared in 25mM sodium citrate, 100mM sodium chloride at pH 5 resulting in a concentration of RNA cargo of approximately 0.45 mg/mL. After mixing, the LNPs were collected in water at the ratio of 3:1. The LNPs were incubated for an hour at room temperature and mixed 1:1 with water. Then they were buffer-exchanged into 1X TSS (50mM Tris, 45mM NaCl, 5% sucrose at pH 7.5) on PD-10 columns (GE Healthcare), using manufacturer's protocol. The LNPs were concentrated using 10kDa Amicon spin filter (centrifugation at 4000g at 4°C) to achieve the desired concentration. The resulting mixture was then filtered using a 0.2 μm sterile filter. The resulting filtrate was stored at -80°C.

[00520] LNP Procedure C: LNPs were formulated with a cationic lipid amine to RNA phosphate (N:P) molar ratio of about 6. The lipid nanoparticle components were dissolved in 100% ethanol with the following molar ratios: 50 mol-% (12.7 mM) cationic lipid (*e.g.*, (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)-carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate, also called 3-((4,4-bis(octyloxy)-butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,12Z)-octadeca-9,12-dienoate); 38 mol-% (12.4 mM) helper lipid (*e.g.*, cholesterol); 9 mol-% (2.53 mM) neutral lipid (*e.g.*, DSPC); and 3 mol-% (.563 mM) PEG (*e.g.*, PEG2k-DMG).

[00521] The LNPs were formed by microfluidic mixing of the lipid and RNA solutions using a Precision Nanosystems NanoAssemblr™ Benchtop Instrument, according to the manufacturer's protocol. A 2:1 ratio of aqueous to organic solvent was maintained during mixing using differential flow rates.

[00522] The RNA cargo was prepared in 25mM sodium citrate, 100mM sodium chloride at pH 5 resulting in a concentration of RNA cargo of approximately 0.45 mg/mL. LNPs were formed by an impinging jet mixing method where one stream of lipids in ethanol were mixed with two streams of RNA in citrate buffer through a 0.25mm ID Cross piece. The two RNA streams mix perpendicular to the ethanol stream. A fourth stream of water for injection (WFI)

meets the resulting particles in an in-line dilution through a 0.5mm ID Tee piece. All four streams are delivered at 10mL/min using a syringe pump. These LNPs were incubated for an hour at room temperature and then they were buffer-exchanged into 1X TSS (50mM Tris, 45mM NaCl, 5% sucrose at pH 7.5) on PD-10 columns (GE Healthcare), using manufacturer's protocol. The LNPs were concentrated using 10kDa Amicon spin filter (centrifugation at 4000g at 4°C) to achieve the desired concentration. The resulting mixture was then filtered using a 0.2 μm sterile filter. The resulting filtrate was stored at -80°C.

[00523] LNP Procedure D: LNPs were formulated with a cationic lipid amine to RNA phosphate (N:P) molar ratio of about 4.5. The lipid nanoparticle components were dissolved in 100% ethanol with the following molar ratios: 45 mol-% (12.7 mM) cationic lipid (*e.g.*, (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate, also called 3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,12Z)-octadeca-9,12-dienoate); 44 mol-% (12.4 mM) helper lipid (*e.g.*, cholesterol); 9 mol-% (2.53 mM) neutral lipid (*e.g.*, DSPC); and 2 mol-% (.563 mM) PEG (*e.g.*, PEG2k-DMG). The RNA cargo were prepared in 25 mM sodium acetate buffer, pH 4.5, resulting in a concentration of RNA cargo of approximately 0.45 mg/mL, with a ratio of Cas9 mRNA: sgRNA of 1:1 (wt/wt).

[00524] LNPs were prepared using a cross-flow technique by impinging jet mixing of the lipid in ethanol with two volumes of RNA solutions and one volume of water. The lipid in ethanol is mixed through a mixing cross with the two volumes of RNA solution. A fourth stream of water is mixed with the outlet stream of the cross through an inline tee. (*See* WO2016010840 Fig. 2.) The LNPs were held for 1 hour at room temperature, and further diluted with water (approximately 1:1 v/v). Diluted LNPs were concentrated using tangential flow filtration on a flat sheet cartridge (Sartorius, 100kD MWCO) and then buffer exchanged by diafiltration into 50 mM Tris, 45 mM NaCl, 5% (w/v) sucrose, pH 7.5 (TSS). Alternatively, the final buffer exchange into TSS was completed with PD-10 desalting columns (GE). If required, formulations were concentrated by centrifugation with Amicon 100 kDa centrifugal filters (Millipore). The resulting mixture was then filtered using a 0.2 μm sterile filter. The final LNP was stored at 4°C or -80°C until further use.

Next-Generation Sequencing ("NGS") and Analysis for On-Target Cleavage Efficiency

[00525] To quantitatively determine the efficiency of editing at the target location in the genome, deep sequencing was utilized to identify the presence of insertions and deletions introduced by gene editing.

[00526] PCR primers were designed around the target site (e.g., within the target gene of interest (e.g., TTR)), and the genomic area of interest was amplified.

[00527] Additional PCR was performed according to the manufacturer's protocols (Illumina) to add the necessary chemistry for sequencing. The amplicons were sequenced on an Illumina MiSeq instrument. The reads were aligned to the human reference genome (*e.g.*, hg38) after eliminating those having low quality scores. The resulting files containing the reads were mapped to the reference genome (BAM files), where reads that overlapped the target region of interest were selected and the number of wild type reads versus the number of reads which contain an insertion, substitution, or deletion was calculated.

[00528] The editing percentage (*e.g.*, the "editing efficiency" or "percent editing") is defined as the total number of sequence reads with insertions or deletions over the total number of sequence reads, including wild type.

LNP Delivery In Vivo

[00529] CD-1 female mice, ranging 6-10 weeks of age were used in each study involving mice. Sprague-Dawley female rats, ranging 6-10 weeks of age were used in each study involving rats. Animals were weighed and grouped according to body weight for preparing dosing solutions based on group average weight. LNPs were dosed via the lateral tail vein in a volume of 0.2 mL per animal (approximately 10 mL per kilogram body weight). The animals were observed at approximately 6 hours post dose for adverse effects. Body weight was measured at twenty-four hours post-administration, and animals were euthanized at various time points by exsanguination via cardiac puncture under isoflourane anesthesia. Blood was collected into serum separator tubes or into tubes containing buffered sodium citrate for plasma as described herein. For studies involving *in vivo* editing, liver tissue was collected from the median lobe from each animal for DNA extraction and analysis.

Genomic DNA Isolation

[00530] For the *in vivo* studies, genomic DNA was extracted from 10 mg of tissue using a bead-based extraction kit, MagMAX-96 DNA Multi-Sample Kit (ThermoFisher, Cat #4413020) according to the manufacturer's protocol, which includes homogenizing the tissue

in lysis buffer (approximately 400 µL/10 mg tissue). All DNA samples were normalized to 100 ng/µL concentration for PCR and subsequent NGS analysis, as described herein.

Transthyretin (TTR) ELISA Analysis Used in Animal Studies

[00531] Blood was collected, and the serum was isolated as indicated. The total TTR serum levels were determined using a Mouse Prealbumin (Transthyretin) ELISA Kit (Aviva Systems Biology, Cat. OKIA00111); rat TTR serum levels were measured using a rat specific ELISA kit (Aviva Systems Biology catalog number OKIA00159). Kit reagents and standards were prepared according to the manufacturer's protocol. Mouse serum was diluted to a final dilution of 10,000-fold with 1x assay diluent. This was done by carrying out two sequential 50-fold dilutions resulting in a 2500-fold dilution. A final 4-fold dilution step was carried out for a total sample dilution of 10,000-fold. Both standard curve dilutions (100 µL each) and diluted serum samples were added to each well of the ELISA plate pre-coated with capture antibody. The plate was incubated at room temperature for 30 minutes before washing. Enzyme-antibody conjugate (100 µL per well) was added for a 20-minute incubation. Unbound antibody conjugate was removed and the plate was washed again before the addition of the chromogenic substrate solution. The plate was incubated for 10 minutes before adding 100 µL of the stop solution, *e.g.*, sulfuric acid (approximately 0.3 M). The plate was read on a SpectraMax M5 plate reader at an absorbance of 450 nm. Serum TTR levels were calculated by SoftMax Pro software ver. 6.4.2 using a four parameter logistic curve fit off the standard curve. Final serum values were adjusted for the assay dilution. Percent knockdown (%KD) values were determined relative to controls, which generally were animals sham-treated with vehicle (transport and storage solution or TSS) unless otherwise indicated.

Nuclease Susceptibility Assays

[00532] Assays to determine and quantify where sgRNA cleavage occurs upon exposure to hepatocyte cytosol and to assess the effect of sgRNA modifications on stability were performed as follows. sgRNAs at 15 µM were incubated with human liver cytosol (XenoTech Product H0610.C) (adjusted to 0.01 mg/mL final protein concentration using pH 7.4 phosphate-buffered saline unless otherwise indicated) for a time period as indicated below. Reactions were stopped by adding 67 µL of proteinase K cell lysis buffer solution, which consisted of 3.230 mL water, 2.125 mL of tissue and cell lysis solution (Epicentre

Product MTC096H), and 340 µL of proteinase K (50 mg/mL from Epicentre Product MPRK092) and incubating for 30 minutes at 65°C in a thermo-mixer shaking at 750 RPM. 8 µL of 3M KCl was then added and the mixture was incubated for 10 minutes at 0°C. The mixtures were then centrifuged for 15 minutes at 1500 *g* to precipitate detergent. The supernatant was removed, diluted with 0.95 mL of dilution buffer (consisting of 0.01% Tween20 in water), and mixed with 1mL of pH 4.3 loading/dilution buffer (consisting of 10 mM sodium acetate, 10 % acetonitrile, 0.01 % Tween 20, 10 mM EDTA, and 1 mM TCEP) and the mixture was loaded on a Clarity® OTX™ SPE oligonucleotide purification cartridge. Washes were performed at pH 4.3, 5.5, and about 7, followed by elution at pH 9.0. The eluate was dried under vacuum and resuspended in 100 mM triethyl ammonium acetate (TEAAc).

[00533] Samples were then analyzed by LC/MS.

Example 2 – Modified Dual Guide Survey in HEK293 cells

[00534] A survey of chemical modification within crRNA was performed to identify negative influence of chemical modification at specific positions on editing efficacy. Each crRNA in this survey targeted the identical sequence within the human BCL11A gene. Test guides contained modifications within the spacer region of the crRNA (positions 1-20 from the 5' end) limited to either a single modified base or two adjacent bases with the same chemical modification as described in Table 6. Phosophothioate bonds (PS), inosine substitution, DNA bases, 2'OMe modifications, and unlocked nucleic acids (UNA) were assayed.

[00535] The human embryonic kidney adenocarcinoma cell line HEK293 constitutively expressing Spy Cas9 ("HEK293_Cas9") was cultured in DMEM media supplemented with 10% fetal bovine serum. Cells were plated at a density of 15,000 cells/well in a 96-well plate 20 hours prior to transfection (~70% confluent at time of transfection). Cells were transfected with Lipofectamine RNAiMAX (ThermoFisher, Cat. 13778150) according to the manufacturer's protocol. Cells were transfected with a lipoplex containing individual crRNA (3.1 nM), trRNA TR000002 (3.1 nM), Lipofectamine RNAiMAX (0.45 µL/well) and OptiMem. Cells were lysed 48 hours post transfection, and lysates were used directly in the PCR reaction that was analyzed for editing by NGS.

[00536] The editing results are shown in Table 6 and Figures 29A-F. Editing efficiency was reduced to near background levels by 2'OMe modification at positions 15 and 16 (Figure 29A). Phosphorothioate dinucleotides reduced editing by roughly 20% when placed at positions 19 and 20 of the spacer region (Figure 29B). Inosine substitution in the seed region

led to moderate negative impact on editing, for instance a roughly 30% decrease when modified at position 14 or a roughly 60% decrease at position 18 (Figure 29C). UNA base substitution at any single position from position 11 to position 20 severely reduced editing efficacy (Figure 29D). DNA base substitution at position 15 reduced editing efficiency by about one third (Figure 29E). DNA base substitution at both positions 15 and 16 reduced editing by about two thirds (Figure 29F).

Table 6 – Survey of Chemical Modification in crRNAs

Modification & Position	**Guide**	**Editing %**	**SD**	**Modification & Position**	**Guide**	**Editing %**	**SD**
No crRNA	n/a	0.2%	0.1%	Inosine 5	CR007559	95.8%	0.9%
Unmodified (none)	CR000309	92.2%	5.9%	Inosine 6	CR007560	94.3%	1.5%
2'OMe 1,2	CR005084	95.0%	0.5%	Inosine 7	CR007561	94.7%	0.4%
2'OMe 3,4	CR005085	97.3%	1.3%	Inosine 8	CR007562	92.8%	2.1%
2'OMe 5,6	CR005086	97.6%	0.5%	Inosine 9	CR007563	88.1%	4.2%
2'OMe 7,8	CR005087	89.5%	2.3%	Inosine 10	CR007564	91.8%	4.8%
2'OMe 9,10	CR005088	90.5%	1.4%	Inosine 11	CR007565	87.3%	4.9%
2'OMe 11,12	CR005089	92.5%	3.2%	Inosine 12	CR007566	80.9%	10.3%
2'OMe 13,14	CR005090	96.2%	0.4%	Inosine 13	CR007567	78.7%	5.4%
2'OMe 15,16	CR005091	1.4%	2.2%	Inosine 14	CR007568	61.5%	4.1%
2'OMe 17,18	CR005092	95.5%	1.1%	Inosine 15	CR007569	89.6%	5.3%
2'OMe 19,20	CR005093	84.1%	2.2%	Inosine 16	CR007570	72.7%	10.7%
PS 1,2	CR005100	96.6%	1.4%	Inosine 17	CR007571	77.9%	6.1%
PS 3,4	CR005101	97.8%	0.4%	Inosine 18	CR007572	35.1%	8.9%
PS 5,6	CR005102	97.3%	0.2%	Inosine 19	CR007573	69.7%	3.2%
PS 7,8	CR005103	90.0%	2.1%	Inosine 20	CR007574	88.1%	6.0%
PS 9,10	CR005104	89.7%	0.9%	DNA 1	CR007575	92.3%	1.9%
PS 11,12	CR005105	93.5%	1.2%	DNA 2	CR007576	91.8%	3.5%
PS 13,14	CR005106	86.5%	1.5%	DNA 3	CR007577	93.3%	1.9%
PS 15,16	CR005107	90.4%	5.7%	DNA 4	CR007578	94.0%	2.2%
PS 17,18	CR005108	91.1%	1.6%	DNA 5	CR007579	94.0%	1.3%
PS 19,20	CR005109	72.9%	0.8%	DNA 6	CR007580	94.1%	2.6%
UNA 1	CR007531	95.1%	2.2%	DNA 7	CR007581	94.5%	2.5%
UNA 2	CR007532	94.8%	2.6%	DNA 8	CR007582	94.8%	1.6%
UNA 3	CR007533	91.9%	4.4%	DNA 9	CR007583	94.6%	1.1%
UNA 4	CR007534	90.4%	5.2%	DNA 10	CR007584	95.7%	0.5%
UNA 5	CR007535	84.1%	8.5%	DNA 11	CR007585	93.1%	2.4%
UNA 6	CR007536	87.2%	7.9%	DNA 12	CR007586	95.0%	3.0%
UNA 7	CR007537	88.7%	6.0%	DNA 13	CR007587	91.5%	2.8%
UNA 8	CR007538	91.9%	3.7%	DNA 14	CR007588	88.8%	3.1%
UNA 9	CR007539	90.0%	7.9%	DNA 15	CR007589	59.8%	8.6%

Modification & Position	Guide	Editing %	SD	Modification & Position	Guide	Editing %	SD
UNA 10	CR007540	95.2%	2.2%	DNA 16	CR007590	83.2%	8.2%
UNA 11	CR007541	90.0%	4.1%	DNA 17	CR007591	93.3%	3.1%
UNA 12	CR007542	13.6%	9.8%	DNA 18	CR007592	92.0%	1.8%
UNA 13	CR007543	4.6%	5.9%	DNA 19	CR007593	92.5%	3.5%
UNA 14	CR007544	5.6%	5.3%	DNA 20	CR007594	86.7%	3.5%
UNA 15	CR007545	0.8%	1.2%	DNA 1,2	CR007595	95.8%	1.9%
UNA 16	CR007546	0.2%	0.2%	DNA 3,4	CR007596	92.7%	2.9%
UNA 17	CR007547	8.7%	5.2%	DNA 5,6	CR007597	88.3%	8.4%
UNA 18	CR007548	2.6%	2.1%	DNA 7,8	CR007598	94.4%	2.4%
UNA 19	CR007549	4.0%	1.8%	DNA 9,10	CR007599	92.1%	2.2%
UNA 20	CR007550	8.3%	5.1%	DNA 11,12	CR007600	93.3%	2.8%
Inosine 1	CR007555	94.9%	4.3%	DNA 13,14	CR007601	87.3%	1.3%
Inosine 2	CR007556	95.1%	0.2%	DNA 15,16	CR007602	33.9%	1.6%
Inosine 3	CR007557	92.2%	3.1%	DNA 17,18	CR007603	90.2%	3.4%
Inosine 4	CR007558	91.8%	2.9%	DNA 19,20	CR007604	82.3%	3.6%

Example 3 – Representative dual guide screen

[00537] The impacts of chemical modification type and position were evaluated in an editing screen of modified crRNAs. The screen assayed guides modified with 2'F, 2'OMe and PS. The complete pattern set was applied to guides targeting six distinct sites in the TTR gene. The final data set contained 1704 distinct guides and 284 unique modification patterns.

[00538] Guide modification patterns were computationally selected to minimize the number of modification combinations required to explore the large combinatorial space of possible modification patterns. Patterns were chosen to create a uniform distribution of modifications at each individual position and also at each pair of positions, so that no particular position or combination of positions was over-represented in the final set. This bias-minimization approach allowed for testing of individual positional effects as well as for detection of higher-order interaction effects between positions. Appropriate controls were added to the set to control for nuisance effects such as guide domain sequence, transfection efficiency and other experimental variability.

[00539] Each pattern in this set contained only one type of modification on positions 4 to 20; modification types were not mixed within patterns. The final set of patterns consisted of 3 groups of 96 patterns on positions 4 to 20 having 0-4 2'F modifications, 0-4 2'Ome modifications or 0-15 PS modifications. PS modifications were more heavily applied because previous observations indicated that the PS modification is better tolerated than 2'Flu or 2'Ome, and therefore less likely to show detectable effects when present in small numbers.

[00540] The human embryonic kidney adenocarcinoma cell line HEK293 constitutively expressing Spy Cas9 ("HEK293_Cas9") was cultured in DMEM media supplemented with 10% fetal bovine serum. Cells were plated at a density of 10,000 cells/well in a 96-well plate about 24 hours prior to transfection (~70% confluent at time of transfection). Cells were transfected with Lipofectamine RNAiMAX (ThermoFisher, Cat. 13778150) according to the manufacturer's protocol. Cells were transfected with a lipoplex containing individual crRNA (25 nM), trRNA TR009880 (25 nM), Lipofectamine RNAiMAX (0.3 μL/well) and OptiMem. Cells were lysed 48 hours post transfection, and lysates were used directly in the PCR reaction that was analyzed for editing by NGS.

[00541] The editing results are described in Table 8. Each row number represents a single modification pattern. The first two rows in the table show controls.

[00542] The overall impact of the modification type, targeting location, and guide domain sequence were evaluated in the modified guides. The data show a wide range of activity within the modified oligonucleotides, from close to 0 to nearly 90% editing. In general, the 2'F modifications were more well-tolerated than 2'OMe or PS modified guides, though the PS guides were more heavily modified, on average, than the other modifications. We observed a clear impact of guide domain's nucleobase sequence on response to modification. G480 and G490 variants were strongly impaired by 2'OMe modifications, but were resistant to 2'F and PS modifications, whereas G494, G499 and G502 variants were most strongly impacted by PS modifications, and less so by 2'OMe, and G488 responded similarly to all three modifications.

[00543] A regression-based analysis was conducted to identify the modification types with significant impact on guide activity. The editing data were first corrected for guide sequence and plate effects prior to modeling. Positional modification impacts were then modeled as independent linearly additive factors using standard regression techniques. A separate analysis examined whether there was evidence of interaction and non-linear relationships among positions. No significant higher-order effects were observed; the results reported below come from the initial linear regression analysis. The editing data for all the modified guides were corrected for guide sequence effects and then modeled for modification impact.

[00544] 2' modifications at a number of positions displayed negative impacts on editing as shown in Table 7 and Figure 30A-C. For example, 2'F or 2'OMe modification of positions 15 or 16 resulted in statistically significant inhibition of editing activity, suggesting that gRNAs with ribose at positions 15 and 16 are preferred. In contrast, 2'F modification of

position 19 significantly increased editing. The regression model found that this modification added an additional 13% editing over baseline, on average. 2'OMe had the opposite effect, strongly inhibiting editing. No other positions were consistently significantly impactful, although individual sequences were in many cases affected. PS modifications had a possible small negative effect at some positions, including position 19. Highly modified gRNA performed worse than less modified gRNA, indicating that the amount of PS modification may be relevant.

Table 7 – Editing Influence Scores

	2'F			2'Ome			PS		
Position	Score	SE	P value	Score	SE	P value	Score	SE	P value
4	0.065	0.045	0.151	0.027	0.015	0.084	0.002	0.011	0.885
5	0.058	0.044	0.186	-0.017	0.015	0.249	-0.020	0.010	0.054
6	-0.004	0.044	0.923	-0.009	0.015	0.555	-0.009	0.012	0.438
7	0.042	0.044	0.347	0.013	0.015	0.404	-0.018	0.011	0.100
8	-0.037	0.046	0.431	-0.037	0.016	0.020	-0.008	0.011	0.446
9	0.090	0.044	0.040	0.006	0.015	0.690	-0.023	0.010	0.025
10	0.010	0.045	0.819	-0.048	0.015	0.002	-0.002	0.011	0.821
11	-0.013	0.046	0.773	-0.001	0.015	0.947	-0.032	0.012	0.006
12	-0.051	0.045	0.262	-0.022	0.015	0.158	-0.022	0.011	0.049
13	-0.020	0.045	0.662	0.001	0.015	0.937	-0.023	0.011	0.039
14	0.000	0.045	0.995	0.027	0.015	0.078	-0.014	0.010	0.178
15	-0.160	0.044	< 4E-4	-0.201	0.015	< 2E-16	0.022	0.012	0.067
16	-0.164	0.045	< 3E-4	-0.165	0.015	< 2E-16	0.010	0.011	0.378
17	-0.050	0.045	0.266	-0.043	0.015	0.005	-0.023	0.011	0.047
18	0.026	0.043	0.545	-0.001	0.015	0.930	-0.013	0.011	0.259
19	0.131	0.044	0.003	-0.098	0.015	< 2E-10	-0.062	0.011	< 3E-8
20	-0.020	0.044	0.649	-0.006	0.015	0.694	-0.032	0.011	0.003

Table 8 – Editing in HEKCas9 cells with modified dgRNA

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR09711	51.3	10.8	CR10224	9.2	5.5	CR10319	40.3	7.7	CR10414	18.3	3.8	CR10509	19.8	6.6	CR09618	8.4	3.7
CR03353	57.5	13.9	CR03346	14.2	10.3	CR03366	49.3	7.7	CR03360	38.2	8.2	CR05303	16.6	5.6	CR00689	9.8	4.8
CR10040	70.9	13.6	CR10130	16.7	2.9	CR10225	74.5	6.3	CR10320	51.7	5.5	CR10415	39.6	1.3	CR10510	24.3	3.4
CR10041	70.4	7.0	CR10131	19.4	3.1	CR10226	50.2	10.7	CR10321	56.1	7.1	CR10416	49.9	6.6	CR10511	22.8	0.5
CR10042	41.9	36.5	CR10132	3.8	0.6	CR10227	38.4	3.8	CR10322	46.3	3.8	CR10417	25.9	4.3	CR10512	8.3	4.1
CR10043	72.5	6.8	CR10133	14.1	2.4	CR10228	61.5	2.8	CR10323	48.1	1.2	CR10418	45.9	7.8	CR10513	10.5	1.1
CR10044	61.9	11.7	CR10134	4.1	1.1	CR10229	52.5	4.9	CR10324	48.8	2.6	CR10419	35.3	2.8	CR10514	10.6	0.8
CR10045	70.0	6.7	CR10135	14.0	4.6	CR10230	49.7	3.7	CR10325	53.1	2.7	CR10420	43.4	5.0	CR10515	17.7	7.9
CR10046	79.3	6.9	CR10136	9.1	1.4	CR10231	53.9	3.9	CR10326	48.5	4.4	CR10421	46.0	2.4	CR10516	19.0	5.7
CR10047	63.6	7.1	CR10137	11.2	2.4	CR10232	55.6	1.9	CR10327	56.9	3.1	CR10422	38.0	3.0	CR10517	24.6	4.7
CR10048	77.1	6.2	CR10138	18.3	0.8	CR10233	44.6	4.2	CR10328	52.2	5.7	CR10423	39.4	4.2	CR10518	17.6	0.9
CR10049	71.5	8.2	CR10139	15.3	0.7	CR10234	37.4	2.8	CR10329	55.7	5.5	CR10424	41.7	8.5	CR10519	19.7	3.8
CR10050	77.0	6.7	CR10140	11.8	1.8	CR10235	57.3	2.5	CR10330	54.5	6.4	CR10425	45.4	7.6	CR10520	17.3	15.0
CR10051	65.6	6.1	CR10141	5.5	1.1	CR10236	25.8	4.7	CR10331	42.1	8.6	CR10426	26.7	4.3	CR10521	13.7	3.7
CR10052	65.4	4.1	CR10142	5.4	1.5	CR10237	25.1	2.6	CR10332	43.6	12.6	CR10427	24.3	5.7	CR10522	21.8	4.8
CR10053	58.5	17.0	CR10143	5.5	0.6	CR10238	33.0	5.0	CR10333	36.2	3.8	CR10428	32.3	10.9	CR10523	8.7	1.6
CR10054	59.0	18.4	CR10144	4.2	1.2	CR10239	29.7	3.6	CR10334	28.7	5.9	CR10429	31.3	2.0	CR10524	7.4	0.9
CR10055	50.0	14.7	CR10145	5.7	2.1	CR10240	27.6	5.4	CR10335	31.7	13.3	CR10430	31.9	5.4	CR10525	8.1	0.8
CR10056	50.0	18.2	CR10146	7.4	1.7	CR10241	37.2	8.0	CR10336	20.7	7.5	CR10431	33.4	5.9	CR10526	6.3	1.0
CR10057	47.2	18.0	CR10147	3.9	0.2	CR10242	29.4	5.6	CR10337	28.0	11.1	CR10432	30.4	6.3	CR10527	5.5	0.5
CR10058	37.9	18.0	CR10148	2.4	1.0	CR10243	17.1	1.8	CR10338	12.3	4.0	CR10433	20.2	6.2	CR10528	3.1	0.1
CR10059	66.4	14.4	CR10149	9.1	1.4	CR10244	22.3	3.5	CR10339	22.5	3.2	CR10434	28.1	6.1	CR10529	7.8	1.4
CR10060	76.6	10.2	CR10150	13.6	3.9	CR10245	55.1	11.0	CR10340	45.2	1.8	CR10435	46.9	6.8	CR10530	28.3	6.2
CR10061	63.1	5.9	CR10151	3.1	1.0	CR10246	45.6	5.9	CR10341	41.2	10.3	CR10436	24.7	3.3	CR10531	12.8	2.8
CR10062	60.6	18.6	CR10152	9.6	2.8	CR10247	31.2	4.7	CR10342	18.5	8.5	CR10437	17.7	3.0	CR10532	8.8	2.3

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR10063	47.0	15.2	CR10153	4.7	0.5	CR10248	31.4	9.3	CR10343	16.9	3.6	CR10438	20.7	1.6	CR10533	11.8	1.1
CR10064	46.0	21.0	CR10154	2.4	0.3	CR10249	25.9	1.0	CR10344	16.2	2.9	CR10439	24.1	1.6	CR10534	5.4	1.2
CR10065	51.0	11.0	CR10155	3.6	0.6	CR10250	27.1	4.4	CR10345	18.8	5.3	CR10440	28.4	4.3	CR10535	7.7	2.2
CR10066	48.0	10.5	CR10156	4.9	0.9	CR10251	24.2	3.8	CR10346	10.8	3.2	CR10441	26.0	3.2	CR10536	6.5	0.8
CR10067	45.9	14.7	CR10157	3.5	1.0	CR10252	15.2	1.5	CR10347	19.7	5.8	CR10442	31.8	5.5	CR10537	10.7	0.5
CR09753	48.7	15.0	CR10158	7.1	0.9	CR10253	14.3	2.1	CR10348	19.2	1.5	CR10443	29.7	0.7	CR09660	6.8	1.7
CR10068	39.0	13.6	CR10159	2.5	0.1	CR10254	17.8	2.4	CR10349	12.3	2.5	CR10444	17.9	2.4	CR10538	4.4	0.7
CR10069	57.3	17.3	CR10160	6.8	1.3	CR10255	21.2	5.3	CR10350	24.3	3.8	CR10445	27.2	4.0	CR10539	6.5	0.8
CR10070	62.0	13.3	CR10161	3.5	0.7	CR10256	28.2	24.3	CR10351	35.0	0.5	CR10446	23.1	2.7	CR10540	4.9	0.6
CR10071	42.7	7.8	CR10162	5.9	1.4	CR10257	58.6	4.0	CR10352	35.5	8.6	CR10447	25.9	2.4	CR10541	9.8	3.7
CR10072	54.0	19.1	CR10163	3.3	0.8	CR10258	35.9	5.0	CR10353	31.4	10.1	CR10448	24.0	3.5	CR10542	12.3	4.0
CR10073	45.1	18.8	CR10164	1.4	0.2	CR10259	6.8	1.1	CR10354	15.2	7.0	CR10449	17.7	4.0	CR10543	3.2	0.4
CR10074	56.0	17.1	CR10165	4.1	0.9	CR10260	23.7	0.9	CR10355	27.1	5.2	CR10450	32.3	1.1	CR10544	7.6	1.4
CR10075	60.8	19.1	CR10166	4.5	0.7	CR10261	21.4	1.8	CR10356	27.8	6.5	CR10451	30.7	6.6	CR10545	8.8	1.0
CR10076	14.0	5.9	CR10167	0.9	0.3	CR10262	11.8	1.9	CR10357	8.0	2.5	CR10452	14.1	2.9	CR10546	2.1	0.2
CR10077	50.5	14.1	CR10168	6.4	0.8	CR10263	15.6	2.0	CR10358	15.3	2.1	CR10453	25.4	1.7	CR10547	8.0	1.7
CR10078	47.0	10.3	CR10169	4.0	0.8	CR10264	10.2	2.2	CR10359	16.7	3.9	CR10454	25.2	4.2	CR10548	10.8	1.0
CR10079	54.9	14.3	CR10170	4.6	0.5	CR10265	18.9	3.6	CR10360	28.1	4.6	CR10455	29.7	6.3	CR10549	9.2	2.5
CR10080	71.8	12.2	CR10171	10.5	2.3	CR10266	62.0	2.1	CR10361	35.7	1.6	CR10456	42.0	6.8	CR10550	11.8	0.8
CR10081	67.8	12.0	CR10172	14.0	3.9	CR10267	61.7	2.0	CR10362	44.2	5.6	CR10457	39.8	4.4	CR10551	21.9	12.2
CR10082	26.4	7.1	CR10173	3.5	0.8	CR10268	21.6	1.9	CR10363	22.7	7.7	CR10458	20.0	6.7	CR10552	5.1	2.2
CR10083	51.3	26.1	CR10174	3.9	0.6	CR10269	26.2	2.5	CR10364	36.6	7.1	CR10459	25.7	7.4	CR10553	7.7	4.6
CR10084	43.4	13.4	CR10175	4.3	1.0	CR10270	18.1	3.9	CR10365	19.4	4.3	CR10460	32.3	4.8	CR10554	5.8	0.8
CR10085	53.9	24.9	CR10176	7.9	1.0	CR10271	30.7	0.5	CR10366	16.6	1.0	CR10461	31.5	3.3	CR10555	11.0	4.9
CR10086	40.6	18.3	CR10177	2.2	0.2	CR10272	6.7	1.0	CR10367	14.1	3.5	CR10462	16.6	3.6	CR10556	2.4	0.5
CR10087	45.4	15.9	CR10178	4.9	1.2	CR10273	32.3	5.6	CR10368	15.6	7.0	CR10463	26.4	4.6	CR10557	4.5	0.3

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR10088	45.2	16.7	CR10179	4.1	0.7	CR10274	14.3	2.9	CR10369	15.7	0.8	CR10464	23.5	4.4	CR10558	9.4	0.9
CR10089	51.0	18.7	CR10180	4.5	1.0	CR10275	15.4	5.7	CR10370	14.9	3.6	CR10465	28.1	4.0	CR10559	4.8	1.5
CR10090	60.3	16.7	CR10181	3.8	1.0	CR10276	27.2	1.2	CR10371	28.5	4.4	CR10466	25.2	3.6	CR10560	4.9	1.0
CR10091	60.0	18.9	CR10182	4.4	1.8	CR10277	45.2	3.9	CR10372	28.0	0.3	CR10467	32.1	2.7	CR10561	4.6	1.4
CR10092	52.9	45.7	CR10183	13.9	2.5	CR10278	66.3	5.3	CR10373	38.3	5.1	CR10468	34.8	8.7	CR10562	16.7	7.1
CR10093	50.0	14.6	CR10184	7.3	0.7	CR10279	23.2	3.3	CR10374	18.0	3.9	CR10469	28.6	5.5	CR10563	7.2	1.7
CR10094	60.4	15.5	CR10185	3.9	0.4	CR10280	31.3	4.4	CR10375	15.2	1.8	CR10470	33.5	8.9	CR10564	7.8	1.7
CR10095	29.0	12.4	CR10186	2.6	0.3	CR10281	21.9	3.7	CR10376	12.6	1.2	CR10471	27.3	7.2	CR10565	4.6	1.6
CR10096	51.0	20.1	CR10187	11.6	3.7	CR10282	22.3	0.6	CR10377	17.9	3.5	CR10472	28.9	4.5	CR10566	8.1	3.5
CR10097	41.1	14.6	CR10188	4.7	0.3	CR10283	28.7	2.9	CR10378	14.8	4.9	CR10473	33.8	8.7	CR10567	9.9	4.0
CR10098	35.6	30.7	CR10189	2.3	0.1	CR10284	9.1	3.8	CR10379	12.9	0.9	CR10474	24.5	4.5	CR10568	4.5	1.4
CR10099	47.7	14.1	CR10190	2.6	0.6	CR10285	14.9	2.7	CR10380	14.5	3.2	CR10475	25.7	5.0	CR10569	9.2	3.0
CR10100	30.6	26.9	CR10191	3.9	1.1	CR10286	18.4	3.4	CR10381	20.0	1.3	CR10476	31.5	5.2	CR10570	6.8	2.3
CR10101	44.5	38.9	CR10192	4.4	0.9	CR10287	19.8	2.7	CR10382	19.3	2.4	CR10477	31.3	8.7	CR10571	8.8	2.8
CR10102	56.1	48.5	CR10193	15.1	7.1	CR10288	71.5	4.8	CR10383	42.1	5.9	CR10478	42.0	5.0	CR10572	11.1	2.2
CR10103	55.0	20.0	CR10194	9.8	0.3	CR10289	41.1	4.2	CR10384	36.4	1.5	CR10479	26.9	5.5	CR10573	11.1	3.8
CR10104	53.6	23.1	CR10195	2.0	0.9	CR10290	13.4	2.2	CR10385	18.2	1.1	CR10480	18.4	2.6	CR10574	3.8	0.7
CR10105	41.9	18.3	CR10196	1.8	0.2	CR10291	15.1	2.6	CR10386	12.8	1.9	CR10481	25.1	3.7	CR10575	11.3	11.1
CR10106	52.4	16.5	CR10197	5.1	2.0	CR10292	21.9	6.0	CR10387	16.4	1.0	CR10482	27.1	3.3	CR10576	12.6	2.1
CR10107	33.6	11.2	CR10198	2.2	0.9	CR10293	16.4	5.6	CR10388	14.5	3.7	CR10483	19.2	2.9	CR10577	4.2	1.2
CR10108	61.6	13.7	CR10199	14.0	3.7	CR10294	35.1	7.9	CR10389	16.6	3.4	CR10484	25.8	5.9	CR10578	7.0	2.1
CR10109	50.5	12.9	CR10200	4.5	2.4	CR10295	34.1	2.8	CR10390	18.3	1.9	CR10485	21.6	2.3	CR10579	5.6	1.8
CR10110	40.7	11.5	CR10201	1.0	0.5	CR10296	11.3	3.5	CR10391	11.3	3.1	CR10486	16.3	2.7	CR10580	2.1	0.9
CR10111	59.6	18.7	CR10202	5.2	0.9	CR10297	22.6	1.2	CR10392	21.3	7.3	CR10487	24.2	4.0	CR10581	11.5	2.5
CR10112	13.8	11.5	CR10203	12.4	2.2	CR10298	58.5	5.2	CR10393	43.1	3.4	CR10488	34.7	2.5	CR10582	11.7	5.3
CR10113	82.2	7.0	CR10204	28.6	8.2	CR10299	70.8	10.4	CR10394	53.7	6.0	CR10489	57.2	6.9	CR10583	18.8	13.9

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR10114	36.2	5.7	CR10205	3.4	1.0	CR10300	50.2	14.2	CR10395	45.8	2.5	CR10490	37.2	6.3	CR10584	9.5	4.5
CR10115	77.2	7.1	CR10206	13.6	1.4	CR10301	63.4	10.9	CR10396	49.2	2.3	CR10491	35.3	8.3	CR10585	24.5	7.5
CR10116	38.6	4.4	CR10207	1.6	0.3	CR10302	24.5	12.4	CR10397	34.6	4.7	CR10492	16.5	2.6	CR10586	1.8	0.7
CR10117	73.1	6.8	CR10208	12.3	2.5	CR10303	49.2	11.6	CR10398	53.9	2.6	CR10493	44.8	5.1	CR10587	11.8	6.3
CR10118	76.0	3.3	CR10209	15.9	2.9	CR10304	58.7	13.6	CR10399	39.5	3.5	CR10494	46.5	4.4	CR10588	9.1	2.9
CR10119	78.5	3.6	CR10210	9.7	1.5	CR10305	43.5	10.0	CR10400	45.2	3.4	CR10495	45.3	3.2	CR10589	10.8	4.7
CR10120	72.6	6.7	CR10211	6.2	1.3	CR10306	31.5	10.0	CR10401	44.2	2.4	CR10496	45.6	4.8	CR10590	5.7	2.3
CR10121	71.6	9.8	CR10212	10.7	0.6	CR10307	57.9	16.1	CR10402	43.9	2.2	CR10497	48.9	3.6	CR10591	26.9	10.4
CR10122	77.2	5.8	CR10213	21.1	6.1	CR10308	55.7	5.6	CR10403	33.4	1.4	CR10498	44.9	3.5	CR10592	18.4	6.0
CR10123	50.3	11.7	CR10214	5.7	2.2	CR10309	74.5	4.3	CR10404	35.5	3.4	CR10499	41.1	2.4	CR10593	9.3	7.9
CR09734	66.6	7.6	CR10215	9.5	1.7	CR10310	56.6	4.1	CR10405	55.5	3.4	CR10500	34.5	6.2	CR09641	13.2	1.7
CR09723	62.5	14.2	CR10216	6.0	1.2	CR10311	55.1	6.0	CR10406	43.2	2.1	CR10501	31.6	2.6	CR09630	14.3	6.7
CR09726	46.1	17.4	CR10217	2.8	0.9	CR10312	13.3	3.2	CR10407	24.0	8.6	CR10502	23.7	3.1	CR09633	7.4	1.6
CR10124	23.5	12.2	CR10218	1.2	0.1	CR10313	21.8	2.2	CR10408	21.1	5.2	CR10503	21.3	4.1	CR10594	5.5	3.3
CR10125	49.8	9.5	CR10219	5.0	0.8	CR10314	32.0	5.6	CR10409	38.8	8.0	CR10504	20.6	2.1	CR10595	7.0	1.5
CR10126	46.8	8.4	CR10220	4.2	0.9	CR10315	18.6	0.6	CR10410	17.7	4.8	CR10505	27.6	1.5	CR10596	6.0	0.9
CR10127	42.8	13.7	CR10221	4.1	0.5	CR10316	11.3	0.9	CR10411	20.1	6.8	CR10506	14.7	3.9	CR10597	4.6	0.2
CR10128	37.2	19.3	CR10222	2.1	0.6	CR10317	12.1	3.9	CR10412	19.1	4.2	CR10507	20.9	1.0	CR10598	2.2	0.4
CR10129	49.9	13.5	CR10223	7.3	0.7	CR10318	26.4	5.2	CR10413	18.0	4.5	CR10508	15.6	4.2	CR10599	5.4	1.8
CR10600	64.9	4.7	CR10691	15.2	2.4	CR10785	75.2	3.6	CR10879	39.8	4.8	CR10973	26.3	6.4	CR11067	10.9	3.0
CR10601	33.1	4.2	CR10692	1.4	0.3	CR10786	48.5	7.7	CR10880	12.1	2.7	CR10974	14.2	7.3	CR11068	3.0	1.0
CR10602	2.0	0.2	CR10693	0.9	0.2	CR10787	29.1	3.6	CR10881	5.7	0.2	CR10975	4.8	0.5	CR11069	0.5	0.1
CR10603	45.4	2.9	CR10694	10.6	0.6	CR10788	65.6	6.9	CR10882	42.4	12.3	CR10976	27.5	4.1	CR11070	8.8	3.5
CR10604	49.9	3.4	CR10695	9.7	0.8	CR10789	62.7	1.3	CR10883	38.9	8.2	CR10977	29.1	9.8	CR11071	9.8	0.8
CR10605	42.0	3.4	CR10696	4.2	0.4	CR10790	58.9	4.2	CR10884	50.8	11.5	CR10978	26.1	11.7	CR11072	7.8	2.5
CR10606	57.7	4.7	CR10697	6.5	0.4	CR10791	71.4	3.6	CR10885	44.9	9.2	CR10979	24.6	2.3	CR11073	14.2	4.2

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR10607	66.0	2.2	CR10698	8.8	1.8	CR10792	64.4	8.2	CR10886	45.5	8.8	CR10980	31.5	3.4	CR11074	14.7	5.4
CR10608	72.2	5.1	CR10699	15.0	2.9	CR10793	61.8	2.2	CR10887	34.8	8.0	CR10981	33.3	2.6	CR11075	15.6	3.7
CR10609	50.7	4.1	CR10700	12.2	0.7	CR10794	71.9	5.3	CR10888	44.4	9.7	CR10982	40.0	10.8	CR11076	14.8	7.1
CR10610	75.2	3.6	CR10701	15.0	2.9	CR10795	75.3	6.8	CR10889	49.4	13.9	CR10983	41.7	5.9	CR11077	14.6	0.7
CR10611	2.6	0.5	CR10702	0.3	0.1	CR10796	2.9	1.1	CR10890	3.9	1.6	CR10984	8.3	9.8	CR11078	0.3	0.2
CR10612	25.8	8.3	CR10703	12.2	1.9	CR10797	44.7	7.7	CR10891	27.4	12.8	CR10985	18.4	1.7	CR11079	11.8	1.2
CR10613	30.8	9.2	CR10704	8.7	1.3	CR10798	30.8	5.1	CR10892	19.3	3.2	CR10986	11.3	3.8	CR11080	7.2	1.3
CR10614	28.9	4.8	CR10705	5.1	0.5	CR10799	28.0	4.1	CR10893	26.5	5.3	CR10987	12.5	3.6	CR11081	4.7	0.9
CR10615	25.0	4.3	CR10706	5.7	0.5	CR10800	22.2	2.2	CR10894	25.6	3.0	CR10988	13.8	4.9	CR11082	4.9	0.9
CR10616	28.5	7.6	CR10707	8.7	2.5	CR10801	27.8	4.9	CR10895	28.3	4.3	CR10989	21.9	9.4	CR11083	10.3	3.3
CR10617	24.7	3.1	CR10708	8.6	0.8	CR10802	26.9	5.0	CR10896	27.2	10.0	CR10990	16.9	3.3	CR11084	4.9	0.6
CR10618	0.6	0.1	CR10709	0.8	0.2	CR10803	6.2	0.5	CR10897	4.5	2.4	CR10991	2.8	0.5	CR11085	0.3	0.1
CR10619	39.1	4.5	CR10710	13.3	1.9	CR10804	27.8	4.2	CR10898	24.3	5.1	CR10992	19.1	1.4	CR11086	6.8	0.2
CR10620	56.3	4.2	CR10711	15.1	3.9	CR10805	55.1	9.8	CR10899	25.4	6.5	CR10993	36.9	4.3	CR11087	11.6	0.9
CR10621	3.4	0.4	CR10712	0.4	0.1	CR10806	1.7	0.4	CR10900	4.1	0.4	CR10994	4.4	4.3	CR11088	0.1	0.0
CR10622	8.4	1.4	CR10713	1.2	0.2	CR10807	10.8	2.3	CR10901	6.8	2.0	CR10995	8.0	7.0	CR11089	1.5	0.4
CR10623	19.9	3.8	CR10714	3.2	0.8	CR10808	12.0	1.9	CR10902	17.7	4.0	CR10996	11.8	8.4	CR11090	5.1	0.8
CR10624	22.4	1.6	CR10715	9.2	2.6	CR10809	20.3	5.2	CR10903	15.8	5.9	CR10997	11.5	1.9	CR11091	3.9	0.6
CR10625	24.9	1.1	CR10716	8.8	1.1	CR10810	26.6	4.1	CR10904	22.8	1.1	CR10998	14.7	5.3	CR11092	5.1	1.1
CR10626	11.5	1.1	CR10717	1.1	0.3	CR10811	11.9	2.6	CR10905	5.2	1.6	CR10999	2.6	0.9	CR11093	1.1	0.6
CR10627	19.1	1.5	CR10718	7.5	2.3	CR10812	34.8	4.4	CR10906	14.8	0.9	CR11000	17.3	4.6	CR11094	5.1	3.6
CR10628	25.9	4.8	CR10719	7.1	1.3	CR10813	15.6	3.2	CR10907	27.3	6.9	CR11001	20.2	6.4	CR11095	7.7	5.5
CR10629	23.2	3.3	CR10720	9.3	2.1	CR10814	17.7	2.4	CR10908	14.5	5.2	CR11002	13.4	4.3	CR11096	11.3	4.6
CR10630	34.8	3.2	CR10721	10.2	5.3	CR10815	29.3	6.6	CR10909	19.7	2.8	CR11003	23.4	2.3	CR11097	10.5	4.3
CR10631	6.1	4.9	CR10722	0.2	0.1	CR10816	1.4	0.2	CR10910	1.8	0.3	CR11004	0.9	0.2	CR11098	0.3	0.1
CR10632	3.0	0.4	CR10723	1.2	0.2	CR10817	18.5	3.5	CR10911	5.7	0.6	CR11005	7.1	0.2	CR11099	0.6	0.3

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR10633	25.3	4.4	CR10724	9.5	1.9	CR10818	33.6	5.9	CR10912	15.1	2.1	CR11006	19.6	3.5	CR11100	11.3	1.0
CR10634	1.0	0.0	CR10725	0.3	0.1	CR10819	1.3	0.1	CR10913	2.3	0.9	CR11007	0.7	0.2	CR11101	0.3	0.1
CR10635	34.4	2.7	CR10726	11.5	3.3	CR10820	17.0	2.3	CR10914	24.4	5.5	CR11008	14.7	6.3	CR11102	7.6	1.3
CR10636	11.6	1.4	CR10727	1.0	0.2	CR10821	8.8	1.1	CR10915	6.6	2.2	CR11009	2.5	0.6	CR11103	1.0	0.3
CR10637	0.4	0.1	CR10728	0.9	0.1	CR10822	4.8	0.4	CR10916	4.0	1.6	CR11010	1.6	0.4	CR11104	0.4	0.1
CR10638	21.9	4.6	CR10729	7.4	3.2	CR10823	27.5	5.1	CR10917	18.2	4.0	CR11011	21.7	6.5	CR11105	3.8	0.8
CR10639	22.1	5.6	CR10730	3.1	0.9	CR10824	12.9	1.1	CR10918	25.3	0.7	CR11012	12.8	2.6	CR11106	2.0	0.7
CR10640	30.0	2.0	CR10731	7.9	2.0	CR10825	29.4	6.7	CR10919	18.9	5.9	CR11013	12.9	1.5	CR11107	3.9	0.3
CR10641	54.1	1.9	CR10732	14.0	5.5	CR10826	38.4	2.5	CR10920	22.0	4.1	CR11014	19.8	1.8	CR11108	11.3	1.2
CR10642	34.3	3.0	CR10733	1.7	0.3	CR10827	41.0	3.8	CR10921	16.3	3.6	CR11015	9.3	2.4	CR11109	6.2	1.5
CR10643	1.3	0.4	CR10734	0.8	0.2	CR10828	8.7	2.4	CR10922	2.8	0.6	CR11016	2.6	0.9	CR11110	0.7	0.1
CR10644	19.5	3.9	CR10735	8.2	1.7	CR10829	16.7	3.0	CR10923	24.7	3.5	CR11017	12.7	1.7	CR11111	7.8	1.3
CR10645	22.8	1.5	CR10736	16.5	6.2	CR10830	18.9	6.4	CR10924	23.8	5.1	CR11018	10.9	3.8	CR11112	6.7	2.5
CR10646	29.2	3.2	CR10737	9.9	0.9	CR10831	30.6	1.7	CR10925	16.6	5.1	CR11019	16.0	4.0	CR11113	13.2	3.3
CR10647	1.0	0.1	CR10738	0.3	0.1	CR10832	1.2	0.3	CR10926	2.2	0.2	CR11020	0.8	0.1	CR11114	0.2	0.1
CR10648	20.6	6.6	CR10739	6.7	0.8	CR10833	21.2	5.7	CR10927	17.2	5.4	CR11021	6.4	0.8	CR11115	5.5	0.9
CR10649	19.3	2.5	CR10740	4.9	0.8	CR10834	28.2	4.6	CR10928	18.7	5.7	CR11022	17.3	4.1	CR11116	4.1	0.8
CR10650	22.2	3.1	CR10741	6.2	0.7	CR10835	20.2	0.3	CR10929	20.5	3.7	CR11023	22.6	7.3	CR11117	2.1	0.3
CR10651	29.8	5.7	CR10742	6.0	1.7	CR10836	12.0	2.4	CR10930	22.1	1.8	CR11024	12.1	4.8	CR11118	4.8	1.1
CR10652	1.9	0.2	CR10743	0.3	0.1	CR10837	1.7	0.2	CR10931	3.4	0.9	CR11025	1.1	0.6	CR11119	0.1	0.1
CR10653	2.3	0.4	CR10744	0.3	0.1	CR10838	3.0	1.1	CR10932	1.3	0.2	CR11026	1.2	0.4	CR11120	0.2	0.0
CR10654	25.8	3.6	CR10745	11.8	5.7	CR10839	17.5	3.1	CR10933	18.0	2.8	CR11027	11.2	3.0	CR11121	3.9	0.8
CR10655	23.8	3.4	CR10746	8.5	2.0	CR10840	17.0	0.6	CR10934	10.8	0.6	CR11028	8.7	3.2	CR11122	3.4	0.3
CR10656	0.8	0.4	CR10747	0.5	0.2	CR10841	4.6	1.0	CR10935	1.4	0.2	CR11029	1.5	0.3	CR11123	0.2	0.1
CR10657	18.0	4.6	CR10748	1.4	0.4	CR10842	10.8	3.1	CR10936	2.9	0.5	CR11030	2.2	0.5	CR11124	2.2	0.2
CR10658	21.8	1.9	CR10749	8.5	1.3	CR10843	14.6	1.9	CR10937	13.9	0.9	CR11031	18.5	6.7	CR11125	5.8	0.9

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR10659	1.0	0.1	CR10750	0.2	0.1	CR10844	0.4	0.0	CR10938	1.5	0.3	CR11032	0.7	0.1	CR11126	0.1	0.1
CR10660	26.8	1.6	CR10751	8.4	2.9	CR10845	19.5	2.9	CR10939	20.1	0.7	CR11033	13.2	2.4	CR11127	3.8	0.8
CR10661	20.9	0.6	CR10752	6.7	2.3	CR10846	19.2	2.4	CR10940	14.8	3.3	CR11034	12.8	3.3	CR11128	5.6	0.8
CR10662	34.2	1.4	CR10753	5.6	3.8	CR10847	15.9	1.0	CR10941	18.9	5.8	CR11035	20.6	0.6	CR11129	7.3	1.3
CR10663	54.8	2.7	CR10754	35.2	23.3	CR10848	38.7	2.6	CR10942	22.2	0.5	CR11036	24.9	4.5	CR11130	21.2	8.2
CR10664	46.8	4.0	CR10755	9.5	3.8	CR10849	28.8	4.0	CR10943	22.5	4.2	CR11037	19.3	4.1	CR11131	9.2	3.7
CR10665	0.3	0.2	CR10756	0.2	0.1	CR10850	0.3	0.1	CR10944	1.0	0.2	CR11038	0.5	0.2	CR11132	0.1	0.1
CR10666	0.9	0.2	CR10757	0.5	0.1	CR10851	4.7	1.6	CR10945	1.6	0.6	CR11039	1.0	0.5	CR11133	0.3	0.1
CR10667	40.8	6.0	CR10758	9.4	1.7	CR10852	34.4	8.8	CR10946	16.7	0.8	CR11040	19.4	0.2	CR11134	7.0	1.6
CR10668	0.7	0.3	CR10759	0.5	0.1	CR10853	4.8	1.6	CR10947	2.5	0.8	CR11041	1.5	0.4	CR11135	0.4	0.1
CR10669	32.0	9.7	CR10760	1.9	0.6	CR10854	23.6	6.3	CR10948	11.6	2.6	CR11042	5.0	0.7	CR11136	5.8	1.5
CR10670	37.8	13.5	CR10761	10.2	1.9	CR10855	21.5	7.3	CR10949	15.1	3.3	CR11043	20.4	3.1	CR11137	5.5	1.2
CR10671	1.3	0.4	CR10762	0.2	0.0	CR10856	0.6	0.2	CR10950	2.1	0.4	CR11044	0.8	0.3	CR11138	0.1	0.1
CR10672	38.2	2.8	CR10763	7.8	2.6	CR10857	20.8	2.6	CR10951	15.3	3.1	CR11045	12.2	4.3	CR11139	5.8	0.7
CR10673	7.2	1.1	CR10764	0.3	0.1	CR10858	1.4	0.5	CR10952	1.1	0.2	CR11046	1.5	0.2	CR11140	0.2	0.1
CR10674	81.0	2.3	CR10765	29.6	7.0	CR10859	59.8	8.9	CR10953	42.1	3.7	CR11047	35.8	8.0	CR11141	11.8	3.3
CR10675	2.1	0.3	CR10766	1.2	0.5	CR10860	6.9	3.3	CR10954	3.6	1.0	CR11048	3.2	0.3	CR11142	0.4	0.1
CR10676	41.3	7.7	CR10767	2.0	0.4	CR10861	22.1	10.2	CR10955	5.0	2.1	CR11049	3.6	1.5	CR11143	5.3	2.1
CR10677	0.2	0.1	CR10768	0.2	0.1	CR10862	0.4	0.2	CR10956	1.0	0.3	CR11050	0.6	0.2	CR11144	0.1	0.0
CR10678	26.2	2.7	CR10769	2.7	0.7	CR10863	31.4	10.7	CR10957	16.2	5.9	CR11051	6.0	1.0	CR11145	4.3	4.0
CR10679	71.1	3.1	CR10770	26.4	8.9	CR10864	61.6	13.5	CR10958	33.3	6.7	CR11052	23.5	3.4	CR11146	15.3	2.2
CR10680	57.8	7.9	CR10771	8.7	4.7	CR10865	60.2	10.0	CR10959	38.1	9.3	CR11053	24.4	7.9	CR11147	7.3	2.2
CR10681	3.6	0.6	CR10772	0.3	0.1	CR10866	1.4	0.4	CR10960	2.1	0.8	CR11054	0.5	0.1	CR11148	0.2	0.1
CR10682	69.4	1.6	CR10773	32.8	12.4	CR10867	47.8	6.2	CR10961	17.7	4.7	CR11055	35.3	7.6	CR11149	32.5	6.9
CR10683	33.4	10.7	CR10774	1.2	0.5	CR10868	29.6	6.6	CR10962	8.5	3.9	CR11056	7.4	1.4	CR11150	1.5	0.4
CR10684	5.1	1.8	CR10775	2.0	1.4	CR10869	20.1	7.3	CR10963	3.2	0.9	CR11057	3.1	1.2	CR11151	0.7	0.2

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR09687	38.3	3.2	CR10776	3.2	0.6	CR10870	37.3	2.2	CR10964	45.6	11.5	CR11058	26.3	2.9	CR09583	13.7	5.0
CR09676	67.8	6.9	CR10777	17.2	7.9	CR10871	56.7	4.5	CR10965	39.2	18.0	CR11059	15.6	0.6	CR09586	3.7	0.7
CR09679	25.0	4.3	CR10778	7.6	2.6	CR10872	18.1	2.3	CR10966	21.3	8.8	CR11060	8.0	1.5	CR09594	5.6	2.9
CR10685	0.4	0.3	CR10779	0.5	0.1	CR10873	6.9	1.0	CR10967	2.5	0.4	CR11061	1.6	0.3	CR11152	0.1	0.1
CR10686	24.3	3.8	CR10780	6.4	0.8	CR10874	24.1	5.0	CR10968	17.2	5.8	CR11062	13.6	8.0	CR11153	7.4	1.1
CR10687	34.6	3.5	CR10781	10.6	3.4	CR10875	20.0	3.7	CR10969	17.3	3.9	CR11063	13.0	2.0	CR11154	5.2	1.0
CR10688	27.1	3.4	CR10782	4.0	1.1	CR10876	7.3	0.5	CR10970	16.0	5.2	CR11064	9.1	2.7	CR11155	2.2	0.3
CR10689	0.3	0.0	CR10783	0.2	0.1	CR10877	0.5	0.2	CR10971	2.1	0.2	CR11065	0.7	0.1	CR11156	0.1	0.1
CR10690	11.9	2.4	CR10784	0.4	0.1	CR10878	6.3	1.4	CR10972	3.4	0.3	CR11066	2.5	0.7	CR11157	0.6	0.1
CR11158	79.4	4.1	CR11252	11.9	1.3	CR11346	89.0	2.5	CR11440	38.4	9.5	CR11534	59.1	7.6	CR11628	16.4	0.9
CR11159	74.6	1.2	CR11253	18.6	1.7	CR11347	77.9	5.0	CR11441	20.6	5.0	CR11535	32.2	5.4	CR11629	11.1	0.9
CR11160	63.3	4.1	CR11254	9.2	0.5	CR11348	69.2	3.3	CR11442	27.2	3.7	CR11536	26.8	1.9	CR11630	18.6	0.8
CR11161	58.6	2.6	CR11255	4.9	0.6	CR11349	69.9	6.0	CR11443	16.5	5.0	CR11537	16.8	6.0	CR11631	3.7	1.3
CR11162	67.8	2.3	CR11256	18.5	0.9	CR11350	73.4	2.6	CR11444	23.9	2.2	CR11538	33.6	14.8	CR11632	10.2	1.8
CR11163	53.4	7.1	CR11257	2.5	0.6	CR11351	72.1	5.5	CR11445	13.8	3.4	CR11539	25.0	3.5	CR11633	6.7	2.2
CR11164	63.6	2.2	CR11258	12.4	2.8	CR11352	70.4	1.7	CR11446	31.4	0.8	CR11540	29.4	6.0	CR11634	11.0	1.4
CR11165	65.2	2.2	CR11259	5.2	0.9	CR11353	66.9	2.7	CR11447	25.2	1.6	CR11541	23.4	1.5	CR11635	8.5	1.2
CR11166	52.6	5.2	CR11260	5.9	1.0	CR11354	61.6	3.5	CR11448	18.1	4.7	CR11542	18.0	2.3	CR11636	5.6	0.4
CR11167	68.3	3.6	CR11261	18.9	1.6	CR11355	67.1	3.7	CR11449	12.6	4.6	CR11543	27.9	0.9	CR11637	13.7	2.3
CR11168	67.8	1.5	CR11262	4.0	0.6	CR11356	82.6	1.5	CR11450	23.0	3.5	CR11544	30.4	2.0	CR11638	12.0	1.5
CR11169	59.5	9.5	CR11263	8.4	4.9	CR11357	68.2	4.8	CR11451	21.4	2.8	CR11545	22.7	6.9	CR11639	20.6	7.8
CR11170	60.1	16.5	CR11264	10.4	4.2	CR11358	49.5	0.9	CR11452	18.7	1.5	CR11546	38.6	19.0	CR11640	9.4	3.8
CR11171	61.5	18.2	CR11265	7.3	1.6	CR11359	43.4	4.8	CR11453	11.8	2.7	CR11547	25.5	12.8	CR11641	4.4	0.6
CR11172	30.0	11.7	CR11266	1.6	0.1	CR11360	37.7	5.0	CR11454	11.5	5.4	CR11548	11.2	3.0	CR11642	5.1	1.5
CR11173	44.7	19.6	CR11267	1.6	0.3	CR11361	33.9	1.3	CR11455	12.1	3.5	CR11549	15.2	9.9	CR11643	2.3	0.7
CR11174	56.0	15.1	CR11268	8.5	0.8	CR11362	37.5	6.1	CR11456	17.0	0.4	CR11550	11.9	8.4	CR11644	9.0	2.5

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR11175	35.8	1.6	CR11269	0.8	0.2	CR11363	41.0	7.2	CR11457	6.4	0.3	CR11551	6.9	1.2	CR11645	1.4	0.6
CR11176	32.0	8.9	CR11270	1.3	0.2	CR11364	30.7	1.8	CR11458	4.8	0.2	CR11552	7.0	3.6	CR11646	1.4	0.5
CR11177	61.8	10.4	CR11271	9.3	2.3	CR11365	49.5	3.7	CR11459	9.8	0.7	CR11553	12.2	3.1	CR11647	10.3	1.8
CR11178	71.5	6.7	CR11272	12.1	2.1	CR11366	65.8	1.1	CR11460	12.3	2.0	CR11554	14.4	4.9	CR11648	7.2	1.8
CR11179	73.9	16.4	CR11273	34.8	33.7	CR11367	66.8	2.9	CR11461	13.0	1.8	CR11555	25.5	4.7	CR11649	13.6	3.5
CR11180	64.3	12.3	CR11274	9.0	7.6	CR11368	46.5	7.1	CR11462	14.3	2.0	CR11556	14.6	5.9	CR11650	6.3	0.9
CR11181	48.0	6.8	CR11275	4.2	0.3	CR11369	35.9	6.1	CR11463	11.4	1.1	CR11557	6.1	1.1	CR11651	3.5	0.4
CR11182	35.3	5.6	CR11276	3.2	0.2	CR11370	32.5	11.9	CR11464	8.7	1.4	CR11558	8.5	4.4	CR11652	4.7	1.6
CR11183	41.4	17.1	CR11277	2.7	1.1	CR11371	31.1	10.2	CR11465	5.1	0.6	CR11559	5.0	0.9	CR11653	1.3	0.2
CR11184	51.4	17.7	CR11278	3.6	0.8	CR11372	22.8	4.1	CR11466	8.0	2.3	CR11560	8.6	2.9	CR11654	2.7	0.7
CR11185	44.4	8.5	CR11279	5.6	2.0	CR11373	29.5	8.8	CR11467	9.2	1.4	CR11561	14.4	7.7	CR11655	3.0	0.9
CR11186	46.5	11.0	CR11280	3.9	0.9	CR11374	27.1	8.0	CR11468	12.0	0.3	CR11562	5.6	1.1	CR11656	2.3	0.6
CR11187	24.8	13.7	CR11281	0.6	0.1	CR11375	27.2	2.7	CR11469	6.8	1.6	CR11563	6.0	4.4	CR11657	1.1	0.3
CR11188	66.4	5.4	CR11282	9.3	2.7	CR11376	30.6	2.6	CR11470	5.1	0.1	CR11564	9.7	5.2	CR11658	8.0	2.5
CR11189	55.0	3.7	CR11283	4.3	0.6	CR11377	49.5	7.9	CR11471	11.5	3.5	CR11565	6.9	2.0	CR11659	4.5	1.7
CR11190	61.5	18.4	CR11284	6.4	1.5	CR11378	51.7	6.9	CR11472	16.9	6.4	CR11566	12.7	3.9	CR11660	2.0	0.5
CR11191	55.0	11.2	CR11285	25.5	16.2	CR11379	24.3	8.1	CR11473	5.7	0.3	CR11567	11.5	12.4	CR11661	2.7	0.7
CR11192	38.0	11.0	CR11286	2.2	1.1	CR11380	15.1	2.8	CR11474	8.0	2.1	CR11568	4.2	1.8	CR11662	2.8	0.5
CR11193	53.4	8.0	CR11287	10.3	4.8	CR11381	33.0	12.9	CR11475	5.2	1.1	CR11569	9.4	3.2	CR11663	1.8	0.7
CR11194	20.6	1.2	CR11288	1.0	0.2	CR11382	15.6	5.5	CR11476	3.8	0.4	CR11570	2.5	0.4	CR11664	1.1	0.3
CR11195	39.2	7.3	CR11289	1.8	0.8	CR11383	17.9	5.4	CR11477	5.4	0.6	CR11571	3.6	2.0	CR11665	1.2	0.4
CR11196	59.4	15.0	CR11290	6.2	0.6	CR11384	29.1	11.8	CR11478	4.8	0.0	CR11572	10.0	4.0	CR11666	3.3	0.4
CR11197	29.4	5.1	CR11291	1.4	0.1	CR11385	25.7	8.8	CR11479	5.7	0.1	CR11573	2.3	1.0	CR11667	0.6	0.1
CR11198	35.2	8.1	CR11292	1.5	0.4	CR11386	26.5	2.8	CR11480	7.1	0.8	CR11574	3.2	1.4	CR11668	2.2	0.5
CR11199	72.5	6.7	CR11293	11.5	2.6	CR11387	49.8	10.4	CR11481	7.3	0.1	CR11575	12.0	2.4	CR11669	7.0	1.8
CR11200	64.5	9.7	CR11294	15.4	2.5	CR11388	55.4	2.0	CR11482	13.2	1.3	CR11576	4.7	1.4	CR11670	2.6	0.4

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR11201	45.5	38.7	CR11295	3.3	0.2	CR11389	30.1	10.1	CR11483	5.5	0.2	CR11577	6.9	4.0	CR11671	1.3	0.5
CR11202	37.8	20.4	CR11296	2.6	1.2	CR11390	18.3	2.7	CR11484	4.4	1.1	CR11578	4.3	2.4	CR11672	1.1	0.3
CR11203	19.3	4.5	CR11297	1.6	0.5	CR11391	20.6	3.8	CR11485	2.4	0.3	CR11579	3.1	0.7	CR11673	2.3	0.5
CR11204	61.3	22.2	CR11298	4.5	0.7	CR11392	17.7	3.4	CR11486	4.2	0.1	CR11580	5.7	1.5	CR11674	1.1	0.3
CR11205	58.5	20.1	CR11299	10.5	2.7	CR11393	32.5	3.7	CR11487	8.8	0.6	CR11581	10.4	3.3	CR11675	2.3	0.6
CR11206	40.2	4.2	CR11300	9.2	5.1	CR11394	21.5	2.7	CR11488	6.3	1.7	CR11582	5.3	2.9	CR11676	2.1	0.7
CR11207	28.5	27.5	CR11301	0.8	0.3	CR11395	8.5	1.7	CR11489	1.8	0.1	CR11583	1.4	0.3	CR11677	0.5	0.1
CR11208	39.9	9.6	CR11302	6.7	2.6	CR11396	22.4	3.0	CR11490	4.4	0.1	CR11584	4.3	0.9	CR11678	3.1	0.5
CR11209	43.8	8.4	CR11303	3.1	0.4	CR11397	19.8	3.1	CR11491	6.9	1.8	CR11585	4.7	2.1	CR11679	2.1	0.4
CR11210	58.5	8.6	CR11304	9.4	3.0	CR11398	37.2	5.2	CR11492	6.3	0.3	CR11586	11.7	2.5	CR11680	8.5	2.8
CR11211	61.1	8.1	CR11305	3.3	1.7	CR11399	44.5	6.1	CR11493	10.5	2.5	CR11587	18.6	19.7	CR11681	3.0	0.7
CR11212	16.5	2.4	CR11306	6.9	9.2	CR11400	20.3	3.4	CR11494	2.5	0.4	CR11588	4.2	1.3	CR11682	1.0	0.4
CR11213	35.8	6.5	CR11307	7.3	2.6	CR11401	16.7	5.2	CR11495	3.4	0.4	CR11589	4.3	1.0	CR11683	1.4	0.1
CR11214	42.2	11.5	CR11308	5.8	2.7	CR11402	25.7	5.4	CR11496	4.8	0.3	CR11590	7.0	1.7	CR11684	1.7	0.2
CR11215	29.7	9.3	CR11309	2.3	0.8	CR11403	11.7	1.2	CR11497	2.6	0.7	CR11591	2.5	1.0	CR11685	1.2	0.1
CR11216	25.9	5.1	CR11310	7.2	4.5	CR11404	17.4	5.7	CR11498	3.7	0.6	CR11592	4.6	1.0	CR11686	1.5	0.4
CR11217	16.0	4.6	CR11311	0.9	0.4	CR11405	13.4	3.7	CR11499	2.3	0.1	CR11593	1.1	0.3	CR11687	0.3	0.1
CR11218	32.2	15.3	CR11312	2.4	1.0	CR11406	10.8	4.1	CR11500	6.6	0.5	CR11594	2.6	0.1	CR11688	1.3	0.3
CR11219	25.4	11.6	CR11313	3.6	2.2	CR11407	13.4	6.3	CR11501	3.3	0.0	CR11595	2.0	0.9	CR11689	0.8	0.1
CR11220	41.7	17.9	CR11314	6.7	2.0	CR11408	23.4	3.9	CR11502	5.6	1.1	CR11596	4.7	1.1	CR11690	5.1	3.3
CR11221	30.3	10.1	CR11315	3.0	1.0	CR11409	22.3	5.0	CR11503	4.2	0.2	CR11597	4.2	0.8	CR11691	1.1	0.1
CR11222	45.3	26.9	CR11316	2.9	0.9	CR11410	22.9	9.8	CR11504	2.9	0.1	CR11598	4.0	1.9	CR11692	1.0	0.3
CR11223	17.7	2.8	CR11317	1.2	0.3	CR11411	15.1	4.9	CR11505	3.1	0.4	CR11599	1.3	0.1	CR11693	0.3	0.1
CR11224	29.2	1.9	CR11318	1.5	0.2	CR11412	12.7	3.5	CR11506	2.4	0.2	CR11600	1.7	0.2	CR11694	0.7	0.1
CR11225	17.1	1.1	CR11319	1.5	0.1	CR11413	8.0	2.3	CR11507	3.8	0.8	CR11601	3.5	1.2	CR11695	0.7	0.2
CR11226	25.2	4.1	CR11320	1.5	0.6	CR11414	6.6	1.9	CR11508	2.3	0.4	CR11602	1.9	0.3	CR11696	0.7	0.3

G480 Var	Edit	SD	G488 Var	Edit	SD	G490 Var	Edit	SD	G494 Var	Edit	SD	G499 Var	Edit	SD	G502 Var	Edit	SD
CR11227	22.3	2.0	CR11321	1.7	0.0	CR11415	10.2	4.3	CR11509	2.6	0.0	CR11603	2.0	0.4	CR11697	0.9	0.2
CR11228	21.8	3.4	CR11322	1.5	0.8	CR11416	7.5	3.5	CR11510	1.7	0.6	CR11604	1.2	0.2	CR11698	0.7	0.2
CR11229	11.4	0.8	CR11323	1.1	0.3	CR11417	3.8	1.2	CR11511	3.1	0.1	CR11605	1.8	0.5	CR11699	0.6	0.1
CR11230	28.5	5.8	CR11324	0.2	0.1	CR11418	9.5	2.9	CR11512	3.1	0.8	CR11606	1.7	0.3	CR11700	1.1	0.4
CR11231	52.6	1.7	CR11325	5.0	2.5	CR11419	16.9	2.0	CR11513	4.1	0.6	CR11607	1.7	0.3	CR11701	5.7	4.6
CR11232	58.5	5.3	CR11326	13.3	5.5	CR11420	34.3	8.3	CR11514	3.8	0.2	CR11608	6.1	1.0	CR11702	1.7	0.8
CR11233	51.3	8.3	CR11327	11.0	3.6	CR11421	22.5	6.4	CR11515	3.7	0.7	CR11609	2.9	0.7	CR11703	3.3	0.2
CR11234	48.1	4.1	CR11328	5.4	2.0	CR11422	20.6	6.0	CR11516	4.8	0.5	CR11610	14.3	19.7	CR11704	1.5	0.4
CR11235	40.5	19.6	CR11329	3.6	3.3	CR11423	20.8	6.8	CR11517	7.8	4.5	CR11611	2.6	2.7	CR11705	1.3	0.2
CR11236	47.1	13.6	CR11330	2.7	1.4	CR11424	17.8	4.9	CR11518	5.1	0.1	CR11612	2.3	0.6	CR11706	1.2	0.2
CR11237	47.0	8.3	CR11331	4.9	1.8	CR11425	22.9	7.1	CR11519	5.9	0.3	CR11613	2.5	0.6	CR11707	1.6	0.4
CR11238	39.0	15.6	CR11332	3.6	2.4	CR11426	13.9	4.1	CR11520	2.9	0.3	CR11614	5.0	5.8	CR11708	1.2	0.5
CR11239	56.7	11.8	CR11333	5.4	1.4	CR11427	14.7	3.3	CR11521	3.5	0.1	CR11615	2.2	0.5	CR11709	3.7	1.7
CR11240	52.2	18.7	CR11334	10.8	8.6	CR11428	13.5	2.9	CR11522	3.6	0.5	CR11616	2.7	1.4	CR11710	2.8	1.4
CR11241	64.9	15.8	CR11335	10.8	8.6	CR11429	17.1	3.4	CR11523	4.5	0.1	CR11617	12.0	15.0	CR11711	3.0	1.2
CR11242	74.6	19.2	CR11336	10.8	8.6	CR11430	16.1	4.4	CR11524	4.2	1.4	CR11618	3.5	0.1	CR11712	3.2	0.8
CR11243	33.7	1.5	CR11337	0.9	0.1	CR11431	19.2	1.2	CR11525	2.1	0.3	CR11619	3.9	2.2	CR11713	1.4	0.3
CR11244	48.2	6.2	CR11338	30.1	25.1	CR11432	58.3	7.1	CR11526	22.3	2.8	CR11620	15.9	8.9	CR11714	3.1	0.2
CR11245	32.6	8.0	CR11339	2.8	1.2	CR11433	22.8	8.7	CR11527	13.7	1.1	CR11621	6.2	4.3	CR11715	1.7	0.3
CR11246	54.2	11.1	CR11340	4.0	1.1	CR11434	37.1	5.5	CR11528	15.4	0.4	CR11622	11.7	7.2	CR11716	2.4	0.6
CR11247	39.4	11.5	CR11341	4.4	2.0	CR11435	24.2	2.4	CR11529	12.1	1.1	CR11623	9.0	7.8	CR11717	4.3	2.0
CR11248	41.0	1.9	CR11342	7.1	0.3	CR11436	24.0	5.8	CR11530	5.2	0.9	CR11624	6.6	1.4	CR11718	2.9	0.8
CR11249	69.4	21.0	CR11343	3.7	1.3	CR11437	15.9	5.7	CR11531	7.7	0.2	CR11625	4.8	1.7	CR11719	1.7	0.6
CR11250	17.9	9.4	CR11344	1.0	0.4	CR11438	11.7	3.1	CR11532	5.7	0.4	CR11626	2.5	0.5	CR11720	0.5	0.1
CR11251	20.7	4.7	CR11345	1.6	0.5	CR11439	14.9	4.2	CR11533	6.5	0.9	CR11627	3.7	1.5	CR11721	1.2	0.2

Example 4

[00545] The impacts of chemical modification type and position within the guide domain were evaluated in an editing screen of modified sgRNAs. The screen assayed guides modified with 2'F, 2'OMe and PS. The complete pattern set was applied to the nucleobase sequence of three guides. Test modification patterns in this example were applied to three guide domain nucleobase sequences, specifically those described in Table 1 for G000486, G000502, or G000415. Guide domain modification patterns were assayed either the conserved region described in SEQ ID No. 695 or in a short-sgRNA format using the conserved region described in SEQ ID No. 253. The final data set contained 270 distinct guides and 45 unique modification patterns in the guide domain.

[00546] Rows 1-12 in Tables 9-12 show test guides assessed for editing efficacy with 2'OMe, 2'F, PS, and 2'H modifications at positions 5, 12, and 15. Rows 13-19 in Tables 9-12 show editing data for variants that substitute 2'F single modification for 2'F + PS modifications at positions 8-10. Rows 20-27 in Tables 9-12 show editing data for variants that substitute 2'F for PS at positions 4-20.

[00547] Editing was assayed in PCH and PHH cells as described in Example 1 with the following modifications. Cells were counted and plated at a density of 30,000-35,000 cells/well for PHH, and 40,000-60,000 cells/well for PCH Transfections used pre-mixed lipid formulations in which the lipid components were reconstituted in 100% ethanol at a molar ratio of 50% Lipid A, 9% DSPC, 38% cholesterol, and 3% PEG2k-DMG. The lipid mixture was then mixed with RNA cargos (e.g., Cas9 mRNA and gRNA) at a lipid amine to RNA phosphate (N:P) molar ratio of about 6.0. Transfections were performed with a final concentration of 100 nM gRNA, 3% cyno serum, and 50 ng Cas9 mRNA per well. Cells were incubated for approximately 48 hours before cell lysis and NGS analysis. The experiment was performed in duplicate. The editing results are described in Tables 9 -12. Each row represents a single modification pattern design with the same conserved region. Rows 46-48 are controls.

[00548] The data were analyzed to estimate the impact of several variables, including whether the guide was or was not a short-sgRNA, variable region modification pattern, and individual modification position, where possible. Short-sgRNA guides were significantly more active than non-short-sgRNA guides in PCH (all sites) and PHH (G502 variants). In PCH, short-sgRNA guides added an additional 14% over equivalent non-short-sgRNAs.

[00549] Many of the modification patterns in this study were designed to incorporate and further test well tolerated modifications into highly modified gRNA molecules. In general this was successful; nearly all patterns showed similar activity to controls overall. A number of individual positions were also tested in this study. Position 5, 12 and 15 were modified individually. Position 5 was highly tolerant of modification. Position 12 was tolerant of PS, 2'-F and 2'-OMe, but was significantly sensitive to 2'-H modification (reduction of editing percentage by 7.5, $p < 0.00002$). Position 15 was tolerant of 2'-H modification, but as in other work presented here, highly sensitive to 2'F and 2'OMe ($p<10^{-13}$).

Table 9 – Average Editing % in PHH cells

PHH									
Row	**G000502 Variants**	**%Edit**	**SD**	**G000486 Variants**	**%Edit**	**SD**	**G000415 Variants**	**%Edit**	**SD**
1	G014462	21.7%	0.2%	G014507	57.0%	0.3%	G014554	57.2%	2.1%
2	G014463	21.4%	1.7%	G014508	57.6%	0.2%	G014555	56.0%	0.4%
3	G014464	28.4%	2.9%	G014509	58.6%	2.5%	G014556	54.4%	5.2%
4	G014465	23.7%	1.0%	G014510	52.5%	0.6%	G014557	54.9%	1.3%
5	G014466	22.8%	0.1%	G014511	54.4%	0.6%	G014558	61.0%	4.1%
6	G014467	27.9%	2.3%	G014512	62.1%	2.4%	G014559	63.4%	0.1%
7	G014468	21.5%	1.3%	G014513	57.6%	0.7%	G014560	55.6%	0.8%
8	G014469	12.6%	0.3%	G014514	52.8%	1.9%	G014561	39.0%	0.6%
9	G014470	3.4%	1.1%	G014515	35.5%	1.2%	G014562	32.8%	6.8%
10	G014471	9.1%	0.6%	G014516	48.6%	1.0%	G014563	33.0%	6.7%
11	G014472	21.2%	0.6%	G014517	55.5%	0.1%	G014564	63.1%	0.6%
12	G014473	18.0%	0.9%	G014518	54.2%	0.1%	G014565	55.2%	2.5%
13	G014474	25.4%	3.7%	G014519	52.3%	0.7%	G014566	64.9%	6.8%
14	G014475	31.5%	3.3%	G014520	60.3%	0.1%	G014567	55.2%	0.3%
15	G014476	26.3%	4.5%	G014521	56.5%	0.4%	G014568	54.5%	5.3%
16	G014477	28.2%	2.1%	G014522	56.6%	5.4%	G014569	59.7%	0.7%
17	G014478	30.6%	1.5%	G014523	64.7%	0.2%	G014570	50.4%	3.5%
18	G014479	32.3%	0.3%	G014524	59.9%	7.3%	G014571	56.7%	3.3%
19	G014480	37.9%	0.8%	G014525	65.1%	2.1%	G014572	49.6%	3.2%
20	G014481	27.8%	0.4%	G014526	53.6%	0.9%	G014573	44.0%	0.4%
21	G014482	26.0%	0.4%	G014527	54.1%	1.2%	G014574	59.3%	4.7%
22	G014483	23.8%	3.3%	G014528	53.3%	1.4%	G014575	50.8%	7.6%
23	G014484	21.6%	2.5%	G014529	47.6%	0.5%	G014576	45.8%	13.8%
24	G014485	21.6%	3.7%	G014530	43.9%	4.6%	G014577	56.1%	5.2%
25	G014486	24.2%	2.8%	G014531	52.8%	4.6%	G014578	61.3%	3.6%
26	G014487	25.9%	3.3%	G014532	51.2%	1.3%	G014579	48.9%	7.8%
27	G014488	22.0%	4.1%	G014533	49.9%	5.4%	G014580	50.2%	7.1%

PHH									
Row	G000502 Variants	%Edit	SD	G000486 Variants	%Edit	SD	G000415 Variants	%Edit	SD
28	G014489	34.7%	3.0%	G014534	67.2%	5.1%	G014581	54.2%	5.5%
29	G014490	38.1%	4.4%	G014535	65.6%	4.6%	G014582	62.0%	2.5%
30	G014491	34.8%	1.8%	G014536	69.5%	5.9%	G014583	51.8%	6.6%
31	G014492	23.5%	1.1%	G014537	66.8%	2.0%	G014584	54.4%	2.4%
32	G014493	38.9%	6.1%	G014538	61.4%	12.4%	G014585	53.7%	15.2%
33	G014494	38.1%	3.7%	G014539	61.0%	3.7%	G014586	56.1%	4.2%
34	G014495	33.4%	1.3%	G014540	63.7%	5.9%	G014587	60.0%	5.9%
35	G014496	42.9%	2.5%	G014541	64.0%	4.2%	G014588	52.5%	2.9%
36	G014497	39.0%	3.7%	G014542	51.2%	4.3%	G014589	56.8%	4.3%
37	G014498	37.0%	3.3%	G014543	70.7%	2.7%	G014590	49.8%	7.0%
38	G014499	34.9%	0.3%	G014544	36.7%	0.1%	G014591	50.3%	2.3%
39	G014500	28.2%	1.7%	G014545	52.8%	0.0%	G014592	49.8%	5.8%
40	G014501	30.5%	2.0%	G014546	56.6%	3.8%	G014593	53.4%	4.5%
41	G014502	33.3%	4.2%	G014547	53.4%	3.9%	G014594	51.8%	0.7%
42	G014503	28.8%	2.5%	G014548	36.3%	1.3%	G014595	55.6%	2.5%
43	G014504	5.9%	0.5%	G014549	64.6%	2.3%	G014596	39.2%	4.0%
44	G014505	0.2%	0.0%	G014550	16.0%	3.3%	G014597	0.4%	0.3%
45	G014506	11.0%	0.1%	G014551	49.6%	1.6%	G014598	38.5%	0.9%
46	G000502	51.4%	3.3%	G000502	51.4%	3.3%	G000502	53.5%	3.1%
47	G010039	29.4%	0.1%	G010039	29.4%	0.1%	G010039	22.6%	3.0%
48	G012401	56.9%	0.1%	G012401	56.9%	0.1%	G012401	52.2%	4.7%

Table 10 - Average Editing % in PCH cells

PCH									
Row	G000502 Variants	%Edit	SD	G000486 Variants	%Edit	SD	G000415 Variants	%Edit	SD
1	G014462	54.6%	2.5%	G014507	4.6%	0.1%	G014554	46.8%	8.1%
2	G014463	43.9%	2.1%	G014508	5.2%	0.7%	G014555	38.2%	2.3%
3	G014464	50.6%	5.1%	G014509	4.1%	1.2%	G014556	34.1%	2.1%
4	G014465	49.1%	3.3%	G014510	3.2%	1.8%	G014557	34.9%	7.1%
5	G014466	51.3%	9.2%	G014511	3.1%	1.1%	G014558	37.5%	4.3%
6	G014467	49.4%	9.7%	G014512	6.2%	2.0%	G014559	36.5%	0.9%
7	G014468	48.2%	4.7%	G014513	6.3%	2.3%	G014560	36.1%	7.0%
8	G014469	40.4%	3.8%	G014514	2.5%	1.1%	G014561	28.7%	3.1%
9	G014470	31.2%	7.8%	G014515	0.6%	0.3%	G014562	20.7%	1.4%
10	G014471	37.1%	8.6%	G014516	1.8%	0.5%	G014563	16.5%	1.5%
11	G014472	50.3%	12.4%	G014517	5.6%	2.5%	G014564	45.1%	3.0%
12	G014473	55.1%	9.3%	G014518	7.1%	0.9%	G014565	42.8%	1.1%
13	G014474	47.6%	6.1%	G014519	4.5%	0.4%	G014566	46.8%	2.9%

PCH									
Row	G000502 Variants	%Edit	SD	G000486 Variants	%Edit	SD	G000415 Variants	%Edit	SD
14	G014475	43.8%	1.8%	G014520	5.5%	1.7%	G014567	35.5%	1.8%
15	G014476	38.2%	10.0%	G014521	4.7%	1.4%	G014568	32.7%	4.9%
16	G014477	47.1%	7.2%	G014522	5.7%	3.5%	G014569	38.8%	0.4%
17	G014478	45.9%	4.4%	G014523	5.3%	1.6%	G014570	28.9%	1.8%
18	G014479	49.3%	6.5%	G014524	7.1%	2.1%	G014571	31.1%	0.8%
19	G014480	49.3%	11.9%	G014525	8.7%	5.0%	G014572	28.0%	1.6%
20	G014481	43.9%	8.9%	G014526	6.3%	1.3%	G014573	15.6%	0.4%
21	G014482	43.6%	4.2%	G014527	5.9%	1.2%	G014574	30.6%	4.1%
22	G014483	45.4%	4.7%	G014528	5.4%	0.4%	G014575	18.8%	2.7%
23	G014484	43.6%	6.7%	G014529	6.5%	2.4%	G014576	33.2%	9.5%
24	G014485	38.5%	3.5%	G014530	6.8%	1.6%	G014577	34.3%	2.1%
25	G014486	32.0%	0.3%	G014531	6.1%	1.7%	G014578	44.1%	7.9%
26	G014487	42.5%	4.0%	G014532	5.8%	0.7%	G014579	28.8%	5.4%
27	G014488	32.3%	7.6%	G014533	4.6%	1.1%	G014580	31.9%	4.7%
28	G014489	40.2%	7.3%	G014534	9.0%	0.6%	G014581	26.7%	4.8%
29	G014490	35.3%	7.7%	G014535	7.0%	2.6%	G014582	32.4%	1.5%
30	G014491	48.9%	7.1%	G014536	7.9%	1.3%	G014583	28.8%	4.1%
31	G014492	38.8%	9.2%	G014537	5.8%	1.8%	G014584	29.5%	1.6%
32	G014493	50.4%	8.5%	G014538	7.6%	1.9%	G014585	23.3%	5.4%
33	G014494	50.5%	6.7%	G014539	7.6%	0.7%	G014586	27.2%	3.1%
34	G014495	57.7%	0.7%	G014540	7.4%	1.8%	G014587	33.1%	1.6%
35	G014496	49.3%	1.9%	G014541	5.0%	0.6%	G014588	34.5%	10.9%
36	G014497	36.5%	6.9%	G014542	16.7%	1.8%	G014589	25.2%	1.5%
37	G014498	39.2%	7.5%	G014543	7.0%	1.6%	G014590	21.9%	1.6%
38	G014499	46.7%	4.5%	G014544	1.8%	0.6%	G014591	26.8%	4.0%
39	G014500	37.1%	10.0%	G014545	5.2%	1.5%	G014592	19.9%	1.2%
40	G014501	40.1%	5.7%	G014546	4.9%	0.7%	G014593	26.0%	3.6%
41	G014502	43.1%	3.7%	G014547	2.5%	0.5%	G014594	22.8%	1.8%
42	G014503	52.5%	4.7%	G014548	1.7%	0.8%	G014595	22.6%	5.4%
43	G014504	13.1%	8.0%	G014549	3.1%	0.1%	G014596	20.6%	7.4%
44	G014505	3.0%	0.3%	G014550	0.6%	0.0%	G014597	0.9%	0.8%
45	G014506	44.1%	2.0%	G014551	1.9%	1.1%	G014598	24.6%	9.1%
46	G000502	55.8%	18.1%	G000502	55.8%	18.1%	G000502	47.9%	0.1%
47	G010039	44.4%	8.0%	G010039	44.4%	8.0%	G010039	39.4%	10.6%
48	G012401	65.4%	9.0%	G012401	65.4%	9.0%	G012401	53.3%	4.5%

Table 11 - Average Editing % in PHH cells for short-sgRNA guides

PHH - short-sgRNA									
Row	G000502 Variants	%Edit	SD	G000486 Variants	%Edit	SD	G000415 Variants	%Edit	SD
1	G014644	57.1%	5.9%	G014689	43.4%	0.4%	G014734	57.5%	1.1%
2	G014645	49.4%	2.5%	G014690	59.2%	12.9%	G014735	63.2%	2.2%
3	G014646	43.1%	0.1%	G014691	63.6%	0.6%	G014736	57.0%	3.7%
4	G014647	41.0%	1.0%	G014692	62.7%	2.4%	G014737	61.1%	1.6%
5	G014648	36.7%	0.8%	G014693	60.6%	2.5%	G014738	61.9%	5.7%
6	G014649	44.9%	0.8%	G014694	42.7%	0.8%	G014739	61.7%	1.9%
7	G014650	24.7%	1.2%	G014695	61.1%	2.5%	G014740	63.9%	0.4%
8	G014651	25.9%	2.3%	G014696	52.7%	2.7%	G014741	47.9%	0.4%
9	G014652	2.6%	0.3%	G014697	33.4%	3.0%	G014742	1.0%	0.4%
10	G014653	12.0%	0.6%	G014698	56.6%	2.2%	G014743	39.4%	2.4%
11	G014654	37.2%	2.5%	G014699	59.1%	3.0%	G014744	67.0%	4.0%
12	G014655	34.4%	2.8%	G014700	60.7%	2.2%	G014745	22.1%	5.2%
13	G014656	46.9%	1.8%	G014701	52.3%	14.2%	G014746	59.9%	0.1%
14	G014657	48.7%	1.9%	G014702	60.1%	5.7%	G014747	56.0%	10.7%
15	G014658	47.9%	4.9%	G014703	62.9%	2.0%	G014748	54.8%	3.4%
16	G014659	43.4%	3.0%	G014704	63.9%	3.0%	G014749	59.7%	0.4%
17	G014660	49.8%	2.8%	G014705	68.4%	2.1%	G014750	51.1%	1.6%
18	G014661	44.1%	4.1%	G014706	58.8%	7.8%	G014751	55.0%	4.5%
19	G014662	50.3%	0.4%	G014707	68.3%	2.2%	G014752	48.8%	5.4%
20	G014663	45.0%	1.2%	G014708	65.3%	2.4%	G014753	62.8%	5.9%
21	G014664	38.4%	5.2%	G014709	54.7%	0.6%	G014754	59.9%	0.1%
22	G014665	34.6%	1.2%	G014710	55.9%	6.4%	G014755	36.8%	1.8%
23	G014666	36.0%	0.6%	G014711	57.5%	2.8%	G014756	55.0%	2.0%
24	G014667	44.8%	1.7%	G014712	56.1%	10.4%	G014757	55.8%	4.1%
25	G014668	44.7%	1.1%	G014713	61.2%	0.8%	G014758	57.9%	6.1%
26	G014669	44.7%	2.2%	G014714	59.5%	5.4%	G014759	51.3%	11.9%
27	G014670	48.3%	6.2%	G014715	60.2%	1.6%	G014760	57.4%	0.4%
28	G014671	50.4%	1.3%	G014716	66.0%	9.4%	G014761	7.0%	0.1%
29	G014672	56.9%	4.5%	G014717	68.9%	4.9%	G014762	10.0%	1.6%
30	G014673	51.0%	1.1%	G014718	68.3%	0.7%	G014763	12.5%	0.0%
31	G014674	52.1%	0.6%	G014719	68.6%	0.1%	G014764	13.4%	2.1%
32	G014675	51.4%	2.7%	G014720	67.3%	3.1%	G014765	36.2%	3.2%
33	G014676	53.3%	3.6%	G014721	69.2%	1.9%	G014766	46.4%	5.7%
34	G014677	52.2%	3.9%	G014722	68.4%	4.6%	G014767	37.9%	4.5%
35	G014678	57.6%	4.2%	G014723	64.3%	4.1%	G014768	37.3%	8.8%
36	G014679	53.2%	4.6%	G014724	61.2%	4.4%	G014769	39.6%	0.6%
37	G014680	50.1%	5.6%	G014725	63.6%	0.8%	G014770	27.4%	0.1%
38	G014681	40.4%	2.5%	G014726	58.0%	4.2%	G014771	60.0%	0.5%

PHH - short-sgRNA									
Row	G000502 Variants	%Edit	SD	G000486 Variants	%Edit	SD	G000415 Variants	%Edit	SD
39	G014682	48.5%	3.7%	G014727	60.0%	3.1%	G014772	63.5%	4.7%
40	G014683	48.3%	6.6%	G014728	63.3%	0.9%	G014773	57.9%	0.6%
41	G014684	51.6%	0.4%	G014729	65.3%	1.8%	G014774	54.3%	4.7%
42	G014685	21.6%	3.4%	G014730	65.8%	0.4%	G014775	49.8%	2.4%
43	G014686	32.3%	0.6%	G014731	64.0%	5.1%	G014776	2.3%	0.6%
44	G014687	0.2%	0.0%	G014732	0.4%	0.1%	G014777	0.1%	0.0%
45	G014688	18.6%	0.6%	G014733	45.2%	4.8%	G014778	11.3%	1.5%
46	G000502	46.5%	0.4%	G000502	46.5%	0.4%	G000502	44.9%	12.2%
47	G010039	29.4%	1.1%	G010039	29.4%	1.1%	G010039	20.5%	1.2%
48	G012401	51.8%	5.8%	G012401	51.8%	5.8%	G012401	59.8%	1.6%

Table 12 - Average Editing % in PCH cells for short-sgRNA guides

PCH - short-sgRNA									
Row	G000502 Variants	%Edit	SD	G000486 Variants	%Edit	SD	G000415 Variants	%Edit	SD
1	G014644	76.6%	2.2%	G014689	10.7%	1.4%	G014734	53.2%	0.4%
2	G014645	73.9%	2.1%	G014690	20.4%	2.8%	G014735	64.0%	0.5%
3	G014646	73.0%	1.9%	G014691	21.9%	0.2%	G014736	50.5%	2.0%
4	G014647	69.8%	3.1%	G014692	20.1%	2.3%	G014737	57.7%	2.7%
5	G014648	71.1%	1.5%	G014693	20.8%	1.6%	G014738	58.0%	2.0%
6	G014649	70.9%	1.0%	G014694	13.2%	0.2%	G014739	57.3%	0.7%
7	G014650	69.3%	3.2%	G014695	26.7%	0.3%	G014740	56.3%	7.8%
8	G014651	67.4%	0.3%	G014696	10.1%	0.6%	G014741	41.4%	2.0%
9	G014652	51.4%	2.6%	G014697	2.5%	0.1%	G014742	2.7%	0.4%
10	G014653	60.2%	0.6%	G014698	8.4%	2.2%	G014743	45.4%	2.3%
11	G014654	70.5%	0.0%	G014699	22.0%	3.2%	G014744	62.8%	2.4%
12	G014655	72.5%	0.1%	G014700	19.4%	2.8%	G014745	38.9%	2.8%
13	G014656	72.3%	0.0%	G014701	29.7%	4.7%	G014746	59.6%	5.2%
14	G014657	71.4%	0.8%	G014702	27.8%	3.5%	G014747	47.5%	3.5%
15	G014658	70.9%	3.5%	G014703	25.5%	3.8%	G014748	46.9%	4.4%
16	G014659	69.6%	1.2%	G014704	27.0%	1.6%	G014749	54.6%	3.3%
17	G014660	68.2%	1.1%	G014705	25.0%	0.8%	G014750	44.3%	1.5%
18	G014661	64.7%	0.1%	G014706	23.0%	0.7%	G014751	51.3%	2.2%
19	G014662	67.7%	2.8%	G014707	25.4%	1.2%	G014752	43.0%	0.8%
20	G014663	69.3%	1.8%	G014708	26.2%	1.3%	G014753	47.6%	3.9%
21	G014664	67.7%	0.3%	G014709	25.7%	5.9%	G014754	52.5%	3.5%
22	G014665	66.5%	0.1%	G014710	20.6%	0.8%	G014755	35.8%	0.9%
23	G014666	66.5%	5.7%	G014711	22.6%	0.9%	G014756	52.4%	3.6%
24	G014667	68.7%	4.8%	G014712	27.3%	1.9%	G014757	55.6%	0.8%

PCH - short-sgRNA									
Row	G000502 Variants	%Edit	SD	G000486 Variants	%Edit	SD	G000415 Variants	%Edit	SD
25	G014668	66.7%	0.5%	G014713	27.9%	2.0%	G014758	51.3%	4.2%
26	G014669	65.9%	1.2%	G014714	24.1%	4.2%	G014759	50.8%	1.5%
27	G014670	64.9%	2.5%	G014715	24.3%	2.2%	G014760	49.6%	1.1%
28	G014671	68.6%	3.0%	G014716	21.4%	5.0%	G014761	9.6%	1.0%
29	G014672	66.3%	2.1%	G014717	24.5%	2.1%	G014762	10.4%	1.8%
30	G014673	65.3%	1.6%	G014718	21.7%	2.7%	G014763	13.5%	0.5%
31	G014674	67.8%	9.9%	G014719	20.1%	1.7%	G014764	13.9%	1.4%
32	G014675	63.3%	0.0%	G014720	31.6%	6.9%	G014765	35.0%	3.1%
33	G014676	67.6%	0.5%	G014721	24.8%	2.8%	G014766	36.5%	1.8%
34	G014677	66.3%	3.4%	G014722	31.9%	0.8%	G014767	36.7%	0.9%
35	G014678	73.3%	1.0%	G014723	33.8%	5.5%	G014768	38.8%	0.8%
36	G014679	64.1%	2.3%	G014724	25.9%	1.6%	G014769	31.7%	1.0%
37	G014680	66.0%	0.8%	G014725	25.8%	1.4%	G014770	23.3%	2.1%
38	G014681	65.9%	1.0%	G014726	22.4%	1.5%	G014771	50.9%	0.0%
39	G014682	72.4%	1.9%	G014727	28.0%	1.8%	G014772	56.6%	0.4%
40	G014683	69.2%	1.6%	G014728	24.3%	0.9%	G014773	52.9%	1.6%
41	G014684	66.5%	0.8%	G014729	27.3%	0.9%	G014774	47.8%	1.5%
42	G014685	48.5%	5.3%	G014730	27.4%	0.9%	G014775	41.7%	4.9%
43	G014686	62.8%	1.6%	G014731	12.5%	3.4%	G014776	3.4%	0.6%
44	G014687	0.5%	0.3%	G014732	0.6%	0.0%	G014777	0.3%	0.1%
45	G014688	64.0%	0.8%	G014733	6.5%	1.1%	G014778	19.8%	1.3%
46	G000502	67.2%	0.5%	G000502	67.2%	0.5%	G000502	63.6%	2.3%
47	G010039	53.0%	0.4%	G010039	53.0%	0.4%	G010039	49.8%	4.6%
48	G012401	68.3%	3.5%	G012401	68.3%	3.5%	G012401	73.2%	3.4%

Example 5 – *In vitro* editing in Primary Human Hepatocytes (PHH), Primary Cynomolgus Hepatocytes (PCH), and HepG2

[00550] sgRNAs targeting the human *TTR* gene were designed as shown in Table 1 and transfected into primary cyno hepatocytes (PCH), primary human hepatocytes (PHH), and HepG2 cells in vitro at concentrations as indicated in the figures and editing efficiency (e.g., percent editing) was measured by NGS, as described in Example 1. The LNPs used in these transfections were made according to LNP Procedure C in Example 1(F).

[00551] Dose response curves of editing efficiency by concentration are shown in Figures 9A (PHH), 9B (PCH), and 9C (HepG2). Tables 13A (PHH), 13B (PCH), and 13C (HepG2) summarize the results of Figures 9A-9C.

Table 13A (PHH)

sgRNA	min	max	EC50	EC50error
G000698	0.43	87	0.981624	0.224339
G000699	0.37	83.33	1.275023	0.243757
G000700	0.73	90.73	0.757331	0.270775
G000701	0.2	84.93	1.000807	0.248197
G000481	0.17	81.3	1.305533	0.28657
G000499	0.4	85.17	1.15425	0.237993

Table 13B (PCH)

sgRNA	min	max	EC50	EC50error
G000698	0.65	97.15	0.482751	0.085198
G000699	0.55	97.25	1.295555	0.242115
G000700	0.65	88.15	1.287722	0.279182
G000701	0.2	87.05	1.619526	0.350191
G000481	0.55	95.6	1.070419	0.241465
G000499	0.25	84.15	3.242486	0.847014

Table 13C (HepG2)

sgRNA	min	max	EC50
G000698	1.4	97.55	0.290574
G000699	0.6	98.65	0.452265
G000700	1	97.5	0.37081
G000701	0.35	96.85	0.496062
G000481	0.35	98.6	0.537527
G000499	0.1	97.9	1.136589

Example 6 – Nuclease Susceptibility and Stability of sgRNAs

[00552] 5'- and 3'-end-labeled versions of G282, G480, G481, G502, and G504 were assayed as described in Example 1(K). Fragment lengths were mapped onto the G282 sequence (Fig. 11A) and cleavage was noted predominantly at CpA and UpA (i.e., pyrimidine-adenine or "YA") sites (illustrated in Fig. 10B), consistent with an RNase A-like

endonucleolytic pattern. *See* Leu et. al., *J. Biol Chem*, 278:7300-09 (2003) (reporting RNase A cleavage at CpA and UpA sites). The cleavage sites observed for G282 are illustrated schematically on a possible secondary structure of this molecule in Fig. 10B.

[00553] Cleavage was consistently observed following nucleotides 25, 45, 50, 64, and 67 in G282, G480, G481, G502, and G504 (except that for G481, there was little to no cleavage at position 25) (Fig. 11A-D). All of these positions are YA sites (labeled YA sites 1, 5, 6, 7, 8, and 9 in Fig. 10B). Furthermore, in the spacer region, cleavage was observed in a generally YA-dependent manner, for example, following position 16 of G480; positions 15 and 18 of G481; and positions 4, 8, 11, and 16 of G502 (Fig. 11B-D). Notably, modifications at YA positions led to reduced cleavage (e.g., following positions 2, 31, 37, 40, and 83). YA positions in which at least the Y was a 2'-OMe nucleotide did not show significant cleavage, consistent with 2'-O-methylation protecting the adjacent 3'linkage from cleavage by RNAse A.

[00554] G502 was compared to sgRNAs with additional modifications in the guide domain (Figs. 12A-C). In particular, G9571 includes 2'-fluoro modifications at certain positions including 8-11 and PS modifications at certain positions including 8-10 as shown in the Sequence Table. G10015 includes a 2'-OMe modification at position 4, 2'-fluoro modifications at positions 8 and 11, and a PS modification at position 16.

[00555] In G9571, cleavage after positions 8 and 11 was reduced or eliminated, consistent with nuclease protection by the 2'-fluoro modifications of these positions (Fig. 12B).

[00556] In G10015, cleavage after positions 4, 8, and 11 was reduced or eliminated, consistent with nuclease protection by the 2'-OMe modification of position 4 and the 2'-fluoro modifications of positions 8 and 11 (Fig. 12C). Cleavage after position 16 also occurred at a somewhat reduced level relative to G502, suggesting partial protection by the phosphorothioate modification at that position.

[00557] Assays on G282, G480, G481, G502, G504, and G509 assembled into ribonucleoproteins (RNPs) with Cas9 were also performed using a higher HLC concentration of 8.5 mg/ml but otherwise following the procedure described above. The RNPs showed reduced susceptibility compared to the experiments using sgRNA alone despite the higher HLC concentration, indicating that the sgRNA within an RNP is less accessible to nuclease, but the cleavage pattern remained qualitatively similar, with most cleavage occurring at YA sites (data not shown).

[00558] G10039, which comprises modifications at all YA sites, was assayed with 0.01 mg/ml HLC and found to show only a very small amount of cleavage at position 16, consistent with protection by the phosphorothioate modification at that position (Fig. 13A). Minimal amounts of cleavage were detectable at certain additional (non-YA) sites, but nearly all of the starting material remained intact throughout the incubation.

[00559] G10039 (as free sgRNA) was also treated with 8.5 mg/ml HLC. Degradation increased at position 16 and was also observed at several other positions, some of which were not YA sites (Fig. 13B).

Example 7 – Editing following transfection with sgRNAs with modifications at YA sites

[00560] A series of sgRNAs were designed by systematically introducing 2'-OMe modifications at individual YA sites in the conserved regions that were unmodified in G282. Thus, the sgRNAs sequentially numbered from G9989-G9994 have 2'-OMe modifications at positions 25, 45, 50, 56, 64, and 67, respectively, which are positions LS5, LS7, LS12, N6, N14, and N17 as shown in Fig. 10A. These are the pyrimidines of YA sites 1, 5, 6, 7, 8, and 9 as shown in Fig. 10B. The sgRNAs sequentially numbered from G10019-G10024 have the same 2'-OMe modifications as G9989-G9994, respectively, but the nucleobase sequence is identical to that of G502 instead of G282.

[00561] Similarly, a series of sgRNAs were designed by systematically introducing 2'-fluoro modifications at individual YA sites in the conserved regions that were unmodified in G282. Thus, the sgRNAs sequentially numbered from G9995-G10000 have 2'-fluoro modifications at positions 25, 45, 50, 56, 64, and 67, respectively. The sgRNAs sequentially numbered from G10025-G10030 have the same 2'-fluoro modifications as G9995-G10000, respectively, but the nucleobase sequence is identical to that of G502 instead of G282.

[00562] A further series of sgRNAs were designed by systematically introducing phosphorothioate modifications at individual YA sites in the conserved regions that were unmodified in G282. Thus, the sgRNAs sequentially numbered from G10001-G10006 have 2'-fluoro modifications at positions 25, 45, 50, 56, 64, and 67. The sgRNAs sequentially numbered from G10031-G10036 have the same phosphorothioate modifications as G10001-G10006, respectively, but the nucleobase sequence is identical to that of G502 instead of G282.

[00563] Also tested were guides modified with ENA (G9878, G10007, and G10008 had the G282 sequence, and G10037 and G10038 had the G502 sequence). The modifications in G10007 and G10037 were at the 45th and 50th nucleotides (positions LS7 and LS12 as

indicated in Fig. 10A). The ENA in G9878 was at the three 5'-terminal nucleotides and the fourth to second nucleotides from the 3' end. The ENA in G10008 and G10038 was at the 46th and 49th nucleotides (positions LS8 and LS11 as indicated in Fig. 10A).

[00564] Also tested were guides modified with deoxyribonucleotides (G9423-G9427) and UNA (G9879), all of which had the G282 sequence. The positions of the modifications in these guides are shown in the Sequence Table.

[00565] The guides described above were incorporated into lipoplexes and transfected into PMH as described above and percent editing was determined (Fig. 14 for guides matching the sequence of G282 and Fig. 15A for guides matching the sequence of G502). The guides with the sequence of G502 were also transfected into PCH and PHH as described above and percent editing was determined (Fig. 15B for PCH and Fig. 15C for PHH). The baseline reference (corresponding to the level of editing indicated by the dotted line) was G282 in Fig. 14 and G502 in Fig. 15A. All of the 2'-OMe, 2'-fluoro, and phosphorothioate modifications introduced in G9989-G10006 and G10019-G10036 were tolerated in that editing activity did not substantially decrease. Additionally, the other modifications were generally tolerated as well. The ENA modification of positions 45-50 in G10007 and G10037 showed lower percent editing activity.

Example 8 – Primary cell editing following transfection with sgRNAs

[00566] Several series of modified sgRNAs were designed based on the nucleobase sequences of G000282 and G000502. Specific modifications are described in Table 1. G00282 variants were assayed for editing in duplicate (unless otherwise noted) in primary mouse hepatocyte cells (PMH) *in vitro*. G000502 variants were similarly assayed in duplicate (unless otherwise noted) in primary cyno hepatocyte (PCH) and PMH cells *in vitro*. All data is reported in Tables 14 and 15 below.

[00567] A series of sgRNAs were designed assaying modifications in the guide domain combined with the modified conserved region described in SEQ ID No. 201. The sgRNAs sequentially numbered from G012421-G012425, G012689, G012690, G012426-G012431 have the same modifications as G012693-G012705, respectively, but the nucleobase sequence is identical to that of G000502 instead of G000282. Data for these guides are presented in Table 14.

[00568] Similarly, a series of sgRNAs were designed assaying modifications in the conserved region combined with the modified guide domain of either the G0000502 variant,

G012402, or the modified guide domain of G000282 variant, G009533. The sgRNAs sequentially numbered from G012432-G012438, G012691, G012439-G012440, G012692 have the same modifications as G012706-G12716, respectively, but the nucleobase sequence is identical to that of G000502 instead of G000282. Data for these guides are presented in Table 14.

[00569] A further series of sgRNAs were designed combining various guide domain and conserved region modification patterns. The sgRNAs sequentially numbered from G012441-G012451 sequentially have the same modifications as G012717-G012727, respectively, but the nucleobase sequence is identical to that of G000502 instead of G000282. Data for these guides are presented in Table 14 and Figure 31A-C.

[00570] Similarly, a series of sgRNAs were designed assaying modifications in the context of short single guide variants of G000282 and G000502. The sgRNAs sequentially numbered from G012452-G012461 are based on the short guide variant of G000502, specifically G012401. These modified variants have the same modifications as G012728-G12737, respectively, but the nucleobase sequence of G012728-G12737 is identical to that of G000639, the short guide variant of G000282. Data for this series of guides are presented in Table 14.

[00571] Lastly, a series of sgRNAs as indicated in Table 15 were designed assaying modifications in the nucleobase sequence of G000502 (See Table 1 for sgRNA nucleotide sequences). Data for this series of guides are presented in Table 15 and Figure 23A-B.

Table 14 – Primary cell editing with modified guides

G000282 Variants	PMH		G000502 Variants	PCH		PMH	
	% Editing	SD		% Editing	SD	% Editing	SD
G000282	81.0%	3.7%	G000502	76.5%	4.9%	92.3%	2.6%
G000639	83.4%	1.6%	G012401	71.7%	3.3%	91.1%	0.0%
G009559	70.9%	0.4%	G009571	72.3%	2.4%	79.9%	2.1%
G009985	91.3%	2.1%	ND	ND	ND	ND	ND
G010009	72.9%	0.5%	G010039	72.4%	4.3%	76.1%	1.0%
G012693	90.2%	0.4%	G012421	78.1%	1.0%	92.0%	2.0%
G012694	89.9%	0.4%	G012422	80.1%	1.3%	92.0%	0.8%
G012695	88.7%	0.7%	G012423	76.4%	4.7%	92.6%	0.4%
G012696	85.7%	0.8%	G012424	79.1%	3.6%	93.1%	0.6%
G012697	87.8%	0.7%	G012425	82.0%	1.3%	94.6%	0.3%
G012698	68.7%	0.8%	G012689	60.6%	1.6%	86.1%	2.1%
G012699	68.1%	1.8%	G012690	67.0%	2.3%	89.6%	0.5%

G000282 Variants	PMH		G000502 Variants	PCH		PMH	
	% Editing	SD		% Editing	SD	% Editing	SD
G012700	73.9%	0.1%	G012426	78.6%	2.9%	93.2%	1.8%
G012701	75.7%	1.6%	G012427	66.2%	3.0%	80.4%	1.0%
G012702	69.4%	0.1%	G012428	66.1%	0.5%	81.8%	0.8%
G012703	86.3%	2.6%	G012429	59.7%	ND	79.3%	1.7%
G012704	64.6%	2.3%	G012430	65.6%	0.8%	75.8%	1.8%
G012705	67.3%	1.1%	G012431	64.1%	0.6%	76.3%	2.5%
G012706	68.4%	0.4%	G012432	53.8%	5.1%	70.8%	1.7%
G012707	62.9%	0.4%	G012433	63.2%	1.6%	76.7%	0.1%
G012708	64.0%	0.1%	G012434	53.1%	3.0%	67.0%	0.4%
G012709	65.8%	0.7%	G012435	62.2%	0.4%	70.7%	0.4%
G012710	43.8%	0.5%	G012436	47.3%	3.3%	64.9%	2.8%
G012711	54.6%	1.6%	G012437	51.2%	4.7%	67.7%	0.2%
G012712	65.9%	1.6%	G012438	60.0%	1.3%	68.7%	2.1%
G012713	67.6%	0.3%	G012691	61.5%	9.0%	74.4%	0.5%
G012714	66.3%	2.1%	G012439	39.4%	1.8%	58.0%	4.3%
G012715	59.3%	1.8%	G012440	40.4%	3.2%	65.5%	3.3%
G012716	60.9%	0.5%	G012692	43.8%	1.5%	63.1%	0.1%
G012717	78.8%	0.4%	G012441	56.8%	0.3%	85.3%	0.8%
G012718	74.1%	3.3%	G012442	65.6%	1.5%	90.0%	0.3%
G012719	75.3%	3.1%	G012443	67.0%	2.0%	88.8%	0.6%
G012720	80.1%	0.0%	G012444	68.7%	1.2%	90.9%	0.1%
G012721	60.6%	1.1%	G012445	44.9%	1.1%	79.3%	2.3%
G012722	67.8%	1.1%	G012446	56.4%	4.2%	85.2%	1.6%
G012723	83.3%	0.7%	G012447	68.4%	1.5%	88.5%	0.6%
G012724	82.9%	0.7%	G012448	79.0%	3.0%	94.5%	0.5%
G012725	88.5%	2.5%	G012449	66.4%	10.3%	84.7%	0.4%
G012726	62.6%	1.3%	G012450	53.3%	0.9%	70.2%	2.5%
G012727	80.4%	1.9%	G012451	54.4%	2.0%	81.6%	0.7%
G012728	65.7%	2.0%	G012452	65.2%	ND	73.4%	0.8%
G012729	65.9%	3.7%	G012453	67.5%	0.5%	75.4%	0.1%
G012730	63.4%	2.7%	G012454	60.7%	0.1%	75.3%	0.4%
G012731	67.4%	3.8%	G012455	63.8%	1.1%	71.9%	1.4%
G012732	69.7%	0.0%	G012456	65.5%	0.1%	73.3%	0.8%
G012733	70.1%	2.9%	G012457	70.0%	10.9%	76.5%	1.1%
G012734	65.2%	1.4%	G012458	52.5%	2.1%	73.8%	3.5%
G012735	59.9%	0.7%	G012459	55.7%	4.4%	74.7%	0.3%
G012736	55.0%	0.8%	G012460	38.7%	1.1%	61.6%	4.1%
G012737	61.7%	2.8%	G012461	51.1%	0.1%	69.6%	1.1%
G012741	70.7%	3.6%	G012402	71.3%	2.8%	77.7%	0.8%

Table 15 – Primary Cell editing with Modified guides

G000502 Variants	PCH		PMH	
	% Editing	SD	% Editing	SD
G000502	76.5%	4.9%	92.3%	2.6%
G012742	51.6%	4.2%	63.1%	1.8%
G012743	49.9%	3.5%	64.1%	1.6%
G012973	0.5%	0.4%	0.6%	0.2%
G012974	3.3%	1.5%	4.4%	1.7%
G012975	19.3%	4.0%	39.1%	2.2%
G012976	2.8%	0.5%	7.3%	1.5%
G012977	20.1%	0.6%	22.4%	3.3%
G012978	38.3%	3.5%	60.1%	3.3%
G012979	23.0%	0.2%	29.3%	3.7%

Example 9 – In vitro editing of modified guides targeting HAO1 and SERPINA1

[00572] Lipid nanoparticle (LNP) formulations of modified sgRNAs targeting were tested on primary human hepatocytes and primary cynomolgus hepatocytes in a dose response assay with guides targeting the human genes HAO1 or LDHA. All methods are as described in Example 1 unless otherwise noted. Both cell lines were incubated at 37°C, 5% CO_2 for 48 hours prior to treatment with LNPs. LNPs were incubated in media containing 3% cynomolgus serum at 37°C for 10 minutes and administered to cells in amounts as further provided herein. Post-incubation the LNPs were added to the human or cynomolgus hepatocytes in an 8 point 3-fold dose response curve starting at 300ng Cas9 mRNA. The cells were lysed 96 hours post-treatment for NGS analysis as described in Example 1

[00573] Table 16 shows the average editing and standard deviation the tested control sgRNAs at 10.75 nM delivered with *Spy Cas9* via LNP in PHH and PCH. These samples were generated in triplicate.

Table 16: Primary cell editing with modified guides targeting HAO1 at 10.75 nM guide.

Cell type	GUIDE	Edit	SD
PHH	G000480	0.990	0.002
	G000502	0.909	0.022
PCH	G000480	0.095	0.018
	G000502	0.912	0.012

[00574] Table 17 shows the average editing and standard deviation for sgRNAs targing HAO1 delivered with *Spy Cas9* via LNP to PHH or PCH. These samples were generated in at

least duplicate. The dose response curve plot for these data are shown in Figures 27A-D and 28A-D.

[00575] Table 18 shows the average editing and standard deviation for sgRNAs targeting SerpinA1 delivered with *Spy Cas9* via LNP to PHH. G000480 and G000502 are controls that target TTR. These samples were generated in at least duplicate. The dose response curve plot for these data are shown in Figures 25A-E.

[00576] Table 19 shows the average editing and standard deviation for sgRNAs targeting SerpinA1 delivered with *Spy Cas9* via LNP to PCH. G000480 and G000502 are controls that target TTR. These samples were generated in at least duplicate. The dose response curve plot for these data are shown in Figures 26A-E.

Table 17 – Editing in primary cells with modified guides targeting HAO1

Guide (nM)		32.260		10.753		3.584		1.195		0.398		0.133		0.044		0.015	
	Guide	%Edit	SD	Edit	SD	Edit	SD	Edit	SD	Edit	SD	Edit	SD	Edit	SD	Edit	SD
PHH	G009428	97.7	0.2	98.0	0.5	94.5	1.5	86.9	2.2	67.4	2.5	39.7	3.8	13.6	0.9	2.7	1.0
	G013964	98.5	0.4	98.5	0.4	96.1	0.8	91.0	1.3	77.1	1.6	59.1	14.7	19.6	2.5	3.9	0.8
	G013968	96.8	0.8	97.5	0.4	90.8	1.4	78.1	1.7	46.4	3.5	25.9	19.9	2.9	0.8	0.8	0.3
	G009429	98.9	0.1	98.4	0.5	91.3	0.6	80.9	1.9	52.9	1.3	21.7	3.0	5.5	0.7	0.7	0.3
	G013965	98.4	0.6	98.2	0.2	93.9	1.2	83.0	1.1	59.6	2.1	45.3	21.4	7.5	0.6	1.1	0.1
	G013969	98.8	0.3	98.6	0.2	94.9	0.3	85.3	0.3	62.9	1.8	38.9	20.6	6.5	1.0	0.6	0.3
	G009430	96.2	0.4	96.3	0.3	88.4	1.8	76.9	0.4	47.8	2.0	20.0	3.8	4.3	1.1	0.5	0.1
	G013966	97.0	0.5	97.1	0.3	92.4	1.0	80.6	2.8	52.6	1.2	31.2	16.9	3.7	0.7	0.5	0.2
	G013970	97.5	0.1	97.0	0.2	90.8	0.4	76.4	3.4	47.2	3.5	25.6	16.8	3.5	0.7	0.5	0.1
	G009432	94.8	2.1	93.1	0.7	83.9	1.9	69.8	2.1	41.9	2.0	15.8	1.5	3.2	0.5	0.5	0.3
	G013967	94.2	0.4	93.5	0.8	84.8	0.6	68.5	4.2	40.6	1.8	24.0	14.3	3.5	0.8	0.5	0.2
	G013971	93.6	0.2	92.6	0.6	83.2	2.0	61.6	1.6	36.5	2.5	21.6	14.1	2.2	0.6	0.3	0.3
PCH	G009428	92.8	2.4	83.6	5.5	65.1	5.5	30.8	4.8	9.9	2.9	3.7	1.5	0.7	0.2	0.4	0.2
	G013964	96.3	0.5	92.4	3.1	77.6	3.9	51.4	6.6	24.7	0.0	5.8	ND	3.2	1.3	0.8	0.2
	G013968	87.5	0.1	84.9	4.6	57.4	1.2	22.0	ND	6.2	0.3	1.8	0.8	1.4	0.7	0.4	0.3
	G009429	96.3	1.6	81.5	9.8	53.3	1.9	21.9	5.5	4.0	0.6	1.2	0.5	0.3	0.2	0.2	0.1
	G013965	95.2	0.6	89.5	1.1	62.6	0.5	28.4	3.2	7.7	0.9	2.1	0.3	0.3	0.2	0.2	0.1
	G013969	98.1	0.7	93.1	3.1	70.0	0.5	38.5	1.6	11.6	1.4	2.6	0.2	0.7	0.3	0.3	0.1
	G009430	94.4	2.8	90.4	3.9	74.6	1.0	42.3	2.8	15.6	0.4	3.0	0.9	0.8	0.1	0.2	0.1
	G013966	95.3	0.7	93.8	1.0	77.9	0.8	51.8	4.2	23.2	1.7	6.5	1.0	1.5	0.5	0.3	0.2
	G013970	95.9	1.6	95.3	0.2	79.3	1.4	50.6	0.3	23.4	0.7	6.2	1.0	1.4	0.2	0.2	0.1
	G009432	94.1	0.8	89.2	3.6	67.5	3.5	39.2	1.8	13.3	1.2	2.3	0.9	1.3	0.6	0.5	0.1
	G013967	92.2	0.8	88.7	0.8	67.3	3.9	38.0	1.9	15.3	1.3	4.3	1.0	1.5	0.2	0.4	0.1
	G013971	95.5	1.0	94.4	1.2	74.2	2.1	45.1	2.4	17.2	3.2	4.5	1.4	1.0	0.1	0.4	0.1

Table 18 - Editing in PHH with modified guides targeting SerpinA1.

guide (nM)		33.3		11.1		3.7		1.23		0.41		0.14		0.05	
	Guide	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**
PHH	G000480	96.6	0.1	95.5	0.1	94.7	0.7	91.9	0.4	85.2	0.6	70.4	4.7	41.4	1.8
	G000486	95.0	0.8	91.8	0.6	87.1	0.6	71.7	1.6	47.3	4.5	22.3	2.1	8.5	1.3
	G000407	77.3	1.7	79.9	3.7	66.7	7.4	48.0	2.1	27.2	5.3	12.0	1.1	5.2	0.6
	G013954	76.2	4.2	73.1	6.4	65.1	7.0	39.2	8.9	22.5	3.3	10.9	2.7	4.4	0.8
	G013959	73.6	0.4	77.3	2.9	69.1	1.3	48.8	5.5	29.5	6.7	13.4	4.3	7.0	1.3
	G000415	93.4	0.8	91.6	1.3	90.6	1.2	86.6	1.7	77.0	3.3	56.7	6.8	34.7	4.3
	G013958	93.6	0.1	92.1	1.8	89.4	1.3	85.5	1.5	73.8	2.7	52.4	5.9	28.7	2.6
	G013963	90.9	0.1	90.7	1.3	91.7	1.8	88.4	1.1	83.6	1.5	68.6	7.2	37.4	6.8
	G000408	91.7	2.4	88.0	0.0	84.3	1.5	74.6	2.7	48.8	6.3	21.7	2.5	6.7	0.7
	G000413	49.3	59.1	85.1	60.2	77.9	55.1	58.1	41.1	31.1	22.0	14.8	10.5	5.1	3.6
	G000409	93.2	0.6	91.1	2.3	86.9	0.4	80.9	1.4	57.7	2.9	31.9	0.8	9.3	0.4
	G013955	95.3	0.8	93.1	1.3	88.0	1.2	82.5	0.4	63.4	2.3	37.8	0.1	13.4	0.8
	G013960	94.8	0.1	91.6	1.8	89.5	1.2	85.9	0.6	73.6	4.5	43.4	0.6	19.3	0.5
	G000412	96.0	67.9	88.6	62.6	88.1	62.3	80.8	57.1	68.8	48.6	30.6	21.6	9.0	6.4
	G013956	46.0	65.1	91.0	0.4	89.7	63.4	83.1	58.8	64.2	45.4	30.4	21.5	15.2	10.7
	G013961	95.0	67.2	92.6	65.5	90.8	64.2	79.3	56.1	51.3	36.3	20.8	14.7	7.0	4.9
	G000414	95.0	0.4	91.6	1.6	89.8	0.4	82.9	0.2	63.6	1.7	34.0	1.7	14.0	0.3
	G013962	57.6	53.5	48.5	58.7	89.0	62.9	80.8	57.1	62.7	44.3	14.4	20.3	14.7	10.4
	G013957	92.3	65.3	46.0	62.4	88.8	62.8	80.9	57.2	60.4	42.7	30.3	21.4	13.9	9.8

Table 19 - Editing in PCH with modified guides targeting SerpinA1.

guide (nM)		33.3		11.1		3.7		1.23		0.41		0.14		0.05	
	Guide	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**	**Edit**	**SD**
PCH	G000480	19.0	1.9	3.7	0.9	1.2	0.3	0.3	0.1	0.1	0.0	0.1	0.0	0.1	0.0
	G000502	82.8	9.8	73.0	10.2	61.8	11.0	41.2	2.3	18.5	1.2	6.3	0.4	3.0	0.2
	G000407	64.4	9.0	48.2	6.7	27.8	7.4	13.3	0.8	5.4	0.1	1.9	0.9	0.6	0.1
	G013954	52.3	16.3	39.3	6.4	23.4	7.4	10.8	2.1	4.4	3.1	2.1	1.6	1.1	0.1
	G013959	65.6	9.8	46.3	9.4	31.4	7.2	15.7	4.5	4.9	0.8	2.2	0.1	1.2	0.6
	G000415	87.0	7.0	74.2	5.7	59.3	7.4	32.4	3.5	10.3	2.4	4.3	0.5	1.7	0.1
	G013958	90.7	4.9	77.0	9.3	60.3	7.5	33.7	0.2	11.9	0.7	4.8	1.1	1.9	0.5
	G013963	89.2	4.9	83.5	2.2	71.9	4.7	47.5	1.8	19.9	3.0	7.7	1.1	2.5	0.4
	G000408	22.4	0.2	7.1	0.6	1.7	0.1	0.6	0.1	0.1	0.1	0.0	0.0	0.1	0.1
	G000413	7.0	0.1	1.7	0.1	0.4	0.1	0.1	0.0	0.1	0.0	0.2	0.0	0.2	0.1
	G000409	71.9	0.5	46.8	0.7	14.7	0.3	3.4	0.0	1.2	0.1	0.2	0.1	0.2	0.1
	G013955	85.0	4.1	60.7	1.1	35.2	2.8	10.8	0.8	3.4	1.4	1.4	0.6	0.3	0.1
	G013960	86.4	0.8	63.9	0.6	37.5	2.0	12.4	3.6	4.6	2.3	1.0	0.5	0.3	0.3
	G000412	82.7	6.0	57.1	0.5	34.1	1.4	11.0	2.6	4.4	1.5	1.2	0.8	0.1	0.0
	G013956	81.9	2.0	64.2	0.9	40.7	1.6	18.8	1.2	7.3	0.7	1.3	0.8	0.4	0.1
	G013961	72.8	18.2	70.6	3.6	43.3	3.5	22.8	3.9	6.1	1.7	1.4	0.1	0.4	0.1
	G000414	76.5	1.6	42.2	3.3	25.1	3.4	8.1	0.1	2.8	0.5	0.8	0.6	0.1	0.0
	G013957	82.3	5.2	50.6	7.0	26.4	2.1	10.2	1.0	3.8	0.4	1.2	0.3	1.2	0.3
	G013962	76.8	0.4	46.1	1.5	24.3	2.5	10.2	1.8	2.8	0.6	0.9	0.1	0.6	0.2

Example 10 – In Vivo Studies of Short-sgRNA

[00577] LNPs prepared as described above in Example 1(F), comprising chemically synthesized sgRNAs (including short-sgRNAs) targeting the mouse *TTR* gene and IVT Cas9 mRNA in a 1:1 weight ratio, were administered to CD-1 female mice (N indicated below) or Sprague-Dawley female rats as described above in Example 1(H). Eight days post dose at necropsy, livers and blood were collected for NGS measurements of editing efficiency and serum TTR analysis, respectively, as described above in Example 1. Animals were weighed 24 hours post dose for overall wellness assessment.

[00578] Figures 1A and 1B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Tables 20A and 20B, which all target the same sequence in the TTR gene (See Table 1 for sgRNA nucleotide sequences). G000211 and G000282 served as reference comparators. The LNPs were made according to LNP Procedure B in Example 1(F). The data shown in Figures 1A and 1B are from mice administered 0.1 mg/kg (mpk) or 0.3 mg/kg of LNPs and are summarized in Tables 20A and 20B.

Table 20A

Guide	Average Editing (%)	Std. Dev.	N
TSS	0.14	0.05477	5
G000282 - 0.3 mpk	59.64	6.213	5
G000282 - 0.1 mpk	14.12	2.286	5
G000515 - 0.3 mpk	37.28	11.9	5
G000515 - 0.1 mpk	15.56	8.138	5
G000621 - 0.3 mpk	37.04	12.41	5
G000621 - 0.1 mpk	6.88	2.826	5
G000632 - 0.3 mpk	38.72	6.406	5
G000632 - 0.1 mpk	8.58	7.482	5
G000638 - 0.3 mpk	42.1	12.23	5
G000638 - 0.1 mpk	15.08	7.851	5
G000639 - 0.3 mpk	54.58	17.3	5
G000639 - 0.1 mpk	20.1	6.038	5
G000640 -0.3 mpk	48.62	11.09	5
G000640 - 0.1 mpk	19.52	10.68	5

G000641 - 0.3 mpk	46.96	6.204	5
G000641 - 0.1 mpk	9.68	1.63	5
G000211 - 0.3 mpk	18.62	12.89	5
G000211 - 0.1 mpk	2.08	0.8044	5

Table 20B

Guide	Average Serum TTR (µg/mL)	SD	N
TSS	969.4	215.2	5
G000282 - 0.3 mpk	178.7	131.2	5
G000282 - 0.1 mpk	883.1	92.82	5
G000515 - 0.3 mpk	529.5	174.9	5
G000515 - 0.1 mpk	869.4	227.8	5
G000621 - 0.3 mpk	523	167.9	5
G000261 - 0.1 mpk	920.8	162.6	5
G000632 - 0.3 mpk	449.4	66.61	5
G000632 - 0.1 mpk	971.5	195.1	5
G000638 - 0.3 mpk	452.4	163.8	5
G000638 - 0.1 mpk	934	242.6	5
G000639 - 0.3 mpk	261.9	202.9	5
G000639 - 0.1 mpk	726.2	122.1	5
G000640 -0.3 mpk	363.3	172	5
G000640 - 0.1 mpk	752.7	233.8	5
G000641 - 0.3 mpk	419	77.43	5
G000641 - 0.1 mpk	1018	58.16	5
G000211 - 0.3 mpk	692.4	157	5
G000211 - 0.1 mpk	970.3	113.7	5

[00579] Figures 2A and 2B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Tables 21A and 21B, which all target the same sequence in the TTR gene (See Table 1 for sgRNA nucleotide sequences). G000269 and G000283 served as reference comparators. The LNPs were made according to LNP Procedure B in Example 1(F). The data shown in Figures 2A and 2B are from mice administered 0.1 mg/kg (mpk) or 0.3 mg/kg of LNPs and are summarized in Tables 21A and 21B.

Table 21A

Guide	Average Editing (%)	Std. Dev.	N
TSS	0.12	0.0447214	5
G000269 - 0.3mpk	8.94	2.65763	5
G000269 - 0.1mpk	2.86	1.94756	5
G000620 - 0.3mpk	24.62	5.66675	5
G000620 - 0.1mpk	10.48	12.0136	5
G000622 - 0.3mpk	14.08	3.20422	5
G000622 - 0.1mpk	4.5	2.01122	5
G000623 - 0.3mpk	14.8	9.48868	5
G000623 - 0.1mpk	3.08	1.26768	5
G000624 - 0.3mpk	32.86	12.3545	5
G000624 - 0.1mpk	7.76	4.60196	5
G000625 - 0.3mpk	41.28	6.99085	5
G000625 - 0.1mpk	15.62	5.79974	5
G000626 - 0.3mpk	37.7	13.1164	5
G000626 - 0.1mpk	7.42	3.25146	5
G000627 - 0.3mpk	27.86	12.5293	5
G000627 - 0.1mpk	6.46	1.60094	5
G000283 - 0.3mpk	40.14	6.59416	5
G000283 - 0.1mpk	19.42	12.1568	5

Table 21B

Guide	Average Serum TTR (µg/mL)	Std. Dev.	N
TSS	970.798	154.875	5
G000269 - 0.3mpk	859.012	244.538	5
G000269 - 0.1mpk	769.096	101.675	5
G000620 - 0.3mpk	595.108	218.142	5
G000620 - 0.1mpk	614.304	117.668	5
G000622 - 0.3mpk	537.89	35.5731	5
G000622 - 0.1mpk	816.786	190.52	5
G000623 - 0.3mpk	515.142	189.776	5

G000623 - 0.1mpk	713.03	158.231	5
G000624 - 0.3mpk	352.896	157.573	5
G000624 - 0.1mpk	584.678	143.396	5
G000625 - 0.3mpk	329.386	72.7329	5
G000625 - 0.1mpk	595.212	90.3979	5
G000626 - 0.3mpk	328.34	142.975	5
G000626 - 0.1mpk	649.298	72.829	5
G000627 - 0.3mpk	443.848	156.222	5
G000627 - 0.1mpk	692.942	187.783	5
G000283 - 0.3mpk	315.128	112.059	5
G000283 - 0.1mpk	535.656	186.657	5

[00580] Figures 3A and 3B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Tables 22A and 22B, which all target the same sequence in the TTR gene (See Table 1 for sgRNA nucleotide sequences). G000502 served as a reference comparator. The LNPs were made according to LNP Procedure C in Example 1(F). The data shown in Figures 3A and 3B are from mice administered 0.1 mg/kg (mpk) or 0.3 mg/kg of LNPs and are summarized in Tables 22A and 22B.

Table 22A

Guide	Average Editing (%)	Std. Dev.	N
TSS	0.133333	0.057735	3
G000502 0.1 mpk	37.4	12.106	5
G000502 0.3 mpk	64.86	2.62545	5
G009571 0.1 mpk	47.6	6.98665	4
G009571 0.3 mpk	69.8	1.59217	5
G010015 0.1 mpk	47.86	6.09451	5
G010015 0.3 mpk	69.325	2.20662	4

Table 22B

Guide	Average Serum TTR (µg/mL)	Std. Dev.	N
TSS	1844.59	542.644	5
G000502 0.1 mpk	768.714	390.311	5
G000502 0.3 mpk	169.707	102.03	5
G009571 0.1 mpk	658.269	303.19	5

G009571 0.3 mpk	84.6392	33.3813	5
G010015 0.1 mpk	602.506	354.455	5
G010015 0.3 mpk	86.236	38.391	5

[00581] Figures 4A and 4B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Tables 23A and 23B, which all target the same sequence in the TTR gene (See Table 1 for sgRNA nucleotide sequences). G000211 and G000282 served as reference comparators. The LNPs were made according to LNP Procedure A in Example 1(F) using IVT Cas9 mRNA corresponding to SEQ ID NO: 501. The data shown in Figures 4A and 4B are from mice administered 0.5 mg/kg (mpk) or 1.0 mg/kg of LNPs and are summarized in Tables 23A and 23B.

Table 23A

Guide	Average Editing (%)	Std. Dev.	N
PBS	0.08	0.04472	5
G000513 - 1 mpk	12.7	15.11	5
G000513 - 0.5 mpk	3.76	2.359	5
G000514 - 1 mpk	0.82	0.3271	5
G000514 - 0.5 mpk	0.34	0.08944	5
G000515 - 1 mpk	30.12	12.44	5
G000515 - 0.5 mpk	7.98	2.111	5
G000516 - 1 mpk	3.96	2.035	5
G000516 - 0.5 mpk	0.92	0.3564	5
G000517 - 1 mpk	0.96	0.2302	5
G000517 - 0.5 mpk	0.42	0.1304	5
G000518 - 1 mpk	0.62	0.1304	5
G000518 - 0.5 mpk	0.22	0.04472	5
G000211 - 1 mpk	2.66	1.346	5
G000211 - 0.5 mpk	0.74	0.1517	5
G000282 - 1 mpk	20.3	12.21	5
G000282 - 0.5 mpk	14.24	9.371	5

Table 23B

Guide	Average Serum TTR (µg/mL)	Std. Dev.	N
PBS	1386	147.5	5
G000513 - 1 mpk	880.9	278.6	5
G000513 - 0.5 mpk	1095	86.52	5
G000514 - 1 mpk	1199	119.3	5
G000514 - 0.5 mpk	1131	139	4
G000515 - 1 mpk	629	288	5
G000515 - 0.5 mpk	1173	170.7	5

G000516 - 1 mpk	1091	118.6	5
G000516 - 0.5 mpk	1416	174.7	5
G000517 - 1 mpk	1336	137.2	5
G000517 - 0.5 mpk	1321	181.3	5
G000518 - 1 mpk	1508	289.9	5
G000518 - 0.5 mpk	1267	376.7	5
G000211 - 1 mpk	1393	256.9	5
G000211 - 0.5 mpk	1318	223.3	5
G000282 - 1 mpk	929.2	250.4	5
G000282 - 0.5 mpk	1162	282	5

[00582] The same sgRNAs listed in Tables 23A and 23B (Table 1) were tested in vitro by transfection into Neuro2A cells, as per Example 1(C). Results are shown in Figure 5.

[00583] Figures 6A and 6B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Tables 24A and 24B, which all target the same sequence in the TTR gene (See Table 1 for sgRNA nucleotide sequences). G000211 and G000282 served as reference comparators. The LNPs were made according to LNP Procedure B in Example 1(F). The data shown in Figures 6A and 6B are from mice administered 0.1 mg/kg (mpk) of LNPs and are summarized in Tables 24A and 24B.

Table 24A

Guide	Average Editing (%)	SD	N
TSS	0.12	0.0447214	5
G000282	16.98	8.49453	5
G000211	1.34	0.497996	5
G000612	8.74	5.38266	5
G000613	17.96	9.23488	5
G000614	0.5	0.339116	5
G000615	11.76	2.81034	5
G000616	8.28	7.08428	5
G000617	5.08	1.96647	5
G000618	6.7	1.81934	5
G000619	10.32	11.9485	5
G000642	16.34	6.9877	5
G000643	18.62	5.83841	5

Table 24B

Guide	Average Serum TTR (µg/mL)	SD	N
TSS	962.636	271.526	5
G000282	936.624	190.211	5
G000211	1239.13	179.194	5

G000612	1011.85	215.796	5
G000613	810.72	156.082	5
G000614	1150.81	362.492	5
G000615	1007.04	179.37	5
G000616	879.592	180.917	5
G000617	1031.62	184.594	5
G000618	921.65	71.1735	5
G000619	924.728	348.938	5
G000642	692.038	162.344	5
G000643	696.416	51.8907	5

[00584] Figures 7A and 7B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Tables 25A and 25B, which all target the same sequence in the TTR gene (See Table 1 for sgRNA nucleotide sequences). G000534 served as a reference comparator. The LNPs were made according to LNP Procedure C in Example 1(F). The data shown in Figures 7A and 7B are from rats administered 0.3 mg/kg (mpk) of LNPs and are summarized in Tables 25A and 25B.

Table 25A

Guide	Average Editing (%)	SD	N
TSS	0.02	0.0447214	5
G000534	20.26	4.73477	5
G000637	11.66	5.93827	5
G000694	20.8	5.62894	5
G000695	11.28	5.66719	5

Table 25B

Guide	Average Serum TTR (µg/mL)	SD	N
TSS	983.078	138.405	5
G000534	1008.92	220.498	5
G000637	1027.73	199.071	5
G000694	682.964	163.519	5
G000695	889.5	270.242	5

[00585] Figures 8A and 8B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Tables 26A and 26B, which all target the same sequence in the TTR gene (See Table 1 for sgRNA nucleotide sequences). G000534 served as a reference comparator. The LNPs were made according to LNP Procedure C in Example 1(F). The data shown in Figures 8A and 8B are from rats

administered 0.3 mg/kg (mpk) and 1.0 mg/kg of LNPs and are summarized in Tables 26A and 26B.

Table 26A

Guide	Average Editing (%)	SD	N
TSS	0.02	0.0447214	5
G000534 - 1MPK	53.48	4.34879	5
G000534 - 0.3MPK	19	2.96395	5
G000694 - 1MPK	39.32	6.93087	5
G000694 - 0.3MPK	13.46	5.50391	5

Table 26B

Guide	Average Serum TTR (µg/mL)	SD	N
TSS	1178.71	75.8721	5
G000534 - 1MPK	266.136	63.6724	5
G000534 - 0.3MPK	676.446	107.07	5
G000694 - 1MPK	503.888	30.8714	5
G000694 - 0.3MPK	789.686	91.9034	5

Example 11 - In Vivo Studies of sgRNAs

[00586] LNPs prepared as described above in Example 1(F) (LNP Procedure D), comprising chemically synthesized sgRNAs targeting the mouse *TTR* gene and IVT Cas9 mRNA in a 1:1 weight ratio, were administered to CD-1 female mice (N indicated below) as described above in Example 1(E). Eight days post dose at necropsy, livers and blood were collected for NGS measurements of editing efficiency and serum TTR analysis, respectively, as described above in Example 1. Animals were weighed 24 hours post dose for overall wellness assessment.

[00587] Figures 17A and 17B show the editing efficiency and TTR protein levels, respectively, for LNPs containing G282, G9981-G9986, and G10009, which all have the same nucleotide sequence as G282. The data shown in Figures 17A and 17B are from mice administered 0.1 mg/kg of LNPs, and are summarized in Tables 27A and 27B.

Table 27A

Guide ID	Average % Editing	Std. Dev.	N
TSS	0.1	0	5
G000282	18.12	3.27826	5
G009981	9.84	3.01297	5
G009982	12.94	3.3709	5

G009983	14.08	6.19007	5
G009984	13.62	11.0981	5
G009985	37.9	12.406	5
G009986	11.9	9.25122	5
G010009	36.14	10.7162	5

Table 27B

Guide ID	Serum TTR (µg/mL)	Std. Dev.	N
TSS	1002.47	185.909	5
G000282	727.622	126.773	5
G009981	764.096	147.486	5
G009982	768.886	246.038	5
G009983	733.138	119.212	5
G009984	724.15	210.047	5
G009985	353.746	277.917	5
G009986	694.538	206.566	5
G010009	542.53	138.99	5

[00588] Figures 18A and 18B show the editing efficiency and TTR protein levels, respectively, for LNPs containing G502 and G10011-G10016, which all have the same nucleotide sequence as G502. The data shown in Figures 18A and 18B are from mice administered 0.1 mg/kg of LNPs, and are summarized in Tables 28A and 28B.

Table 28A

Guide ID	Average % Editing	Std. Dev.	N
TSS	0.1	0	5
G000502	31.58	7.40993	5
G010011	13.44	4.90184	5
G010012	28.42	2.98613	5
G010013	20	3.83536	5
G010014	9.12	4.75994	5
G010015	48.08	6.12552	5
G010016	22.92	4.32169	5

Table 28B

Guide ID	Serum TTR (µg/mL)	Std. Dev.	N
TSS	931.178	141.193	5
G000502	570.332	179.698	5
G010011	589.487	31.5553	4
G010012	454.848	99.7835	5
G010013	597.594	314.78	5
G010014	381.214	169.623	5

G010015	181.184	54.3217	5
G010016	317.66	203.218	5

[00589] Figures 19A and 19B show the editing efficiency and TTR protein levels, respectively, for LNPs containing G502 and G9965-G9976, which all have the same nucleotide sequence as G502. The data shown in Figures 19A and 19B are from mice administered 0.1 mg/kg of LNPs, and are summarized in Tables 29A and 29B.

Table 29A

Guide ID	Average % Editing	Std. Dev.	N
TSS	0.6	0.0816497	4
G000502	39.18	9.50616	5
G009565	18.32	2.58592	5
G009566	18	10.5654	4
G009567	52.22	5.29641	5
G009568	42.64	12.5763	5
G009569	44.525	15.3743	4
G009570	46.52	9.6699	5
G009571	52.58	14.8569	5
G009572	10.18	4.80749	5
G009573	48.04	8.35063	5
G009574	28.1	3.80592	5
G009575	40.26	10.7549	5
G009576	15.36	6.01731	5

Table 29B

Guide ID	Serum TTR (µg/mL)	Std. Dev.	N
TSS	1992.98	364.252	5
G000502	594.954	199.578	5
G009565	1024.87	681.864	5
G009566	1120.52	361.314	4
G009567	378.082	108.791	5
G009568	613.27	290.386	5
G009569	312.825	324.585	4
G009570	410.94	175.285	5
G009571	365.506	365.327	5
G009572	1267.14	295.1	5
G009573	564.246	53.4768	5
G009574	685.998	178.199	5
G009575	664.69	507.897	5
G009576	1087.78	325.185	5

[00590] Figures 19C and 19D show the editing efficiency and TTR protein levels, respectively, for LNPs containing G282 and G9553-G9564, which all have the same nucleotide sequence as G282. The data shown in Figures 19C and 19D are from mice administered 0.1 mg/kg of LNPs, and are summarized in Tables 30A and 30B.

Table 30A

Guide ID	Average % Editing	Std. Dev.	N
TSS	0.1	0	5
G000282	37.56	8.50194	5
G009553	7.35	2.93201	4
G009554	9.85	5.35257	4
G009555	54	10.5376	5
G009556	20.72	5.53281	5
G009557	30.86	5.2491	5
G009558	26.5	14.046	5
G009559	52	8.22283	5
G009560	9.82	7.95217	5
G009561	33.62	5.01568	5
G009562	21.8	7.32427	5
G009563	28.5	4.48497	5
G009564	8.3	6.59735	5

Table 30B

Guide ID	Serum TTR (µg/mL)	Std. Dev.	N
TSS	609.04	85.4341	5
G000282	341.19	111.876	5
G009553	704.38	55.5751	4
G009554	578.958	222.003	5
G009555	271.606	212.904	5
G009556	656.606	176.012	5
G009557	549.578	346.277	5
G009558	820.098	368.242	5
G009559	402.612	270.913	5
G009560	1050.99	211.752	5
G009561	546.352	134.462	5
G009562	771.896	268.971	5
G009563	703.896	345.506	5
G009564	702.558	158.096	5

[00591] Figures 20A and 20B show the editing efficiency and TTR protein levels, respectively, for LNPs containing G502, G9567, G9569, and G9570, which all have the same nucleotide sequence as G502. The data shown in Figures 20A and 20B are from mice

administered 0.03 mg/kg, 0.1 mg/kg, or 0.3 mg/kg of LNPs, and are summarized in Tables 31A and 31B.

Table 31A

Guide ID	Average % Editing	Std. Dev.	N
TSS	0.26	0.250998	5
G000502 0.3mpk	73.26	1.61802	5
G000502 0.1mpk	47.1	10.0135	5
G000502 0.03mpk	15.02	9.31649	5
G009567 0.3mpk	72.5	3.06105	5
G009567 0.1mpk	54.86	7.43525	5
G009567 0.03mpk	21.7	7.22565	5
G009569 0.3mpk	71.7	2.60576	5
G009569 0.1mpk	56.42	8.42033	5
G009569 0.03mpk	23.42	4.62136	5
G009570 0.3mpk	68.1	3.99166	4
G009570 0.1mpk	51.08	11.5764	5
G009570 0.03mpk	20.38	8.62827	5

Table 31B

Guide ID	Serum TTR (µg/mL)	Std. Dev.	N
TSS	858.846	34.7566	5
G000502 0.3mpk	31.962	36.7047	5
G000502 0.1mpk	382.614	113.613	5
G000502 0.03mpk	686.612	96.3004	5
G009567 0.3mpk	20.1267	13.6911	3
G009567 0.1mpk	230.032	64.7601	5
G009567 0.03mpk	620.4	130.126	5
G009569 0.3mpk	25.91	11.9748	4
G009569 0.1mpk	231.09	102.557	5
G009569 0.03mpk	582.208	124.496	5
G009570 0.3mpk	73.82	13.3713	5
G009570 0.1mpk	334.308	163.522	5
G009570 0.03mpk	661.48	171.449	5

[00592] Figures 20C and 20D show the editing efficiency and TTR protein levels, respectively, for LNPs containing G502, G9571, and G10039, which all have the same nucleotide sequence as G502. The data shown in Figures 20C and 20D are from mice administered 0.03 mg/kg, 0.1 mg/kg, or 0.3 mg/kg of LNPs, and are summarized in Tables 32A and 32B.

Table 32A

Guide ID	Average % Editing	Std. Dev.	N
TSS	0.08	0.0447214	5
G000502 0.3mpk	50.7	23.7015	5
G000502 0.1mpk	38.2	3.14245	5
G000502 0.03mpk	12.78	8.84064	5
G0009571 0.3mpk	72.24	2.21653	5
G0009571 0.1mpk	56.48	6.50092	5
G0009571 0.03mpk	15.6	5.6	5
G010039 0.3mpk	65.98	4.22694	5
G010039 0.1mpk	31.74	10.0179	5
G010039 0.03mpk	13.34	6.50446	5

Table 32B

Guide ID	Serum TTR (µg/mL)	Std. Dev.	N
TSS	1062.23	240.945	5
G000502 0.3mpk	224.37	242.604	4
G000502 0.1mpk	814.642	264.733	5
G000502 0.03mpk	922.306	235.495	5
G0009571 0.3mpk	123.52	43.2127	4
G0009571 0.1mpk	317.752	100.059	5
G0009571 0.03mpk	860.7	114.188	5
G010039 0.3mpk	160.613	83.6036	4
G010039 0.1mpk	662.048	274.764	5
G010039 0.03mpk	759.892	166.829	5

[00593] Figures 20E and 20F show the editing efficiency and TTR protein levels, respectively, for LNPs containing G502, G9571, and G10015, which all have the same nucleotide sequence as G502. The data shown in Figures 20E and 20F are from mice administered 0.1 mg/kg or 0.3 mg/kg of LNPs, and are summarized in Tables 33A and 33B.

Table 33A

Guide ID	Average Editing (%)	Std. Dev.	N
TSS	0.133333	0.057735	3
G000502 0.1 mpk	37.4	12.106	5
G000502 0.3 mpk	64.86	2.62545	5
G009571 0.1 mpk	47.6	6.98665	4
G009571 0.3 mpk	69.8	1.59217	5
G010015 0.1 mpk	47.86	6.09451	5
G010015 0.3 mpk	69.325	2.20662	4

Table 33B

Guide ID	Serum TTR (µg/mL)	Std. Dev.	N
TSS	1844.59	542.644	5
G000502 0.1 mpk	768.714	390.311	5
G000502 0.3 mpk	169.707	102.03	5
G009571 0.1 mpk	658.269	303.19	5
G009571 0.3 mpk	84.6392	33.3813	5
G010015 0.1 mpk	602.506	354.455	5
G010015 0.3 mpk	86.236	38.391	5

Example 12 – In Vivo Studies

[00594] Figures 8C and 8D show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Table 34 (See Table 1 for sgRNA nucleotide sequences) which all target the same sequence in the TTR gene. G000282 served as a reference comparator. The LNPs were made according to LNP Procedure D in Example 1(F). The data shown in Figures 8C and 8D are from CD-1 mice administered 0.1 mg/kg and 0.3 mg/kg of total RNA and are summarized in Table 34.

Table 34 – Liver Editing and Serum TTR

Guide	Dose (mpk)	% Editing	SD	N	Serum TTR (µg/ml)	SD	N	Serum TTR %TSS
TSS	TSS	4.8	1.8	5	746	259	5	100%
G000282	0.1	50.8	4.1	5	173	46	5	23%
G000282	0.3	64.9	1.9	5	55	51	5	7%
G000639	0.1	43.3	7.6	4	246	82	4	33%
G000639	0.3	63.4	5.1	5	104	85	5	14%
G000640	0.1	42.7	8.4	4	260	70	4	35%
G000640	0.3	65.4	1.1	4	55	19	4	7%
G011771	0.1	49.3	7.7	5	205	82	5	27%
G011771	0.3	66.4	4.3	5	38	15	5	5%

[00595] Figures 21A and 21B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Table 35 (See Table 1 for sgRNA nucleotide sequences) which all target the same sequence in the TTR gene. The LNPs were made according to LNP Procedure D in Example 1(F). The data shown in Figures 21A and 21B are from CD-1 female mice (n=5) administered 0.1 mg/kg and 0.3 mg/kg of total RNA and are summarized in Table 35.

Table 35- Liver Editing and Serum TTR

Guide	Dose (mpk)	% Editing	SD	Serum TTR µg/ml	SD	Serum TTR %TSS
TSS	TSS	0.1	0.0	1845	543	100%
G000502	0.1	37.4	12.1	769	390	42%
G000502	0.3	64.9	2.6	170	102	9%
G009571	0.1	49.5	7.3	658	303	36%
G009571	0.3	69.8	1.6	85	33	5%
G010015	0.1	47.9	6.1	603	354	33%
G010015	0.3	69.1	2.0	86	38	5%
G012401	0.1	28.2	10.0	1183	298	64%
G012401	0.3	59.0	7.7	264	127	14%
G012402	0.1	45.7	4.6	872	293	47%
G012402	0.3	67.8	3.8	117	64	6%

[00596] Figures 18C-D show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Table 36 (See Table 1 for sgRNA nucleotide sequences) which all target the same sequence in the TTR gene. The LNPs were made according to LNP Procedure D in Example 1(F). The data shown in Figures 18C-D are from CD-1 female mice administered 0.1 mg/kg (mpk) and 0.3 mg/kg of total RNA and are summarized in Table 36.

Table 36 - Liver Editing and Serum TTR

Guide	Dose (mpk)	% Editing	SD	Serum TTR (ug/ml)	SD	N	Serum TTR %TSS
TSS	TSS	0.4	0.6	1935	443	5	100%
G000282	0.1	40.2	13.5	174	94	5	9%
G000282	0.3	67.9	0.9	351	54	5	18%
G009559	0.1	49.6	6.2	132	73	5	7%
G009559	0.3	61.0	15.8	165	32	5	9%
G009985	0.1	45.5	3.8	143	42	5	7%
G009985	0.3	65.6	5.1	232	71	5	12%
G010009	0.1	60.5	6.4	58	40	5	3%
G010009	0.3	58.2	18.6	159	77	4	8%

[00597] Figures 18E-F show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Table 37 (See Table 1 for sgRNA nucleotide sequences) which all target the same sequence in the TTR gene. The LNPs were

made according to LNP Procedure D in Example 1(F). The data shown in Figures 18E-F are from CD-1 female mice (n=5) administered 0.1 mg/kg (mpk) and 0.3 mg/kg of total RNA and are summarized in Table 37.

Table 37 – Liver Editing and Serum TTR

Guide	Dose (mpk)	% Editing	SD	Serum TTR (ug/ml)	SD	Serum TTR %TSS
TSS	TSS	0.1	0.0	666	103	100%
G000502	0.1	46.9	8.1	199	52	30%
G000502	0.3	66.3	1.7	51	12	8%
G010018	0.1	42.5	7.8	211	38	32%
G010018	0.3	69.6	1.7	36	20	5%
G010022	0.1	45.0	12.8	290	131	44%
G010022	0.3	70.4	1.4	20	13	3%
G010024	0.1	44.0	7.9	235	95	35%
G010024	0.3	71.2	1.4	14	6	2%
G010038	0.1	34.4	9.6	291	96	44%
G010038	0.3	64.6	2.7	63	27	9%

[00598] Figures 3C-D show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Table 38 (See Table 1 for sgRNA nucleotide sequences) which all target the same sequence in the TTR gene. The LNPs were made according to LNP Procedure D in Example 1(F). The data shown in Figures 3C-D are from CD-1 female mice (n=5) administered 0.1 mg/kg (mpk) and 0.3 mg/kg of total RNA and are summarized in Table 38.

Table 38 - Liver Editing and Serum TTR

Guide	Dose (mpk)	% Editing	SD	Serum TTR ug/ml	SD	Serum TTR %TSS
TSS	TSS	0.1	0.0	1035	100	100%
G000282	0.1	35.3	7.7	494	103	48%
G000282	0.3	62.9	2.6	95	27	9%
G000639	0.1	28.0	1.1	597	144	58%
G000639	0.3	57.7	5.0	157	35	15%
G012741	0.1	37.2	14.6	420	167	41%
G012741	0.3	58.6	3.8	147	30	14%

[00599] Figures 22A-B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Table 39 (See Table 1 for sgRNA

nucleotide sequences) which all target the same sequence in the TTR gene. The LNPs were made according to LNP Procedure P4.3 in Example 1(F). The data shown in Figures 22A-B are from Sprague Dawley rats administered 0.1 mg/kg and 0.03 mg/kg of total RNA and are summarized in Table 39.

Table 39 - Liver Editing and Serum TTR in rat

Guide	Dose (mpk)	% Editing	SD	Serum TTR (µg/ml)	SD	N	Serum TTR %TSS
TSS	TSS	0.2	0.1	1239	195	5	100%
G000534	0.03	12.4	3.0	1195	230	5	96%
G000534	0.10	46.6	0.77	450	94	5	36%
G013496	0.03	9.9	1.3	1028	300	5	83%
G013496	0.10	47.6	6.2	471	116	5	38%
G013771	0.03	18.7	2.7	1006	147	5	81%
G013771	0.10	58.0	9.1	331	150	4	27%

[00600] Table 40 shows the editing efficiency and TTR protein levels, respectively, for LNPs containing the indicated sgRNAs (See Table 1 for sgRNA nucleotide sequences) which all target the same sequence in the TTR gene. The LNPs were made according to LNP Procedure D in Example 1(F). The data shown in Table 40 are from CD-1 female mice administered 0.1 mg/kg of total RNA.

Table 40 – Liver Editing and Serum TTR

Guide	Editing	SD	N	Serum TTR (µg/ml)	SD	N	Serum TTR %TSS
TSS	0.3	0.1	5	759	106	5	100%
G000502	26.7	6.4	5	480	148	5	63%
G012421	17.2	4.9	5	642	137	5	85%
G012422	33.5	9.5	5	479	170	5	63%
G012423	12.4	2.7	5	626	82	5	82%
G012424	18.4	6.1	5	614	106	5	81%
G012426	31.4	4.8	5	481	122	5	63%
G012443	36.6	10.5	4	406	115	4	53%
G012448	37.6	6.6	5	400	194	5	53%
G012453	16.5	4.0	5	644	126	5	85%
G012456	3.6	1.3	5	795	89	5	105%
G012457	14.8	5.5	5	675	167	5	89%

[00601] Figures 24A-B show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Table 41 (See Table 1 for sgRNA

nucleotide sequences) which all target the same sequence in the TTR gene. The LNPs were made according to LNP Procedure D in Example 1(F). The data shown in Figures 24A-B are from CD-1 female mice administered 0.1 mg/kg of total RNA and are summarized in Table 41.

Table 41 – Liver Editing and Serum TTR

Guide	% Editing	SD	N	Serum TTR (µg/ml)	SD	N	Serum TTR %TSS
TSS	0.1	0.1	5	763	66	5	100%
G000502	22.9	8.5	5	610	196	5	80%
G012973	0.1	0.1	5	818	47	5	107%
G012974	0.5	0.2	5	949	140	5	124%
G012975	6.6	3.0	5	787	190	5	103%
G012976	0.2	0.1	5	671	71	5	88%
G012977	3.0	1.6	5	636	65	5	83%
G012978	19.3	9.2	5	559	128	5	73%
G012979	1.0	0.8	5	1234	206	5	162%
CR012980	0.2	0.2	4	837	223	5	110%

[00602] Figures 3E-F show the editing efficiency and TTR protein levels, respectively, for LNPs containing the sgRNAs indicated in Table 42 (See Table 1 for sgRNA nucleotide sequences) which all target the same sequence in the TTR gene. The LNPs were made according to LNP Procedure D in Example 1(F). The data shown in Figures 3E-F are from Sprague Dawley female rats (n=5) administered 0.1 mg/kg and 0.03 mg/kg of total RNA and are summarized in Table 42.

Table 42 – Liver editing & Serum TTR in Rat

Guide	Dose (mpk)	% Editing	SD	Serum TTR ug/ml	SD	Serum TTR %TSS
TSS	TSS	0.1	0.0	1635	301	100%
G013498	0.03	13.7	5.9	1054	225	64%
G013498	0.10	51.0	9.1	325	133	20%
G000534	0.03	10.7	1.1	1105	154	68%
G000534	0.10	38.6	13.1	411	90	25%
G000694	0.03	3.1	1.0	1157	223	71%
G000694	0.10	28.2	6.1	656	92	40%

Example 13 – Correlations Between In Vitro and In Vivo Editing with sgRNAs

[00603] Chemically synthesized sgRNAs (G502 and G9565-G9576) and IVT Cas9 mRNA were administered to primary hepatocytes as lipoplex transfections or LNP transfections as described in Example 1(D) and 1(F) (LNP Procedure D), respectively. Editing of the *TTR* gene was determined by NGS as described above in Example 1(G). The same sgRNAs were also administered to CD-1 female mice as described in Example 5, particularly the section describing data shown in Figures 19A and 19B.

[00604] The % editing from in vitro lipoplex transfections of PMH compared to in vivo editing is shown Figure 16A. As shown in Figure 16A, the correlation between in vitro lipoplex transfections of PMH and in vivo editing is not statistically significant. The correlation is not predictive.

[00605] The % editing from in vitro LNP transfections of PMH (at 0.3 ng, 1 ng, 3 ng, 10 ng, and 30 ng) compared to in vivo editing are shown in Figures 16B to 16F. As shown in Figures 16B to 16F, the correlation between in vitro LNP transfections of PMH and in vivo editing was statistically significant. The correlation is predictive.

[00606] Figure 16G shows a comparison of % editing with the indicated guides delivered to PMH by lipoplex transfection (data above left box), to PMH in LNP (data above center box), or to mice in vivo (data above right box). Figure 16H shows a comparison of % editing with the indicated guides delivered to PMH in LNP (1 ng, 3 ng, 10 ng) or to mice in vivo (0.1 mpk, 0.3 mpk). Although the rank order of the indicated guides may generally be considered to be the same in each set of data, the in vivo editing shows greater differentiation of the editing results.

[00607] Figure 16I shows the results from Figure 16G replotted to indicate differences in editing between G000282 and G000211. The barplot values were generated by dividing % editing of the G000282 value by the % editing of the G000211 value to indicate fold differences in editing. The indicated guides were delivered to PMH by lipoplex transfection (data above left box), to PMH in LNP (data above center box), or to mice in vivo (data above right box).

[00608] Figure 16J shows the results from Figure 16H replotted to indicate differences in editing between G000283 and G000269. The barplot values were generated by dividing % editing of the G000283 value by the % editing of the G000269 value to indicate fold differences in editing. The indicated guides were delivered to PMH in LNP (data above left box) or to mice in vivo (data above right box).

We claim:

1. A guide RNA (gRNA) which is a short-single guide RNA (short-sgRNA) comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides and wherein the short-sgRNA comprises a 5' end modification or a 3' end modification.
2. The gRNA of claim 1, wherein the short-sgRNA comprises a 5' end modification.
3. The gRNA of any one of the preceding claims, wherein the short-sgRNA comprises a 3' end modification.
4. The gRNA of any one of the preceding claims, wherein the short-sgRNA comprises a 5' end modification and a 3' end modification.
5. The gRNA of any one of the preceding claims, wherein the short-sgRNA comprises a 3' tail.
6. The gRNA of claim 5, wherein the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.
7. The gRNA of claim 5, wherein the 3' tail comprises about 1-2, 1-3, 1-4, 1-5, 1-7, 1-10, at least 1-5, at least 1-3, at least 1-4, at least 1-5, at least 1-5, at least 1-7, or at least 1-10 nucleotides.
8. The gRNA of any one of the preceding claims, wherein the short-sgRNA does not comprise a 3' tail.
9. The gRNA of any one of the preceding claims, comprising a modification in the hairpin region.
10. The gRNA of any one of the preceding claims, comprising a 3' end modification, and a modification in the hairpin region.
11. The gRNA of any one of the preceding claims, comprising a 3' end modification, a modification in the hairpin region, and a 5' end modification.
12. The gRNA of any one of the preceding claims, comprising a 5' end modification, and a modification in the hairpin region.
13. The gRNA of any one of the preceding claims, wherein the at least 5-10 lacking nucleotides are consecutive.
14. The gRNA of any one of the preceding claims, wherein the at least 5-10 lacking nucleotides:

i. are within hairpin 1;
ii. are within hairpin 1 and the "N" between hairpin 1 and hairpin 2;
iii. are within hairpin 1 and the two nucleotides immediately 3' of hairpin 1;
iv. include at least a portion of hairpin 1;
v. are within hairpin 2;
vi. include at least a portion of hairpin 2;
vii. are within hairpin 1 and hairpin 2;
viii. include at least a portion of hairpin 1 and include the "N" between hairpin 1 and hairpin 2;
ix. include at least a portion of hairpin 2 and include the "N" between hairpin 1 and hairpin 2;
x. include at least a portion of hairpin 1, include the "N" between hairpin 1 and hairpin 2, and include at least a portion of hairpin 2;
xi. are within hairpin 1 or hairpin 2, optionally including the "N" between hairpin 1 and hairpin 2;
xii. are consecutive;
xiii. are consecutive and include the "N" between hairpin 1 and hairpin 2;
xiv. are consecutive and span at least a portion of hairpin 1 and a portion of hairpin 2;
xv. are consecutive and span at least a portion of hairpin 1 and the "N" between hairpin 1 and hairpin 2; or
xvi. are consecutive and span at least a portion of hairpin 1 and two nucleotides immediately 3' of hairpin 1.

15. The gRNA of any one of the preceding claims, further comprising a guide region.

16. The gRNA of any one of the preceding claims, wherein the 3' and/or 5' end modification comprises a protective end modification, such as a modified nucleotide selected from 2'-O-methyl (2'-OMe) modified nucleotide, 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, an inverted abasic modified nucleotide, or combinations thereof.

17. The gRNA of any one of the preceding claims, wherein the modification in the hairpin region comprises a modified nucleotide selected from 2'-O-methyl (2'-OMe)

modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, a phosphorothioate (PS) linkage between nucleotides, or combinations thereof.

18. The gRNA of any one of the preceding claims, wherein the 3' and/or 5' end modification comprises or further comprises a 2'-O-methyl (2'-OMe) modified nucleotide.

19. The gRNA of any one of the preceding claims, wherein the 3' and/or 5' end modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

20. The gRNA of any one of the preceding claims, wherein the 3' and/or 5' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides.

21. The gRNA of any one of the preceding claims, wherein the 3' and/or 5' end modification comprises or further comprises an inverted abasic modified nucleotide.

22. The gRNA of any one of the preceding claims, wherein the modification in the hairpin region comprises or further comprises a 2'-O-methyl (2'-OMe) modified nucleotide.

23. The gRNA of any one of the preceding claims, wherein the modification in the hairpin region comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

24. The gRNA of any one of the preceding claims, wherein the 3' end modification comprises any of:

    i. a modification of any one or more of the last 7, 6, 5, 4, 3, 2, or 1 nucleotides;
    ii. one modified nucleotide;
    iii. two modified nucleotides;
    iv. three modified nucleotides;
    v. four modified nucleotides;
    vi. five modified nucleotides;
    vii. six modified nucleotides; and
    viii. seven modified nucleotides.

25. The gRNA of any one of the preceding claims, wherein the at least 5-10 nucleotides comprise nucleotides 54-61 of SEQ ID NO:400, nucleotides 53-60 of SEQ ID NO:400; or nucleotides 54-58 of SEQ ID NO:400, optionally wherein the short-sgRNA comprises modifications at least H1-1 to H1-5 and H2-1 to H2-12.

26. The gRNA of any one of the preceding claims, wherein the at least 5-10 nucleotides:

i. consist of 5-10 nucleotides;
ii. consist of 6-10 nucleotides;
iii. consist of 5 nucleotides;
iv. consist of 6 nucleotides;
v. consist of 7 nucleotides;
vi. consist of 8 nucleotides;
vii. consist of 9 nucleotides;
viii. consist of 10 nucleotides;
ix. consist of 5-10 consecutive nucleotides;
x. consist of 6-10 consecutive nucleotides;
xi. consist of 5 consecutive nucleotides;
xii. consist of 6 consecutive nucleotides;
xiii. consist of 7 consecutive nucleotides;
xiv. consist of 8 consecutive nucleotides;
xv. consist of 9 consecutive nucleotides; or
xvi. consist of 10 consecutive nucleotides.

27. The gRNA of any one of the preceding claims, wherein the 3' end modification comprises one or more of:
i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-OMe modified nucleotide;
iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide; and
vi. a combination of one or more of (i.) - (v.).

28. The gRNA of any one of the preceding claims, wherein the short-sgRNA comprises a 3' tail comprising one or more of:
i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-OMe modified nucleotide;
iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide; and
vi. a combination of one or more of (i.) - (v.).

29. The gRNA any one of the preceding claims, wherein the short-sgRNA comprises one or more of:

i. 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 PS linkages between nucleotides;
ii. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, or 18 PS linkages between nucleotides;
iii. about 1-3, 1-5, 1-6, 1-7, 1-8, 1-9, or 1-10 PS linkages between nucleotides;
iv. about 1-3, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 1-12, 1-14, 1-16, 1-18, or 1-20 PS linkages between nucleotides; and
v. PS linkages between each nucleotide.

30. The gRNA of any one of the preceding claims, wherein the 3' end modification comprises at least one PS linkage, and wherein one or more of:
i. there is one PS linkage, and the linkage is between the last and second to last nucleotide;
ii. there are two PS linkages between the last three nucleotides;
iii. there are PS linkages between any one or more of the last four nucleotides;
iv. there are PS linkages between any one or more of the last five nucleotides; and
v. there are PS linkages between any one or more of the last 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

31. The gRNA of claim 30, wherein the 3' end modification further comprises at least one 2'-OMe, 2'-O-moe, inverted abasic, or 2'-F modified nucleotide.

32. The gRNA of any one of the preceding claims, wherein the 3' end modification comprises:
i. a modification of one or more of the last 1-7 nucleotides, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof;
ii. a modification to the last nucleotide with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and an optional one or two PS linkages to the next nucleotide and/or the first nucleotide of the 3' tail;
iii. a modification to the last and/or second to last nucleotide with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages;

iv. a modification to the last, second to last, and/or third to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages;

v. a modification to the last, second to last, third to last, and/or fourth to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages; or

vi. a modification to the last, second to last, third to last, fourth to last, and/or fifth to last nucleotides with 2'-OMe, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

33. The gRNA of any one of the preceding claims, wherein the sgRNA comprise a 3' tail, wherein the 3' tail comprises a modification of any one or more of the nucleotides present in the 3' tail.

34. The gRNA of claim 33, wherein the 3' tail is fully modified.

35. The gRNA of claim 33, wherein the at least 5-10 nucleotides comprise nucleotides 54-61 of SEQ ID NO:400, nucleotides 53-60 of SEQ ID NO:400; or nucleotides 54-58 of SEQ ID NO:400, optionally wherein the short-sgRNA comprises modifications at least H1-1 to H1-5 and H2-1 to H2-12.

36. The gRNA of any one of the preceding claims, wherein the short-sgRNA comprises any one or more of:

i. the 3' end modification as shown in any one of SEQ ID Nos: 1-54;

ii. (i) a 2'-OMe modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, (ii) three consecutive 2'O-moe modified nucleotides immediately 5' to the 2'-OMe modified nucleotide, and (iii) three consecutive PS linkages between the last three nucleotides;

iii. (i) five consecutive 2'-OMe modified nucleotides from the 3' end of the 3' terminus, and (ii) three PS linkages between the last three nucleotides;

iv. an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA;

v. (i) an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, and (ii) three consecutive 2'-OMe modified nucleotides at the last three nucleotides of the conserved region of an sgRNA or short-sgRNA;

vi. (i) 15 consecutive 2'-OMe modified nucleotides from the 3' end of the 3' terminus, (ii) five consecutive 2'-F modified nucleotides immediately 5' to the 2'-OMe modified nucleotides, and (iii) three PS linkages between the last three nucleotides;

vii. (i) alternating 2'-OMe modified nucleotides and 2'-F modified nucleotides at the last 20 nucleotides of the conserved region of an sgRNA or short-sgRNA, and (ii) three PS linkages between the last three nucleotides;

viii. (i) two or three consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides;

ix. one PS linkage between the last and next to last nucleotides; and

x. 15 or 20 consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

37. The gRNA of any one of the preceding claims, wherein the 5' end modification comprises any one or more of:

i. a modification of any one or more of nucleotides 1-7 of the guide region;

ii. one modified nucleotide;

iii. two modified nucleotides;

iv. three modified nucleotides;

v. four modified nucleotides;

vi. five modified nucleotides;

vii. six modified nucleotides; and

viii. seven modified nucleotides.

38. The gRNA of any one of the preceding claims, wherein the 5' end modification comprises a modification of between 1 and 7, between 1 and 5, between 1 and 4, between 1 and 3, or between 1 and 2 nucleotides.

39. The gRNA of any one of the preceding claims, wherein the at least 5-10 nucleotides:

i. comprise nucleotides 54-61 of SEQ ID NO:400;

ii. comprise nucleotides 53-60 of SEQ ID NO:400;

iii. comprise nucleotides 54-58 of SEQ ID NO:400.

iv. consist of nucleotides 54-61 of SEQ ID NO:400;

v. consist of nucleotides 53-60 of SEQ ID NO:400; or

vi. consist of nucleotides 54-58 of SEQ ID NO:400.

40. The gRNA of any one of the preceding claims, wherein the 5' end modification comprises one or more of:
    i. a phosphorothioate (PS) linkage between nucleotides;
    ii. a 2'-OMe modified nucleotide;
    iii. a 2'-O-moe modified nucleotide;
    iv. a 2'-F modified nucleotide;
    v. an inverted abasic modified nucleotide;
    vi. a deoxyribonucleotide;
    vii. an inosine; and
    viii. combinations of one or more of (i.) – (vii.).

41. The gRNA any one of the preceding claims, wherein the 5' end modification comprises:
    i. 1, 2, 3, 4, 5, 6, and/or 7 PS linkages between nucleotides; or
    ii. about 1-2, 1-3, 1-4, 1-5, 1-6, or 1-7 PS linkages between nucleotides.

42. The gRNA of any one of the preceding claims, wherein the 5' end modification comprises at least one PS linkage, and wherein:
    i. there is one PS linkage, and the linkage is between nucleotides 1 and 2 of the guide region;
    ii. there are two PS linkages, and the linkages are between nucleotides 1 and 2, and 2 and 3 of the guide region;
    iii. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;
    iv. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, and 4 and 5 of the guide region;
    v. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region;
    vi. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, 5 and 6, and 6 and 7 of the guide region; or
    vii. there are PS linkages between any one or more of nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, 5 and 6, 6 and 7, and 7 and 8 of the guide region.

43. The gRNA of claim 42, wherein the 5' end modification further comprises at least one 2'-OMe, 2'-O-moe, inverted abasic, or 2'-F modified nucleotide.

44. The gRNA of any one of the preceding claims, wherein the short-sgRNA comprises:

i. a modification of one or more of nucleotides 1-7 of the variable region, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-OMe, 2'-O-moe, 2'-F, 2'-H (a deoxyribonucleotide), an inosine, and/or combinations thereof;

ii. a modification to the first nucleotide of the guide region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and an optional PS linkage to the next nucleotide;

iii. a modification to the first and/or second nucleotide of the variable region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and optionally one or more PS linkages;

iv. a modification to the first, second, and/or third nucleotides of the variable region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and optionally one or more PS linkages;

v. a modification to the first, second, third, and/or fourth nucleotides of the variable region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and optionally one or more PS linkages; or

vi. a modification to the first, second, third, fourth, and/or fifth nucleotides of the variable region with 2'-OMe, 2'-O-moe, 2'-F, 2'-H, an inosine, or combinations thereof, and optionally one or more PS linkages.

45. The gRNA of any one of the preceding claims, wherein the short-sgRNA comprises any one or more of:

i. a 5' end modification as shown in any one of SEQ ID Nos: 1-54;

ii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region;

iii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

iv. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region;

v. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region;

vi. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region;

vii. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

viii. an inverted abasic modified nucleotide at nucleotide 1 of the guide region;

ix. an inverted abasic modified nucleotide at nucleotide 1 of the guide region and 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region; and

x. an inverted abasic modified nucleotide at nucleotide 1 of the guide region, 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region, and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the variable region.

46. The gRNA of any one of the preceding claims, wherein the upper stem region comprises at least one modification.

47. The gRNA of any one of the preceding claims, wherein the upper stem modification comprises any one or more of:

i. a modification to any one or more of US1-US12 in the upper stem region;

ii. a modification of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all 12 nucleotides in the upper stem region; and

iii. a modification of about 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, or 1-12 nucleotides in the upper stem region.

48. The gRNA of claim 47, wherein the upper stem modification comprises one or more of:

i. a 2'-OMe modified nucleotide;

ii. a 2'-O-moe modified nucleotide;

iii. a 2'-F modified nucleotide; and

iv. combinations of one or more of (i.) – (iii.).

49. A guide RNA which is a short-sgRNA comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides and wherein the short-sgRNA comprises a 5' end modification and one or more modification in one or more of:

i. the upper stem region;

ii. the hairpin 1 region; and

iii. the hairpin 2 region,

wherein the 5' end modification comprises a 5' protective end modification, such as at least two phosphorothioate (PS) linkages within the first seven nucleotides.

50. The gRNA of claim 49, wherein at least one modification comprises a 2'-O-methyl (2'-OMe) modified nucleotide.

51. The gRNA of claim 49 or claim 50, wherein at least one modification comprises a 2'-fluoro (2'-F) modified nucleotide.

52. The gRNA of any one of claims 49-51, wherein at least one modification comprises a phosphorothioate (PS) bond between nucleotides.

53. The gRNA of any one of claims 49-52, wherein the short-sgRNA comprises one or more modifications in the upper stem region.

54. The gRNA of claim 53, comprising modifications at any one of US1 to US12.

55. The gRNA of any one of claims 49-54, wherein the short-sgRNA comprises one or more modifications in the hairpin 1 region.

56. The gRNA of claim 55, wherein the short-sgRNA comprises a modification at H1-1.

57. The gRNA of any one of claims 49-56, wherein the short-sgRNA comprises one or more modifications in the hairpin 2 region.

58. The gRNA of claim 57, wherein the short-sgRNA comprises a modification at H2-1.

59. The gRNA of any one of claims 49-58, wherein the short-sgRNA comprises modifications at H1-1 to H1-12.

60. The gRNA of any one of claims 49-59, wherein the short-sgRNA comprises modifications at H2-1 to H2-15.

61. The gRNA of any one of claims 49-60, wherein the short-sgRNA comprises one or more modifications in each of the upper stem region, the hairpin 1 region, and the hairpin 2 region.

62. The gRNA of any one of claims 49-61, wherein the short-sgRNA comprises a modified nucleotide between hairpin 1 and hairpin 2 regions.

63. The gRNA of any one of claims 49-62, further comprising a lower stem region comprising a modification.

64. The gRNA of any one of claims 49-63, further comprising a 3' end modification.

65. The gRNA of claim 64, wherein at least two of the last four nucleotides at the 3' end of the 3' terminus are modified.

66. The gRNA of claim 64, wherein at least two of the last four nucleotides at the 3' end of the 3' terminus are modified with 2'-OMe, 2'-F, or 2'-O-moe.

67. The gRNA of any one of claims 64-66, further comprising phosphorothioate (PS) bonds between one or more of the last four nucleotides at the 3' end of the 3' terminus.

68. The gRNA of any one of claims 49-67, further comprising a bulge region comprising a modification.

69. The gRNA of any one of claims 49-68, further comprising a nexus region comprising a modification.

70. The gRNA of any one of claims 49-69, wherein at least the first three nucleotides at the 5' end of the variable region, and the last three nucleotides at the 3' end of the 3' terminus are modified.

71. The gRNA of any one of claims 49-70, wherein the first four nucleotides at the 5' end of the variable region, and the last four nucleotides at the 3' end of the 3' terminus are linked with phosphorothioate (PS) bonds.

72. The gRNA of any one of claims 70-71, wherein the end modifications comprise 2'-OMe.

73. The gRNA of any one of claims 70-71, wherein the end modifications comprise 2'-F.

74. The gRNA of any one of claims 49-73, wherein the first four nucleotides at the 5' end of the variable region and the last four nucleotides at the 3' end of the 3' terminus are linked with a PS bond, and wherein the first three nucleotides at the 5' end of the variable region and the last three nucleotides at the 3' end of the 3' terminus comprise 2'-OMe modifications.

75. The gRNA of any one of claims 49-74, wherein the first four nucleotides at the 5' terminus and the last four nucleotides at the 3' terminus are linked with a PS bond, and wherein the first three nucleotides at the 5' terminus and the last three nucleotides at the 3' terminus comprise 2'-OMe, 2'-F, and/or 2'-O-moe modifications.

76. The gRNA of any one of claims 49-75, wherein LS1, LS6, LS7, LS8, LS11, and/or LS12 are modified with 2'-OMe.

77. The gRNA of any one of claims 49-76, wherein each of the nucleotides in the bulge region are modified with 2'-OMe.

78. The gRNA of any one of claims 49-77, wherein at least 50% of the nucleotides in the bulge region are modified with 2'-OMe.

79. The gRNA of any one of claims 49-78, wherein each of the nucleotides in the upper stem region are modified with 2'-OMe.

80. The gRNA of any one of claims 49-79, wherein N16, N17, and/or N18 in the nexus region are modified with 2'-OMe.

81. The gRNA of any one of claims 49-80, wherein N15, N16, N17, and/or N18 in the nexus region are modified.

82. The gRNA of claim 80 or 81, wherein the modifications in the nexus region are selected from 2'-OMe and 2'F.

83. The gRNA of any one of claims 80-82, wherein N16, N17, and N18 are linked with PS bonds.

84. The gRNA of any one of claims 49-83, wherein each of the nucleotides remaining in the hairpin 1 region are modified with 2'-OMe.

85. The gRNA of any one of claims 49-84, wherein each of the nucleotides in the hairpin 2 region are modified with 2'-OMe.

86. A guide RNA which is a short-sgRNA comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides and wherein the short-sgRNA comprises a 5' end modification and a 3' end modification, wherein the short-sgRNA further comprises any one or more of:

i. at least one modification in the upper stem region; and
ii. a 3' tail.

87. The gRNA of claim 86, wherein the upper stem modification comprises any one or more of:

i. a modification of each nucleotide (US1-US12) in the upper stem region;
ii. a modification to any one or more of US1-US12 in the upper stem region;
iii. a modification of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all 12 nucleotides in the upper stem region; and
iv. a modification of about 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, or 1-12 nucleotides in the upper stem region.

88. The gRNA of any one of claims 86-87, wherein the 5' end modification comprises any one or more of:

i. a modification of any one or more of nucleotides 1-7 of the variable region;
ii. one modified nucleotide;
iii. two modified nucleotides;
iv. three modified nucleotides;
v. four modified nucleotides;
vi. five modified nucleotides;
vii. six modified nucleotides; and
viii. seven modified nucleotides.

89. The gRNA of any one of claims 86-88, wherein the 5' end modification comprises any one or more of:

i. a 5' end modification as shown in any one of SEQ ID Nos: 1-54, 401-532, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, 3388-3430, or 3549-3552;
ii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the variable region;
iii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the variable region;
iv. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the variable region;
v. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the variable region;
vi. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the variable region;
vii. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the variable region;
viii. an inverted abasic modified nucleotide at nucleotide 1 of the variable region;

ix. an inverted abasic modified nucleotide at nucleotide 1 of the variable region and 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the variable region; and

x. an inverted abasic modified nucleotide at nucleotide 1 of the variable region, 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the variable region, and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the variable region.

90. The gRNA of claim 89, comprising 2'-OMe modified nucleotides at at least nucleotides 1, 2, and 3, of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the variable region.

91. The gRNA of claim 89, comprising 2'-OMe modified nucleotides at at least nucleotides 1, 2, 3, and 4 of the variable region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the variable region.

92. The gRNA of any one of claims 86-91, comprising a 3' end modification comprising any one or more of:

i. a modification of any one or more of the last 7, 6, 5, 4, 3, 2, or 1 nucleotides;

ii. one modified nucleotide;

iii. two modified nucleotides;

iv. three modified nucleotides;

v. four modified nucleotides;

vi. five modified nucleotides;

vii. six modified nucleotides; and

viii. seven modified nucleotides.

93. The gRNA of any one of claims 86-92, wherein the short-sgRNA comprises any one or more of:

i. a 3' end modification shown in any one of SEQ ID Nos: 1-54, 401-532, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, 3388-3430, or 3549-3552;

ii. (i) a 2'-OMe modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, (ii) three consecutive 2'O-moe modified nucleotides immediately 5' to the 2'-OMe modified nucleotide,

and (iii) three consecutive PS linkages between the last three nucleotides;

iii. (i) five consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides;

iv. an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA;

v. (i) an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, and (ii) three consecutive 2'-OMe modified nucleotides at the last three nucleotides of the conserved region of an sgRNA or short-sgRNA;

vi. (i) 15 consecutive 2'-OMe modified nucleotides, (ii) five consecutive 2'-F modified nucleotides immediately 5' to the 2'-OMe modified nucleotides, and (iii) three PS linkages between the last three nucleotides;

vii. (i) alternating 2'-OMe modified nucleotides and 2'-F modified nucleotides at the last 20 nucleotides of the conserved region of an sgRNA or short-sgRNA, and (ii) three PS linkages between the last three nucleotides;

viii. (i) two or three consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides;

ix. one PS linkage between the last and next to last nucleotides; and

x. 15 or 20 consecutive 2'-OMe modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

94. The gRNA of any one of claims 86-93, wherein the sgRNA comprise a 3' tail, wherein the 3' tail comprises a modification of any one or more of the nucleotides present in the 3' tail.

95. The gRNA of claim 94, wherein the 3' tail is fully modified.

96. The gRNA of claim 94 wherein the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, or 1-10 nucleotides, optionally where any one or more of these nucleotides are modified.

97. A guide RNA which is a short-sgRNA comprising any of SEQ ID Nos: 1-54, 201-254, and 301-354, including the modifications of Table 1.

98. A guide RNA which is a short-sgRNA comprising nucleic acids having at least 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% identity to the nucleic

acids of any one of SEQ ID Nos: 1-54, 201-254, and 301-354, wherein the modification at each nucleotide of the short-sgRNA that corresponds to a nucleotide of the reference sequence identifier in Table 1, is identical to or equivalent to the modification shown in the reference sequence identifier in Table 1.

99. The gRNA of any one of the preceding claims, comprising a YA modification at at least one guide region YA site.

100. The gRNA of any one of the preceding claims, comprising a YA modification at at least one guide region YA site that is not a 5' end modification.

101. The gRNA of any one of the preceding claims, comprising a YA modification at one or more guide region YA sites, wherein the guide region YA site is at or after nucleotide 8 from the 5' end of the 5' terminus.

102. The gRNA of any one of the preceding claims comprising a YA modification at one or more guide region YA sites, wherein the short-sgRNA comprises one or more of:

i. a modification at one or more of H1-1 and H2-1;
ii. a YA modification at 1, 2, 3, 4, or 5 guide region YA sites;
iii. a YA modification at 1, 2, 3, 4, or 5 guide region YA sites, wherein the modification of at least one guide region YA site is different from any 5' end modification of the sgRNA;
iv. a YA modification at one or more guide region YA sites, wherein the guide region YA site is at or after nucleotide 8 from the 5' end of the 5' terminus;
v. a YA modification at one or more guide region YA sites, wherein the guide region YA site is within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;
vi. a YA modification at one or more guide region YA sites, wherein the guide region YA site is within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;
vii. a YA modification at a guide region YA site other than a 5' end modification;
viii. a YA modification at two or more guide region YA sites, wherein the guide region YA sites are at or after nucleotide 8 from the 5' end of the 5' terminus;

ix. a YA modification at two or more guide region YA sites, wherein the two guide region YA sites are within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;

x. a YA modification at two or more guide region YA sites, wherein the guide region YA sites are within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;

xi. a YA modification at two or more guide region YA sites other than a 5' end modification; and

xii. a YA modification at two or more guide region YA sites, wherein the modifications of the guide region YA sites comprise a modification that at least one nucleotide located 5' of the guide region YA site does not comprise.

103. The gRNA of any one of the preceding claims, comprising a YA modification wherein the modification comprises 2'-fluoro, 2'-H, 2'-OMe, ENA, UNA, inosine, or PS.

104. The gRNA of any one of the preceding claims, comprising a YA modification wherein the modification alters the structure of the dinucleotide motif to reduce RNA endonuclease activity.

105. The gRNA of any one of the preceding claims, comprising a YA modification wherein the modification interferes with recognition or cleavage of a YA site by an RNase and/or stabilizes an RNA structure.

106. The gRNA of any one of the preceding claims, comprising a YA modification wherein the modification comprises one or more of:

i. a ribose modification selected from 2'-O-alkyl, 2'-F, 2'-moe, 2'-F arabinose, and 2'-H (deoxyribose);

ii. a bicyclic ribose analog, such as LNA, BNA, and ENA;

iii. an unlocked nucleic acid modification;

iv. a base modification, such as inosine, pseudouridine, and 5'-methylcytosine; and

v. an internucleoside linkage modification such as phosphorothioate.

107. The gRNA of any one of the preceding claims, comprising a YA modification at one or more conserved region YA sites.

108. The gRNA of any one of the preceding claims, comprising a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10.

109. The gRNA of any one of the preceding claims, comprising a YA modification at one or more of conserved region YA sites 1 and 8.

110. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 1.

111. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 2.

112. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 3.

113. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 4.

114. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 5.

115. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 6.

116. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 7.

117. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 8.

118. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 9.

119. The gRNA of any one of the preceding claims, comprising a YA modification of conserved region YA site 10.

120. The gRNA of any one of the preceding claims, comprising one or more of:

i. YA modifications of conserved region YA sites 2, 3, 4, and 10;
ii. YA modifications of conserved region YA sites 2, 3, and 4;
iii. YA modifications of conserved region YA sites 2, 3, and 10;
iv. YA modifications of conserved region YA sites 2, 4, and 10;
v. YA modifications of conserved region YA sites 3, 4, and 10;
vi. YA modifications of conserved region YA sites 2 and 10;
vii. YA modifications of conserved region YA sites 2 and 4;
viii. YA modifications of conserved region YA sites 2 and 3;
ix. YA modifications of conserved region YA sites 3 and 4;
x. YA modifications of conserved region YA sites 3 and 10;
xi. YA modifications of conserved region YA sites 4 and 10

xii. YA modifications of conserved region YA sites 1 and 5;
xiii. YA modifications of conserved region YA sites 1 and 6;
xiv. YA modifications of conserved region YA sites 1 and 7;
xv. YA modifications of conserved region YA sites 1 and 8;
xvi. YA modifications of conserved region YA sites 1 and 9;
xvii. YA modifications of conserved region YA sites 8 and 5;
xviii. YA modifications of conserved region YA sites 8 and 6;
xix. YA modifications of conserved region YA sites 8 and 7; and
xx. YA modifications of conserved region YA sites 8 and 9;
xxi. optionally wherein the sgRNA further comprises YA modifications of conserved region YA sites 2, 3, 4, and/or 10.

121. The gRNA of any one of the preceding claims, wherein at least one modified YA site comprises a 2'-OMe modification, optionally at the pyrimidine of the YA site.

122. The gRNA of any one of the preceding claims, wherein at least one modified YA site comprises a 2'-fluoro modification, optionally at the pyrimidine of the YA site.

123. The gRNA of any one of the preceding claims, wherein at least one modified YA site comprises a PS modification, optionally at the pyrimidine of the YA site.

124. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises modifications at at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or all of the following nucleotides: 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18, optionally wherein the modifications are 2'-OMe, 2'-fluoro, 2'-H, inosine, or phosphorothioate modifications.

125. The gRNA of any one of the preceding claims, wherein the short-sgRNA comprises a guide region that comprises modifications at nucleotides 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18, optionally wherein the modifications are 2'-OMe, 2'-fluoro, 2'-H, inosine, or phosphorothioate modifications.

126. The gRNA of claims 124-125, wherein 2'-OMe modifications are not present in the guide region at nucleotides 6-11 and 13-end.

127. The gRNA of claims 124-126, wherein 2'-fluoro modifications are not present in the guide region at nucleotides 1-7, 15, 16, and 19-end.

128. The gRNA of claims 124-127, wherein phosphorothioate modifications are not present in the guide region at nucleotides 4, 5, 11-14, 17, and 18.

129. The gRNA of claims 124-128, wherein the guide region comprises an unmodified nucleotide 20.

130. The gRNA of claims 124-129, wherein the guide region consists of 20 nucleotides.

131. The gRNA of claims 124-130, wherein the guide region comprises a YA site at nucleotides 5-6 and a modification at nucleotide 5.

132. The gRNA of claims 124-131, wherein the guide region comprises a YA site at nucleotides 12-13 and a modification at nucleotide 12.

133. The gRNA of claims 124-132, wherein the guide region comprises a YA site at nucleotides 15-16 and a modification at nucleotide 15.

134. The gRNA of claims 124-133, wherein the guide region comprises a YA site at nucleotides 16-17 and a modification at nucleotide 16.

135. The gRNA of claims 124-134, wherein the guide region comprises a YA site at nucleotides 19-20 and a modification at nucleotide 19.

136. The gRNA of claims 124-130 or 132-135, wherein the guide region does not comprise a YA site at nucleotides 5-6 and nucleotide 5 is unmodified.

137. The gRNA of claims 124-131 or 133-136, wherein the guide region does not comprise a YA site at nucleotides 12-13 and nucleotide 12 is unmodified.

138. The gRNA of claims 124-132 or 134-137, wherein the guide region does not comprise a YA site at nucleotides 15-16 and nucleotide 15 is unmodified.

139. The gRNA of claims 124-133 or 135-138, wherein the guide region does not comprise a YA site at nucleotides 16-17 and nucleotide 16 is unmodified.

140. The gRNA of claims 124-134 or 136-139, wherein the guide region does not comprise a YA site at nucleotides 19-20 and nucleotide 19 is unmodified.

141. The gRNA of claims 124-140, wherein the short-sgRNA comprises a guide region that comprises one or more of the following:

i. 2’-OMe and phosphorothioate modifications at nucleotide 1;
ii. 2’-OMe and phosphorothioate modifications at nucleotide 2;
iii. 2’-OMe and phosphorothioate modifications at nucleotide 3;
iv. a 2'-OMe modification at nucleotide 4;
v. a phosphorothioate modification at nucleotide 6;
vi. a phosphorothioate modification at nucleotide 7;
vii. 2'-fluoro and phosphorothioate modifications at nucleotide 8;
viii. 2'-fluoro and phosphorothioate modifications at nucleotide 9;

ix. 2'-fluoro and phosphorothioate modifications at nucleotide 10;
x. a 2'-fluoro modification at nucleotide 11;
xi. a 2'-fluoro modifications at nucleotide 13;
xii. a 2'-fluoro modifications at nucleotide 14;
xiii. a 2'-fluoro modifications at nucleotide 17; and
xiv. a 2'-fluoro modifications at nucleotide 18.

142. The gRNA of claims 124-141, wherein the guide region comprises each of the modifications set forth in the preceding claim.

143. The gRNA of claims 124-142, wherein the guide region comprises at least 1, 2, 3, or 4 of the following:
i. a 2'-OMe modification at nucleotide 5 if nucleotides 5 and 6 form a YA site;
ii. a 2'-OMe modification at nucleotide 12 if nucleotides 12 and 13 form a YA site;
iii. a phosphorothioate modification at nucleotide 15 if nucleotides 15 and 16 form a YA site;
iv. a phosphorothioate modification at nucleotide 16 if nucleotides 16 and 17 form a YA site; and
v. a phosphorothioate or 2'-fluoro modification at nucleotide 19 if nucleotides 19 and 20 form a YA site.

144. The gRNA of claims 124-143, wherein the guide region comprises a YA site at nucleotides 5-6 and a 2'-OMe modification at nucleotide 5.

145. The gRNA of claims 124-144, wherein the guide region comprises a YA site at nucleotides 12-13 and a 2'-OMe modification at nucleotide 12.

146. The gRNA of claims 124-145, wherein the guide region comprises a YA site at nucleotides 15-16 and a phosphorothioate modification at nucleotide 15.

147. The gRNA of claims 124-146, wherein the guide region comprises a YA site at nucleotides 16-17 and a phosphorothioate modification at nucleotide 16.

148. The gRNA of claims 124-147, wherein the guide region comprises a YA site at nucleotides 19-20 and a phosphorothioate modification at nucleotide 19.

149. The gRNA of claims 124-148, wherein the guide region comprises a 2'-fluoro modification at nucleotide 19.

150. The gRNA of claims 124-149, wherein the guide region comprises an unmodified nucleotide 15 or only a phosphorothioate modification at nucleotide 15.

151. The gRNA of claims 124-150, wherein the guide region comprises an unmodified nucleotide 16 or only a phosphorothioate modification at nucleotide 16.

152. A guide RNA which is a single guide RNA (sgRNA) comprising:

i. a YA modification at two or more guide region YA sites;
ii. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
iii. a YA modification at one or more of conserved region YA sites 1 and 8.

153. A guide RNA which is a single guide RNA (sgRNA) comprising:

i. a YA modification at one or more guide region YA sitesthat are at or after nucleotide 8 from the 5' end of the 5' terminus;
ii. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and optionally
iii. a YA modification at one or more of conserved region YA sites 1 and 8.

154. A guide RNA which is a single guide RNA (sgRNA) comprising:

i. a YA modification at one or more guide region YA sitesthat are within 13 nucleotides of the 3' terminal nucleotide of the guide region;
ii. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
iii. a YA modification at one or more of conserved region YA sites 1 and

155. A guide RNA which is a single guide RNA (sgRNA) comprising:

i. a 5' end modification and a 3' end modification;
ii. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and
iii. a YA modification at one or more of conserved region YA sites 1 and 8.

156. A guide RNA which is a single guide RNA (sgRNA) comprising:

i. a YA modification at at least one guide region YA site, wherein the modification of the guide region YA site comprises a modification at at

least one nucleotide located 5' of the guide region YA site does not comprise;

ii. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and

iii. a YA modification at one or more of conserved region YA sites 1 and 8.

157. A guide RNA which is a single guide RNA (sgRNA) comprising:

i. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and

ii. a YA modification at conserved region YA sites 1 and 8.

158. A guide RNA which is a single guide RNA (sgRNA) comprising:

i. a YA modification at one or more guide region YA sitesthat are at or after nucleotide 8 from the 5' end of the 5' terminus;

ii. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10; and

iii. a modification at one or more of H1-1 and H2-1.

159. A guide RNA which is a single guide RNA (sgRNA) comprising:

i. a YA modification at one or more of conserved region YA sites 2, 3, 4, and 10;

ii. a YA modification at one or more of conserved region YA sites 1, 5, 6, 7, 8, and 9; and

iii. a modification at one or more of H1-1 and H2-1.

160. A guide RNA which is an sgRNA comprising any one or more of the following:

i. a modification, such as a YA modification, at one or more nucleotides located at or after nucleotide 6 from the 5' end of the 5' terminus;

ii. a YA modification at one or more guide sequence YA sites;

iii. a modification at one or more of B3, B4, and B5, wherein B6 does not comprise a 2'-OMe modification or comprises a modification other than 2'-OMe;

iv. a modification at LS10, wherein LS10 comprises a modification other than 2'-fluoro; and/or

v. a modification at N2, N3, N4, N5, N6, N7, N10, or N11;

and

wherein at least one of the following is true:

a. at least one of nucleotides 8-11, 13, 14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;

b. at least one of nucleotides 6-10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;

c. at least one of B2, B3, B4, or B5 does not comprise a 2'-OMe modification;

d. at least one of LS1, LS8, or LS10 does not comprise a 2'-OMe modification;

e. at least one of N2, N3, N4, N5, N6, N7, N10, N11, N16, or N17 does not comprise a 2'-OMe modification;

f. H1-1 comprises a modification;

g. H2-1 comprises a modification; or

h. at least one of H1-2, H1-3, H1-4, H1-5, H1-6, H1-7, H1-8, H1-9, H1-10, H2-1, H2-2, H2-3, H2-4, H2-5, H2-6, H2-7, H2-8, H2-9, H2-10, H2-11, H2-12, H2-13, H2-14, or H2-15 does not comprise a phosphorothioate linkage.

161. A guide RNA comprising any one or more of the following:

i. a modification, such as a YA modification, at one or more nucleotides located at or after nucleotide 6 from the 5' end of the 5' terminus; or

ii. a YA modification at one or more guide sequence YA sites;

wherein at least one of the following is true:

a. at least one of nucleotides 8-11, 13, 14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification; or

b. at least one of nucleotides 6-10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;

and wherein at least one of the following is also true:

c. at least one of nucleotides 7-10 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification;
d. nucleotide 20 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification; or
e. the guide RNA comprises a 2'-fluoro modification at any one or more of nucleotides 1-20 from the 5' end of the 5' terminus and at least one of nucleotides 11, 12, 13, 14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification, optionally wherein nucleotide 12 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

162. A guide RNA which is an sgRNA comprising a guanosine at N14 and/or one or more of the following:

i. a YA modification at one or more guide region YA sitesthat are at or after nucleotide 8 from the 5' end of the 5' terminus;
ii. a YA modification at one or more of conserved region YA sites 1, 5, and 6, wherein if YA site 6 is modified at LS12 and LS9is not modified, then the modification of LS12 is other than 2'-OMe;
iii. a modification at LS9, wherein if LS9 is modified and LS5, LS7, and LS12 are not modified, then the modification of LS9 is other than 2'-fluoro,
iv. a modification at LS12, wherein if LS12 is modified and LS9 is not modified, then the modification of LS12 is other than 2'-OMe;
v. a modification at LS8 or LS11, wherein at least one of LS8 and LS11 comprises a modification other than 2'-OMe; and/or
vi. a modification at N6, N14, or N17, wherein if N17 is modified and N6 and N14 are not modified, then the modification of N17 is other than 2'-fluoro and other than 2'-OMe;

and wherein at least one of the following is true:

a. at least one of nucleotides 8-11, 13-14, 17, or 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
b. at least one of nucleotides 6-10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
c. at least one of B2, B3, B4, or B5 does not comprise a 2'-OMe modification;
d. at least one of LS1, LS8, or LS10 does not comprise a 2'-OMe modification;
e. at least one of N2, N3, N4, N5, N6, N7, N10, N11, N16, or N17 does not comprise a 2'-OMe modification;
f. H1-1 comprises a modification;
g. H2-1 comprises a modification; or
h. at least one of H1-2, H1-3, H1-4, H1-5, H1-6, H1-7, H1-8, H1-9, H1-10, H2-1, H2-2, H2-3, H2-4, H2-5, H2-6, H2-7, H2-8, H2-9, H2-10, H2-11, H2-12, H2-13, H2-14, or H2-15 does not comprise a phosphorothioate linkage.

163. The gRNA of claims 161 or 162, comprising:

i. a YA modification at 1, 2, 3, 4, or 5 guide region YA sites;
ii. a YA modification at 1, 2, 3, 4, or 5 guide region YA sites, wherein the modification of at least one guide region YA site is different from any 5' end modification of the sgRNA;
iii. a YA modification at one or more guide region YA sites that are at or after nucleotide 8 from the 5' end of the 5' terminus;
iv. a YA modification at one or more guide region YA sites that are is within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;
v. a YA modification at one or more guide region YA sites that are within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;
vi. a YA modification at a guide region YA site other than a 5' end modification; or

vii. a YA modification at a guide region YA site, wherein the modification of the guide region YA site comprises a modification at at least one nucleotide located 5' of the guide region YA site does not comprise.

164. The gRNA of claim 163, comprising:

i. a YA modification at two or more guide region YA sites that are at or after nucleotide 8 from the 5' end of the 5' terminus;
ii. a YA modification at two or more guide region YA sites that are within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;
iii. a YA modification at two or more guide region YA sites that are within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;
iv. a YA modification at two or more guide region YA sites other than a 5' end modification; or
v. a YA modification at a two or more guide region YA sites, wherein the modifications of the guide region YA sites comprise a modification at at least one nucleotide located 5' of the guide region YA site does not comprise.

165. The gRNA of claim 163, comprising:

i. a YA modification at three or more guide region YA sites that are at or after nucleotide 8 from the 5' end of the 5' terminus;
ii. a YA modification at three or more guide region YA sites that are within nucleotides 5-end, 6-end, 7-end, 8-end, 9-end, or 10-end from the 5' end of the 5' terminus;
iii. a YA modification at three or more guide region YA sites that are within 17, 16, 15, 14, 13, 12, 11, 10, or 9 nucleotides of the 3' terminal nucleotide of the guide region;
iv. a YA modification at three or more guide region YA sites other than a 5' end modification; or
v. a YA modification at a three or more guide region YA sites, wherein the modifications of the guide region YA sites comprise a modification at at

least one nucleotide located 5' of the guide region YA site does not comprise.

166. The gRNA of any one of claims 161-165, comprising at least one YA modification at nucleotide 6 from the 5' end of the 5' terminus.

167. The gRNA of any one of claims 161-166, comprising at least one YA modification at nucleotide 7 from the 5' end of the 5' terminus.

168. The gRNA of any one of claims 161-167, comprising at least one YA modification at nucleotide 8 from the 5' end of the 5' terminus.

169. The gRNA of any one of claims 161-168, comprising at least one YA modification at nucleotide 9 from the 5' end of the 5' terminus.

170. The gRNA of any one of claims 161-169, comprising at least one YA modification at nucleotide 10 from the 5' end of the 5' terminus.

171. The gRNA of any one of claims 161-170, comprising at least one YA modification at nucleotide 11 from the 5' end of the 5' terminus.

172. The gRNA of any one of claims 161-171, comprising at least one YA modification at nucleotide 12 from the 5' end of the 5' terminus.

173. The gRNA of any one of claims 161-172, comprising at least one YA modification at nucleotide 13 from the 5' end of the 5' terminus.

174. The gRNA of any one of claims 161-173, comprising at least one YA modification at nucleotide 14 from the 5' end of the 5' terminus.

175. The gRNA of any one of claims 161-174, comprising at least one YA modification at nucleotide 15 from the 5' end of the 5' terminus.

176. The gRNA of any one of claims 161-175, comprising at least one YA modification at nucleotide 16 from the 5' end of the 5' terminus.

177. The gRNA of any one of claims 161-176, comprising at least one YA modification at nucleotide 17 from the 5' end of the 5' terminus.

178. The gRNA of any one of claims 161-177, comprising at least one YA modification at nucleotide 18 from the 5' end of the 5' terminus.

179. The gRNA of any one of claims 161-178, comprising at least one YA modification at nucleotide 19 from the 5' end of the 5' terminus.

180. The gRNA of any one of claims 161-179, comprising at least one YA modification at nucleotide 20 from the 5' end of the 5' terminus.

181. The gRNA of any one of claims 161-180, wherein at least 1, 2, 3, 4, 5, 6, 7, or 8 of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus comprise a YA modification, optionally wherein the modification comprises 2'-fluoro, 2'-H, 2'-OMe, or PS.

182. The gRNA of claim 181, wherein the modification is 2'-fluoro.

183. The gRNA of claim 181, wherein the modification is 2'-OMe or 2'-H.

184. The gRNA of claim 181, wherein the modification is PS.

185. The gRNA of any one of claims 161-184, wherein at least 1, 2, 3, 4, or 5 of nucleotides 6-10 from the 5' end of the 5' terminus comprise a YA modification, optionally wherein the modification comprises 2'-fluoro, 2'-H, 2'-OMe, inosine, or PS.

186. The gRNA of claim 185, wherein the modification is PS.

187. The gRNA of claim 185, wherein the modification is 2'-fluoro or 2'-H.

188. The gRNA of claim 185, wherein the modification is 2'-OMe.

189. The gRNA of any one of claims 161-188, comprising any one or more of the following:

i. 1, 2, 3, 4, 5, 6, 7, or 8 YA modifications of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, wherein the YA modifications are optionally 2'-fluoro modifications, and a modification other than 2'-fluoro at one or more of nucleotides 6-10 from the 5' terminus;
ii. a YA modification other than PS at one or more of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, and 1, 2, 3, 4, or 5 YA modifications at nucleotides 6-10 from the 5' end of the 5' terminus, optionally wherein the modifications are PS modifications;

iii. 1, 2, 3, 4, 5, 6, 7, or 8 YA modifications at nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, wherein the YA modifications are optionally 2'-fluoro modifications, and modifications other than 2'-fluoro at nucleotides 6-10 from the 5' end of the 5' terminus;

iv. YA modifications other than PS at each of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, and 1, 2, 3, 4, or 5 YA modifications at nucleotides 6-10 from the 5' end of the 5' terminus, wherein the modifications are optionally PS modifications;

v. 1, 2, 3, 4, 5, 6, 7, or 8 YA modifications at nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, wherein the YA modifications are optionally 2'-fluoro modifications, and one or more PS modification at any one of nucleotides 6-10 from the 5' end of the 5' terminus;

vi. at least one 2'-fluoro modification at any one of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, and 1, 2, 3, 4, or 5 YA modifications of nucleotides 6-10 from the 5' end of the 5' terminus, wherein the modifications are optionally PS modifications;

vii. 1, 2, 3, 4, 5, 6, 7, or 8 YA modifications of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, wherein the YA modifications are optionally 2'-fluoro modifications, and a PS modification at each of nucleotides 6-10 from the 5' end of the 5' terminus; or

viii. a 2'-fluoro modification at each of nucleotides 8-11, 13-14, and 17-18 from the 5' end of the 5' terminus, and 1, 2, 3, 4, or 5 YA modifications of nucleotides 6-10 from the 5' end of the 5' terminus, wherein the modifications are optionally PS modifications.

190. The gRNA of any one of claims 161-189, wherein:

i. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, or 4 modified YA sites including a first modified YA site comprising a 2'-OMe modification and a second modified YA site comprising a 2'-fluoro modification or a PS modification;

ii. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, or 4 modified YA sites including a first modified YA site comprising a 2'-fluoro modification and a second modified YA site comprising a 2'-OMe modification or a PS modification;

iii. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, or 4 modified YA sites including a first modified YA site comprising a PS modification and a second modified YA site comprising a 2'-OMe modification or a 2'-fluoro modification;

iv. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, or 4 modified YA sites including a YA modification;

v. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 3 or 4 modified YA sites including a first modified YA site comprising a 2'-OMe modification, a second modified YA site comprising a 2'-fluoro modification, and a third modified YA site comprising a PS modification;

vi. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 3 or 4 modified YA sites including a first modified YA site comprising a 2'-OMe modification, a second modified YA site comprising a 2'-fluoro modification, a third modified YA site comprising a 2'-fluoro modification, and a fourth modified YA site comprising a PS modification;

vii. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 3 or 4 modified YA sites including a YA modification;

viii. nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 4 modified YA sites including a first modified YA site comprising a 2'-OMe modification, a second modified YA site comprising a 2'-fluoro modification, a third modified YA site comprising a PS modification, and a fourth modified YA site comprising a PS modification; or

ix. nucleotides 4-40 from the 5' end of the 5' terminus comprise at least 4 modified YA sites including a YA modification.

191. The gRNA of any one of claims 161-190, wherein nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 5 modified YA sites.

192. The gRNA of any one of claims 161-191, wherein the at least 5 modified YA sites include a fifth modified YA site comprising a PS modification, optionally wherein the third modified YA site comprises a 2'-fluoro modification.

193. The gRNA of any one of claims 161-192, wherein the first, second, and (if applicable) third, fourth, and fifth of the at least 5 modified YA sites are arranged in the 5' to 3' direction.

194. The gRNA of any one of claims 161-193, wherein the first, second, and (if applicable) third, fourth, and fifth of the at least 5 modified YA sites are not arranged in the 5' to 3' direction.

195. The gRNA of any one of claims 161-194, wherein nucleotides 4-20 from the 5' end of the 5' terminus comprise at least 2, 3, 4, or 5 modified YA sites comprising a deoxyribonucleotide, optionally wherein the deoxyribonucleotide is the pyrimidine of the YA sites.

196. The gRNA of any one of claims 161-195, wherein:

i. at least 1, 2, 3, or 4 of nucleotides 8-11 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-fluoro modification;
ii. at least 1, 2, 3, 4, 5, 6, 7, or 8 of nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus comprise a YA modification, optionally wherein the YA modifications are 2'-OMe if present at nucleotides 8-11 and 2'-fluoro if present at nucleotides 13, 14, 17, or 18;
iii. at least one or both of nucleotides 17 and 18 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-fluoro modification;
iv. at least one or both of nucleotides 17 and 18 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-fluoro modification; or
v. at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 of nucleotides 4-14, 17, and 18 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-fluoro modification.

197. The gRNA of any one of claims 161-196, wherein at least 1, 2, 3, 4, 5, or 6 of nucleotides 4-10 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-OMe modification.

198. The gRNA of any one of claims 161-197, wherein nucleotides 4-10 from the 5' end of the 5' terminus comprise a YA modification, which is optionally a 2'-OMe modification.

199. The gRNA of any one of claims 161-198, wherein:

i. at least one of nucleotides 1-3 from the 5' end of the 5' terminus comprise a 5' protective end modification, which is optionally a 2'-OMe modification;
ii. at least two of nucleotides 1-3 from the 5' end of the 5' terminus comprise a 5' protective end modification, which is optionally a 2'-OMe modification; or
iii. each of nucleotides 1-3 from the 5' end of the 5' terminus comprise a 5' protective end modification, which is optionally a 2'-OMe modification.

200. The gRNA of any one of claims 161-199, wherein at least 1, 2, 3, 4, or 5 of nucleotides 11, 13, 14, 17, and 18 from the 5' end of the 5' terminus comprise a 5' end modification, which is optionally a 2'-fluoro modification.

201. The gRNA of any one of claims 161-200, wherein nucleotide 15 from the 5' end of the 5' terminus is unmodified or modified only with phosphorothioate.

202. The gRNA of any one of claims 161-200, wherein nucleotide 16 from the 5' terminus is unmodified or modified only with phosphorothioate.

203. The gRNA of any one of the preceding claims, wherein nucleotide 3 from the 5' end of the 5' terminus is unmodified or modified only with phosphorothioate.

204. The gRNA of any one of claims 161-203, which is a crRNA or dgRNA.

205. The gRNA of any one of claims 161-203, which is an sgRNA.

206. The gRNA of any one of claims 161-203, which is a short-sgRNA.

207. The gRNA of any one of claim 205 or 206, comprising a YA modification of conserved region YA site 1.

208. The gRNA of any one of claims 205-207, comprising a YA modification of conserved region YA site 2.

209. The gRNA of any one of claims 205-208, comprising a YA modification of conserved region YA site 3.

210. The gRNA of any one of claims 205-209, comprising a YA modification of conserved region YA site 4.

211. The gRNA of any one of claims 205-210, comprising a YA modification of conserved region YA site 5.

212. The gRNA of any one of claims 205-211, comprising a YA modification of conserved region YA site 6.

213. The gRNA of any one of claims 205-212, comprising a YA modification of conserved region YA site 7.

214. The gRNA of any one of claims 205-213, comprising a YA modification of conserved region YA site 8.

215. The gRNA of any one of claims 205-214, comprising a YA modification of conserved region YA site 9.

216. The gRNA of any one of claims 205-215, comprising a YA modification of conserved region YA site 10.

217. The gRNA of any one of claims 205-216, comprising:

i. YA modifications of conserved region YA sites 2, 3, 4, and 10;
ii. YA modifications of conserved region YA sites 2, 3, and 4;
iii. YA modifications of conserved region YA sites 2, 3, and 10;
iv. YA modifications of conserved region YA sites 2, 4, and 10;
v. YA modifications of conserved region YA sites 3, 4, and 10;
vi. YA modifications of conserved region YA sites 2 and 10;
vii. YA modifications of conserved region YA sites 2 and 4;
viii. YA modifications of conserved region YA sites 2 and 3;
ix. YA modifications of conserved region YA sites 3 and 4;
x. YA modifications of conserved region YA sites 3 and 10; or
xi. YA modifications of conserved region YA sites 4 and 10.

218. The gRNA of any one of claims 205-217, comprising:

i. YA modifications of conserved region YA sites 1 and 5;
ii. YA modifications of conserved region YA sites 1 and 6;
iii. YA modifications of conserved region YA sites 1 and 7;
iv. YA modifications of conserved region YA sites 1 and 8;
v. YA modifications of conserved region YA sites 1 and 9;
vi. YA modifications of conserved region YA sites 8 and 5;
vii. YA modifications of conserved region YA sites 8 and 6;
viii. YA modifications of conserved region YA sites 8 and 7; or
ix. YA modifications of conserved region YA sites 8 and 9;

optionally wherein the sgRNA further comprises YA modifications of conserved region YA sites 2, 3, 4, and 10.

219. The gRNA of any one of claims 205-218, wherein at least one modified YA site comprises a 2'-OMe modification, optionally at the pyrimidine of the YA site.

220. The gRNA of any one of claims 205-219, wherein at least one modified YA site comprises a 2'-fluoro modification, optionally at the pyrimidine of the YA site.

221. The gRNA of any one of claims 205-220, wherein at least one modified YA site comprises a PS modification, optionally at the pyrimidine of the YA site.

222. The gRNA of any one of claims 205-221, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified YA sites comprise a 2'-OMe modification, optionally at the pyrimidines of the YA sites.

223. The gRNA of any one of claims205-222, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified YA sites comprise a 2'-fluoro modification, optionally at the pyrimidines of the YA sites.

224. The gRNA of any one of claims205-223, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified YA sites comprise a PS modification, optionally at the pyrimidines of the YA sites.

225. The gRNA of any one of claims205-224, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified YA sites comprise a ribose modification at the 2' position, optionally at the pyrimidines of the YA sites, and optionally chosen from a 2'-O-alkyl, 2'-H, and 2'-fluoro modification.

226. The gRNA of any one of claims 205-225, wherein:

i. conserved region YA sites 1 and 8 comprise 2'-fluoro modifications, optionally at the pyrimidines of the YA sites;
ii. conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
iii. conserved region YA site 1 comprises a 2'-fluoro modification and conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
iv. conserved region YA site 8 comprises a 2'-fluoro modification and conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
v. conserved region YA site 1 comprises a 2'-fluoro modification at the pyrimidine of the YA sites and YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
vi. conserved region YA site 8 comprises a 2'-fluoro modification at the pyrimidine of the YA site and YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites;
vii. conserved region YA sites 1 and 8 comprise 2'-fluoro modifications and conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites; or
viii. conserved region YA sites 1 and 8 comprise 2'-fluoro modifications at the pyrimidines of the YA sites and conserved region YA sites 5 and 6; 5 and 7; 5 and 9; 6 and 7; 6 and 9; 5, 6, and 7; 5, 6, and 9; 6, 7, and 9; or 5, 6, 7, and 9 comprise 2'-OMe modifications, optionally at the pyrimidines of the YA sites.

227. The gRNA of any one of claims 205-226, wherein conserved region YA sites 7 and 9 comprise YA modifications, which are optionally 2'-OMe modifications.

228. The gRNA of any one of claims 205-227, wherein conserved region YA sites 5, 6, 7, and 9 comprise YA modifications, which are optionally 2'-OMe modifications.

229. The gRNA of any one of claims 205-228, wherein conserved region YA site 8 comprises a 2'-fluoro modification.

230. The gRNA of any one of claims 205-229, wherein conserved region YA site 8 comprises a deoxyribonucleotide modification.

231. The gRNA of any one of claims 205-230, wherein conserved region YA site 8 is abolished by a base substitution, optionally wherein the base substitution eliminates the uracil of YA site 8, further optionally wherein the base substitution is a uracil to guanine substitution.

232. The gRNA of any one of claims 205-231, wherein conserved region YA site 1 comprises a 2'-fluoro modification.

233. The gRNA of any one of claims 205-232, wherein conserved region YA site 1 comprises a PS modification.

234. The gRNA of any one of claims 205-233, wherein 1, 2, 3, 4, 5, 6, or 7 of LS5, LS7, LS8, LS9, LS10, LS11, and LS12 comprise modifications, optionally wherein the modifications are 2'-fluoro and/or 2'-OMe modifications.

235. The gRNA of any one of claims 205-234, wherein modifications at LS5, LS7, LS9, and LS11, if present, comprise 2'-fluoro modifications, optionally wherein each of LS5, LS7, LS9, and LS11 comprise 2'-fluoro modifications.

236. The gRNA of any one of claims 205-235, wherein modifications at LS8, LS10, and LS12, if present, comprise 2'-OMe modifications, optionally wherein each of LS8, LS10, and LS12 comprise 2'-OMe modifications.

237. The gRNA of any one of claims 205-236, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of N2, N3, N4, N5, N6, N7, N10, N11, N16, and N17 comprise modifications, which are optionally 2'-OMe modifications.

238. The gRNA of any one of claims 205-237, wherein H2-2 comprises a modification, optionally wherein H2 is otherwise unmodified.

239. The gRNA of any one of claims 205-238, wherein H2-2 comprises a 2'-OMe modification.

240. The gRNA of any one of claims 205-239, wherein US3, US9, and US12 comprise modifications, optionally wherein the US is otherwise unmodified.

241. The gRNA of any one of claims 205-240, wherein US3, US9, and US12 comprise 2'-OMe modifications.

242. The gRNA of any one of claims 205-241, wherein nucleotides 6-10 from the 5' end of the 5' terminus comprise a PS modification and nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus comprise a 2'-fluoro modification.

243. The gRNA of any one of claims 205-242, wherein each guide region YA site comprises a 2'-fluoro modification, optionally excepting nucleotides 15 and/or 16 from the 5' end of the 5' terminus.

244. The gRNA of any one of claims 205-243, wherein nucleotides 4, 8, and 11 from the 5' end of the 5' terminus comprise YA modifications, optionally wherein nucleotide 4 comprises a 2'-OMe modification and nucleotides 8 and 11 comprise a 2'-fluoro modification.

245. The gRNA of any one of claims 205-244, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or more modified YA sites comprise a YA modification at the pyrimidine position of the YA site.

246. The gRNA of claim 245, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified conserved region YA sites comprise a YA modification at the pyrimidine position of the YA site.

247. The gRNA of any one of claims 205-246, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or more modified YA sites comprise a YA modification at the adenine position of the YA site.

248. The gRNA of claim 247, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified conserved region YA sites comprise a YA site modification at the adenine position of the YA site.

249. The gRNA of any one of claims 205-248, comprising:

i. a modification of H1-1;
ii. a modification of H2-1; or
iii. modifications of H1-1 and H2-1.

250. The gRNA of claim 249, wherein H1-1 and/or H2-1 comprises a 2'-OMe modification.

251. The gRNA of claim 250, wherein H1-1 and/or H2-1 comprises a 2'-fluoro modification.

252. The gRNA of claim 251, wherein H1-1 and/or H2-1 comprises a PS modification.

253. The gRNA of any one of claims 205-252, comprising a modification at B3, optionally wherein B6 does not comprise a 2'-OMe modification or comprises a modification other than 2'-OMe.

254. The gRNA of any one of claims 205-253, comprising a modification at B4, optionally wherein B6 does not comprise a 2'-OMe modification or comprises a modification other than 2'-OMe.

255. The gRNA of any one of claims 205-254, comprising a modification at B5, optionally wherein B6 does not comprise a 2'-OMe modification or comprises a modification other than 2'-OMe.

256. The gRNA of any one of claims 205-255, comprising a modification at LS10, optionally wherein LS10 comprises a modification other than 2'-fluoro.

257. The gRNA of any one of claims 205-256, comprising a modification at N2.

258. The gRNA of any one of claims 205-257, comprising a modification at N3.

259. The gRNA of any one of claims 205-258, comprising a modification at N4.

260. The gRNA of any one of claims 205-259, comprising a modification at N5.

261. The gRNA of any one of claims 205-260, comprising a modification at N6.

262. The gRNA of any one of claims 205-261, comprising a modification at N7.

263. The gRNA of any one of claims 205-262, comprising a modification at N10.

264. The gRNA of any one of claims 205-263, comprising a modification at N11.

265. The gRNA of any one of claims 205-264,, wherein:

i. nucleotide 8 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
ii. nucleotide 9 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
iii. nucleotide 10 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
iv. nucleotide 11 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
v. nucleotide 13 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
vi. nucleotide 14 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
vii. nucleotide 17 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification; and/or
viii. nucleotide 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

266. The gRNA of any one of claims 205-265, wherein:

i. nucleotide 6 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
ii. nucleotide 7 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
iii. nucleotide 8 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
iv. nucleotide 9 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification; and/or
v. nucleotide 10 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

267. The gRNA of any one of claims 205-266, wherein:

i. nucleotide 6 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
ii. nucleotide 7 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
iii. nucleotide 8 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage;
iv. nucleotide 9 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage; and/or
v. nucleotide 10 from the 5' end of the 5' terminus does not comprise a phosphorothioate linkage.

268. The gRNA of any one of claims 205-267, wherein:

i. nucleotide 7 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification;
ii. nucleotide 8 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification;
iii. nucleotide 9 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification; and/or
iv. nucleotide 10 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification.

269. The gRNA of any one of claims 205-268, wherein nucleotide 20 from the 5' end of the 5' terminus does not comprise a 2'-OMe modification.

270. The gRNA of any one of claims 205-269, wherein the guide RNA comprises a 2'-fluoro modification at any one or more of nucleotides 1-11 and 13-20 from the 5' end of the 5' terminus and nucleotide 12 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

271. The gRNA of any one of claims 205-270, wherein the guide RNA comprises a 2'-fluoro modification at any one or more of nucleotides 1-20 from the 5' end of the 5' terminus and:

i. nucleotide 11 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;

ii. nucleotide 12 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
iii. nucleotide 13 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
iv. nucleotide 14 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification;
v. nucleotide 17 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification; and/or
vi. nucleotide 18 from the 5' end of the 5' terminus does not comprise a 2'-fluoro modification.

272. The gRNA of any one of claims 205-271, wherein:

i. B2 does not comprise a 2'-OMe modification;
ii. B3 does not comprise a 2'-OMe modification;
iii. B4 does not comprise a 2'-OMe modification; and/or
iv. B5 does not comprise a 2'-OMe modification.

273. The gRNA of any one of claims 205-272, wherein:

i. LS1 does not comprise a 2'-OMe modification;
ii. LS8 does not comprise a 2'-OMe modification; and/or
iii. LS10 does not comprise a 2'-OMe modification.

274. The gRNA of any one of claims 205-273, wherein:

i. N2 does not comprise a 2'-OMe modification;
ii. N3 does not comprise a 2'-OMe modification;
iii. N4 does not comprise a 2'-OMe modification;
iv. N5 does not comprise a 2'-OMe modification;
v. N6 does not comprise a 2'-OMe modification;
vi. N7 does not comprise a 2'-OMe modification;
vii. N10 does not comprise a 2'-OMe modification;
viii. N11 does not comprise a 2'-OMe modification;
ix. N16 does not comprise a 2'-OMe modification; and/or
x. N17 does not comprise a 2'-OMe modification.

275. The gRNA of any one of claims 205-274, wherein:

i. H1-2 does not comprise a phosphorothioate linkage;
ii. H1-3 does not comprise a phosphorothioate linkage;
iii. H1-4 does not comprise a phosphorothioate linkage;
iv. H1-5 does not comprise a phosphorothioate linkage;
v. H1-6 does not comprise a phosphorothioate linkage;
vi. H1-7 does not comprise a phosphorothioate linkage;
vii. H1-8 does not comprise a phosphorothioate linkage;
viii. H1-9 does not comprise a phosphorothioate linkage;
ix. H1-10 does not comprise a phosphorothioate linkage;
x. H2-1 does not comprise a phosphorothioate linkage;
xi. H2-2 does not comprise a phosphorothioate linkage;
xii. H2-3 does not comprise a phosphorothioate linkage;
xiii. H2-4 does not comprise a phosphorothioate linkage;
xiv. H2-5 does not comprise a phosphorothioate linkage;
xv. H2-6 does not comprise a phosphorothioate linkage;
xvi. H2-7 does not comprise a phosphorothioate linkage;
xvii. H2-8 does not comprise a phosphorothioate linkage;
xviii. H2-9 does not comprise a phosphorothioate linkage;
xix. H2-10 does not comprise a phosphorothioate linkage;
xx. H2-11 does not comprise a phosphorothioate linkage;
xxi. H2-12 does not comprise a phosphorothioate linkage;
xxii. H2-13 does not comprise a phosphorothioate linkage;
xxiii. H2-14 does not comprise a phosphorothioate linkage; and/or
xxiv. H2-15 does not comprise a phosphorothioate linkage.

276. A gRNA which is an sgRNA comprising modifications at:

i. nucleotides 6-10 from the 5' end of the 5' terminus, which are optionally PS modifications;
ii. nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus, which are optionally 2'-fluoro modifications; and
iii. H1-1 and H2-1, which are optionally 2'-OMe modifications, or conserved region YA site 1 or 8.

277. A gRNA which is an sgRNA comprising YA modifications at:

i. conserved region YA sites 1, 5, 6, 7, and 9, which are optionally 2'-OMe modifications; and
ii. conserved region YA site 8, which is optionally a 2'-fluoro modification.

278. A gRNA comprising YA modifications at four guide region YA sites, wherein at least one of the YA sites is at or after nucleotide 8 from the 5' end of the 5' terminus, and wherein:

i. the first YA site comprises a 2'-OMe modification;
ii. the second YA site comprises a 2'-fluoro modification;
iii. the third YA site comprises a 2'-fluoro or PS modification; and
iv. the fourth YA site comprises a PS modification,

optionally wherein the first, second, third, and fourth YA sites are arranged in the 5' to 3' direction.

279. The gRNA of claim 278, wherein the third YA site comprises a PS modification.

280. The gRNA of any one of claims 278-279, wherein the third YA site comprises a 2'-fluoro modification.

281. The gRNA of any one of claims 278-280, further comprising a fifth YA site comprising a PS modification, which is optionally 3' of the fourth YA site.

282. The gRNA of any one of the claims 205-281, wherein conserved region YA sites 1, 5, 6, 7, and 9 comprise YA modifications, which are optionally 2'-OMe modifications; and conserved region YA site 8 comprises a modification, which is optionally a 2'-fluoro modification.

283. A gRNA which is an sgRNA comprising YA modifications at:

i. nucleotide 4 from the 5' end of the 5' terminus, wherein the YA modification is optionally a 2'-OMe modification;
ii. nucleotides 6-10 from the 5' end of the 5' terminus, which are optionally PS modifications;
iii. nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus, which are optionally 2'-fluoro modifications;

iv. LS5, LS7, LS9, and LS11, which are optionally 2'-fluoro modifications;
v. LS8, LS10, and LS12, which are optionally 2'-OMe modifications;
vi. N2, N3, N4, N5, N6, N7, N10, N11, N16, and N17, which are optionally 2'-OMe modifications; and
vii. N14, which is optionally a 2'-fluoro modification.

284. The gRNA of any one of claim 161-, wherein one or more of the following are true:

i. nucleotide 4 from the 5' end of the 5' terminus comprises a 2'-OMe modification;
ii. nucleotides 6-10 from the 5' end of the 5' terminus comprise PS modifications;
iii. nucleotides 8-11, 13, 14, 17, and 18 from the 5' end of the 5' terminus comprise 2'-fluoro modifications;
iv. LS5, LS7, LS9, and LS11 comprise 2'-fluoro modifications;
v. LS8, LS10, and LS12 comprise 2'-OMe modifications;
vi. N2, N3, N4, N5, N6, N7, N10, N11, N16, and N17 comprise 2'-OMe modifications; and
vii. N14 comprises a 2'-fluoro modification.

285. The gRNA of any one of claims 161-284, wherein at least one YA modification comprises a modification of the pyrimidine position of the YA site.

286. The gRNA of any one of claims 161-285, wherein at least one YA modification comprises a modification of the adenine position of the YA site.

287. The gRNA of any one of claims 161-286, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 YA sites comprise YA modifications at the pyrimidines positions of the YA sites.

288. The gRNA of any one of claims 161-287, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 YA sites comprise YA modifications at the adenine positions of the YA sites.

289. The gRNA of any one of claims 161-288, wherein at least one YA modification comprises a 2'-OMe modification.

290. The gRNA of any one of claims 161-289, wherein at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 YA sites comprise a 2'-OMe modification.

291. The gRNA of any one of claims 161-290, wherein each modified conserved region YA site comprises a modification at the pyrimidine position of the YA site.

292. The gRNA of any one of claims 161-291, wherein each modified guide region YA site, or each modified conserved region and guide region YA site, comprises a modification at the pyrimidine position of the YA site.

293. The gRNA of any one of claims 161-292, wherein each modified conserved region YA site comprises a modification at the adenine position of the YA site.

294. The gRNA of any one of claims 161-293, wherein each modified guide region YA site, or each modified conserved region and guide region YA site, comprises a modification at the adenine position of the YA site.

295. The gRNA of any one of claims 161-294, which is an sgRNA comprising a modification at LS5.

296. The gRNA of any one of claims 161-295, which is an sgRNA comprising a modification at LS7.

297. The gRNA of any one of claims 161-296, which is an sgRNA comprising a modification at LS9, optionally wherein if LS9 is modified and LS5, LS7, and LS12 are not, then the modification of LS9 is other than 2'-fluoro.

298. The gRNA of any one of claims 161-297, which is an sgRNA comprising a modification at LS12, optionally wherein if LS12 is modified and LS9 is not, then the modification of LS12 is other than 2'-OMe.

299. The gRNA of any one of claims 161-298, which is an sgRNA comprising at least one YA modification that stabilizes a secondary structure, optionally wherein the secondary structure is the lower stem.

300. The gRNA of any one of claims 161-299, which is an sgRNA comprising at least one modification of LS8 and/or LS11, optionally wherein the modification of LS8 and/or LS11 stabilizes a secondary structure.

301. The gRNA of any one of claims 161-300, comprising a YA modification that stabilizes a secondary structure chosen from:

i. ENA;
ii. LNA; or
iii. a bicyclic ribose modification.

302. The gRNA of any one of claims 161-301, which is an sgRNA comprising a modification at N6.

303. The gRNA of any one of claims 161-302, which is an sgRNA comprising a modification at N14.

304. The gRNA of any one of claims 161-303, which is an sgRNA comprising a modification at N17, optionally wherein if N17 is modified and N6 and N14 are not, then the modification of N17 is other than 2'-fluoro and other than 2'-OMe.

305. The gRNA of any one of claims 161-304, wherein at least 1, 2, or 3 of nucleotides 1-3 from the 5' end of the 5' terminus comprise deoxyribonucleotides, optionally wherein nucleotides 1-3 from the 5' end of the 5' terminus comprise PS modifications.

306. The gRNA of any one of claims 161-305, wherein the gRNA is an sgRNA and at least 1, 2, or 3 of nucleotides 1-3 from the 3' end of the 3' terminus comprise deoxyribonucleotides, optionally wherein nucleotides 2-3 from the 3' end of the 3' terminus comprise PS modifications.

307. The gRNA of any one of claims 161-306, wherein the gRNA is an sgRNA and nucleotide 4 from the 3' end of the 3' terminus comprises a PS modification, optionally wherein nucleotide 4 from the 3' end of the 3' terminus comprises a 2'-OMe modification.

308. The gRNA of any one of claims 161-307, wherein the gRNA is an sgRNA and hairpin 2 comprises deoxyribonucleotides, optionally wherein all or all but 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides of hairpin 1 and hairpin 2 are deoxyribonucleotides.

309. The gRNA of any one of claims 161-308, wherein the gRNA is an sgRNA and hairpin 1 and hairpin 2 comprise deoxyribonucleotides, optionally wherein all or all

but 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 nucleotides of hairpin 1 and hairpin 2 are deoxyribonucleotides.

310. The gRNA of any one of claims 161-309, wherein the gRNA is an sgRNA and all or all but 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 nucleotides from the beginning of hairpin 1 to the 3' end of the sgRNA are deoxyribonucleotides, optionally wherein nucleotides 1-3 from the 3' end of the 3' terminus are deoxyribonucleotides.

311. The gRNA of any one of claims 161-310, wherein the gRNA is an sgRNA and the upper stem comprises deoxyribonucleotides.

312. The gRNA of any one of claims 161-311, wherein the gRNA is an sgRNA and all or all but 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides of the upper stem are deoxyribonucleotides.

313. The gRNA of any one of claims 161-312, wherein at least 1, 2, or 3 of nucleotides 1-3 from the 5' end of the 5' terminus comprise ENA, optionally wherein nucleotides 1-3 from the 5' end of the 5' terminus comprise PS modifications.

314. The gRNA of any one of claims 161-313, wherein the gRNA is an sgRNA and at least 1, 2, or 3 of nucleotides 2-4 from the 3' end of the 3' terminus comprise ENA, optionally wherein nucleotides 2-3 from the 3' end of the 3' terminus comprise PS modifications.

315. The gRNA of any one of claims 161-314, wherein at least 1, 2, or 3 of nucleotides 1-3 from the 5' end of the 5' terminus comprise UNA, optionally wherein nucleotides 1-3 from the 5' end of the 5' terminus comprise PS modifications.

316. The gRNA of any one of claims 161-315, wherein the gRNA is an sgRNA and at least 1, 2, or 3 of nucleotides 2-4 from the 3' end of the 3' terminus comprise UNA, optionally wherein nucleotides 2-3 from the 3' end of the 3' terminus comprise PS modifications.

317. The gRNA of any one of claims 161-316, wherein the gRNA is an sgRNA and nucleotide 4 from the 3' end of the 3' terminus comprises a PS modification, optionally wherein nucleotide 4 from the 3' end of the 3' terminus comprises a 2'-OMe modification.

318. The gRNA of any one claims 161-317, wherein the gRNA is an sgRNA that comprises a 3' end modification.

319. The gRNA of any one of claims 161-318, which is an sgRNA comprising a 3' end modification, wherein the 3' end modification is a protective 3' end modification.

320. The gRNA of any one claims 161-319, wherein the gRNA is an sgRNA that comprises a 3' tail.

321. The gRNA of claim 320, wherein the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

322. The gRNA of claim 320, wherein the 3' tail comprises about 1-2, 1-3, 1-4, 1-5, 1-7, 1-10, at least 1-5, at least 1-3, at least 1-4, at least 1-5, at least 1-5, at least 1-7, or at least 1-10 nucleotides.

323. The gRNA of any one of claims 161-322, which is an sgRNA comprising a modification in the hairpin region.

324. The gRNA of any one of claims 161-323, which is an sgRNA comprising a 3' end modification, and a modification in the hairpin region.

325. The gRNA of claim 323 or 324, wherein the modification in the hairpin region comprises a modified nucleotide selected from 2'-O-methyl (2'-O-Me) modified nucleotide, a 2'-fluoro (2'-F) modified nucleotide, or combinations thereof.

326. The gRNA of any one of claims 323-325, wherein the modification in the hairpin region comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

327. The gRNA of any one of claims 323-326, wherein the modification in the hairpin region comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

328. The gRNA of any one of claims 161-327, comprising 3' and/or 5' protective end modification(s).

329. The gRNA of claim 328, wherein the 3' and/or 5' end modification comprises a modified nucleotide selected from 2'-O-methyl (2'-O-Me) modified nucleotide, 2'-O-(2-methoxyethyl) (2'-O-moe) modified nucleotide, a 2'-fluoro (2'-F) modified

nucleotide, a phosphorothioate (PS) linkage between nucleotides, an inverted abasic modified nucleotide, or combinations thereof.

330. The gRNA of claim 328 or 329, wherein the 3' and/or 5' end modification comprises or further comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

331. The gRNA of claim 328 or 329, wherein the 3' and/or 5' end modification comprises or further comprises a 2'-fluoro (2'-F) modified nucleotide.

332. The gRNA of claim 328 or 329, wherein the 3' and/or 5' end modification comprises or further comprises a phosphorothioate (PS) linkage between nucleotides.

333. The gRNA of claim 328 or 329, wherein the 3' and/or 5' end modification comprises or further comprises an inverted abasic modified nucleotide.

334. The gRNA of any one any one of claims 161-333, wherein the gRNA is an sgRNA and if the sgRNA comprises a 3' end modification, the 3' end modification comprises any one or more of the following:

i. a modification of any one or more of the last 7, 6, 5, 4, 3, 2, or 1 nucleotides;
ii. one modified nucleotide;
iii. two modified nucleotides;
iv. three modified nucleotides;
v. four modified nucleotides;
vi. five modified nucleotides;
vii. six modified nucleotides; and
viii. seven modified nucleotides.

335. The gRNA of claim 334, wherein the 3' end modification comprises a modification of between 1 and 7, between 1 and 5, between 1 and 4, or between 2 and 4 nucleotides.

336. The gRNA of any one of claims 161-335, wherein the gRNA is an sgRNA comprising a 3' end modification and the 3' end modification comprises one or more of the following:

i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-O-Me modified nucleotide;

iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide
vi. ENA, UNA, and/or DNA; and
vii. or a combination thereof.

337. The gRNA of any one of claims 161-336, wherein the gRNA is an sgRNA comprising a 3' tail, and the 3' tail comprises any one or more of:

i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-O-Me modified nucleotide;
iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide
vi. ENA, UNA, and/or DNA; and
vii. or a combination thereof.

338. The gRNA of claim 336, wherein the 3' end modification comprises:

i. 1, 2, 3, 4, 5, 6, or 7 PS linkages between nucleotides;
ii. about 1-3, 1-5, 1-6, or 1-7 PS linkages between nucleotides; or
iii. PS linkages between each nucleotide.

339. The gRNA of any one of claims claim 326-328, wherein the 3' end modification further comprises at least one 2'-O-Me, 2'-O-moe, inverted abasic, or 2'-F modified nucleotide.

340. The gRNA of any one of claims 326-329, wherein the 3' end modification comprises at least one PS linkage, and wherein:

i. there is one PS linkage, and the linkage is between the last and second to last nucleotide;
ii. there are two PS linkages between the last three nucleotides;
iii. there are PS linkages between any one or more of the last four nucleotides;
iv. there are PS linkages between any one or more of the last five nucleotides; or

v. there are PS linkages between any one or more of the last 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

341. The gRNA of any one of claims 336-340, wherein the 3' end modification comprises:

i. a modification of one or more of the last 1-7 nucleotides, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof;
ii. a modification to the last nucleotide with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and an optional one or two PS linkages to the next nucleotide and/or the first nucleotide of the 3' tail;
iii. a modification to the last and/or second to last nucleotide with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages;
iv. a modification to the last, second to last, and/or third to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages;
v. a modification to the last, second to last, third to last, and/or fourth to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages; or
vi. a modification to the last, second to last, third to last, fourth to last, and/or fifth to last nucleotides with 2'-O-Me, 2'-O-moe, 2'-F, or combinations thereof, and optionally one or more PS linkages.

342. The gRNA of any one of claims 161-341, wherein the gRNA is an sgRNA comprising a 3' tail, wherein the 3' tail comprises a modification of any one or more of the nucleotides present in the 3' tail.

343. The gRNA of claim 342, wherein the 3' tail is fully modified.

344. The gRNA of claim 342, wherein the 3' tail comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, or 1-10 nucleotides, optionally where any one or more of these nucleotides are modified.

345. The gRNA of any one of claims 336-344, wherein the 3' end modification comprises any one or more of the following:

i. the 3' end modification as shown in any one of SEQ ID Nos: 401-532;
ii. (i) a 2'O-Me modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, (ii) three consecutive 2'O-moe modified nucleotides immediately 5' to the 2'O-Me modified nucleotide, and (iii) three consecutive PS linkages between the last three nucleotides;
iii. (i) five consecutive 2'O-Me modified nucleotides from the 3' terminus, and (ii) three PS linkages between the last three nucleotides;
iv. an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA;
v. (i) an inverted abasic modified nucleotide at the last nucleotide of the conserved region of an sgRNA or short-sgRNA, and (ii) three consecutive 2'O-Me modified nucleotides at the last three nucleotides of the conserved region of an sgRNA or short-sgRNA;
vi. (i) 15 consecutive 2'O-Me modified nucleotides from the 3' terminus, (ii) five consecutive 2'-F modified nucleotides immediately 5' to the 2'O-Me modified nucleotides, and (iii) three PS linkages between the last three nucleotides;
vii. (i) alternating 2'O-Me modified nucleotides and 2'-F modified nucleotides at the last 20 nucleotides of the conserved region of an sgRNA or short-sgRNA, and (ii) three PS linkages between the last three nucleotides;
viii. (i) two or three consecutive 2'O-Me modified nucleotides, and (ii) three PS linkages between the last three nucleotides;
ix. one PS linkage between the last and next to last nucleotides; and
x. 15 or 20 consecutive 2'O-Me modified nucleotides, and (ii) three PS linkages between the last three nucleotides.

346. The gRNA of any one of claims 161-345, comprising a 5' end modification comprising any one or more of the following:

i. a modification of any one or more of nucleotides 1-7 of the guide region;
ii. one modified nucleotide;
iii. two modified nucleotides;
iv. three modified nucleotides;

v. four modified nucleotides;
vi. five modified nucleotides;
vii. six modified nucleotides; and
viii. seven modified nucleotides.

347. The gRNA of any one of claims 161-346, comprising a 5' end modification, wherein the 5' end modification is a protective 5' end modification.

348. The gRNA of any one of claims 161-347, comprising a 5' end modification, wherein the 5' end modification comprises a modification of between 1 and 7, between 1 and 5, between 1 and 4, between 1 and 3, or between 1 and 2 nucleotides.

349. The gRNA of any one of claims 161-348, comprising a 5' end modification wherein the 5' end modification comprises any one or more of the following:

i. modifications of 1, 2, 3, 4, 5, 6, or 7 of the first 7 nucleotides;
ii. modifications of about 1-3, 1-4, 1-5, 1-6, or 1-7 of the first 7 nucleotides; and
iii. modifications at the first, second, third, fourth, fifth, sixth, and/or seventh nucleotide at the 5' end, optionally wherein the modifications are consecutive.

350. The gRNA of any one of claims 161-349, comprising a 5' end modification, wherein the 5' end modification comprises one or more of:

i. a phosphorothioate (PS) linkage between nucleotides;
ii. a 2'-O-Me modified nucleotide;
iii. a 2'-O-moe modified nucleotide;
iv. a 2'-F modified nucleotide;
v. an inverted abasic modified nucleotide
vi. ENA, UNA, and/or DNA; and
vii. combinations thereof.

351. The gRNA any one of claims 161-350, comprising a 5' end modification wherein the 5' end modification comprises:

i. 1, 2, 3, 4, 5, 6, and/or 7 PS linkages between nucleotides; or
ii. about 1-2, 1-3, 1-4, 1-5, 1-6, or 1-7 PS linkages between nucleotides.

352. The gRNA of any one of claims 161-351, wherein the sgRNA comprises a 5' end modification and the 5' end modification comprises at least one 2'-O-Me, 2'-O-moe, inverted abasic, 2'-H, inosine, or 2'-F modified nucleotide.

353. The gRNA of claim 352, wherein the 5' end modification comprises at least one PS linkage, and wherein:

i. there is one PS linkage, and the linkage is at nucleotide 1 of the guide region;
ii. there are two PS linkages, and the linkages are at nucleotides 1 and 2 of the guide region;
iii. there are PS linkages at any one or more of nucleotides 1, 2, and 3 of the guide region;
iv. there are PS linkages at any one or more of nucleotides 1, 2, 3, and 4 of the guide region;
v. there are PS linkages at any one or more of nucleotides 1, 2, 3, 4, and 5 of the guide region;
vi. there are PS linkages at any one or more of nucleotides 1, 2, 3, 4, 5, and 6 of the guide region; or
vii. there are PS linkages at any one or more of nucleotides 1, 2, 3, 4, 5, 6, and 7 of the guide region.

354. The gRNA of any one of claims 352-353, wherein the 5' end modification comprises:

i. a modification of one or more of nucleotides 1-7 of the variable region, wherein the modification is a PS linkage, inverted abasic nucleotide, 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, and/or combinations thereof;
ii. a modification to the first nucleotide of the guide region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and an optional PS linkage to the next nucleotide;
iii. a modification to the first and/or second nucleotide of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and optionally one or more PS linkages;

iv. a modification to the first, second, and/or third nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and optionally one or more PS linkages;

v. a modification to the first, second, third, and/or fourth nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and optionally one or more PS linkages; or

vi. a modification to the first, second, third, fourth, and/or fifth nucleotides of the variable region with 2'-O-Me, 2'-O-moe, 2'-F, 2'-H, inosine, or combinations thereof, and optionally one or more PS linkages.

355. The gRNA of any one of claims 161-354, comprising a 5' end modification, wherein the 5' end modification comprises any one or more of the following:

i. a 5' end modification as shown in any one of SEQ ID Nos: 1-54, 401-532, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, 3388-3430, or 3549-3552;

ii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region;

iii. 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

iv. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region;

v. 2'-OMe modified nucleotides at nucleotides 1, 2, 3, 4, and 5 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the guide region;

vi. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region;

vii. 2'O-moe modified nucleotides at nucleotides 1, 2, and 3 of the guide region and PS linkages between nucleotides 1 and 2, 2 and 3, and 3 and 4 of the guide region;

viii. an inverted abasic modified nucleotide at nucleotide 1 of the guide region;

ix. an inverted abasic modified nucleotide at nucleotide 1 of the guide region and 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region; and

x. an inverted abasic modified nucleotide at nucleotide 1 of the guide region, 2'-OMe modified nucleotides at nucleotides 1, 2, and 3 of the guide region, and PS linkages between nucleotides 1 and 2, 2 and 3, 3 and 4, 4 and 5, and 5 and 6 of the variable region.

356. The gRNA of any one of claims 161-355, wherein the gRNA is an sgRNA and the upper stem region comprises at least one modification.

357. The gRNA of claim 346, wherein the upper stem modification comprises any one or more of the following:

i. a modification to any one or more of US1-US12 in the upper stem region;

ii. a modification of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all 12 nucleotides in the upper stem region; and

iii. a modification of about 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, or 1-12 nucleotides in the upper stem region.

358. The gRNA of any one of claims 356-357, wherein the upper stem modification comprises one or more of:

i. a 2'-O-Me modified nucleotide;

ii. a 2'-H modified nucleotide;

iii. a 2'-F modified nucleotide; and

iv. combinations thereof.

359. The gRNA of any one of claims 161-358, wherein the gRNA is an sgRNA comprising one or more modifications in the hairpin 1 region.

360. The gRNA of claim 359 wherein the sgRNA comprises a modification at H1-1.

361. The gRNA of any one of claims 161-360, wherein the gRNA is an sgRNA comprising one or more modifications in the hairpin 2 region.

362. The gRNA of claim 361, wherein the sgRNA comprises a modification at H2-1.

363. The gRNA of any one of claims 161-362, wherein the gRNA is an sgRNA comprising comprises modifications at H1-1 to H1-12.

364. The gRNA of any one of claims 161-363, wherein the gRNA is an sgRNA comprising comprises modifications at H2-1 to H2-15.

365. The gRNA of any one of claims 161-364, wherein the gRNA is an sgRNA comprising one or more modifications in each of the upper stem region, the hairpin 1 region, and the hairpin 2 region.

366. The gRNA of any one of claims 161-365, wherein the gRNA is an sgRNA comprising a modified nucleotide between hairpin 1 and hairpin 2 regions.

367. The gRNA of any one of claims 161-366, which is an sgRNA further comprising a lower stem region comprising a modification.

368. The gRNA of any one of claims 161-367, further comprising a 3' end modification.

369. The gRNA of claim 368, wherein at least two of the last four nucleotides at the 3' end of the 3' terminus are modified.

370. The gRNA of claim 369, wherein at least two of the last four nucleotides at the 3' end of the 3' terminus are modified with 2'-O-Me, 2'-F, or 2'-O-moe.

371. The gRNA of any one of claims 368-370, further comprising phosphorothioate (PS) bonds between one or more of the last four nucleotides at the 3' end of the 3' terminus.

372. The gRNA of any one of claims 161-371, which is an sgRNA further comprising a bulge region comprising a modification.

373. The gRNA of any one of claims 161-372, which is an sgRNA further comprising a nexus region comprising a modification.

374. An sgRNA comprising any of SEQ ID Nos: 401-535, 601, 607-732, 801, 807-932, 1001, or 1007-1132, including the modifications of Table 1.

375. An sgRNA comprising nucleic acids having at least 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 85, 80, 75, or 70% identity to the nucleic acids of any one of SEQ ID Nos: 401-535, 601, 607-732, 801, 807-932, 1001, or 1007-1132, wherein the modification at each nucleotide of the sgRNA that corresponds to a nucleotide of the reference sequence identifier in Table 1, is identical to or equivalent to the modification shown in the reference sequence identifier in Table 1.

376. The gRNA of any one of claims 161-375, wherein the modification reduces gRNA degradation without significantly altering the ability of the guide to cleave a target nucleic acid.

377. The gRNA of any one of claims 161-376, comprising a YA modification wherein the modification comprises 2'-fluoro, 2'-H, 2'-O-Me, ENA, UNA, or PS.

378. The gRNA of any one of claims 161-377, comprising a YA modification wherein the modification alters the structure of the dinucleotide motif to reduce RNA endonuclease activity.

379. The gRNA of any one of claims 161-378, comprising a YA modification wherein the modification interferes with recognition or cleavage of a YA site by an RNase and/or stabilizes an RNA structure.

380. The gRNA of any one of claims 161-379, comprising a YA modification wherein the modification comprises one or more of:

i. a ribose modification selected from 2'-O-alkyl, 2'-F, 2'-moe, 2'-F arabinose, and 2'-H (deoxyribose);
ii. a bicyclic ribose analog, such as LNA, BNA, and ENA;
iii. an unlocked nucleic acid modification;
iv. a base modification, such as inosine, pseudouridine, and 5'-methylcytosine; and
v. an internucleoside linkage modification such as phosphorothioate.

381. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises a modification at nucleotide 5, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

382. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises a modification at nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

383. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises a 2'-OMe modification at nucleotide 5 and/or nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

384. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises a 2'-F modification at nucleotide 5 and/or nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

385. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises a 2'-H modification at nucleotide 5 and/or nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

386. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises a phosphorothioate modification at nucleotide 5 and/or nucleotide 12, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

387. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises modifications at:

i. nucleotides 8-10;
ii. nucleotides 8 and 9;
iii. nucleotides 8 and 10; or
iv. nucleotides 9 and 10,

optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

388. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-F modifications at:

i. nucleotides 8-10;
ii. nucleotides 8 and 9;
iii. nucleotides 8 and 10;
iv. nucleotides 9 and 10; or
v. nucleotide 8;

optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

389. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-F modifications at:

i. nucleotides 8-10;
ii. nucleotides 8 and 9;
iii. nucleotides 8 and 10;
iv. nucleotides 9 and 10; or
v. nucleotide 8;

wherein nucleotides 8-10 do not comprise phosphorothioate modifications, and optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

390. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-F modifications at nucleotides 8-10 and:

i. phosphorothioate modifications at 1, 2, or 3 of nucleotides 8-10;
ii. a phosphorothioate modification at nucleotide 8;
iii. a phosphorothioate modification at nucleotide 9;
iv. a phosphorothioate modification at nucleotide 10;
v. a phosphorothioate modification at nucleotides 8 and 9;

vi. a phosphorothioate modification at nucleotides 8 and 10;
vii. a phosphorothioate modification at nucleotides 9 and 10; or
viii. a phosphorothioate modification at nucleotides 8-10

optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 11, 13, 14, 17, and 18.

391. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises:

i. a 2'-F or phosphorothioate modification at nucleotides 5 and 6;
ii. a 2'-F modification at nucleotides 5 and 6;
iii. a phosphorothioate modification at nucleotides 5 and 6;
iv. a 2'-F modification at nucleotide 5 and a phosphorothioate modification at nucleotide 6; or
v. a 2'-F modification at nucleotide 6 and a phosphorothioate modification at nucleotide 5;

optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 7-10, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

392. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-F modifications at at least 1, 2, 3, 4, 5, or 6 of nucleotides 6-11, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3, and/or 2'-F modifications at nucleotides 13, 14, 17, and 18.

393. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-F modifications at at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of nucleotides 1-4 and 6-11, optionally wherein the guide region comprises phosphorothioate modifications at nucleotides 1-3 and/or 2'-F modifications at nucleotides 13, 14, 17, and 18.

394. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-F modifications at nucleotides 6-11, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4,

phosphorothioate modifications at nucleotides 1-3, and/or 2'-F modifications at nucleotides 13, 14, 17, and 18.

395. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-F modifications at nucleotides 1-4, optionally wherein the guide region comprises phosphorothioate modifications at nucleotides 1-3 and 6-10, and/or 2'-F modifications at nucleotides 6-11, 13, 14, 17, and 18.

396. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises a 2'-F modification at nucleotide 9 and not a phosphorothioate modification at nucleotide 9, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-8 and 10, and/or 2'-F modifications at nucleotides 8, 10, 11, 13, 14, 17, and 18.

397. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that does not comprise 2'-F modifications at at least 1, 2, 3, 4, 5, 6, 7, or 8 of nucleotides 8-11, 13, 14, 17, and 18, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

398. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that does not comprise 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

399. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-OMe modifications at at least 1, 2, 3, or 4 of nucleotides 9, 11, 13, and 14, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

400. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises 2'-OMe modifications at nucleotides 9, 11, 13, and 14, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4 and/or phosphorothioate modifications at nucleotides 1-3 and 6-10.

401. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises phosphorothioate modifications at one or both of nucleotides 8 and 10, optionally wherein the guide region comprises 2'-OMe modifications at nucleotides 1-4, phosphorothioate modifications at nucleotides 1-3 and 6-7, and/or 2'-F modifications at nucleotides 8-11, 13, 14, 17, and 18.

402. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises modifications at at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or all of the following nucleotides: 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18, optionally wherein the modifications are 2'-OMe, 2'-fluoro, or phosphorothioate modifications.

403. The gRNA of any one of the the preceding claims, wherein the gRNA comprises a guide region that comprises modifications at nucleotides 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 17, and 18, optionally wherein the modifications are 2'-OMe, 2'-fluoro, or phosphorothioate modifications.

404. The gRNA of any one of the preceding claims, wherein 2'-OMe modifications are not present in the guide region at nucleotides 6-11 and 13-end.

405. The gRNA of any one of the preceding claims, wherein 2'-fluoro modifications are not present in the guide region at nucleotides 1-7, 15, 16, and 19-end.

406. The gRNA of any one of the preceding claims, wherein phosphorothioate modifications are not present in the guide region at nucleotides 4, 5, 11-14, 17, and 18.

407. The gRNA of any one of the preceding claims, wherein the guide region comprises an unmodified nucleotide 20.

408. The gRNA of any one of the preceding claims, wherein the guide region consists of 20 nucleotides.

409. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 5-6 and a modification at nucleotide 5.

410. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 12-13 and a modification at nucleotide 12.

411. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 15-16 and a modification at nucleotide 15.

412. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 16-17 and a modification at nucleotide 16.

413. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 19-20 and a modification at nucleotide 19.

414. The gRNA of any one of the preceding claims, wherein the guide region does not comprise a YA site at nucleotides 5-6 and nucleotide 5 is unmodified.

415. The gRNA of any one of the preceding claims, wherein the guide region does not comprise a YA site at nucleotides 12-13 and nucleotide 12 is unmodified.

416. The gRNA of any one of the preceding claims, wherein the guide region does not comprise a YA site at nucleotides 15-16 and nucleotide 15 is unmodified.

417. The gRNA of any one of the preceding claims, wherein the guide region does not comprise a YA site at nucleotides 16-17 and nucleotide 16 is unmodified.

418. The gRNA of any one of the preceding claims, wherein the guide region does not comprise a YA site at nucleotides 19-20 and nucleotide 19 is unmodified.

419. The gRNA of any one of the preceding claims, wherein the gRNA comprises a guide region that comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or all of the following:

i. 2'-OMe and phosphorothioate modifications at nucleotide 1;
ii. 2'-OMe and phosphorothioate modifications at nucleotide 2;
iii. 2'-OMe and phosphorothioate modifications at nucleotide 3;
iv. a 2'-OMe modification at nucleotide 4;
v. a phosphorothioate modification at nucleotide 6;
vi. a phosphorothioate modification at nucleotide 7;
vii. 2'-fluoro and phosphorothioate modifications at nucleotide 8;
viii. 2'-fluoro and phosphorothioate modifications at nucleotide 9;
ix. 2'-fluoro and phosphorothioate modifications at nucleotide 10;
x. a 2'-fluoro modification at nucleotide 11;
xi. a 2'-fluoro modifications at nucleotide 13;

xii. a 2'-fluoro modifications at nucleotide 14;
xiii. a 2'-fluoro modifications at nucleotide 17; and
xiv. a 2'-fluoro modifications at nucleotide 18.

420. The gRNA of any one of the preceding claims, wherein the guide region comprises each of the modifications set forth in the preceding claim.

421. The gRNA of any one of the preceding claims, wherein the guide region comprises at least 1, 2, 3, or 4 of the following:

i. a 2'-OMe modification at nucleotide 5 if nucleotides 5 and 6 form a YA site;
ii. a 2'-OMe modification at nucleotide 12 if nucleotides 12 and 13 form a YA site;
iii. a phosphorothioate or 2'-H modification at nucleotide 15 if nucleotides 15 and 16 form a YA site;
iv. a phosphorothioate modification at nucleotide 16 if nucleotides 16 and 17 form a YA site; and
v. a phosphorothioate or 2'-fluoro modification at nucleotide 19 if nucleotides 19 and 20 form a YA site.

422. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 5-6 and a a 2'-OMe modification at nucleotide 5.

423. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 12-13 and a 2'-OMe modification at nucleotide 12.

424. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 15-16 and a phosphorothioate modification at nucleotide 15.

425. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 16-17 and a phosphorothioate modification at nucleotide 16.

426. The gRNA of any one of the preceding claims, wherein the guide region comprises a YA site at nucleotides 19-20 and a phosphorothioate modification at nucleotide 19.

427. The gRNA of any one of the preceding claims, wherein the guide region comprises a 2'-fluoro modification at nucleotide 19.

428. The gRNA of any one of the preceding claims, wherein the guide region comprises an unmodified nucleotide 15 or only a phosphorothioate modification at nucleotide 15.

429. The gRNA of any one of the preceding claims, wherein the guide region comprises an unmodified nucleotide 16 or only a phosphorothioate modification at nucleotide 16.

430. The gRNA of any one of the preceding claims, wherein the gRNA is an sgRNA comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides.

431. The gRNA of claim 430, wherein the at least 5-10 lacking nucleotides are consecutive.

432. The gRNA of claim 430 or 431, wherein the at least 5-10 lacking nucleotides:

i. are within hairpin 1;
ii. are within hairpin 1 and the "N" between hairpin 1 and hairpin 2;
iii. are within hairpin 1 and the two nucleotides immediately 3' of hairpin 1;
iv. include at least a portion of hairpin 1;
v. are within hairpin 2;
vi. include at least a portion of hairpin 2;
vii. are within hairpin 1 and hairpin 2;
viii. include at least a portion of hairpin 1 and include the "N" between hairpin 1 and hairpin 2;
ix. include at least a portion of hairpin 2 and include the "N" between hairpin 1 and hairpin 2;
x. include at least a portion of hairpin 1, include the "N" between hairpin 1 and hairpin 2, and include at least a portion of hairpin 2;
xi. are within hairpin 1 or hairpin 2, optionally including the "N" between hairpin 1 and hairpin 2;
xii. are consecutive;
xiii. are consecutive and include the "N" between hairpin 1 and hairpin 2;

xiv. are consecutive and span at least a portion of hairpin 1 and a portion of hairpin 2;

xv. are consecutive and span at least a portion of hairpin 1 and the "N" between hairpin 1 and hairpin 2; or

xvi. are consecutive and span at least a portion of hairpin 1 and two nucleotides immediately 3' of hairpin 1.

433. The gRNA of any one of claims 430-432, wherein the at least 5-10 nucleotides comprise nucleotides 54-61 of SEQ ID NO:400, nucleotides 53-60 of SEQ ID NO:400; or nucleotides 54-58 of SEQ ID NO:400, optionally wherein the sgRNA comprises modifications at least H1-1 to H1-5 and H2-1 to H2-12.

434. The gRNA of any one of claims 430-433, wherein the at least 5-10 nucleotides:

i. consist of 5-10 nucleotides;

ii. consist of 6-10 nucleotides;

iii. consist of 5 nucleotides;

iv. consist of 6 nucleotides;

v. consist of 7 nucleotides;

vi. consist of 8 nucleotides;

vii. consist of 9 nucleotides;

viii. consist of 10 nucleotides;

ix. consist of 5-10 consecutive nucleotides;

x. consist of 6-10 consecutive nucleotides;

xi. consist of 5 consecutive nucleotides;

xii. consist of 6 consecutive nucleotides;

xiii. consist of 7 consecutive nucleotides;

xiv. consist of 8 consecutive nucleotides;

xv. consist of 9 consecutive nucleotides; or

xvi. consist of 10 consecutive nucleotides.

435. The gRNA of claim 434, wherein the at least 5-10 nucleotides comprise nucleotides 54-61 of SEQ ID NO:400, nucleotides 53-60 of SEQ ID NO:400; or nucleotides 54-58 of SEQ ID NO:400, optionally wherein the sgRNA comprises modifications at least H1-1 to H1-5 and H2-1 to H2-12.

436. The gRNA of any one of claims 430-435, wherein the at least 5-10 nucleotides:

i. comprise nucleotides 54-61 of SEQ ID NO:400;
ii. comprise nucleotides 53-60 of SEQ ID NO:400;
iii. comprise nucleotides 54-58 of SEQ ID NO:400.
iv. consist of nucleotides 54-61 of SEQ ID NO:400;
v. consist of nucleotides 53-60 of SEQ ID NO:400; or
vi. consist of nucleotides 54-58 of SEQ ID NO:400.

437. The gRNA of any one of the preceding claims, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 15 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

438. The gRNA of any one of the preceding claims, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 16 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

439. The gRNA of any one of the preceding claims, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 17 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of a gRNA, wherein the gRNA is any one of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

440. The gRNA of any one of the preceding claims, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 18 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601,

607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

441. The gRNA of any one of the preceding claims, wherein the gRNA comprises modifications and/or unmodified nucleotides at at least 19 of nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

442. The gRNA of any one of the preceding claims, wherein the gRNA comprises modifications and/or unmodified nucleotides at nucleotides 1-20 from the 5' end of the 5' terminus that match the modification pattern at nucleotides 1-20 of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

443. The gRNA of any one of the preceding claims, wherein the gRNA comprises a modification pattern that matches at least 75% of the modification pattern of any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

444. The gRNA of any one of the preceding claims, wherein the gRNA comprises the modification pattern of any one of the gRNAs in Table 1, wherein the modification pattern is the same as any one of the gRNAs of SEQ ID NOs: 1-54, 201-254, 301-354, 401-535, 601, 607-732, 801, 807-932, 1001, 1007-1132, 1205-1212, 1322-1406, 1417-1501, 1511-1596, 3018-3059, 3063-3104, 3108-3149, 3153-3194, 3198-3239, 3243-3284, 3295-3341, 3343-3385, or 3388-3430.

445. The gRNA of any one of claims 437-444, further comprising a sequence having at least 75% identity to the sequence of nucleotides 21-end of the gRNA.

446. The gRNA of any one of claims 437-444, further comprising a sequence having at least 80% identity to the sequence of nucleotides 21-end of the gRNA.

447. The gRNA of any one of claims 437-444, further comprising a sequence having at least 85% identity to the sequence of nucleotides 21-end of the gRNA.

448. The gRNA of any one of claims 437-444, further comprising a sequence having at least 90% identity to the sequence of nucleotides 21-end of the gRNA.

449. The gRNA of any one of claims 437-444, further comprising a sequence having at least 95% identity to the sequence of nucleotides 21-end of the gRNA.

450. The gRNA of any one of claims 437-444, further comprising a sequence having at least 98% identity to the sequence of nucleotides 21-end of the gRNA.

451. The gRNA of any one of claims 437-444, further comprising a sequence having 100% identity to the sequence of nucleotides 21-end of the gRNA.

452. An LNP composition comprising a gRNA of any one of the preceding claims.

453. A composition comprising a gRNA of any one of claims 1-451 associated with a lipid nanoparticle (LNP).

454. A composition comprising the gRNA of any one of claims 1-451, or the composition of any one of claims 452-453, further comprising a nuclease or an mRNA which encodes the nuclease.

455. The composition of claim 454, wherein the nuclease is a Cas protein.

456. The composition of claim 455, wherein the Cas protein is a Cas9.

457. The composition of claim 456, wherein the Cas9 is an *S. pyogenes* Cas9 or an *S. aureus* Cas9.

458. The composition of any one of claims 453-457, wherein the nuclease is a nickase or a dCas.

459. The composition of any one of claims 453-458, wherein the nuclease is modified.

460. The composition of claim 459 wherein the modified nuclease comprises a nuclear localization signal (NLS).

461. The composition of any one of claims 452-460, comprising an mRNA which encodes the nuclease.

462. The composition of claim 461, wherein the mRNA comprises the sequence of any one of SEQ ID NOs: 3499-3527 or 3529-3546.

463. A pharmaceutical formulation comprising the gRNA of any one of claims 1-451 or the composition of any one of claims 452-462 and a pharmaceutically acceptable carrier.

464. A method of modifying a target DNA comprising, delivering a Cas protein or a nucleic acid encoding a Cas protein, and any one or more of the following to a cell:

i. the gRNA of any one of claims 1-451;

ii. the composition of any one of claims 452-462; and

iii. the pharmaceutical formulation of claim 463.

465. The method of claim 464, wherein the method results in an insertion or deletion in a gene.

466. The method of claim 464 or claim 465, further comprising delivering to the cell a template, wherein at least a part of the template incorporates into a target DNA at or near a double strand break site induced by the Cas protein.

467. The gRNA of any one of claims 1-451, the composition of claims 452-462, or the pharmaceutical formulation of claim 463 for use in preparing a medicament for treating a disease or disorder.

468. Use of the gRNA of any one of claims 1-451, the composition of claims 452-462, or the pharmaceutical formulation of claim 463 in the manufacture of a medicament for treating a disease or disorder.

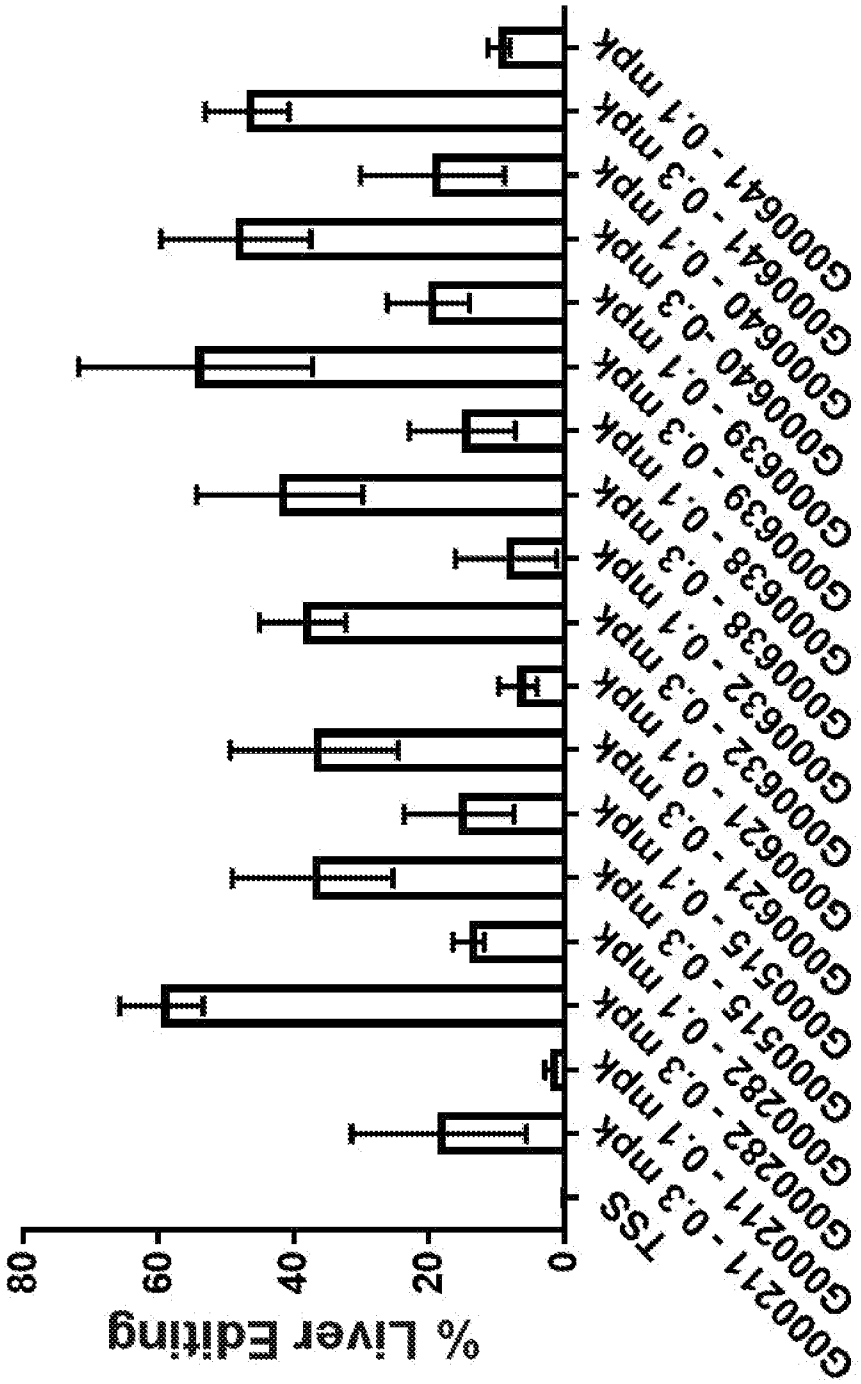

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20
40
60
80
TSS
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G000271 - 0.1 mpk
G000282 - 0.3 mpk
G000282 - 0.1 mpk
G000515 - 0.3 mpk
G000515 - 0.1 mpk
G000621 - 0.3 mpk
G000621 - 0.1 mpk
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Fig. 1A

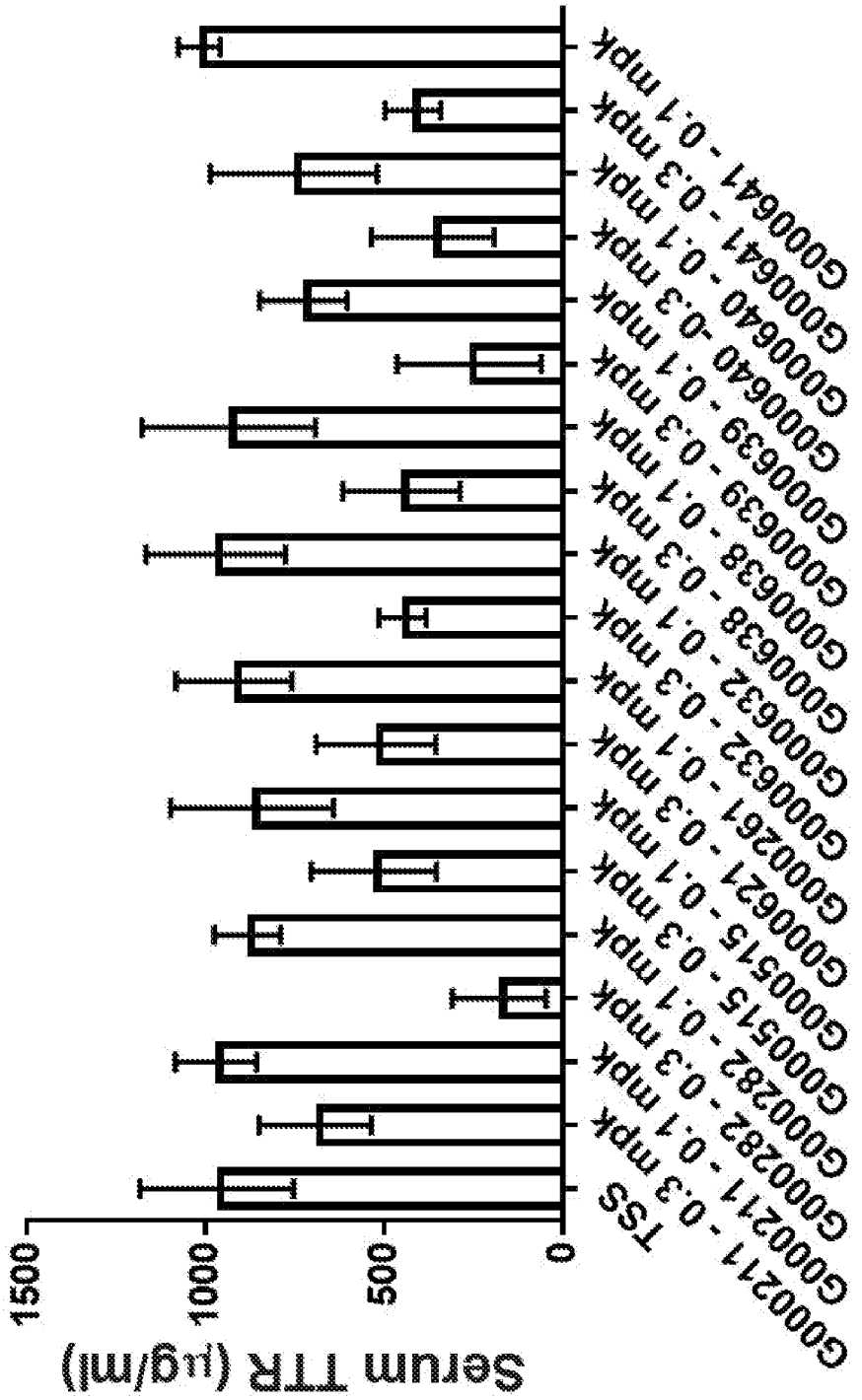

Serum TTR (µg/ml)
1500
1000
500
0
TSS
G000211 - 0.3 mpk
G000211 - 0.1 mpk
G000282 - 0.3 mpk
G000282 - 0.1 mpk
G000515 - 0.3 mpk
G000515 - 0.1 mpk
G000621 - 0.3 mpk
G000621 - 0.1 mpk
G000261 - 0.3 mpk
G000632 - 0.1 mpk
G000632 - 0.3 mpk
G000638 - 0.1 mpk
G000638 - 0.3 mpk
G000639 - 0.1 mpk
G000639 - 0.3 mpk
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G000641 - 0.1 mpk
G000641 - 0.3 mpk
G000647 - 0.1 mpk

Fig. 1B

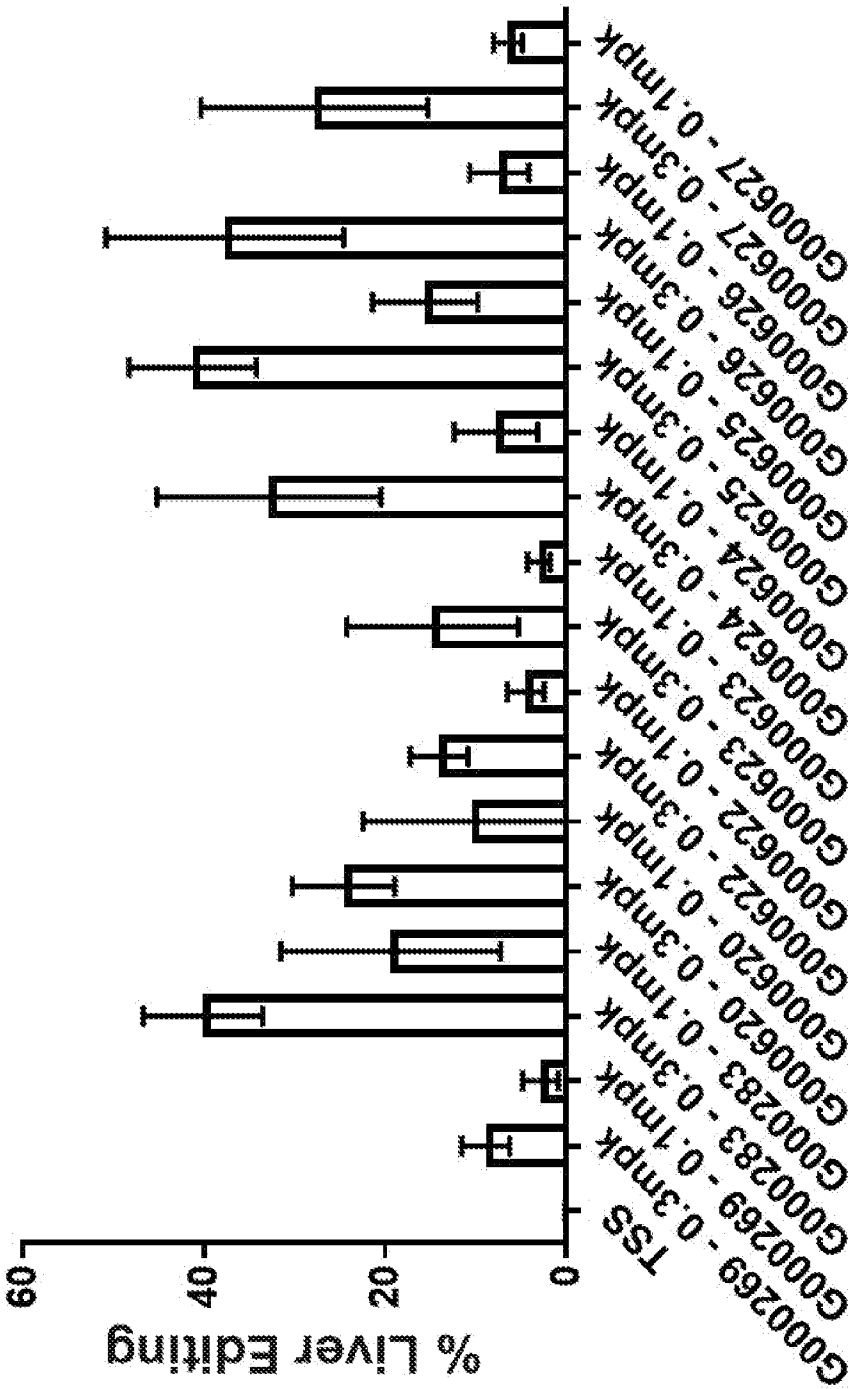

% Liver Editing
0
20
40
60
TSS
G000269 - 0.3mpk
G000269 - 0.1mpk
G000283 - 0.3mpk
G000283 - 0.1mpk
G000620 - 0.3mpk
G000620 - 0.1mpk
G000622 - 0.3mpk
G000622 - 0.1mpk
G000623 - 0.3mpk
G000623 - 0.1mpk
G000624 - 0.3mpk
G000624 - 0.1mpk
G000625 - 0.3mpk
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G000627 - 0.3mpk
G000627 - 0.1mpk

Fig. 2A

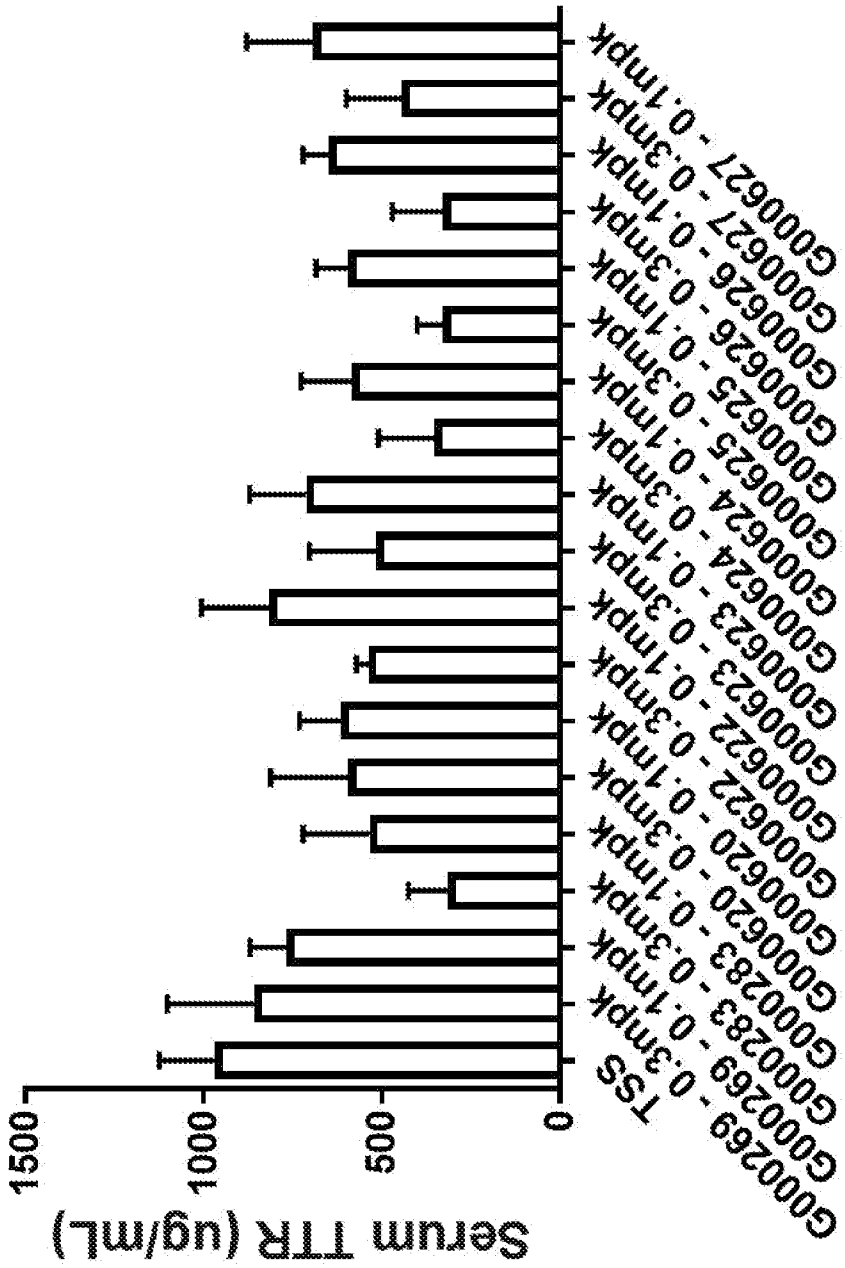

Serum TTR (ug/mL)
1500
1000
500
0
TSS
G000269 - 0.3mpk
G000269 - 0.1mpk
G000283 - 0.3mpk
G000283 - 0.1mpk
G000620 - 0.3mpk
G000620 - 0.1mpk
G000622 - 0.3mpk
G000622 - 0.1mpk
G000623 - 0.3mpk
G000623 - 0.1mpk
G000624 - 0.3mpk
G000624 - 0.1mpk
G000625 - 0.3mpk
G000625 - 0.1mpk
G000626 - 0.3mpk
G000626 - 0.1mpk
G000627 - 0.3mpk
G000627 - 0.1mpk

Fig. 2B

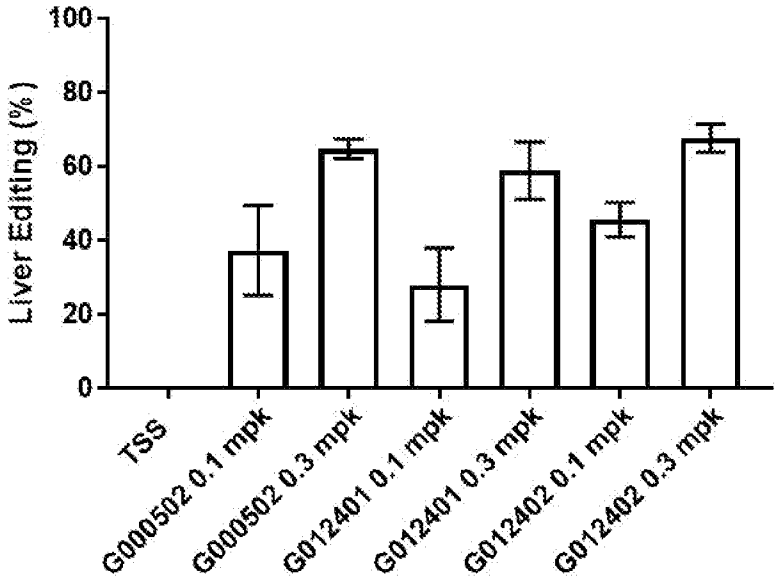

Liver Editing (%)
100
80
60
40
20
0
TSS
G000502 0.1 mpk
G000502 0.3 mpk
G012401 0.1 mpk
G012401 0.3 mpk
G012402 0.1 mpk
G012402 0.3 mpk

Fig. 3A

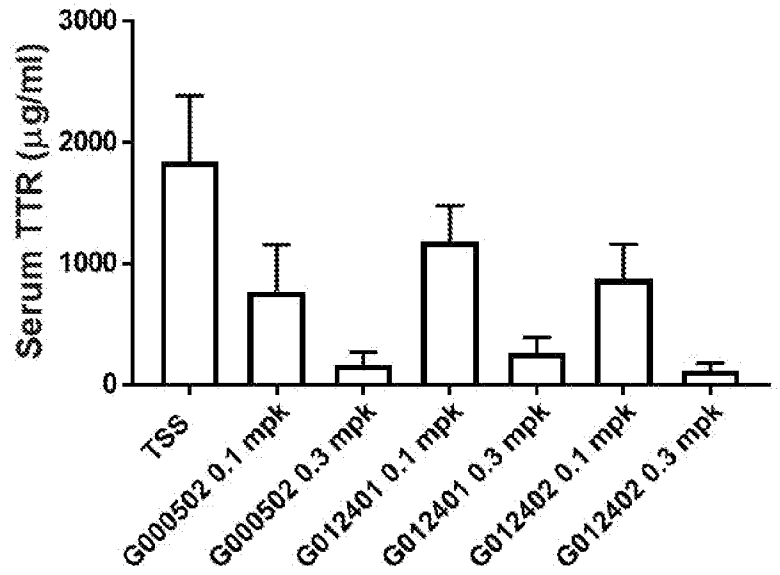

Serum TTR (µg/ml)
3000
2000
1000
0
TSS
G000502 0.1 mpk
G000502 0.3 mpk
G012401 0.1 mpk
G012401 0.3 mpk
G012402 0.1 mpk
G012402 0.3 mpk

Fig. 3B

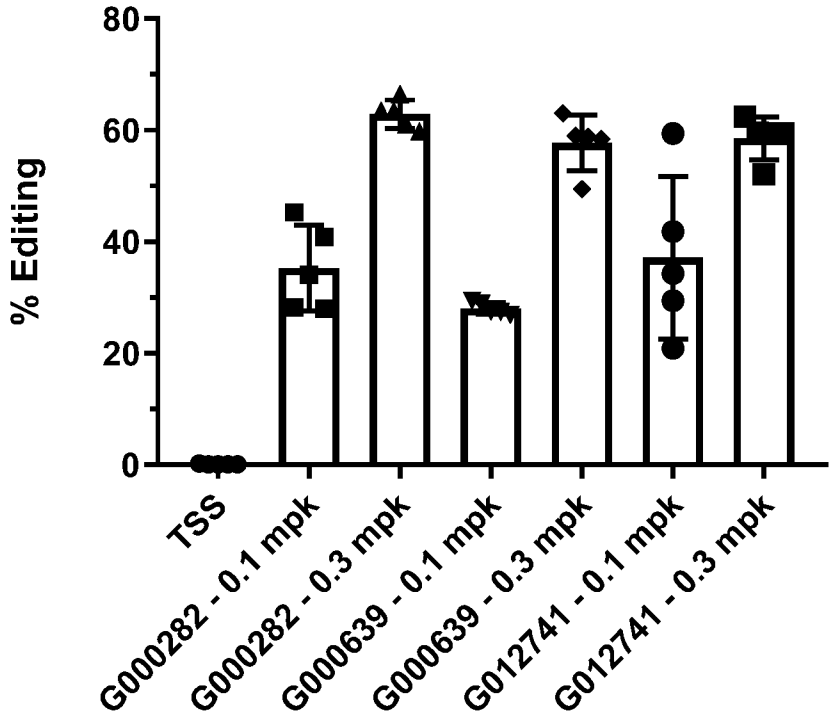

% Editing
80
60
40
20
0
TSS
G000282 - 0.1 mpk
G000282 - 0.3 mpk
G000639 - 0.1 mpk
G000639 - 0.3 mpk
G012741 - 0.1 mpk
G012741 - 0.3 mpk

Fig. 3C

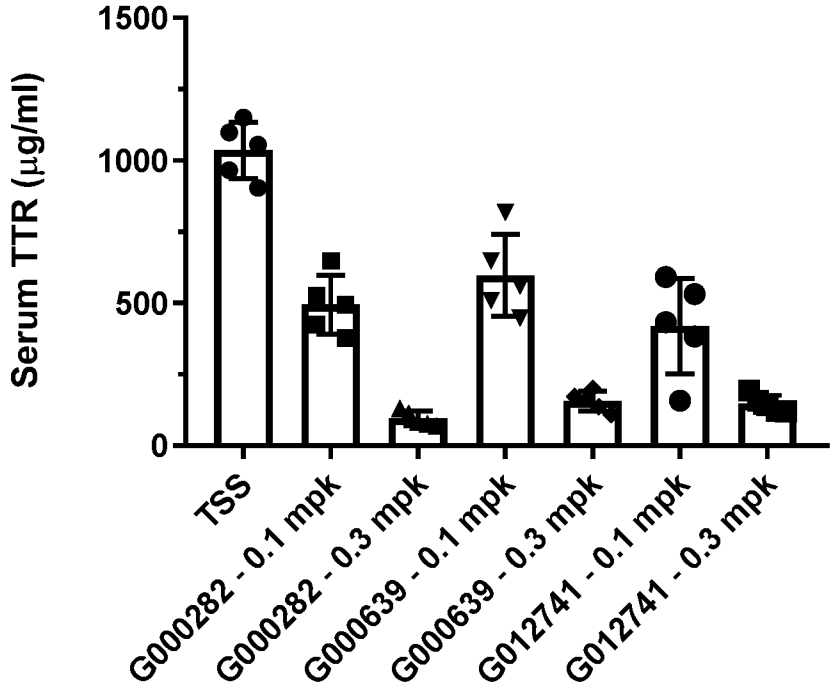

Serum TTR (μg/ml)
1500
1000
500
0
TSS
G000282 - 0.1 mpk
G000282 - 0.3 mpk
G000639 - 0.1 mpk
G000639 - 0.3 mpk
G012741 - 0.1 mpk
G012741 - 0.3 mpk

Fig. 3D

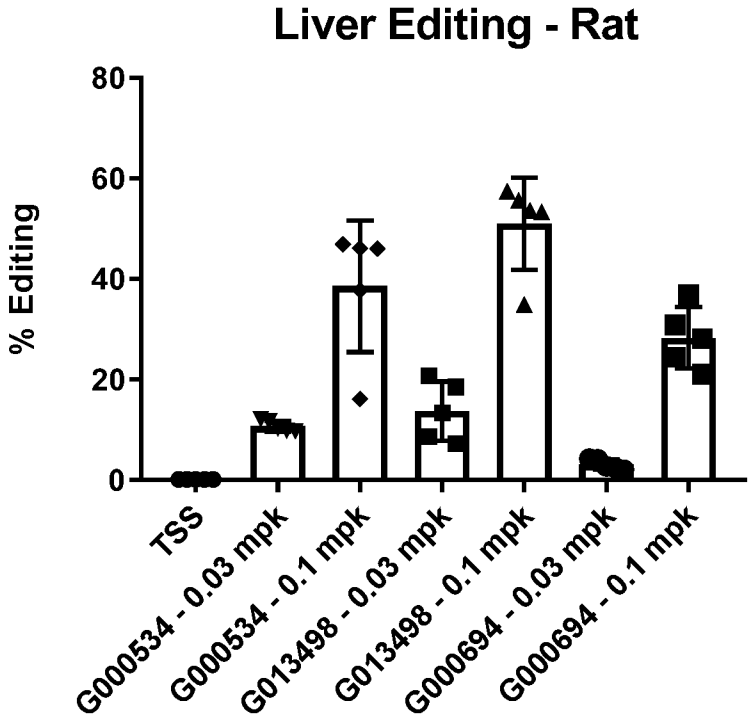

Liver Editing - Rat
% Editing
80
60
40
20
0
TSS
G000534 - 0.03 mpk
G000534 - 0.1 mpk
G013498 - 0.03 mpk
G013498 - 0.1 mpk
G000694 - 0.03 mpk
G000694 - 0.1 mpk

Fig. 3E

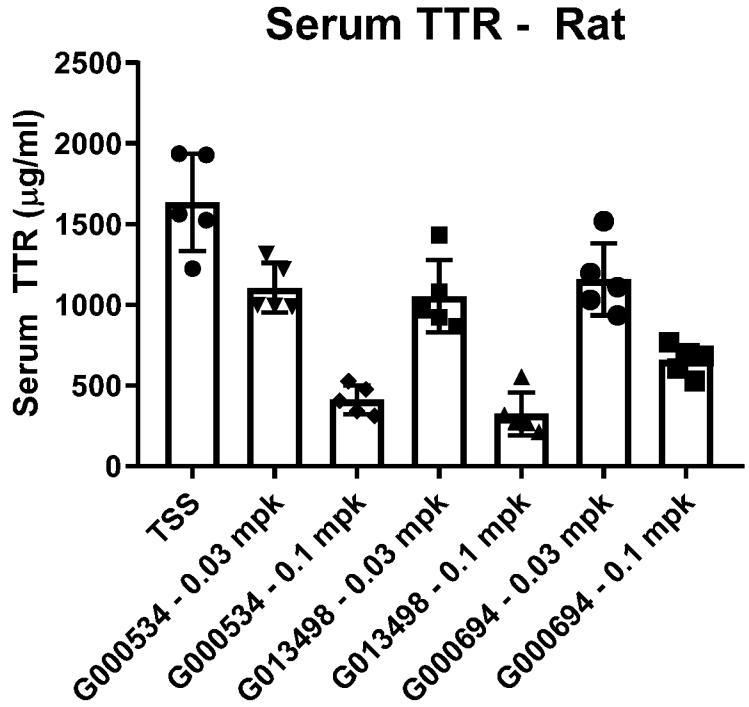

Serum TTR - Rat
Serum TTR (µg/ml)
2500
2000
1500
1000
500
0
TSS
G000534 - 0.03 mpk
G000534 - 0.1 mpk
G013498 - 0.03 mpk
G013498 - 0.1 mpk
G000694 - 0.03 mpk
G000694 - 0.1 mpk

Fig. 3F

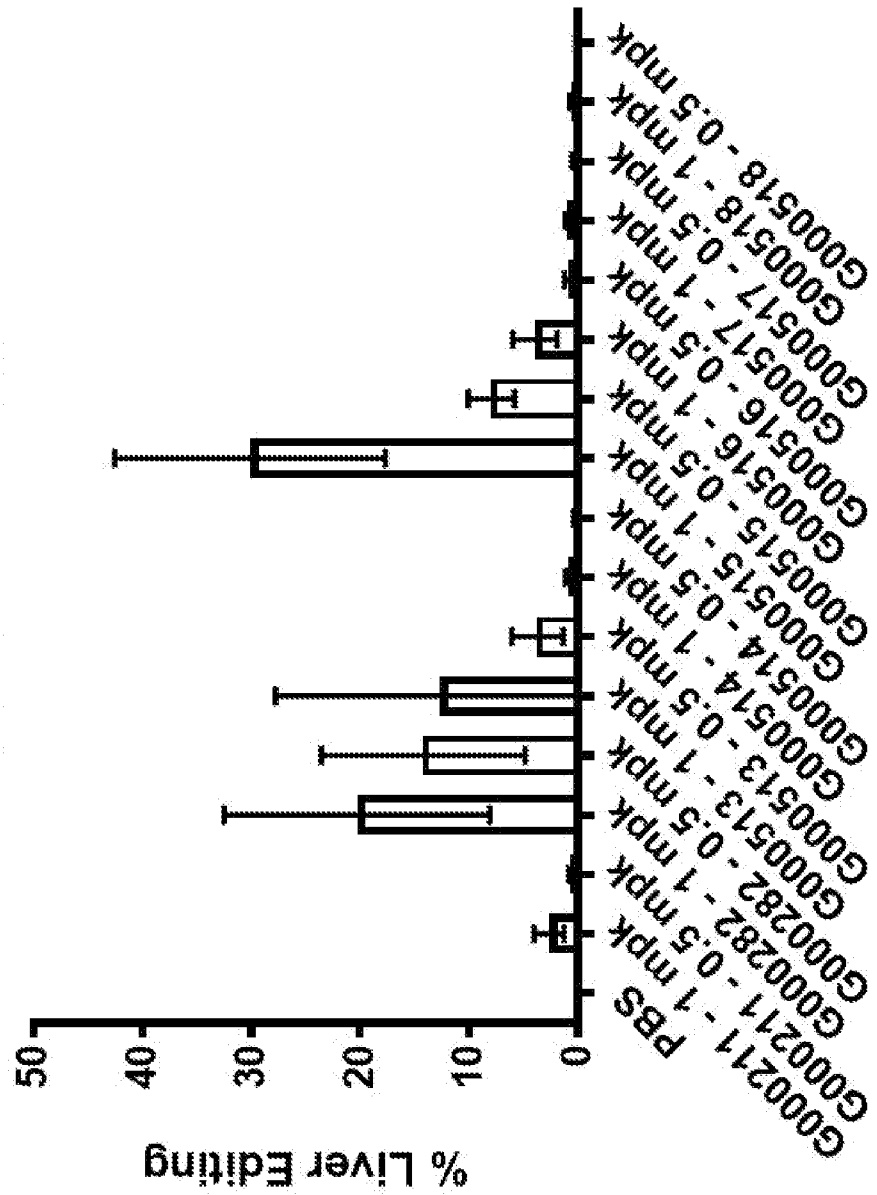

% Liver Editing
0
10
20
30
40
50
PBS
G000211 - 1 mpk
G000211 - 0.5 mpk
G000282 - 1 mpk
G000282 - 0.5 mpk
G000513 - 1 mpk
G000513 - 0.5 mpk
G000514 - 1 mpk
G000514 - 0.5 mpk
G000515 - 1 mpk
G000515 - 0.5 mpk
G000516 - 1 mpk
G000516 - 0.5 mpk
G000517 - 1 mpk
G000517 - 0.5 mpk
G000518 - 1 mpk
G000518 - 0.5 mpk

Fig. 4A

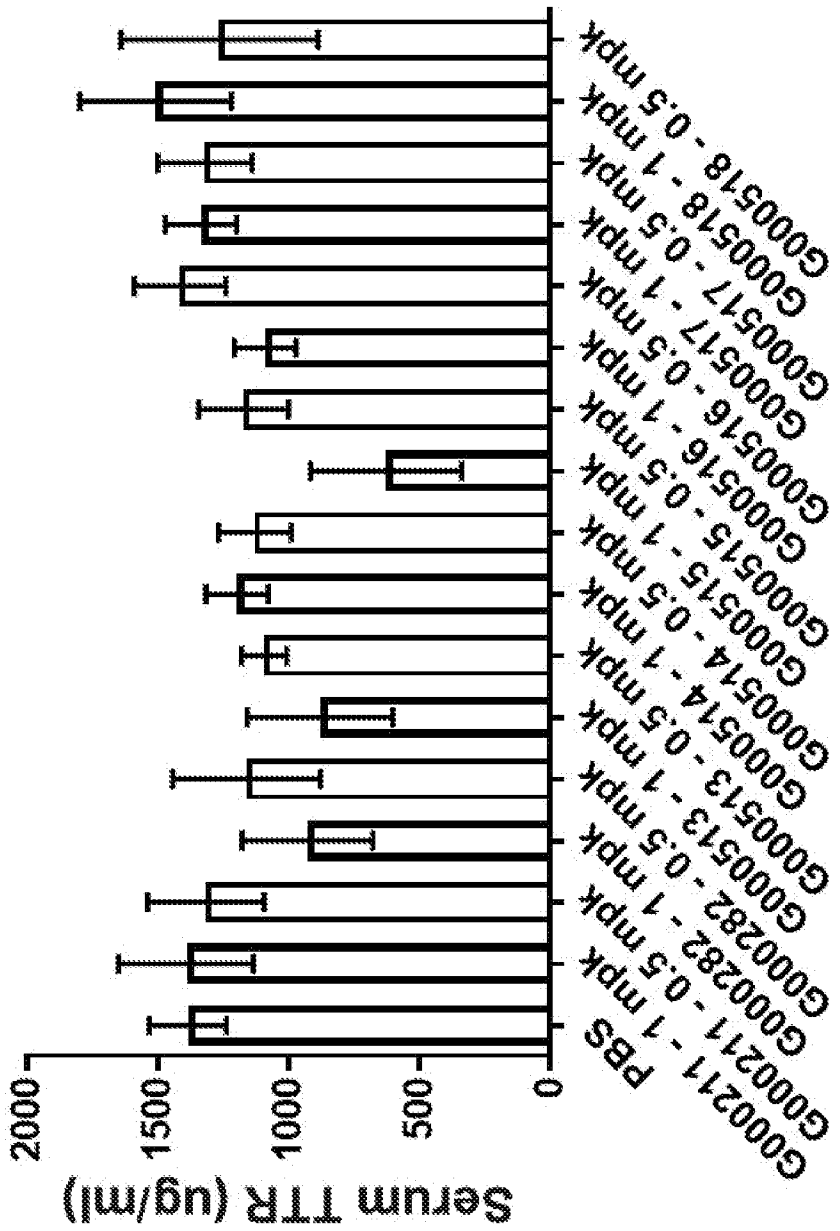

Serum TTR (ug/ml)
2000
1500
1000
500
0
PBS
G000214 - 1 mpk
G000214 - 0.5 mpk
G000282 - 1 mpk
G000282 - 0.5 mpk
G000513 - 1 mpk
G000513 - 0.5 mpk
G000514 - 1 mpk
G000514 - 0.5 mpk
G000515 - 1 mpk
G000515 - 0.5 mpk
G000516 - 1 mpk
G000516 - 0.5 mpk
G000517 - 1 mpk
G000517 - 0.5 mpk
G000518 - 1 mpk
G000518 - 0.5 mpk

Fig. 4B

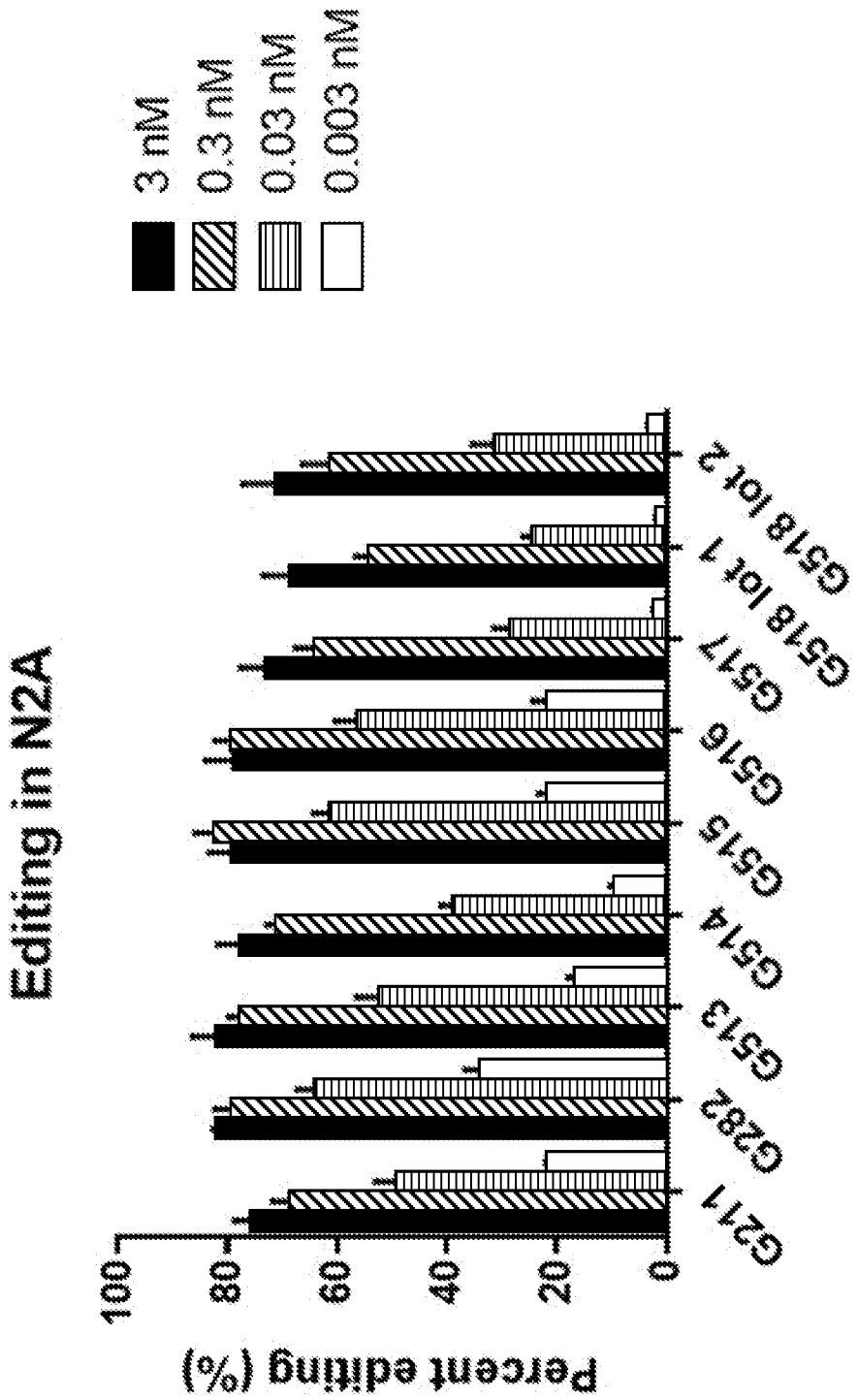

Editing in N2A
3 nM
0.3 nM
0.03 nM
0.003 nM
Percent editing (%)
100
80
60
40
20
0
G21
G282
G513
G514
G515
G516
G517
G518 lot 1
G518 lot 2

Fig. 5

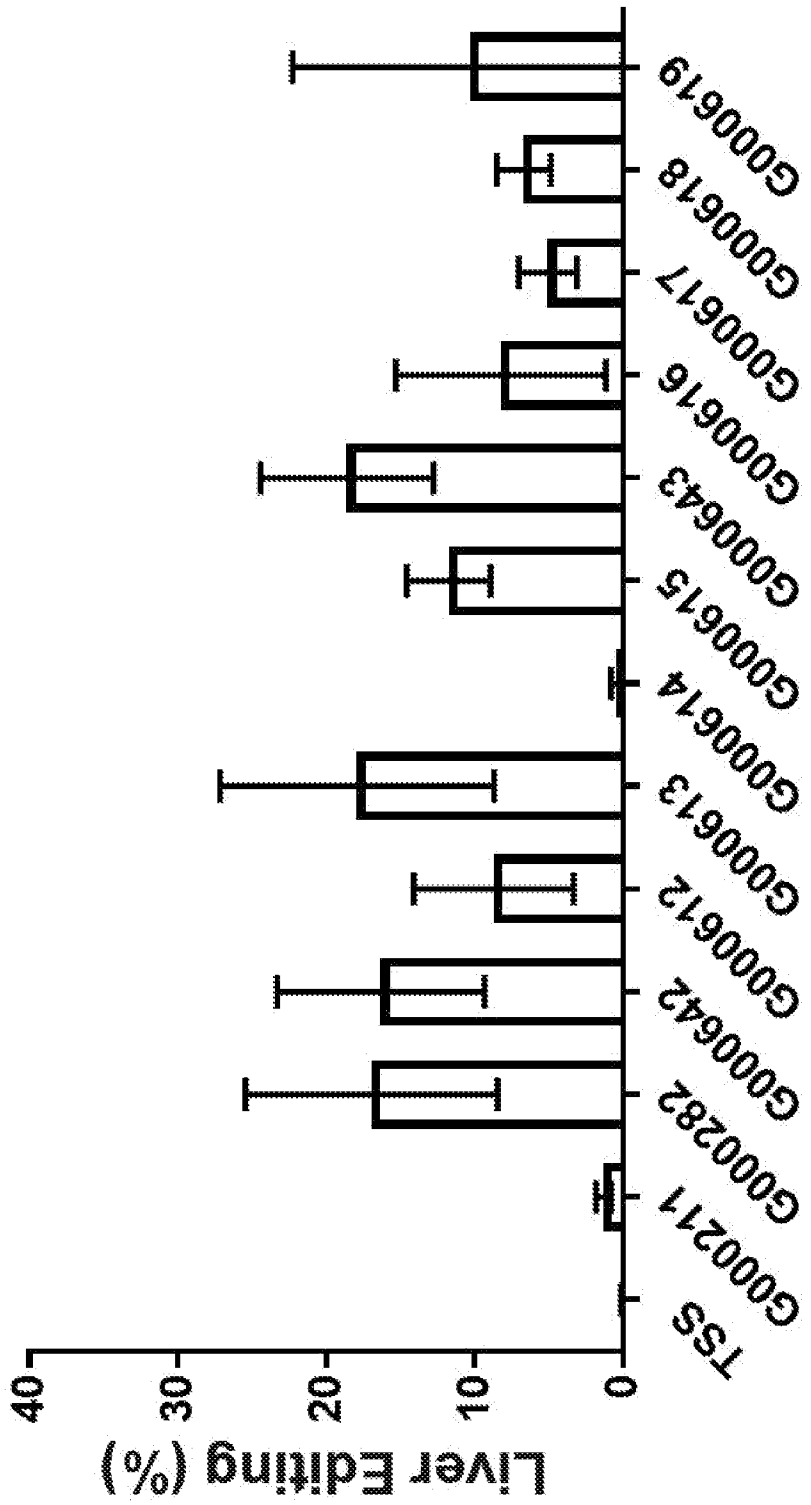

Liver Editing (%)
0
10
20
30
40
TSS
G000211
G000282
G000642
G000612
G000613
G000614
G000615
G000643
G000616
G000617
G000618
G000619

Fig. 6A

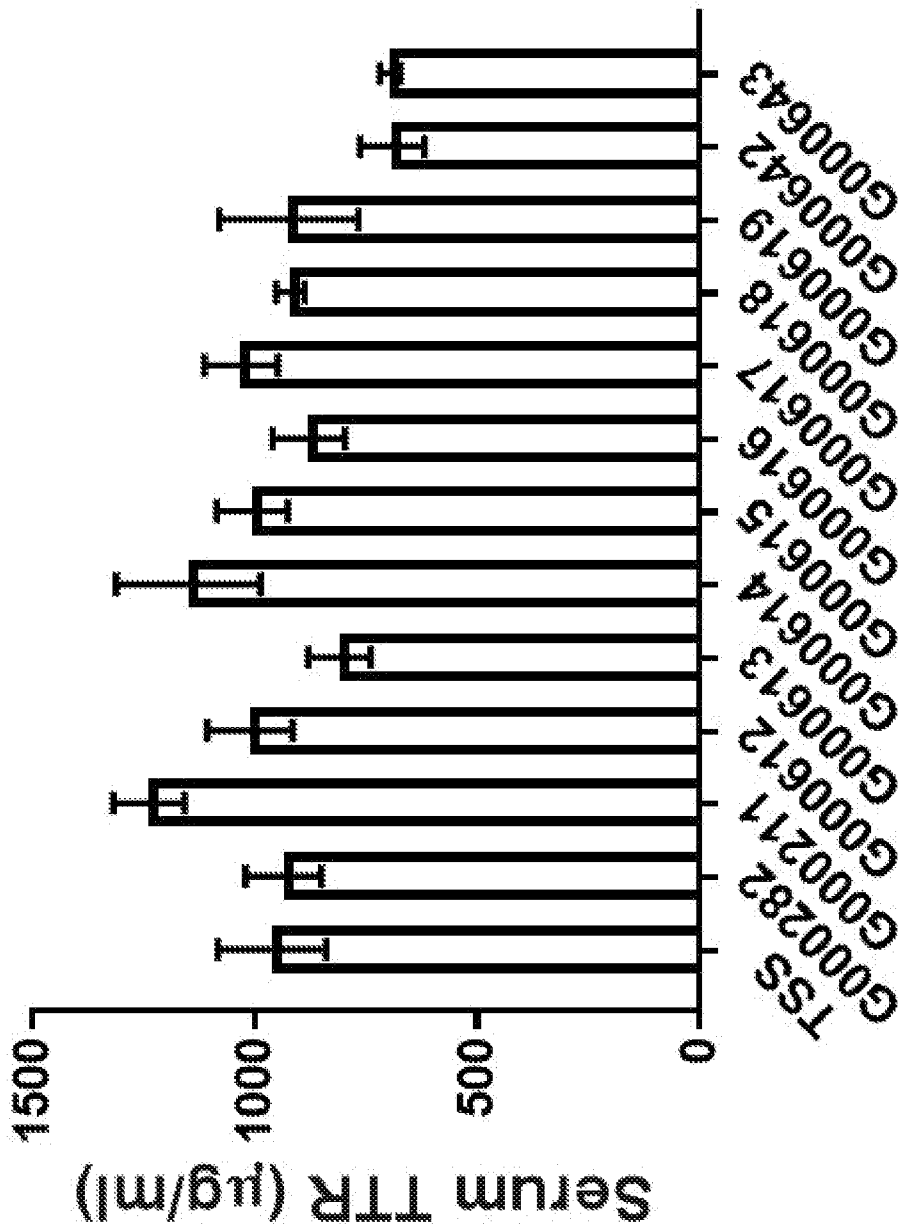

Serum TTR (µg/ml)
1500
1000
500
0
TSS
G000282
G000271
G000612
G000613
G000614
G000615
G000616
G000617
G000618
G000619
G000642
G000643

Fig. 6B

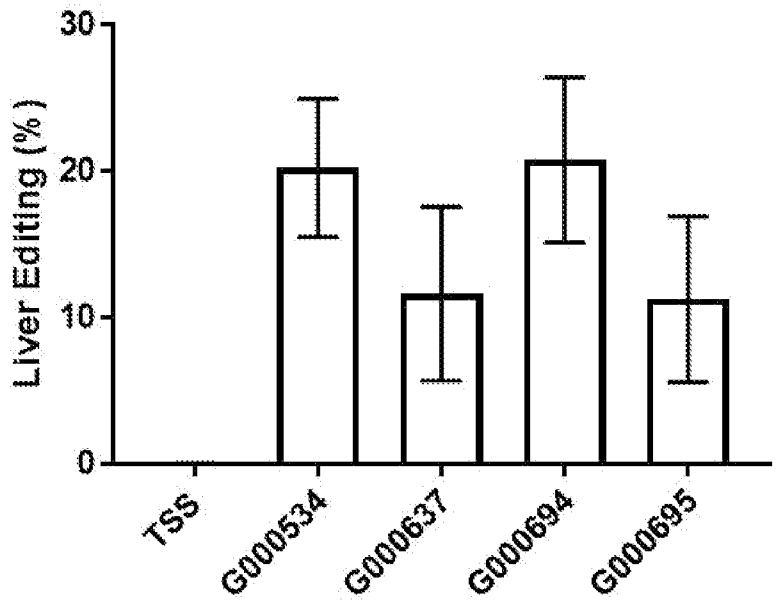

Liver Editing (%)
30
20
10
0
TSS
G000534
G000637
G000694
G000695

Fig. 7A

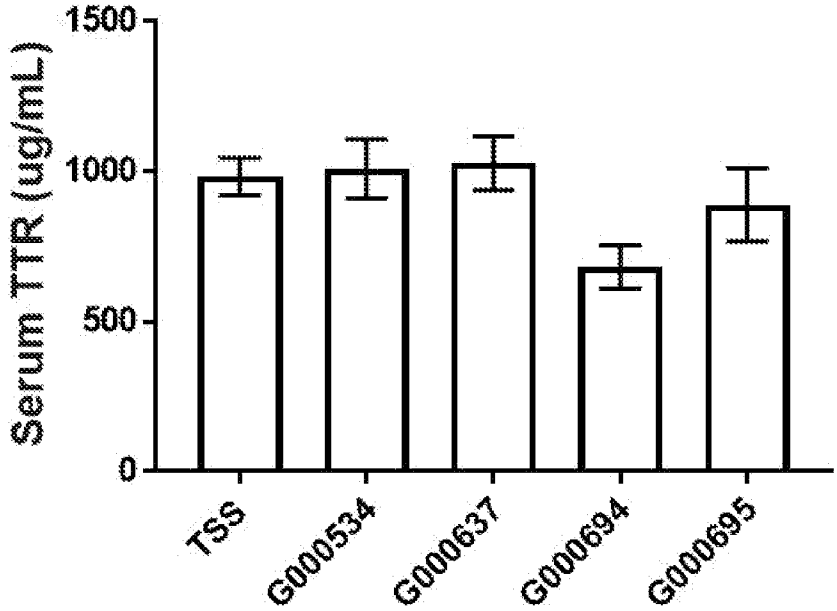

Serum TTR (ug/mL)
1500
1000
500
0
TSS
G000534
G000637
G000694
G000695

Fig. 7B

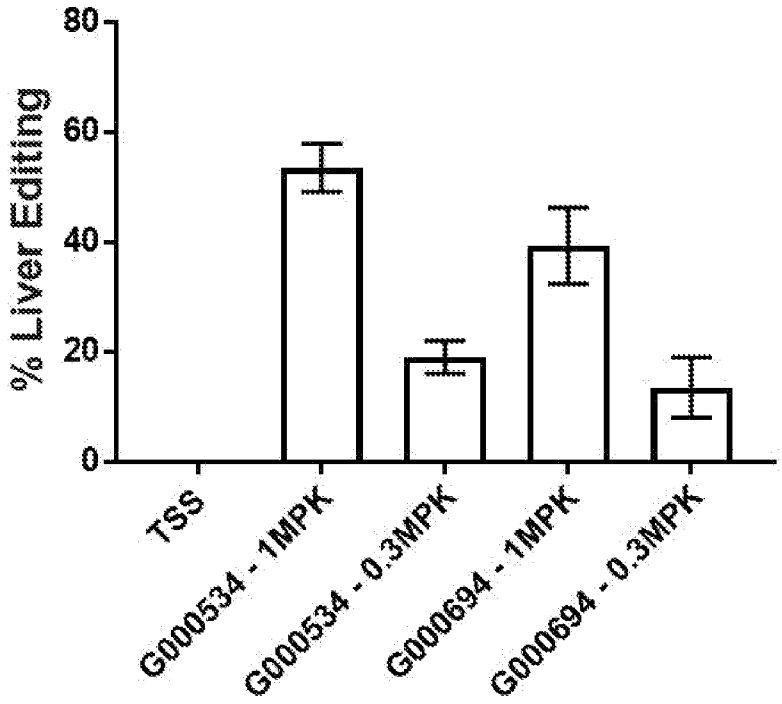

% Liver Editing
80
60
40
20
0
TSS
G000534 - 1MPK
G000534 - 0.3MPK
G000694 - 1MPK
G000694 - 0.3MPK

Fig. 8A

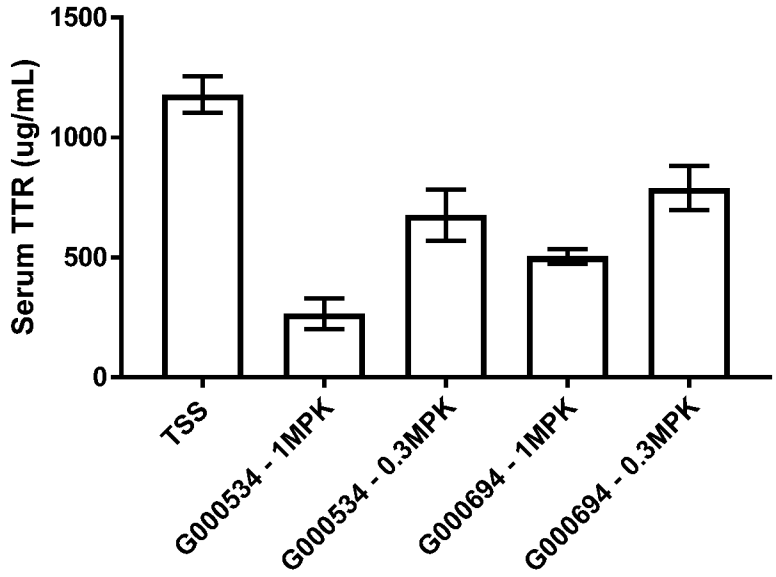

Serum TTR (ug/mL)
1500
1000
500
0
TSS
G000534 - 1MPK
G000534 - 0.3MPK
G000694 - 1MPK
G000694 - 0.3MPK

Fig. 8B

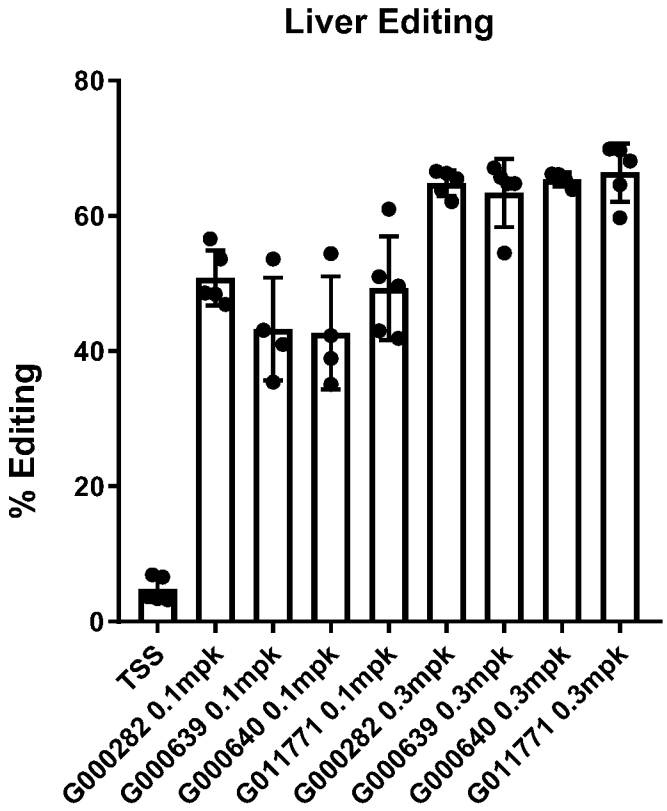

Liver Editing
% Editing
80
60
40
20
0
TSS
G000282 0.1mpk
G000639 0.1mpk
G000640 0.1mpk
G011771 0.1mpk
G000282 0.3mpk
G000639 0.3mpk
G000640 0.3mpk
G011771 0.3mpk

Fig. 8C

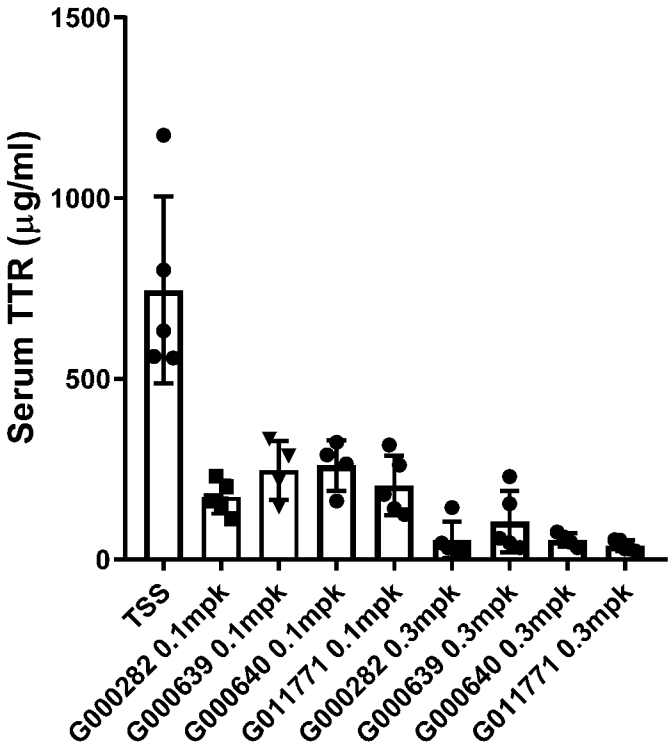

Serum TTR (μg/ml)
1500
1000
500
0
TSS
G000282 0.1mpk
G000639 0.1mpk
G000640 0.1mpk
G011771 0.1mpk
G000282 0.3mpk
G000639 0.3mpk
G000640 0.3mpk
G011771 0.3mpk

Fig. 8D

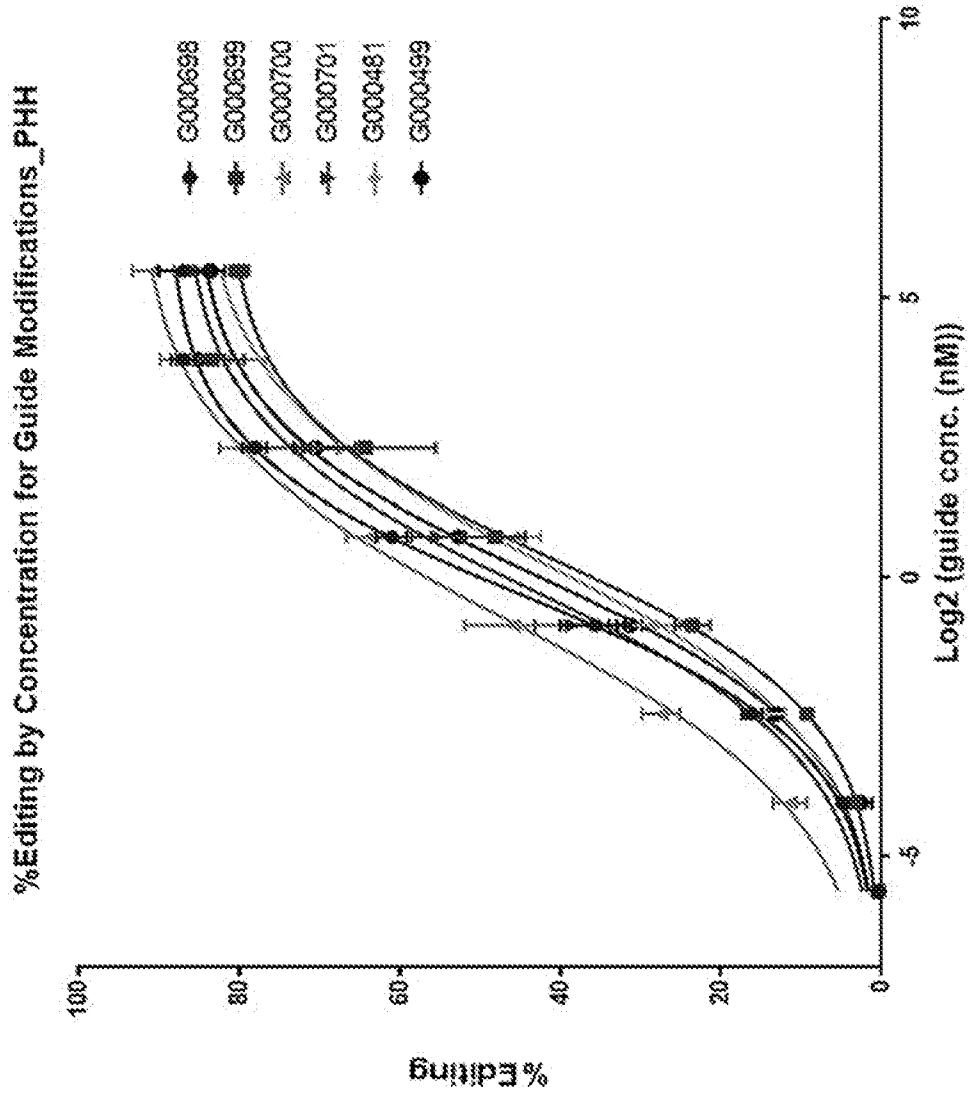

%Editing by Concentration for Guide Modifications_PHH
G000698
G000699
G000700
G000701
G000481
G000499
% Editing
100
80
60
40
20
0
-5
0
5
10
Log2 (guide conc. (nM))

Fig. 9A

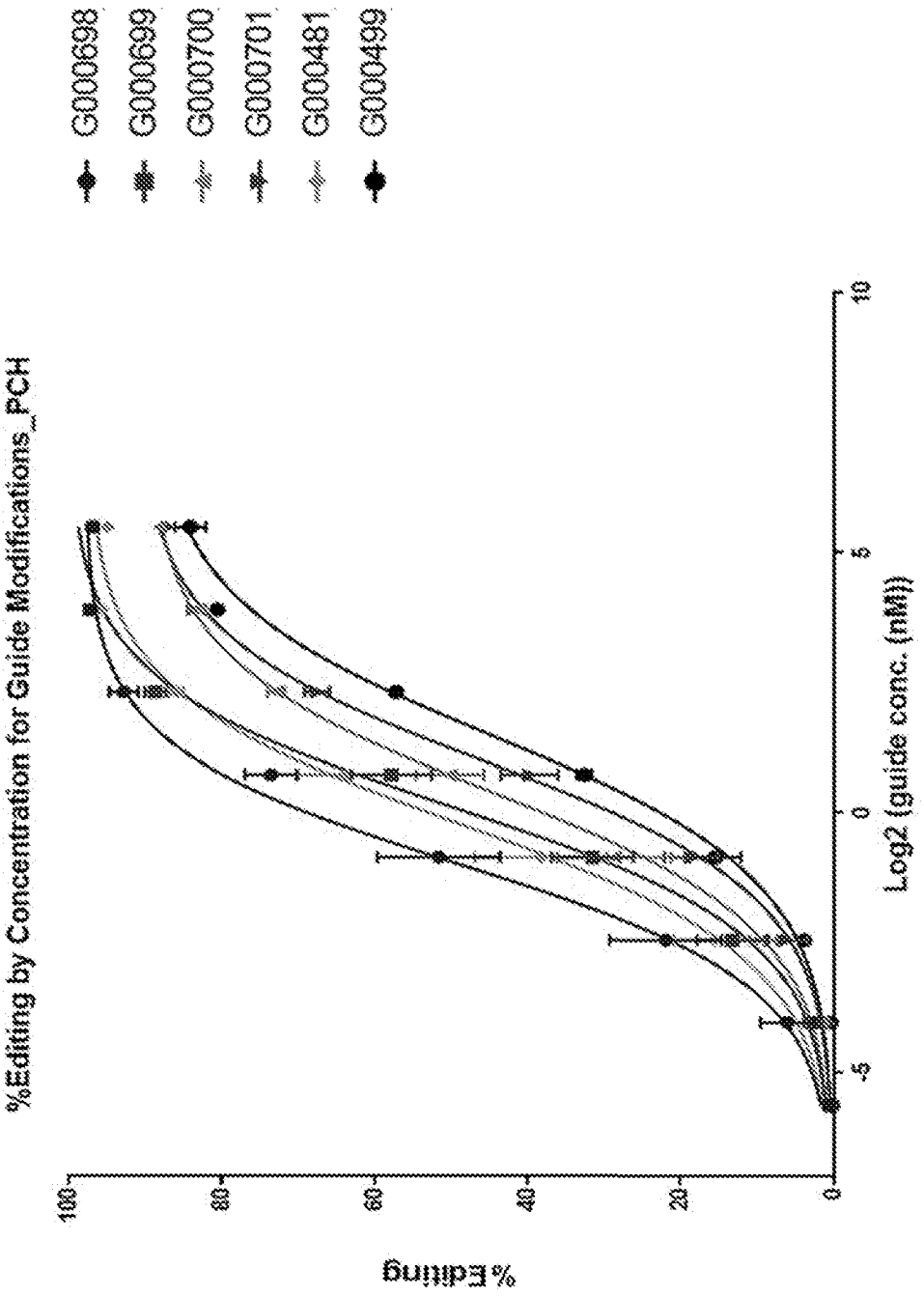

%Editing by Concentration for Guide Modifications_PCH
G000698
G000699
G000700
G000701
G000481
G000499
%Editing
100
80
60
40
20
0
-5
0
5
10
Log2 (guide conc. (nM))

Fig. 9B

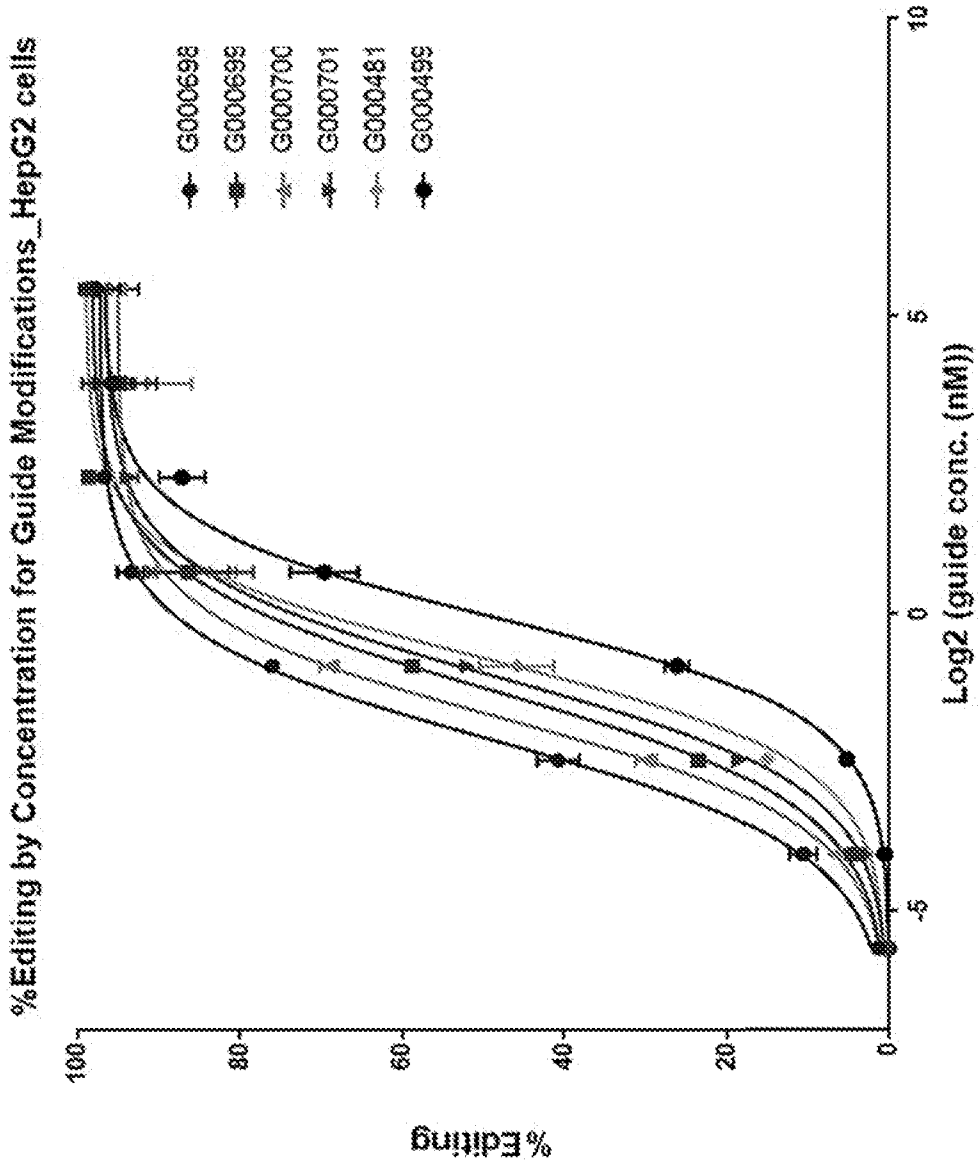

%Editing by Concentration for Guide Modifications_HepG2 cells
G000698
G000699
G000700
G000701
G000481
G000495
% Editing
100
80
60
40
20
0
-5
0
5
10
Log2 (guide conc. (nM))

Fig. 9C

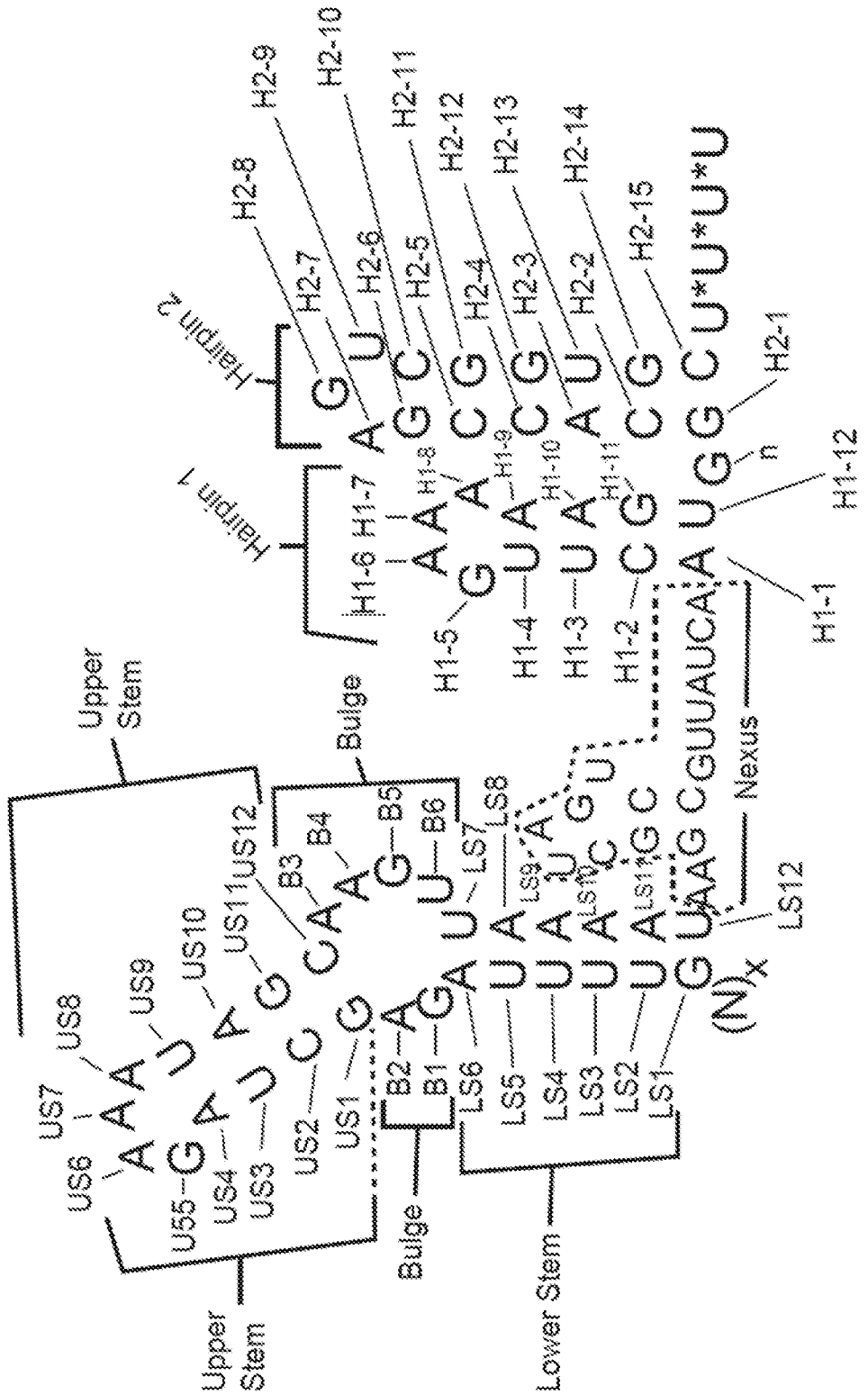

Upper Stem
Bulge
Hairpin 1
Hairpin 2
Nexus
Bulge
Lower Stem
Upper Stem
US7
US8
US9
US10
US11
US12
US6
US5
US4
US3
US2
US1
B3
B4
B5
B6
B2
B1
LS8
LS7
LS6
LS5
LS4
LS3
LS2
LS1
LS9
LS10
LS11
LS12
H1-6
H1-7
H1-8
H1-5
H1-4
H1-3
H1-2
H1-1
H1-12
n
H2-9
H2-10
H2-8
H2-7
H2-6
H2-11
H2-5
H2-12
H2-4
H2-13
H2-3
H2-14
H2-2
H2-15
H2-1

Fig. 10A

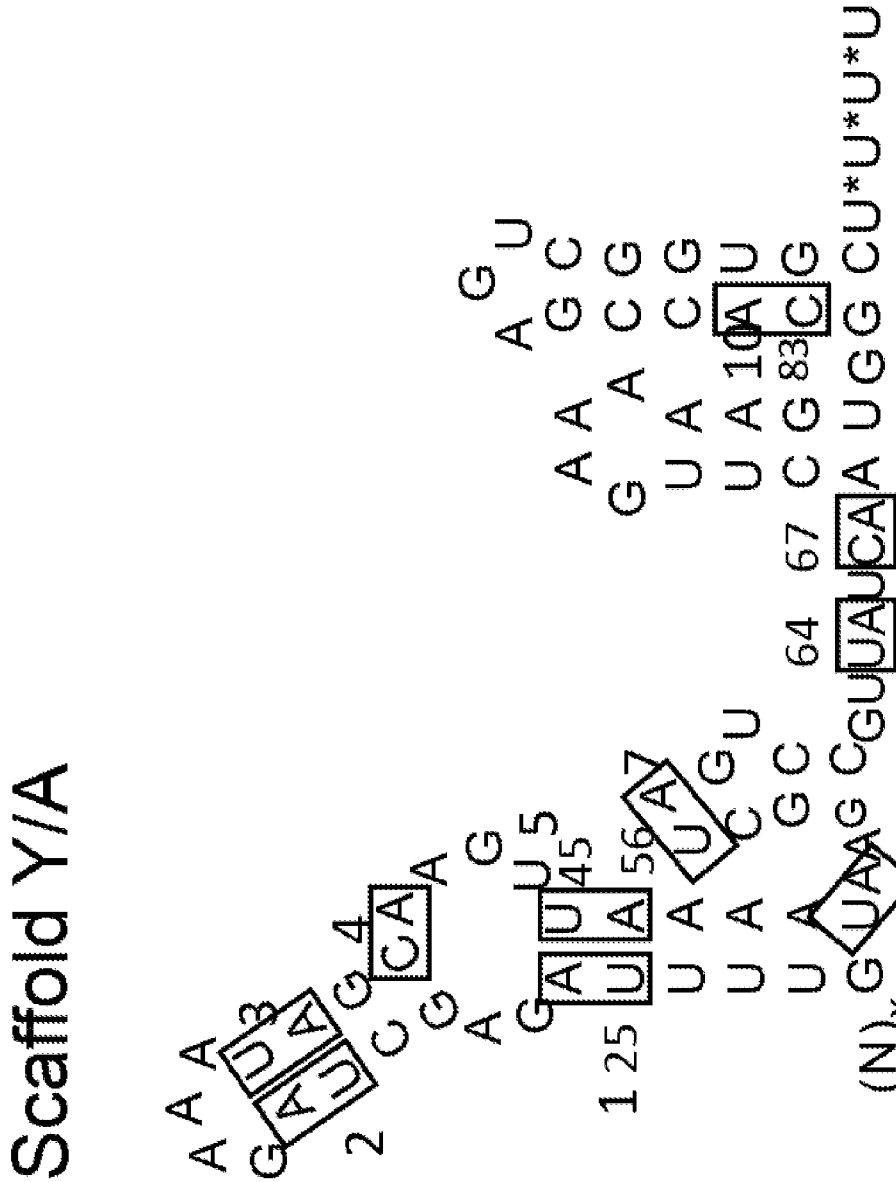

Scaffold Y/A
A A A
G A U 3
A U G 4
2 C G C A
A G
G A U 5
1 25 U A 45
U A 56 A 7
U A C G U
U A G C
U A G C 64 67
G U U A U C A A
(N)x 50 6
8 9
A G U
A G C
A A C G
G A C G
U A C G
U A 10 A U
U A 83 C G
A U G G C U*U*U*U

Fig. 10B

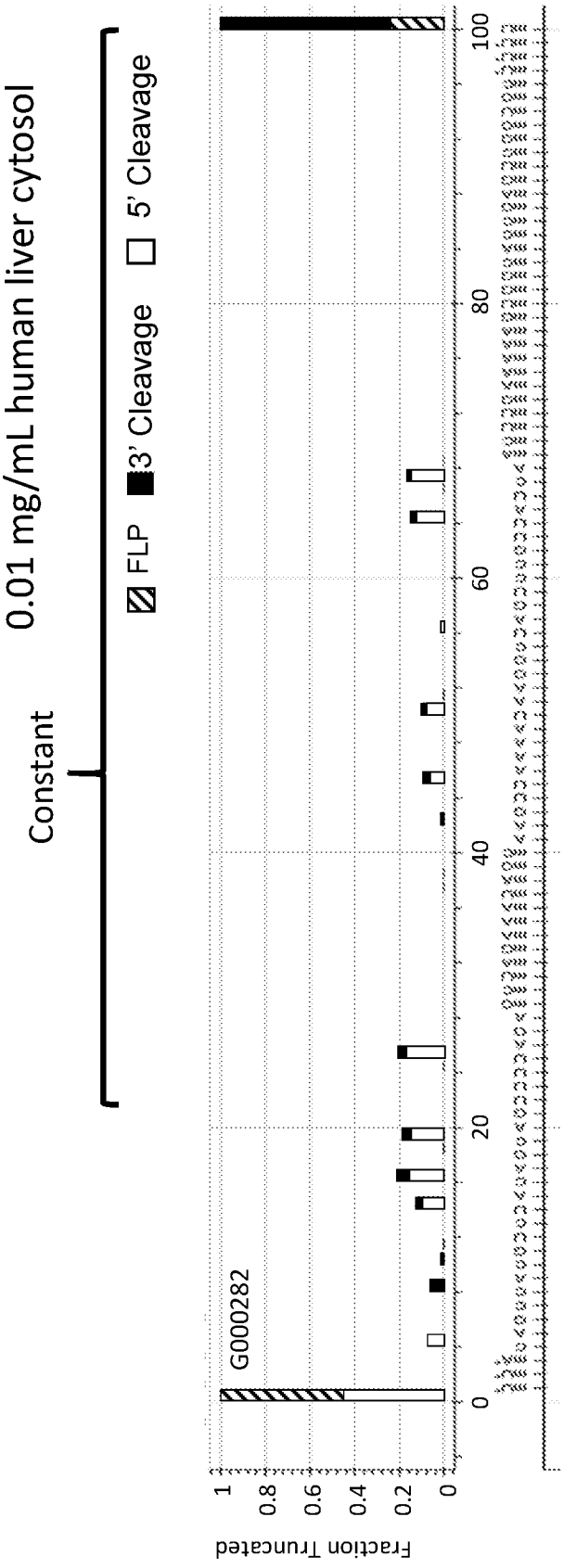

Constant
0.01 mg/mL human liver cytosol
FLP
3' Cleavage
5' Cleavage
G000282
Fraction Truncated
0
0.2
0.4
0.6
0.8
1
0
20
40
60
80
100

Fig. 11A

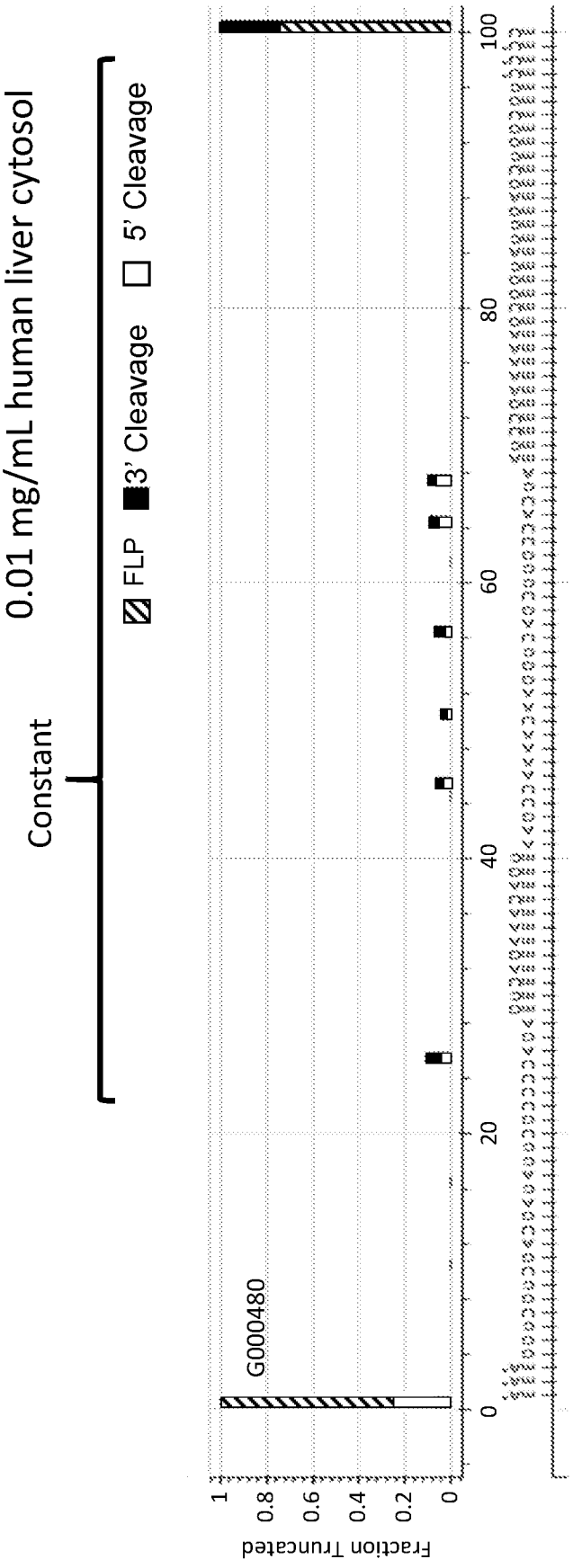

Constant
0.01 mg/mL human liver cytosol
FLP
3' Cleavage
5' Cleavage
G000480
Fraction Truncated
0
0.2
0.4
0.6
0.8
1
0
20
40
60
80
100

Fig. 11B

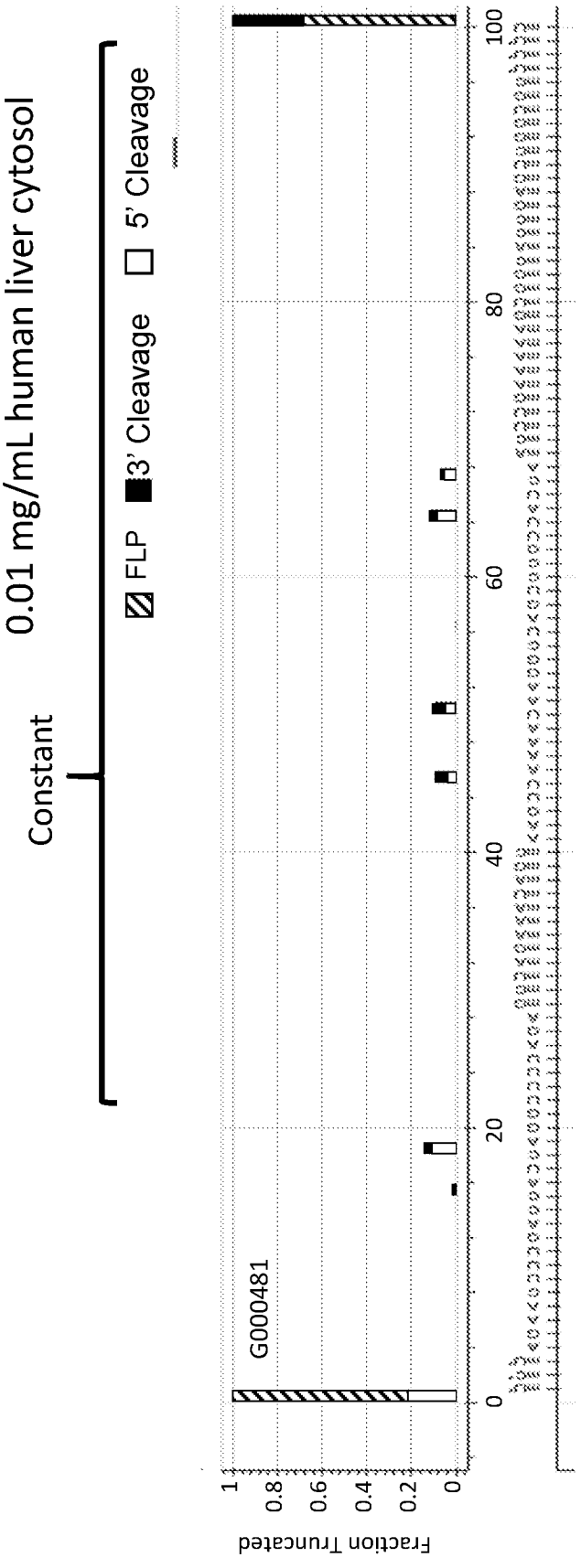

Constant
0.01 mg/mL human liver cytosol
FLP
3' Cleavage
5' Cleavage
G000481
Fraction Truncated
0
0.2
0.4
0.6
0.8
1
0
20
40
60
80
100

Fig. 11C

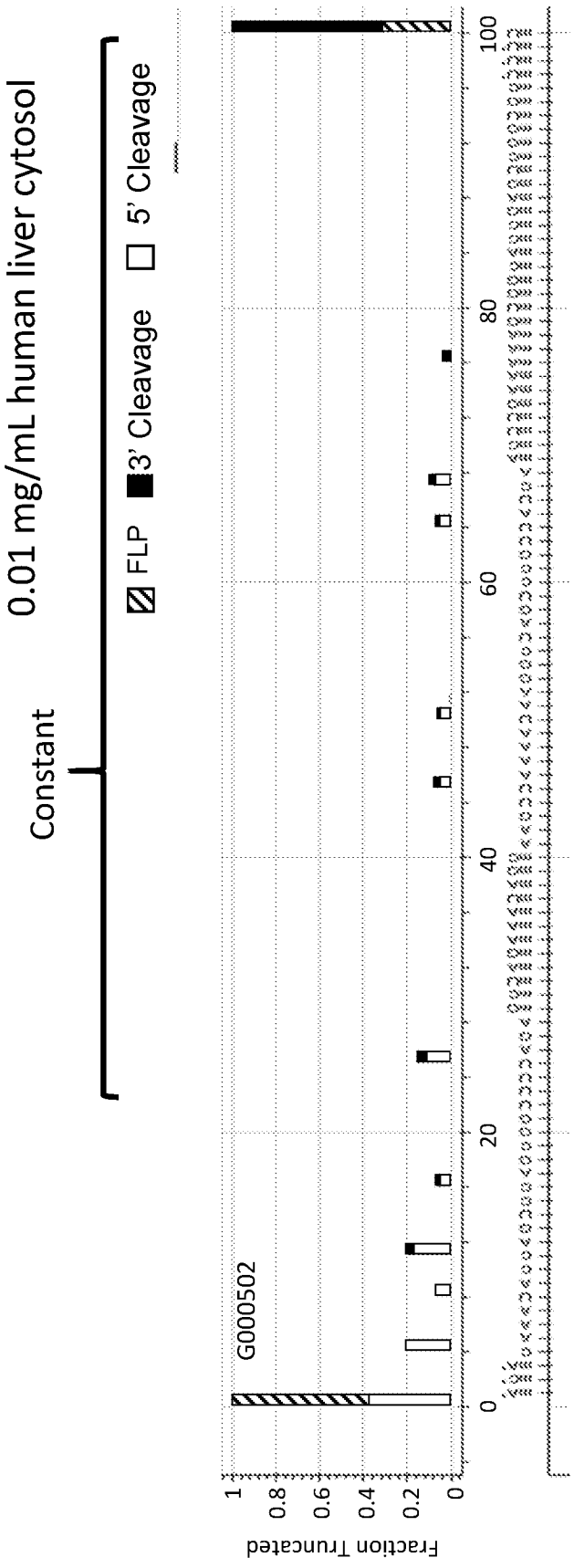

Constant
0.01 mg/mL human liver cytosol
FLP
3' Cleavage
5' Cleavage
G000502
Fraction Truncated
0
0.2
0.4
0.6
0.8
1
0
20
40
60
80
100

Fig. 11D

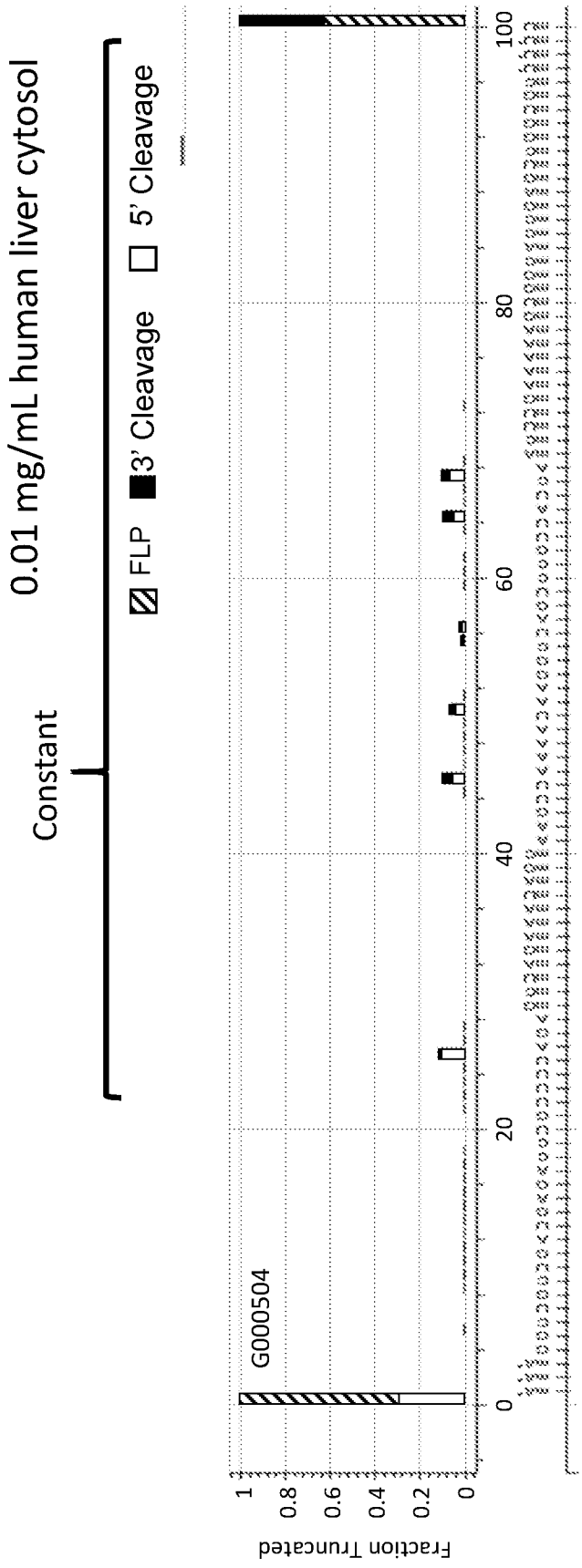

Constant
0.01 mg/mL human liver cytosol
FLP
3' Cleavage
5' Cleavage
G000504
Fraction Truncated
0
0.2
0.4
0.6
0.8
1
0
20
40
60
80
100

Fig. 11E

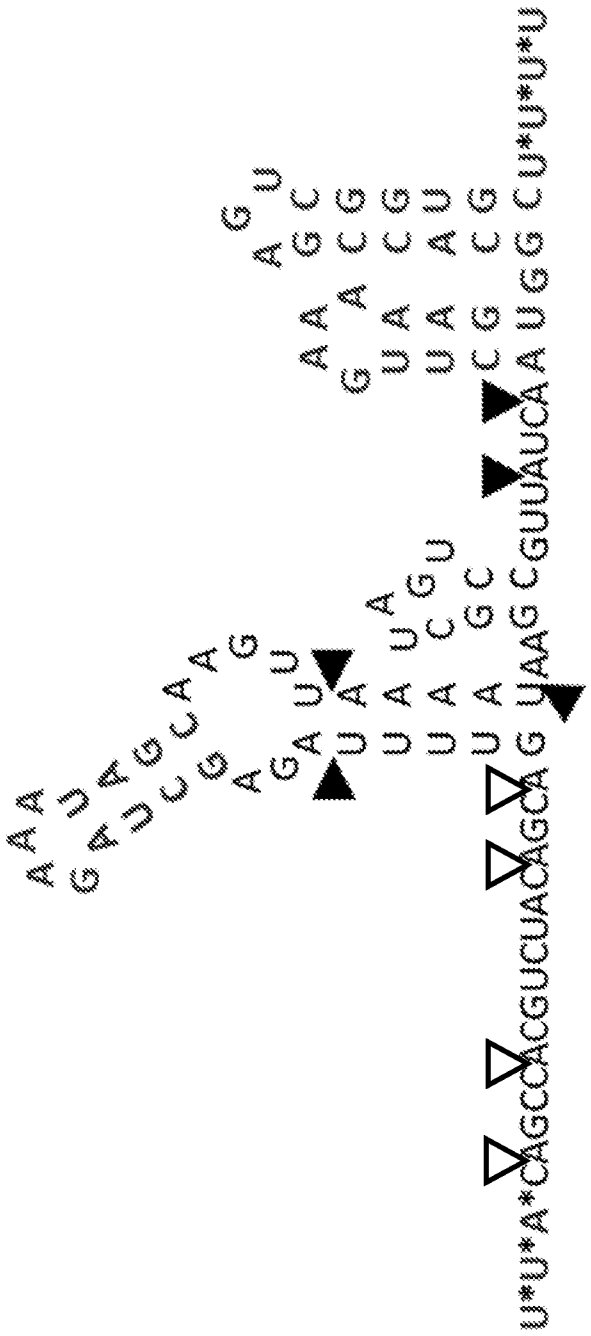


Fig. 11F

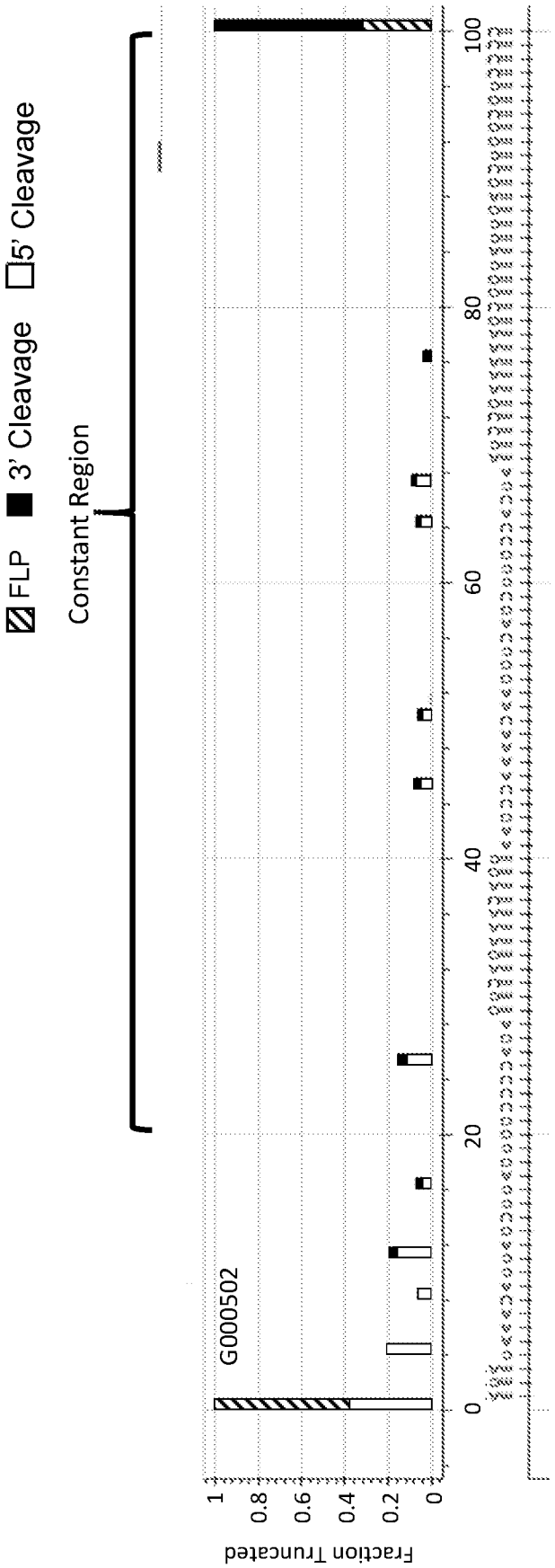

FLP
3' Cleavage
5' Cleavage
Constant Region
G000502
Fraction Truncated
0
0.2
0.4
0.6
0.8
1
0
20
40
60
80
100

Fig. 12A

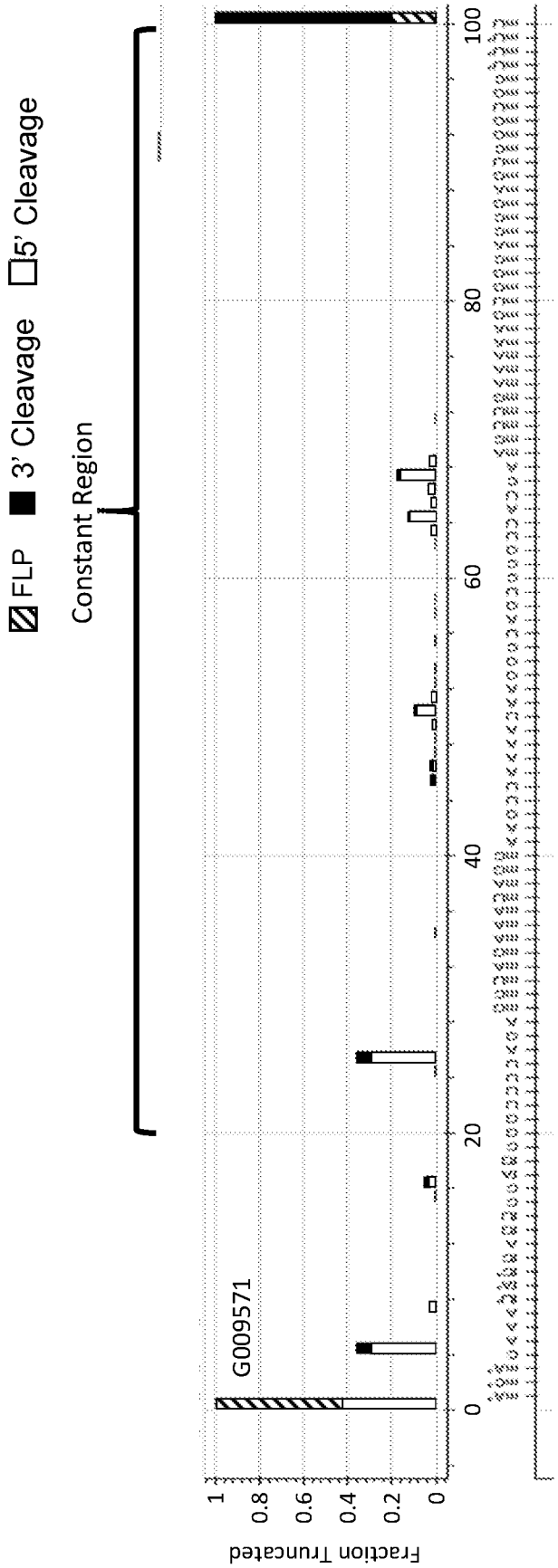

FLP
3' Cleavage
5' Cleavage
Constant Region
G009571
Fraction Truncated
0
0.2
0.4
0.6
0.8
1
0
20
40
60
80
100

Fig. 12B

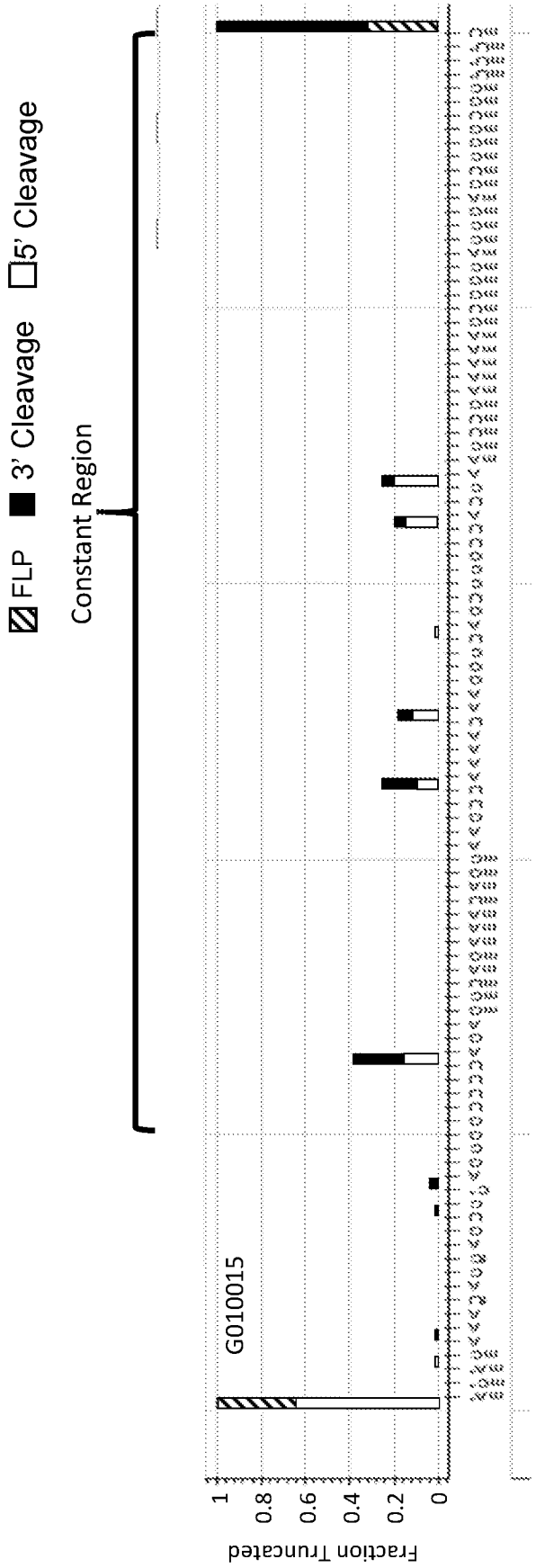

FLP
3' Cleavage
5' Cleavage
Constant Region
G010015
Fraction Truncated
0
0.2
0.4
0.6
0.8
1

Fig. 12C

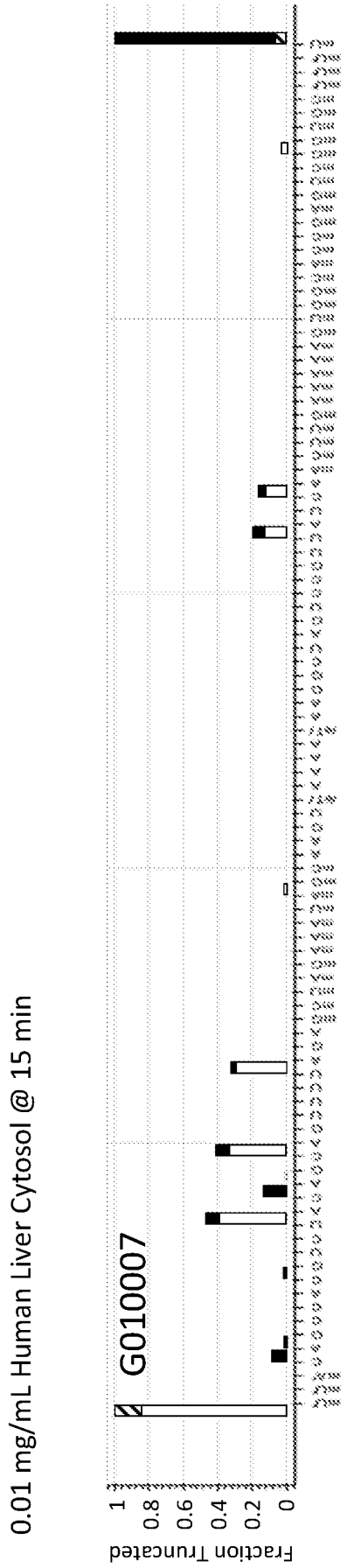


Fig. 12D

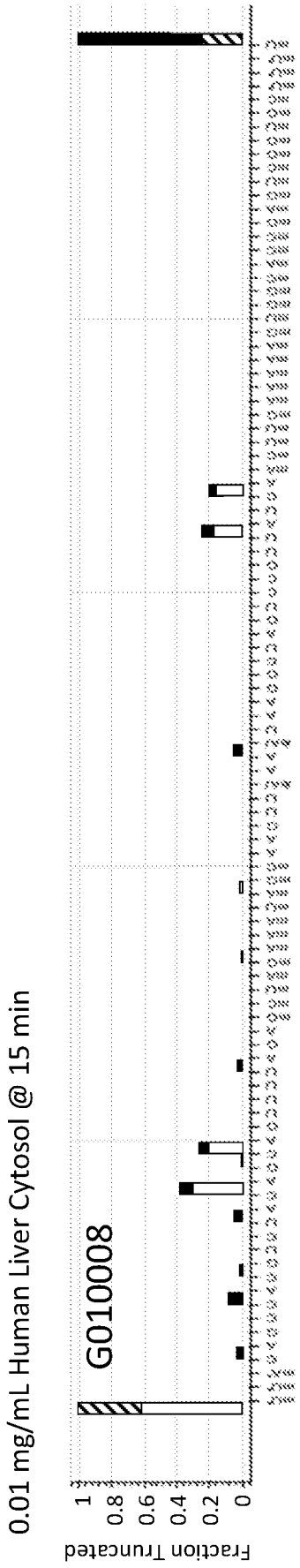


Fig. 12E

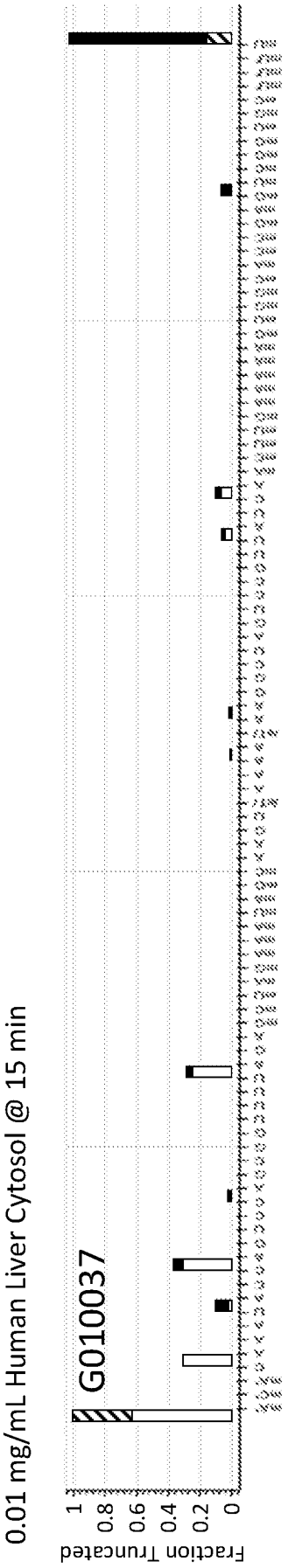


Fig. 12F

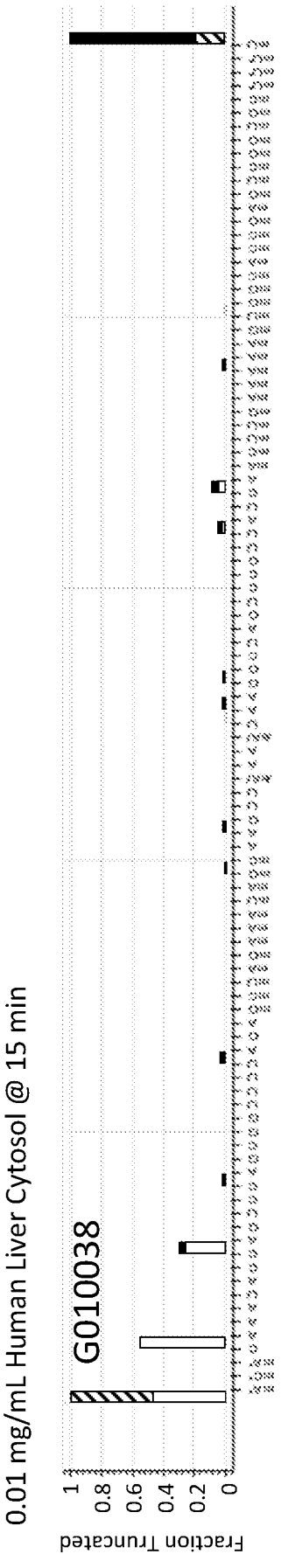


Fig. 12G

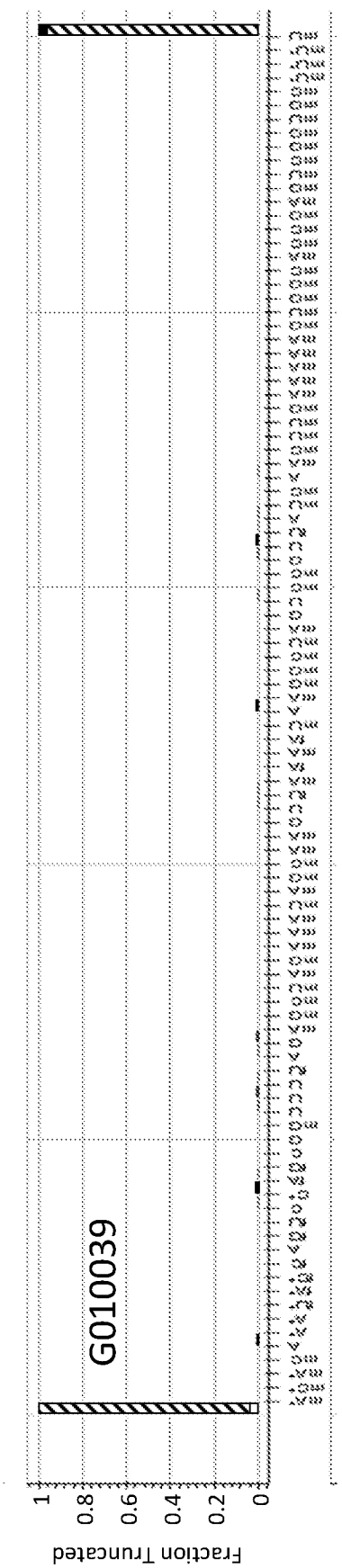


Fig. 13A

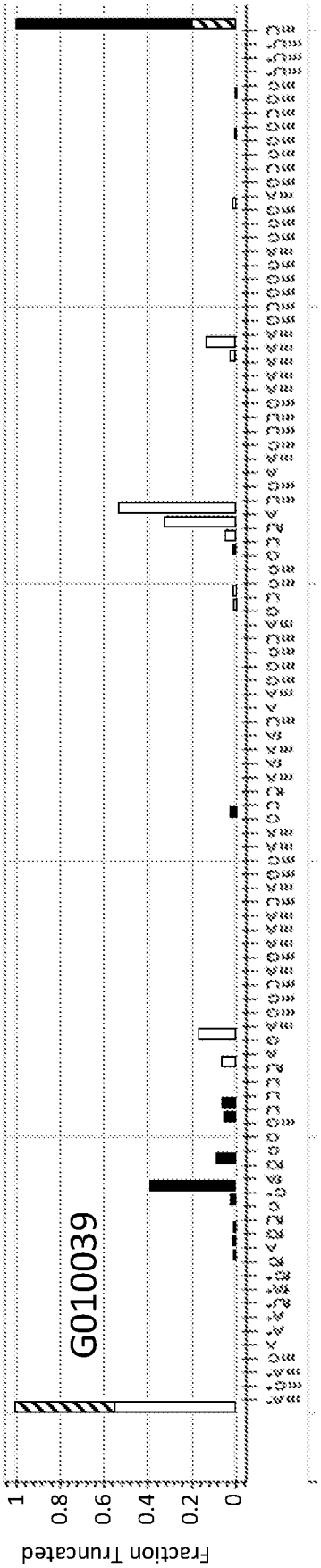


Fig. 13B

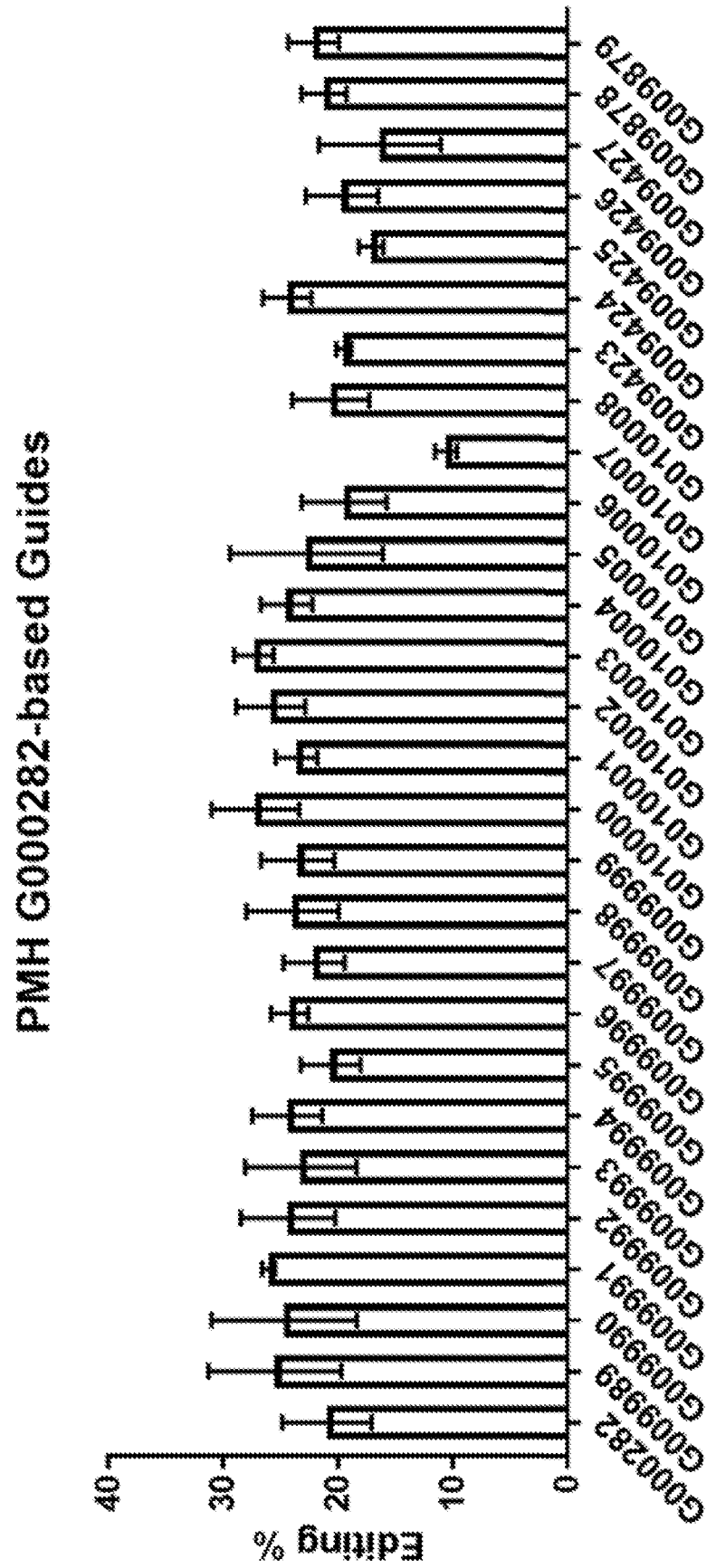

PMH G000282-based Guides
Editing %
0
10
20
30
40
G000282
G000989
G000990
G000991
G000992
G000993
G000994
G000995
G000996
G000997
G000998
G000999
G001000
G001001
G001002
G001003
G001004
G001005
G001006
G001007
G001008
G009423
G009424
G009425
G009426
G009427
G009878
G009879

Fig. 14

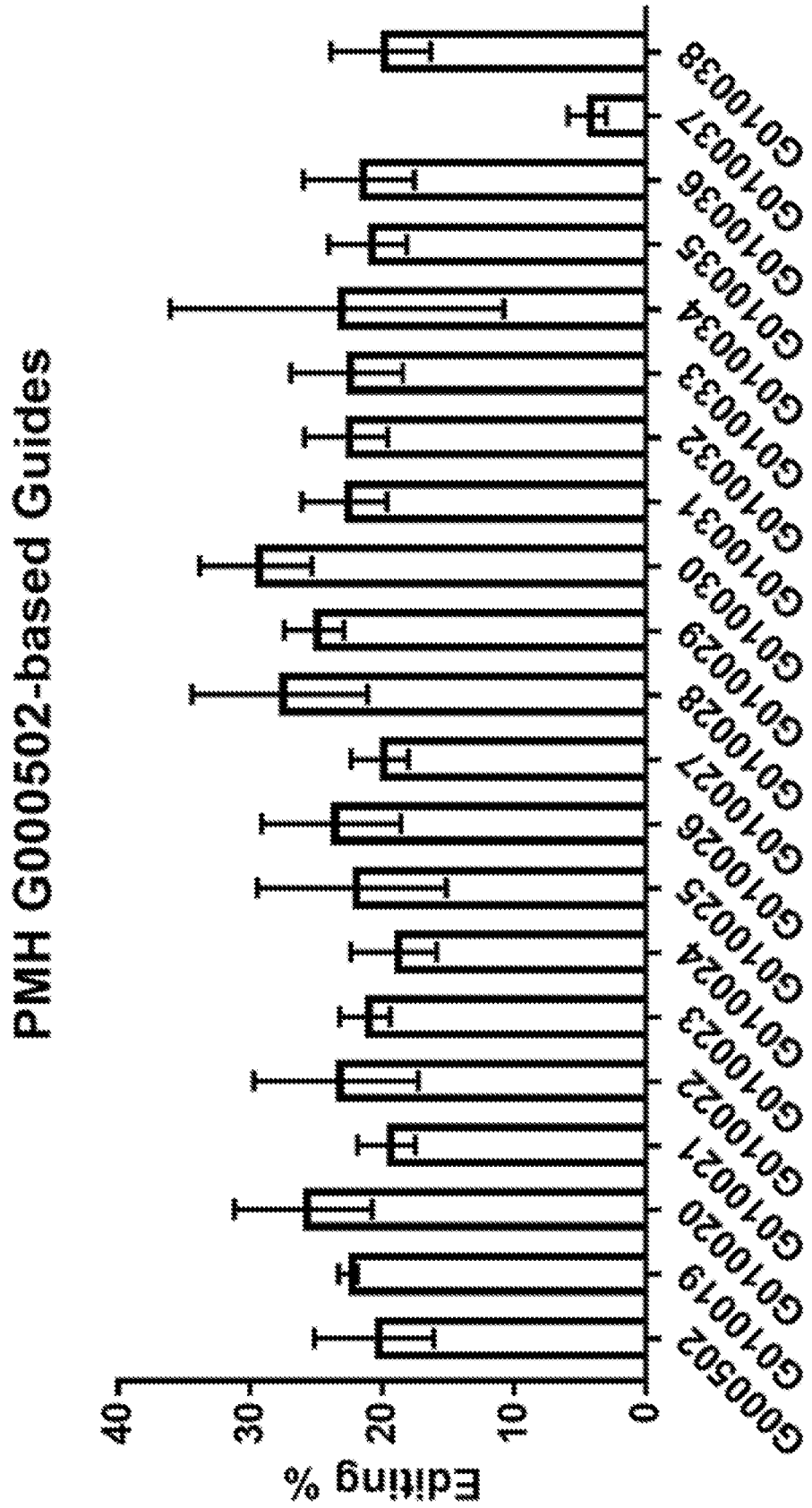

PMH G000502-based Guides
Editing %
0
10
20
30
40
G000502
G0100019
G0100020
G0100021
G0100022
G0100023
G0100024
G0100025
G0100026
G0100027
G0100028
G0100029
G0100030
G0100031
G0100032
G0100033
G0100034
G0100035
G0100036
G0100037
G0100038

Fig. 15A

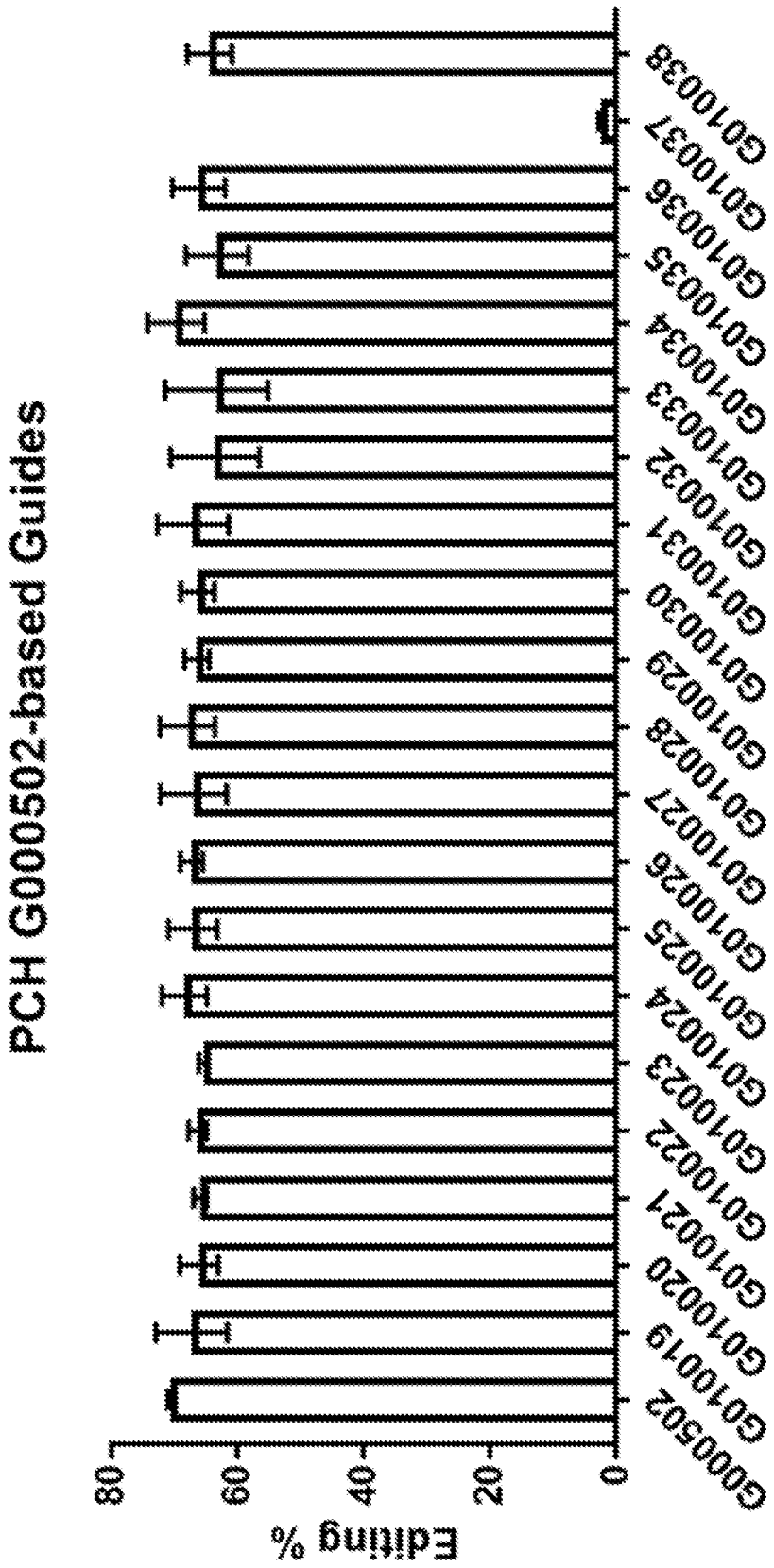

PCH G000502-based Guides
Editing %
80
60
40
20
0
G000502
G100519
G100520
G100521
G100522
G100523
G100524
G100525
G100526
G100527
G100528
G100529
G100530
G100531
G100532
G100533
G100534
G100535
G100536
G100537
G100538

Fig. 15B

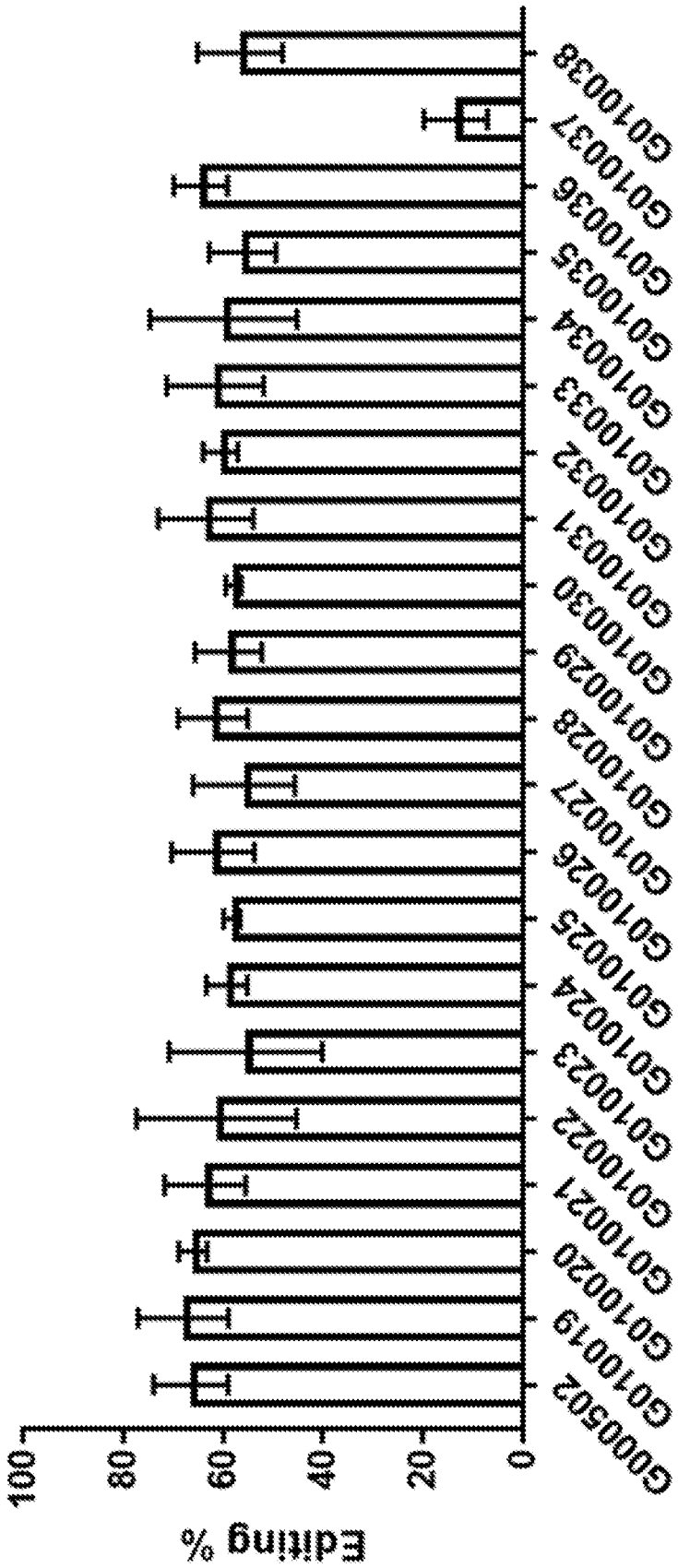

PHH G000502-based Guides
Editing %
100
80
60
40
20
0
G000502
G100019
G100020
G100021
G100022
G100023
G100024
G100025
G100026
G100027
G100028
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G100033
G100034
G100035
G100036
G100037
G100038

Fig. 15C

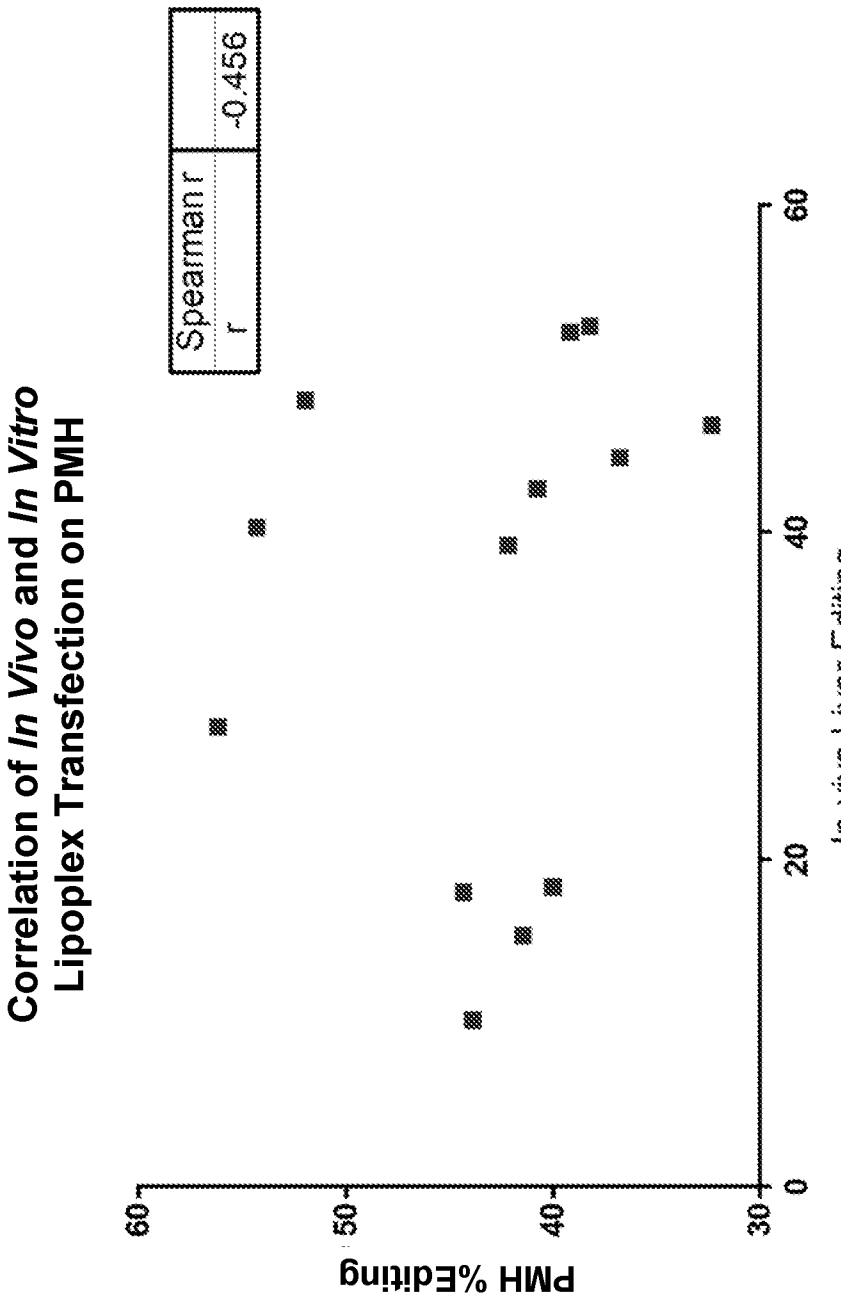

Correlation of In Vivo and In Vitro
Lipoplex Transfection on PMH
Spearman r
r
-0.456
PMH %Editing
In-vivo Liver Editing
60
50
40
30
0
20
40
60

Fig. 16A

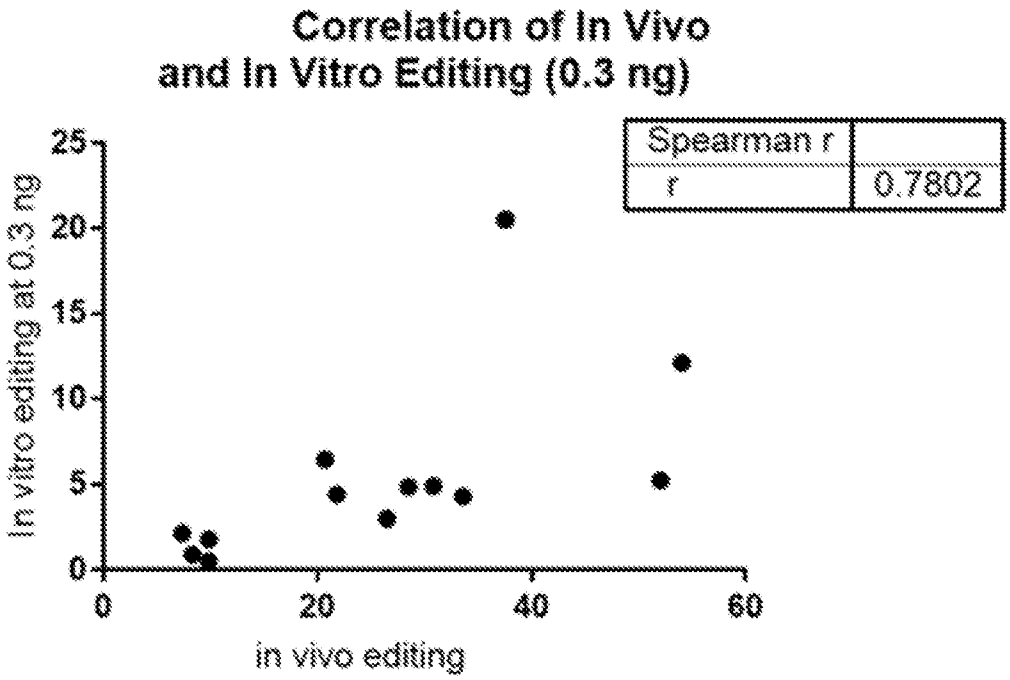


Fig. 16B

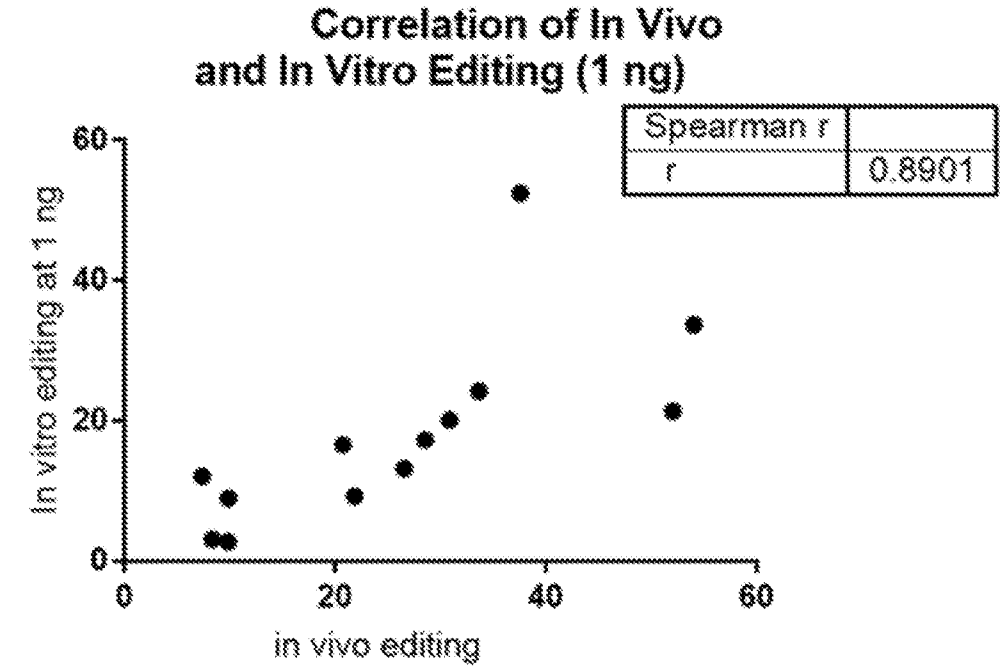


Fig. 16C

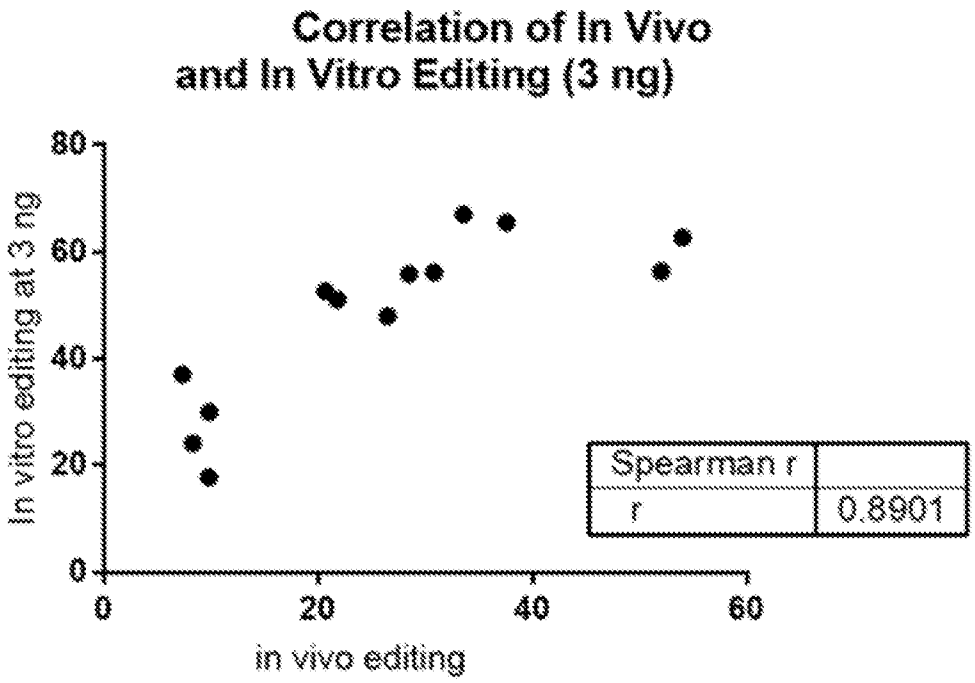


Fig. 16D

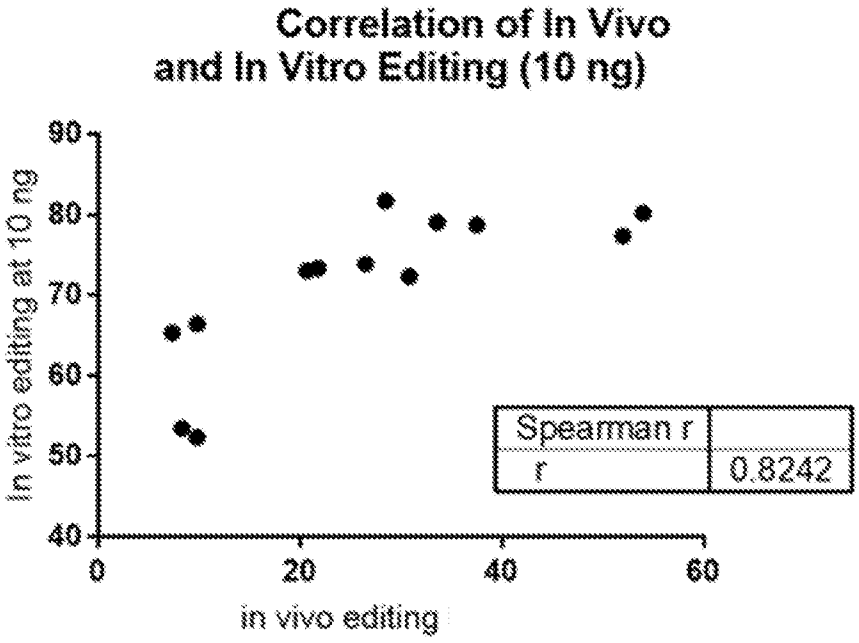


Fig. 16E

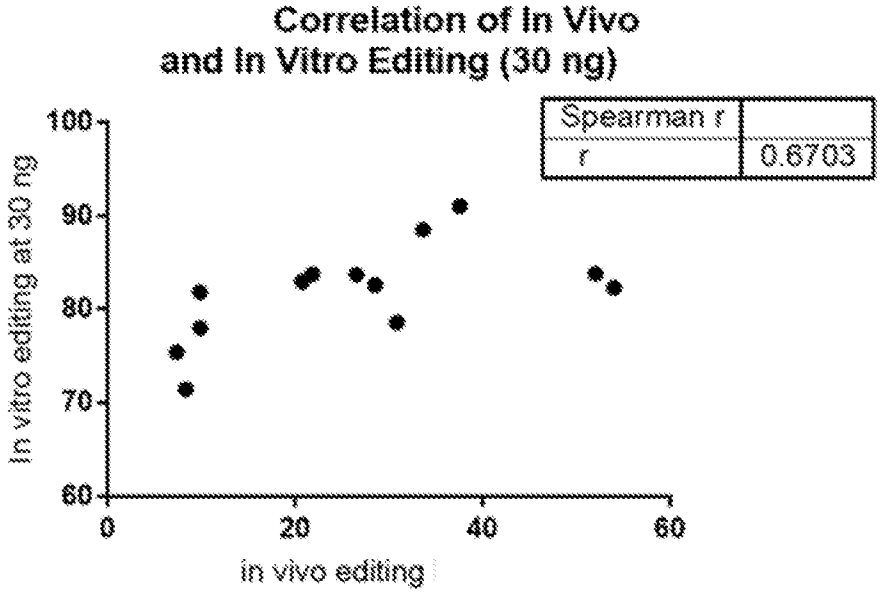


Fig. 16F

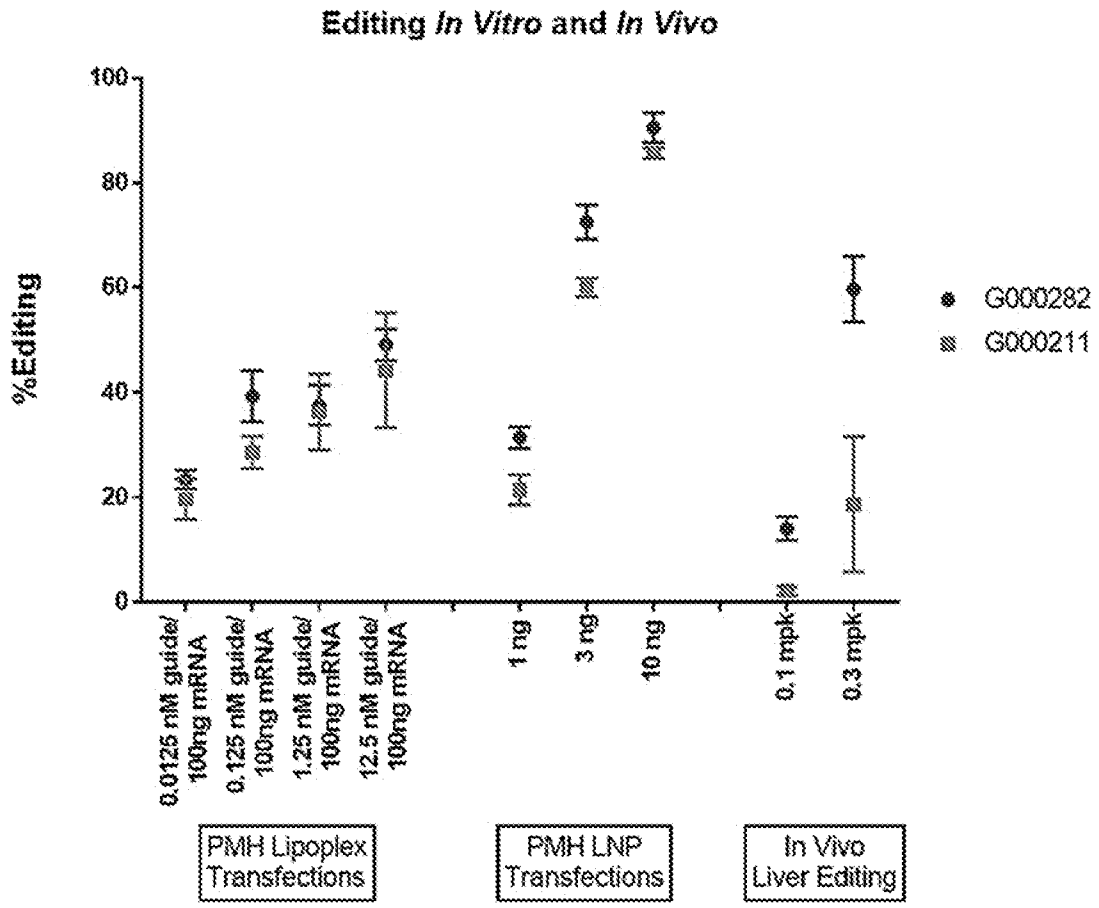


Fig. 16G

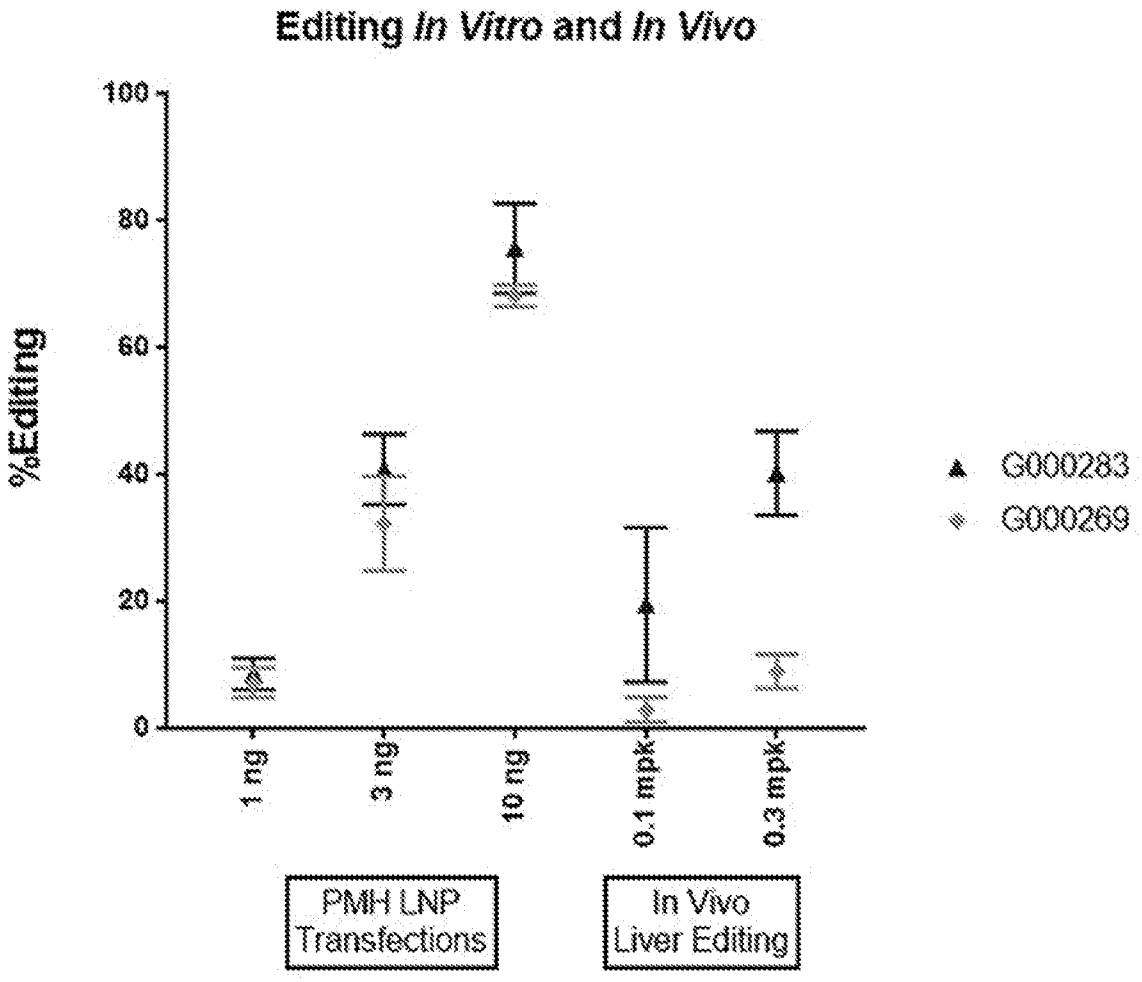

Editing *In Vitro* and *In Vivo*
%Editing
100
80
60
40
20
0
1 ng
3 ng
10 ng
0.1 mpk
0.3 mpk
PMH LNP Transfections
In Vivo Liver Editing
G000283
G000269

Fig. 16H

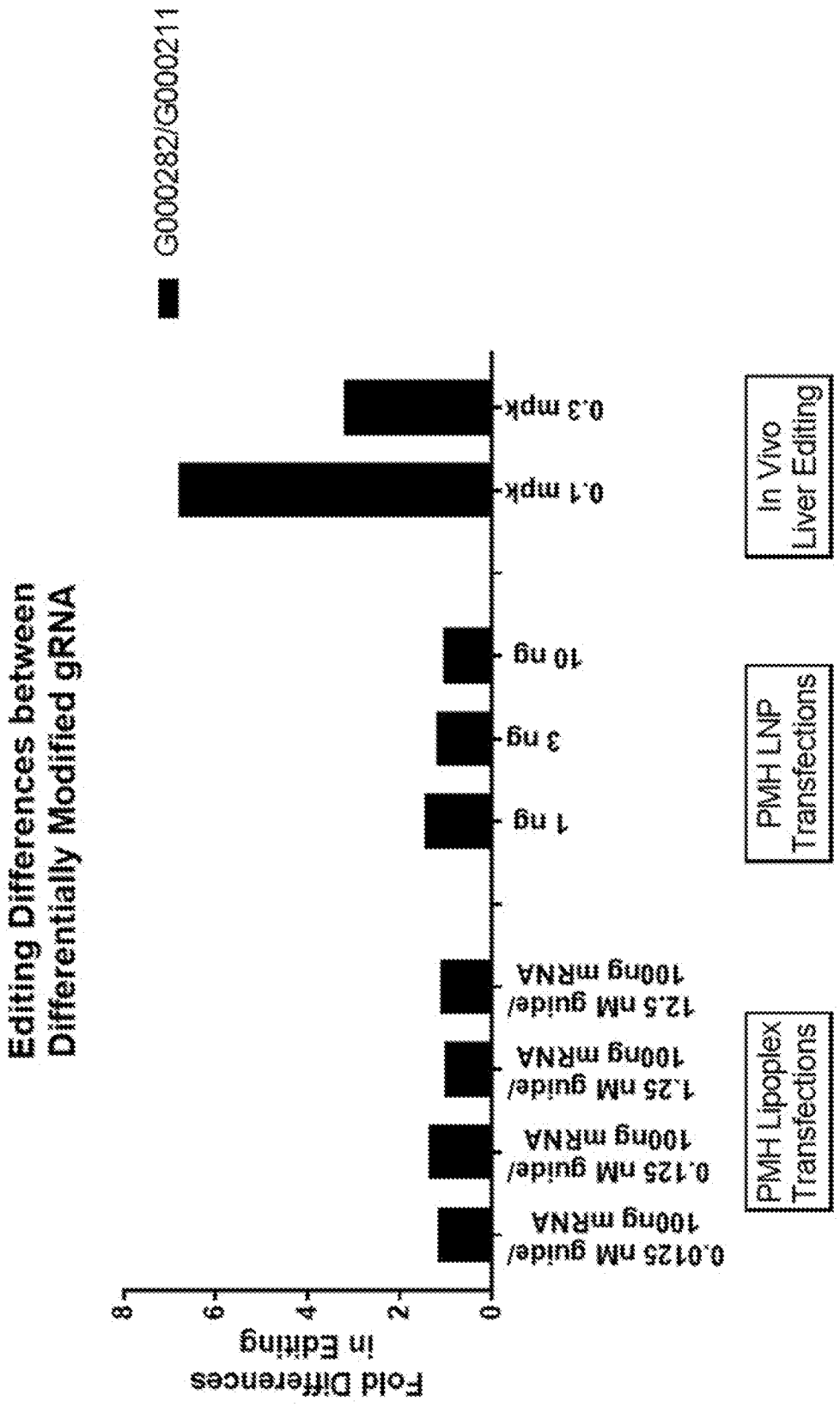

Editing Differences between Differentially Modified gRNA
G000282/G000211
Fold Differences in Editing
0
2
4
6
8
0.0125 nM guide/ 100ng mRNA
0.125 nM guide/ 100ng mRNA
1.25 nM guide/ 100ng mRNA
12.5 nM guide/ 100ng mRNA
1 ng
3 ng
10 ng
0.1 mpk
0.3 mpk
PMH Lipoplex Transfections
PMH LNP Transfections
In Vivo Liver Editing

Fig. 16I

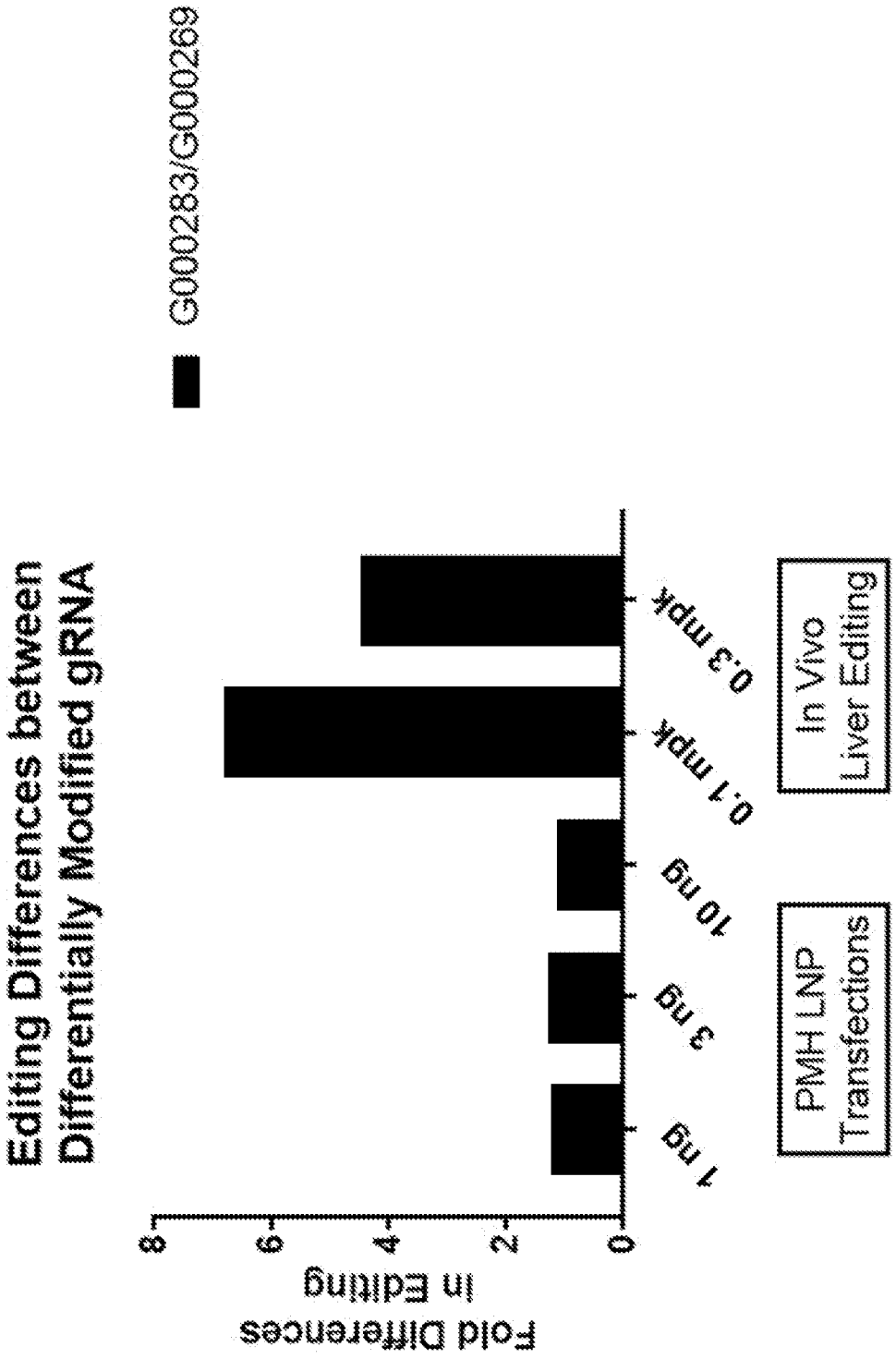

Editing Differences between Differentially Modified gRNA
G000283/G000269
Fold Differences in Editing
0
2
4
6
8
1 ng
3 ng
10 ng
0.1 mpk
0.3 mpk
PMH LNP Transfections
In Vivo Liver Editing

Fig. 16J

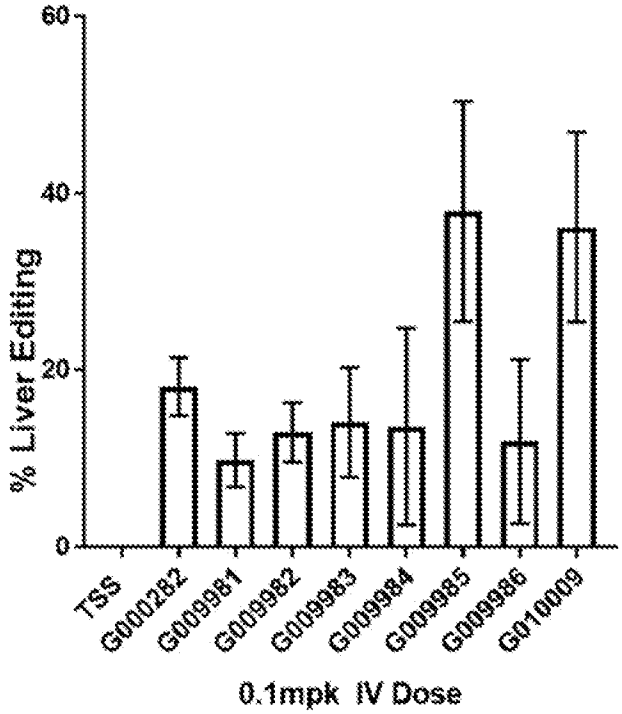


Fig. 17A

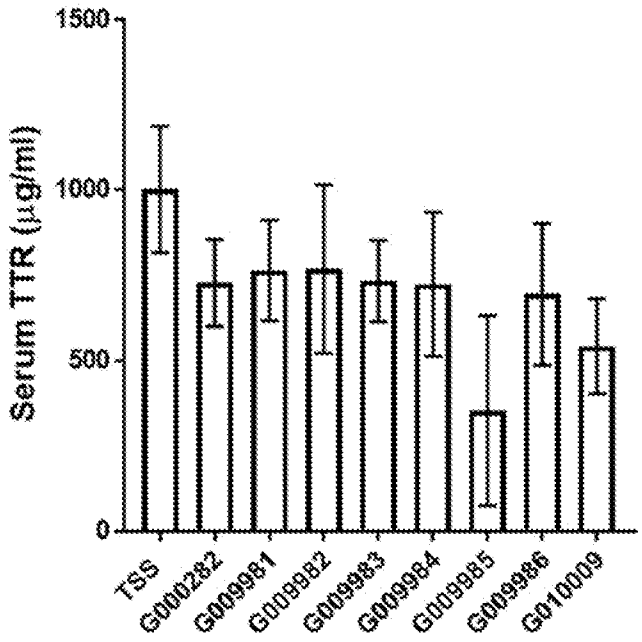


Fig. 17B

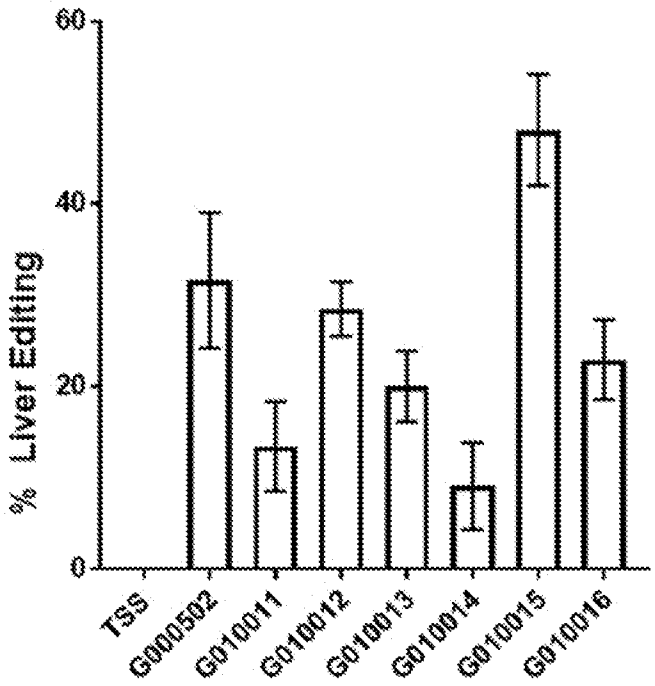


Fig. 18A

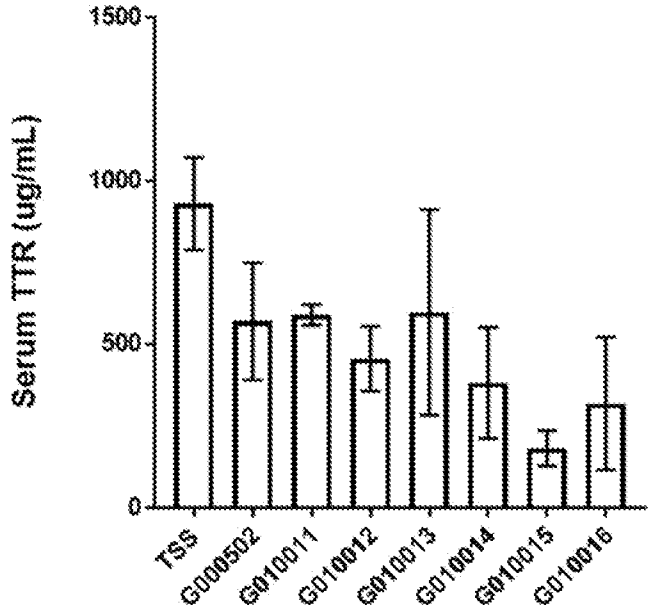


Fig. 18B

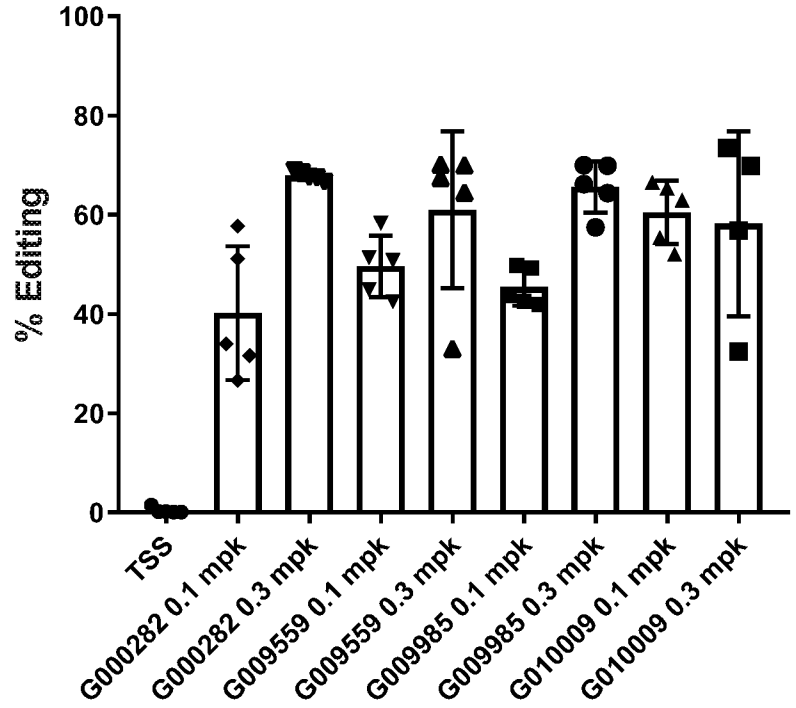


Fig. 18C

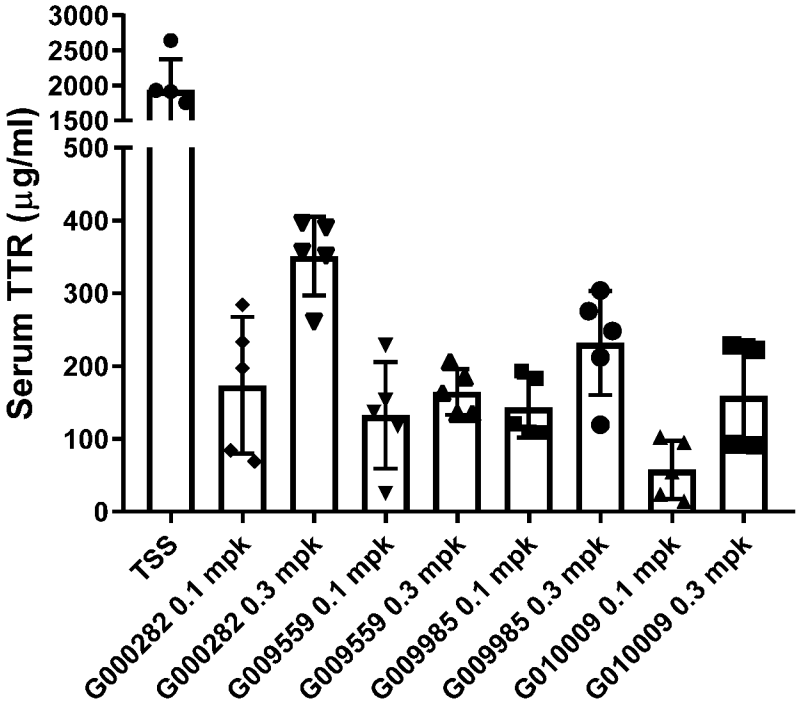


Fig. 18D

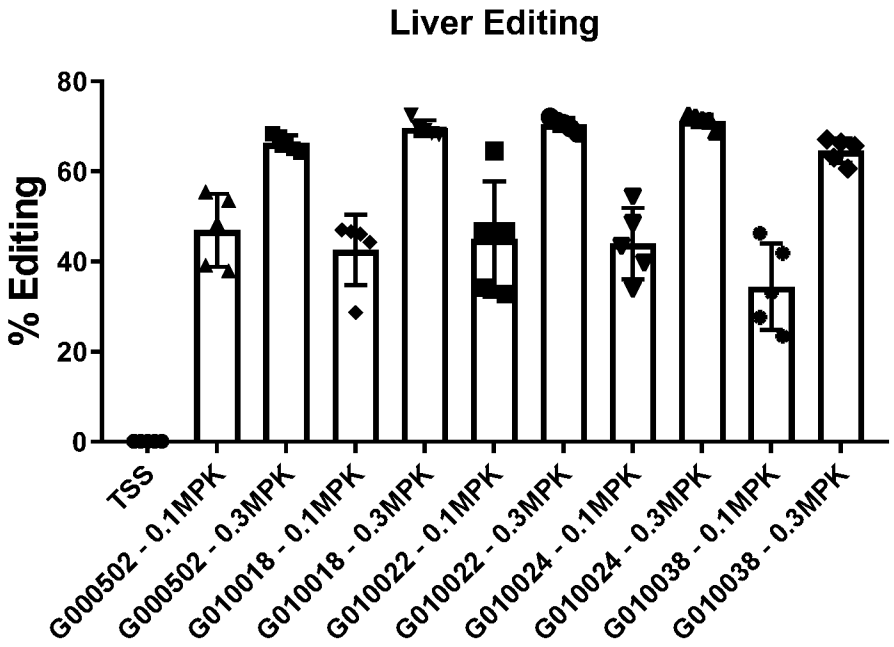


Fig. 18E

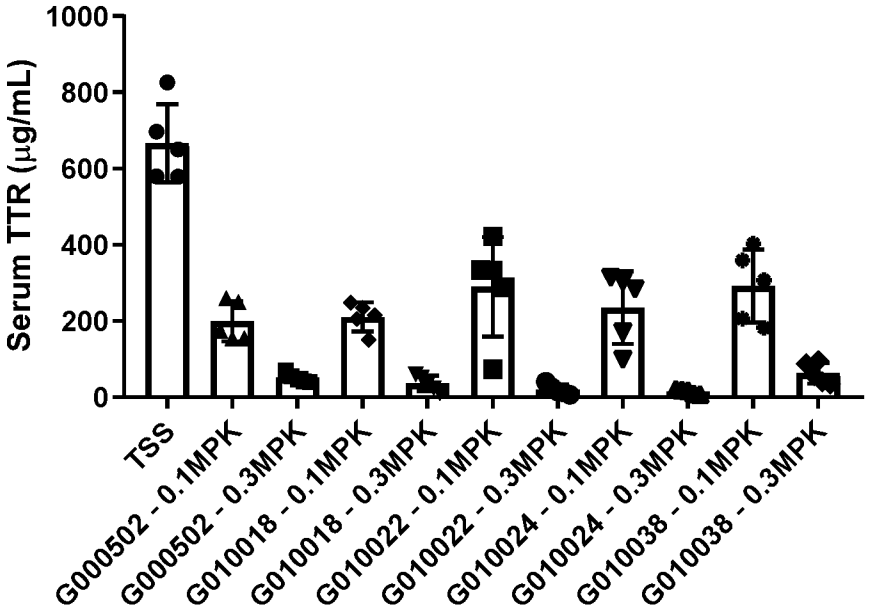


Fig. 18F

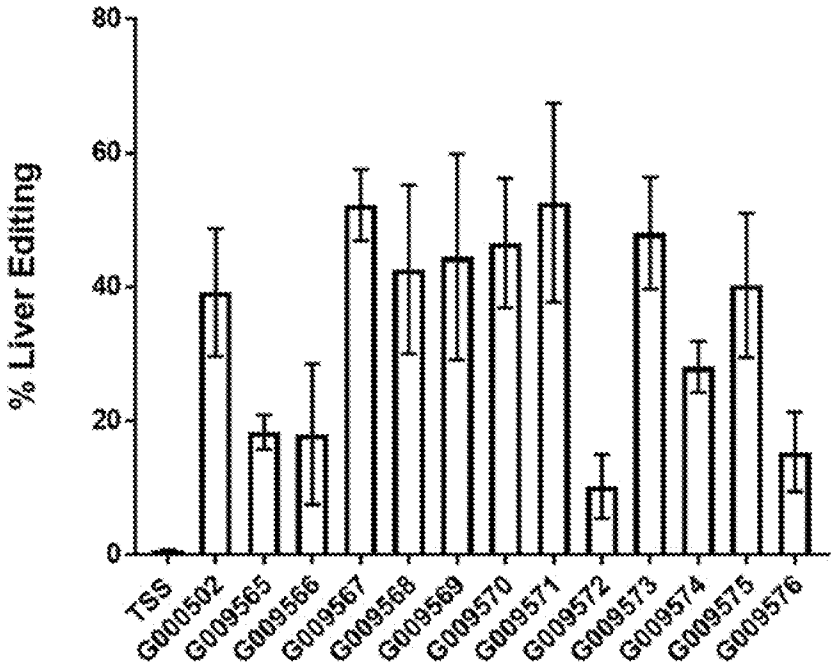


Fig. 19A

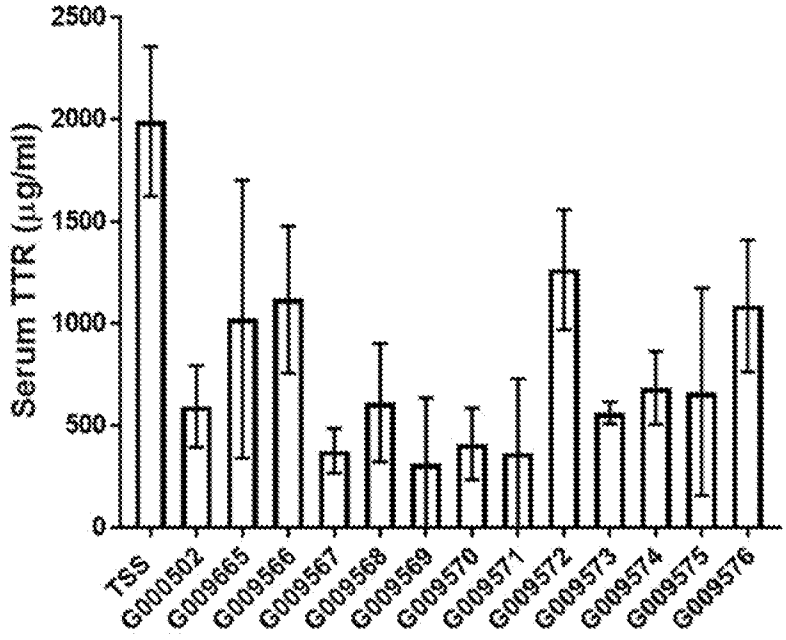


Fig. 19B

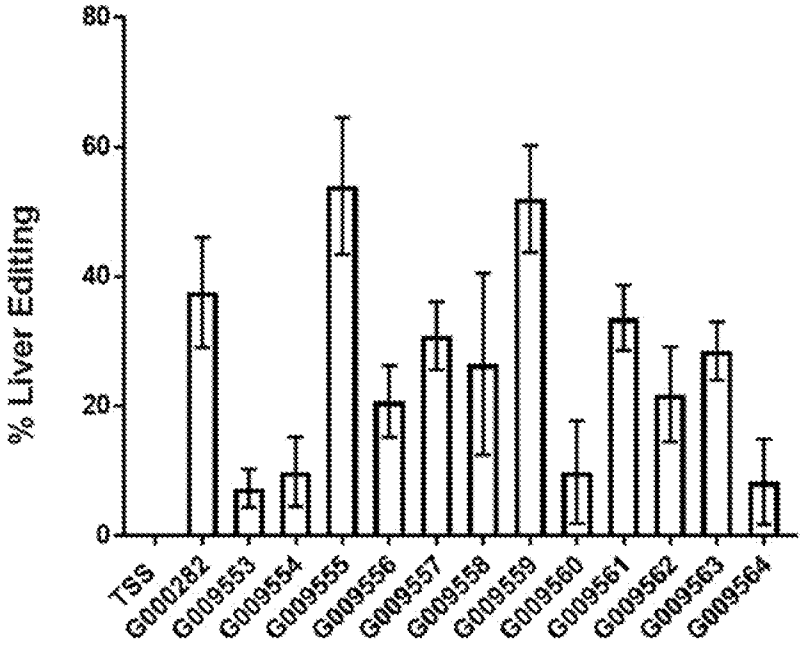


Fig. 19C

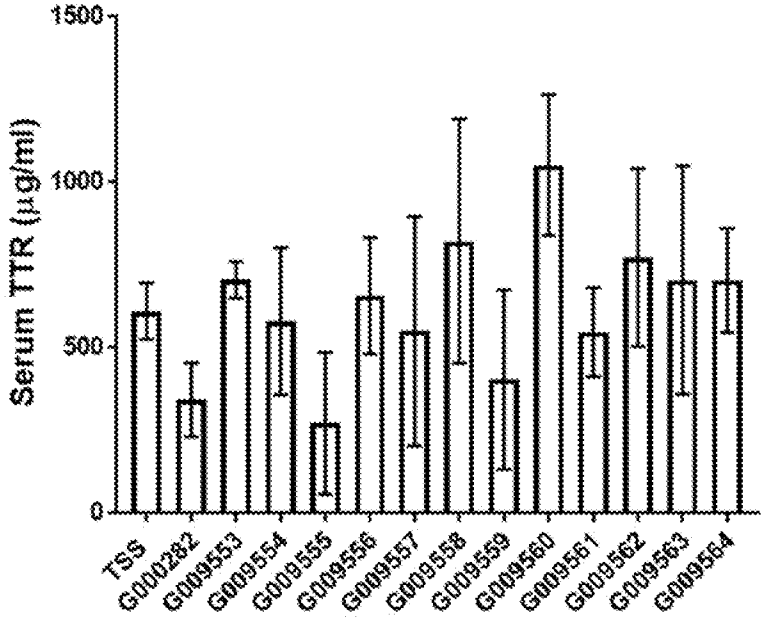


Fig. 19D

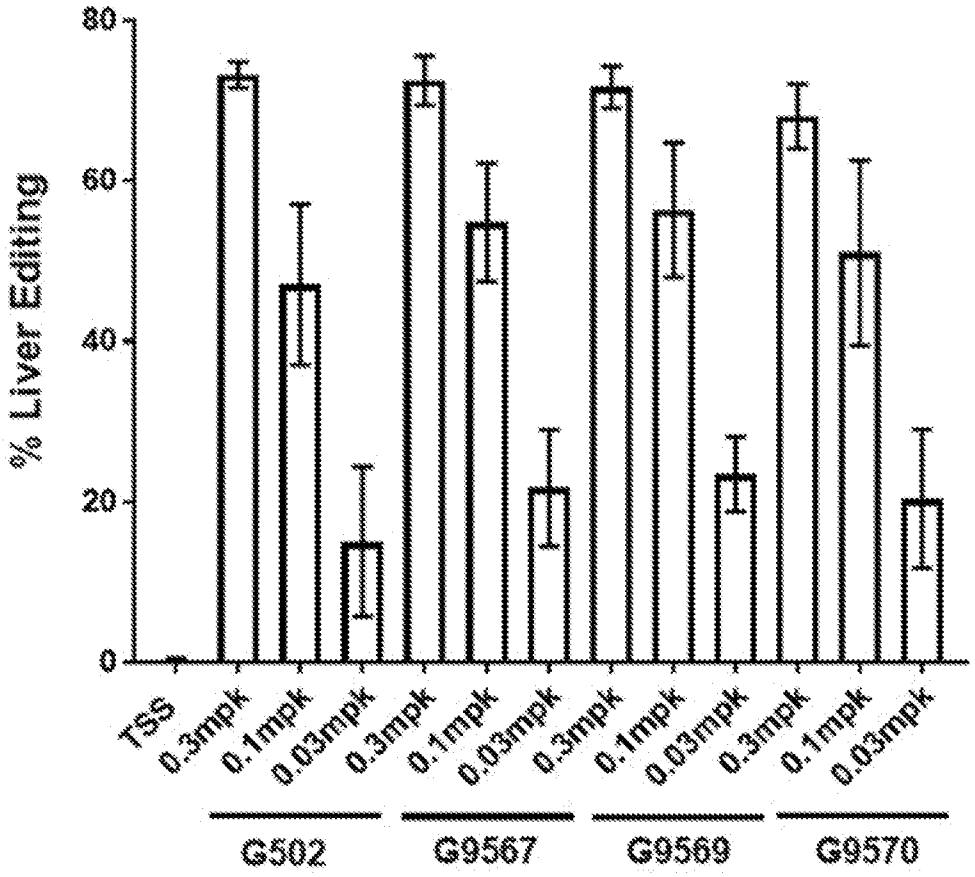

% Liver Editing
80
60
40
20
0
TSS
0.3mpk
0.1mpk
0.03mpk
0.3mpk
0.1mpk
0.03mpk
0.3mpk
0.1mpk
0.03mpk
0.3mpk
0.1mpk
0.03mpk
G502
G9567
G9569
G9570

Fig. 20A

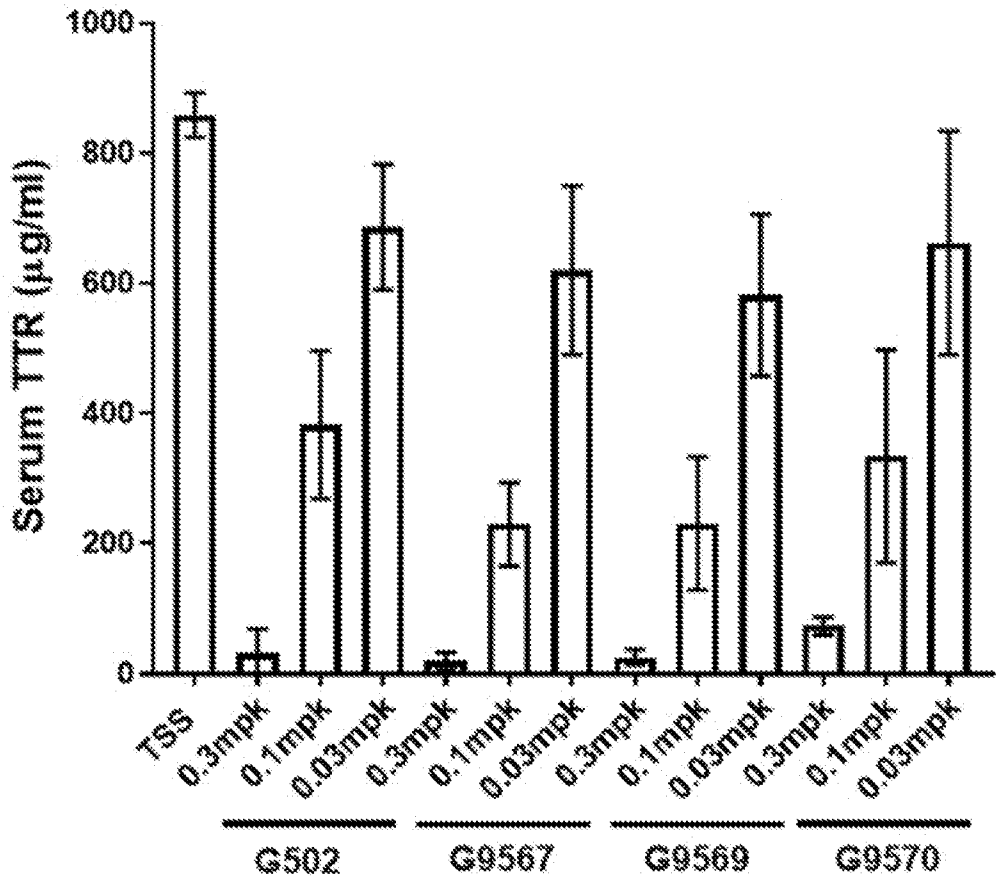

Serum TTR (µg/ml)
1000
800
600
400
200
0
TSS
0.3mpk
0.1mpk
0.03mpk
0.3mpk
0.1mpk
0.03mpk
0.3mpk
0.1mpk
0.03mpk
0.3mpk
0.1mpk
0.03mpk
G502
G9567
G9569
G9570

Fig. 20B

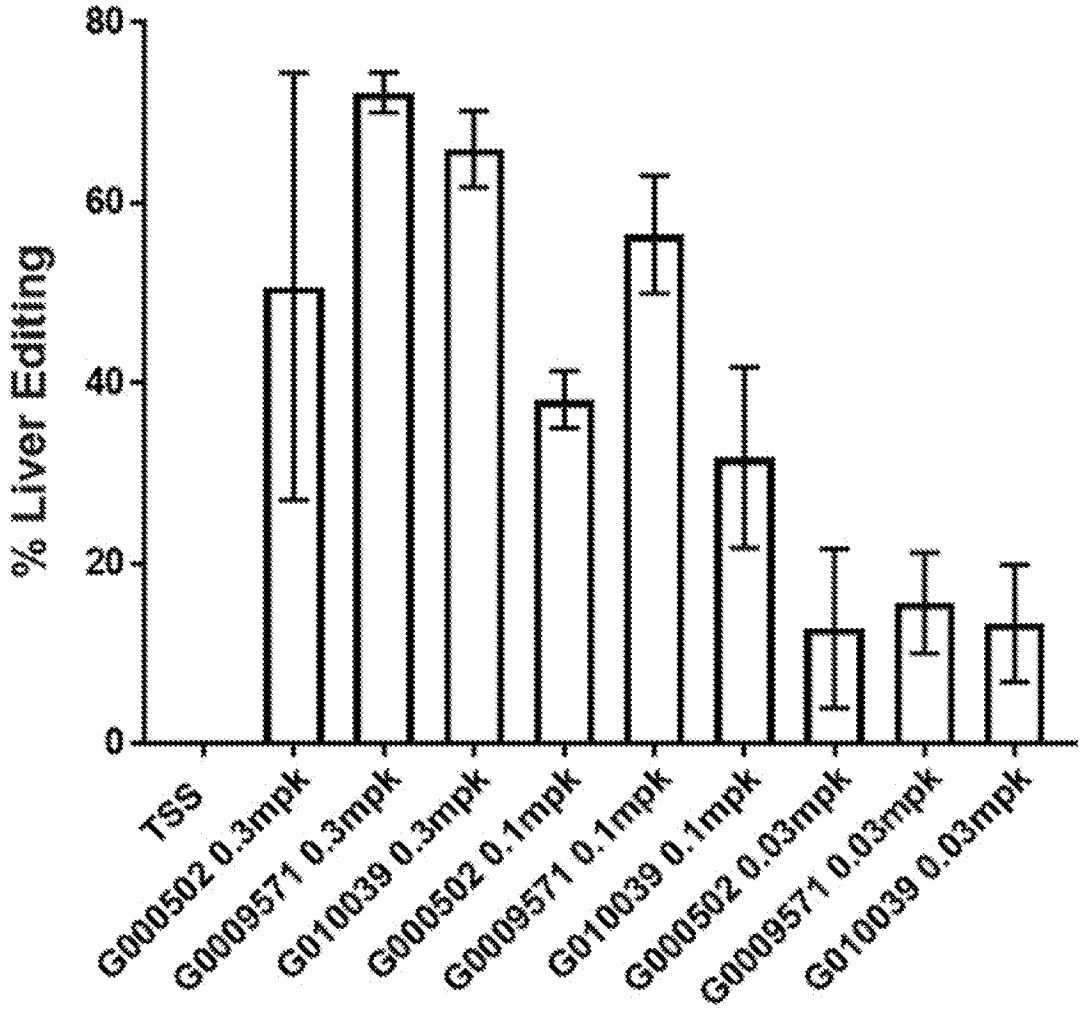

% Liver Editing
80
60
40
20
0
TSS
G000502 0.3mpk
G0009571 0.3mpk
G010039 0.3mpk
G000502 0.1mpk
G0009571 0.1mpk
G010039 0.1mpk
G000502 0.03mpk
G0009571 0.03mpk
G010039 0.03mpk

Fig. 20C

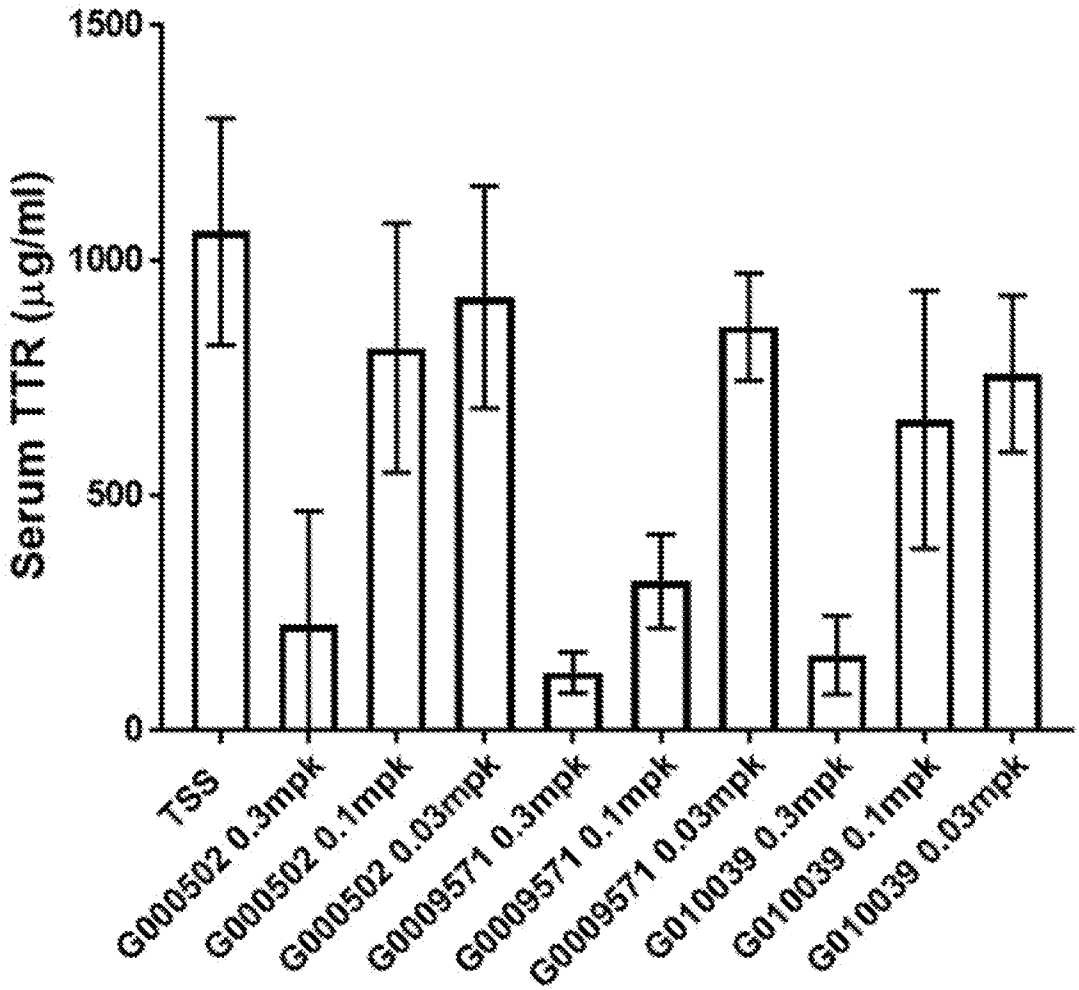

Serum TTR (µg/ml)
1500
1000
500
0
TSS
G000502 0.3mpk
G000502 0.1mpk
G000502 0.03mpk
G0009571 0.3mpk
G0009571 0.1mpk
G0009571 0.03mpk
G010039 0.3mpk
G010039 0.1mpk
G010039 0.03mpk

Fig. 20D

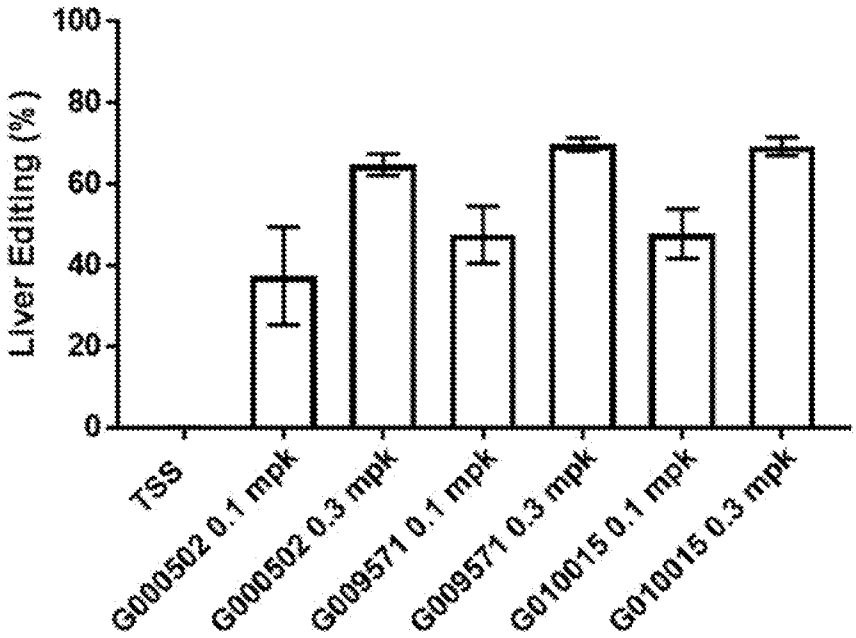


Fig. 20E

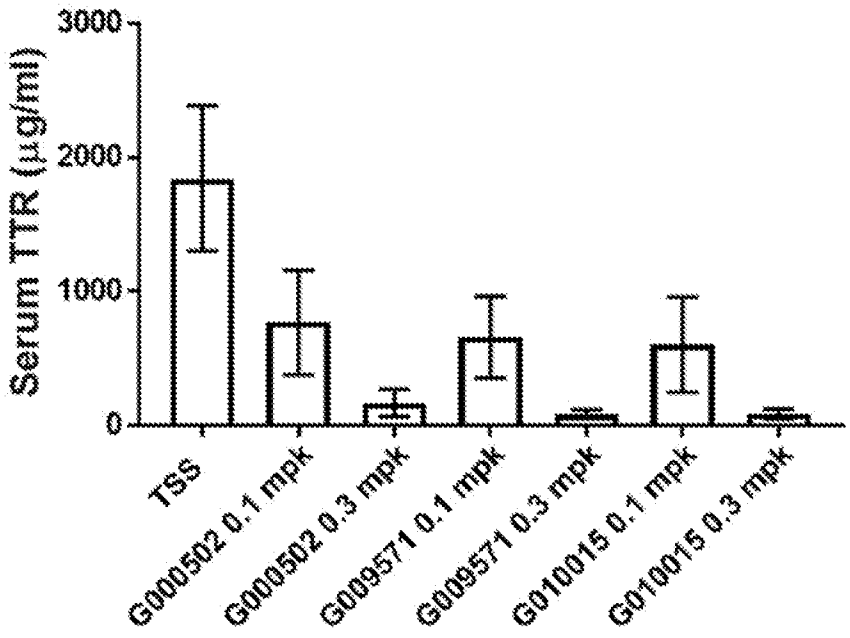


Fig. 20F

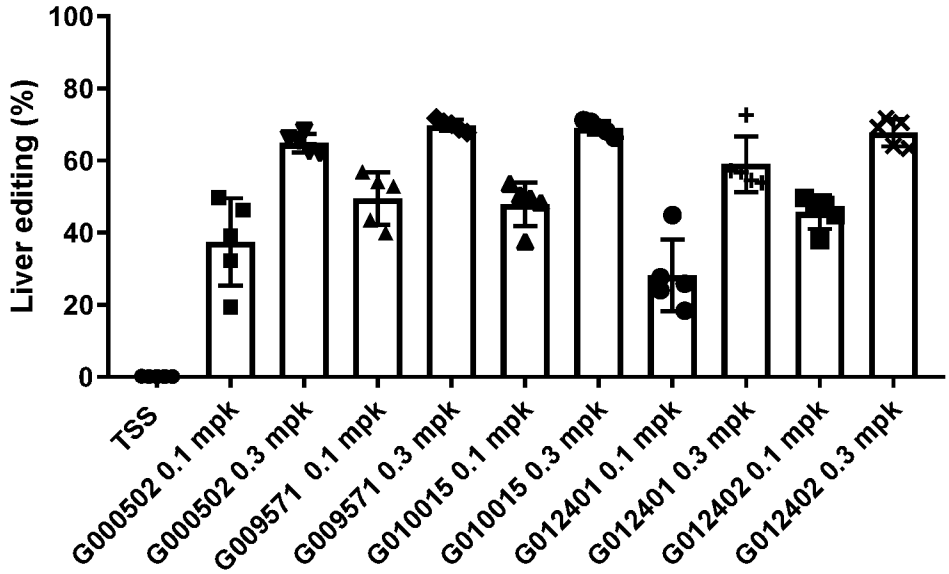


Fig. 21A

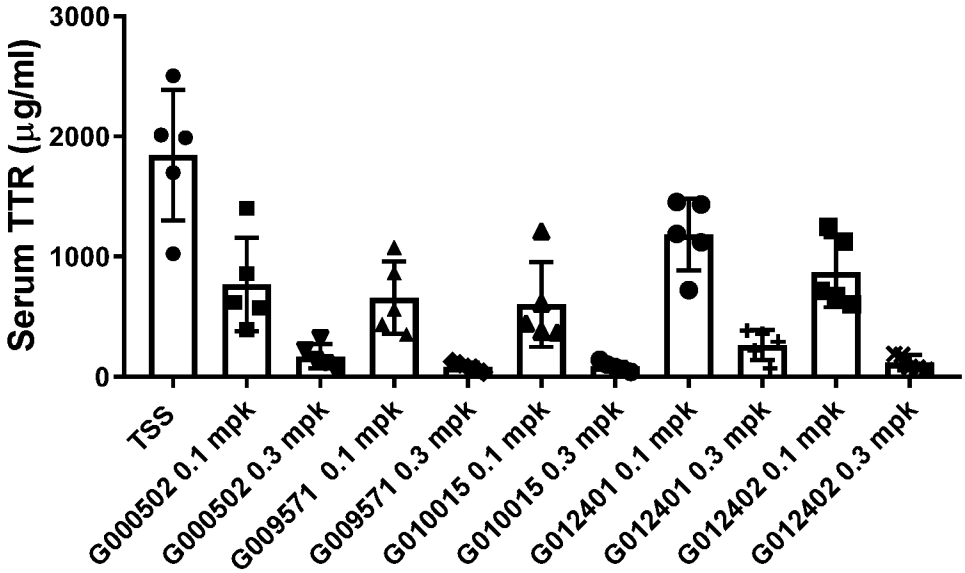


Fig. 21B

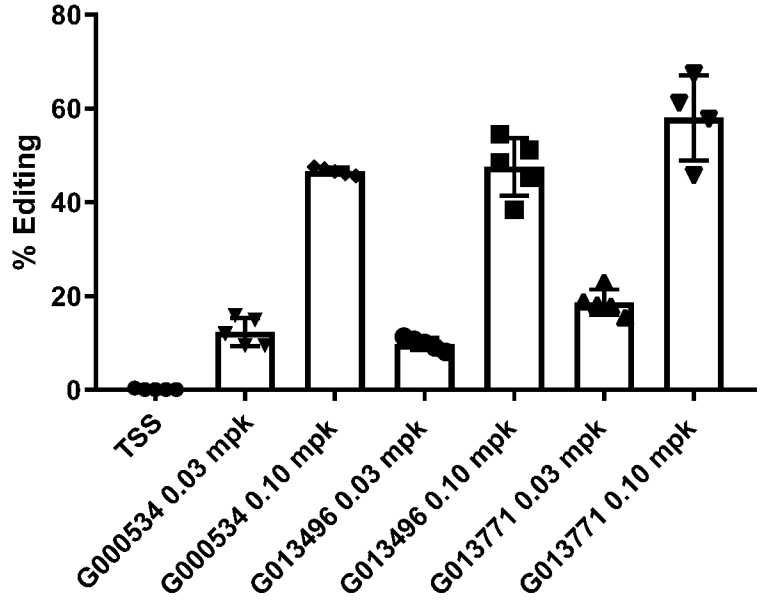


Fig. 22A

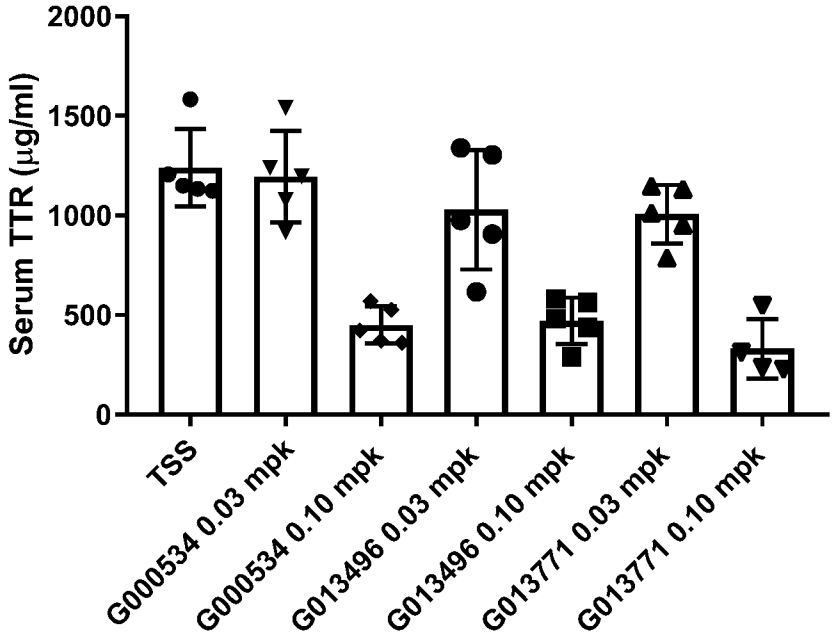


Fig. 22B

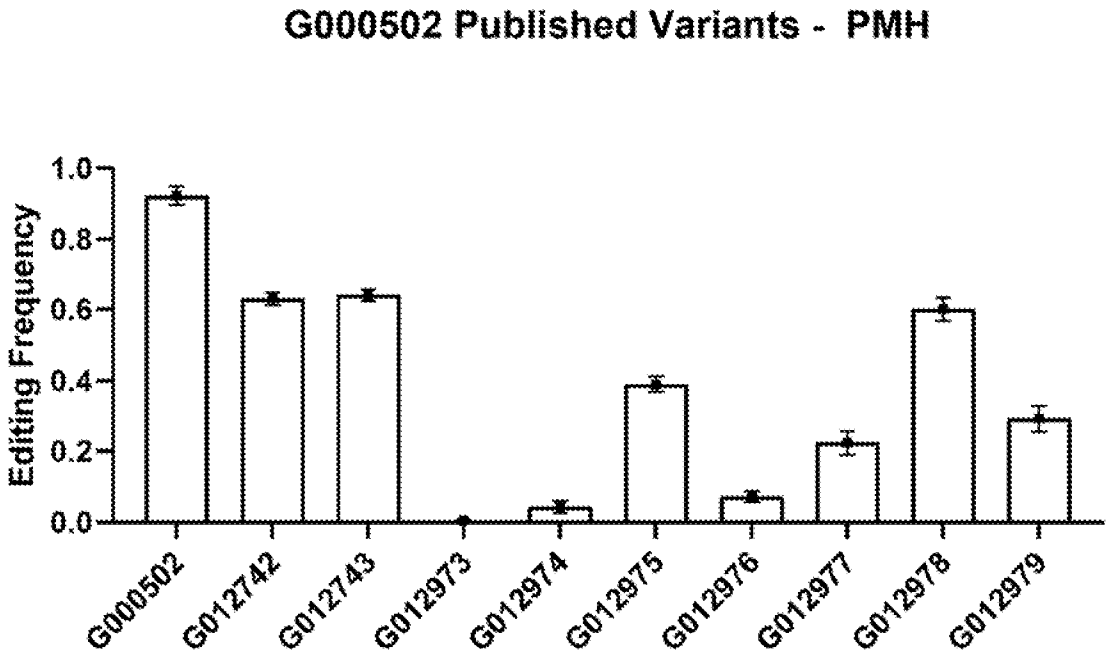


Fig. 23A

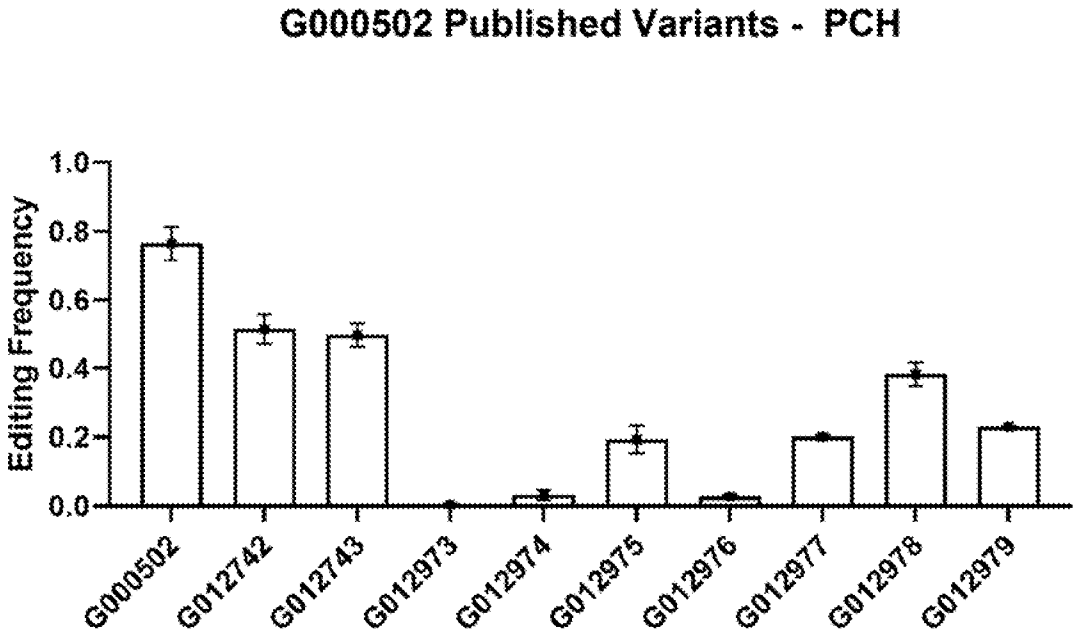


Fig. 23B

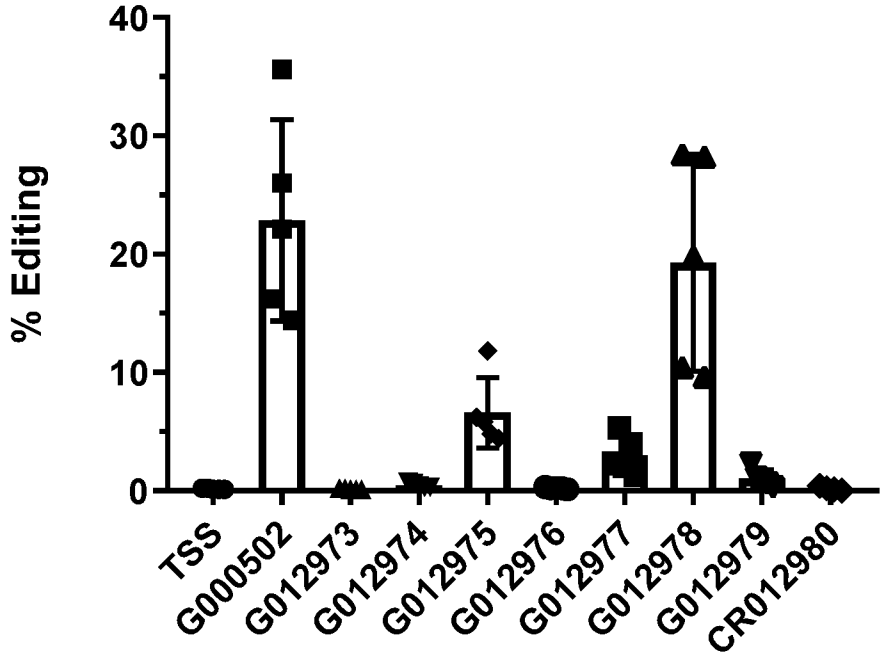


Fig. 24A

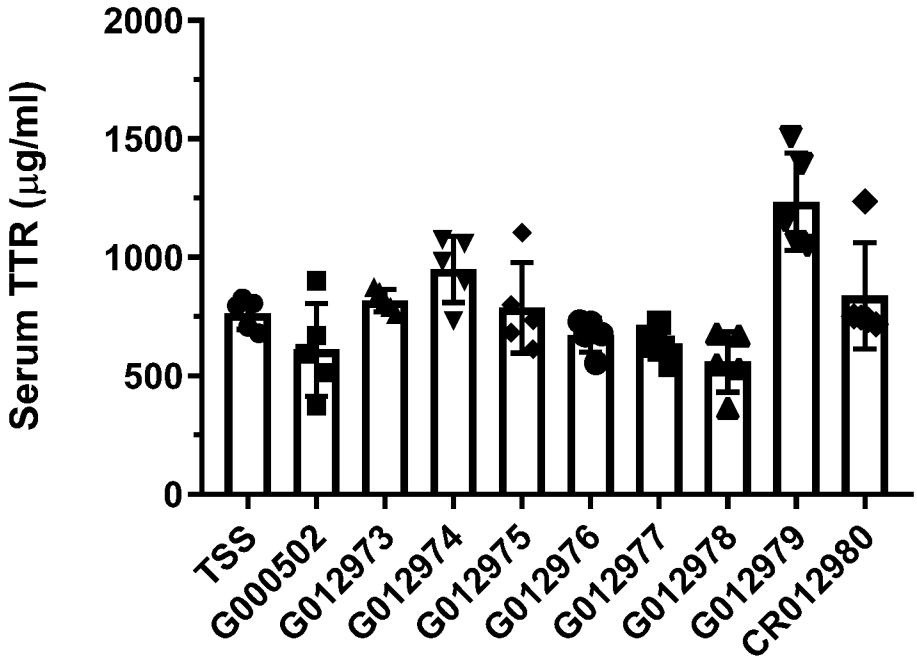


Fig. 24B

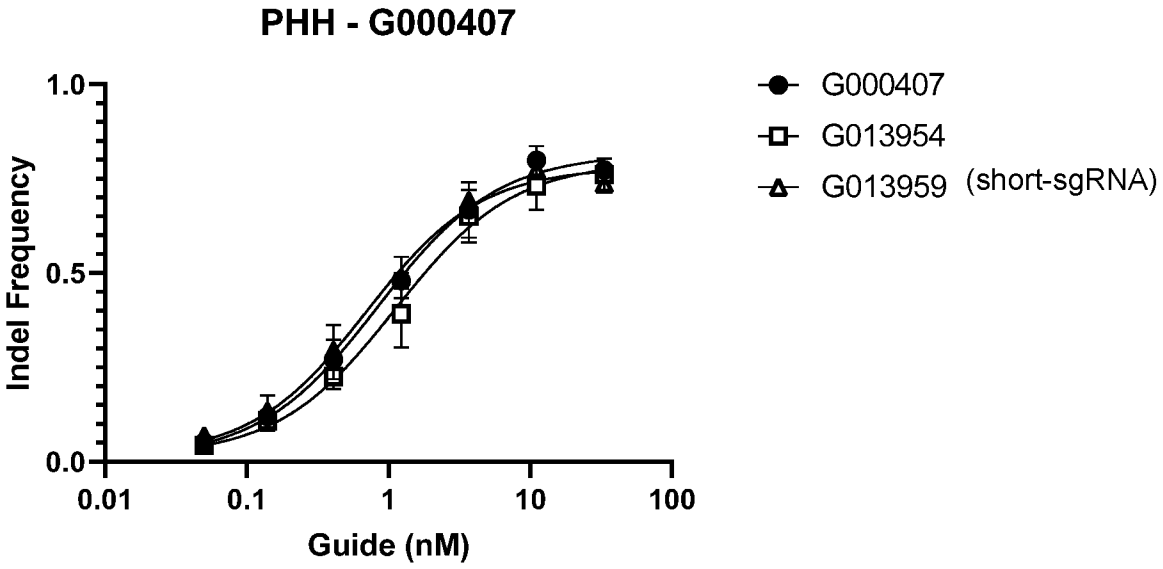


Fig. 25A

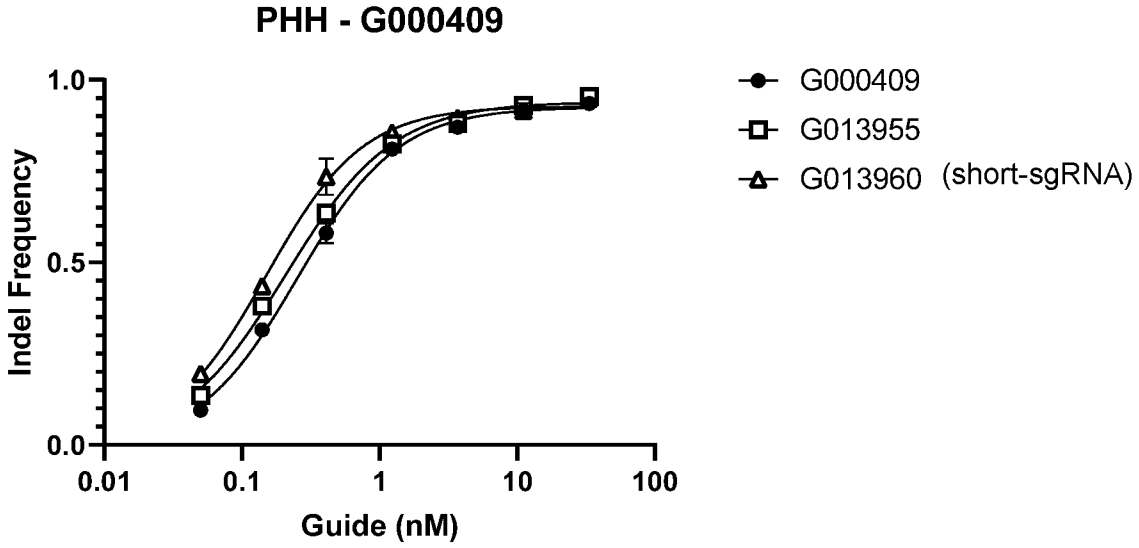


Fig. 25B

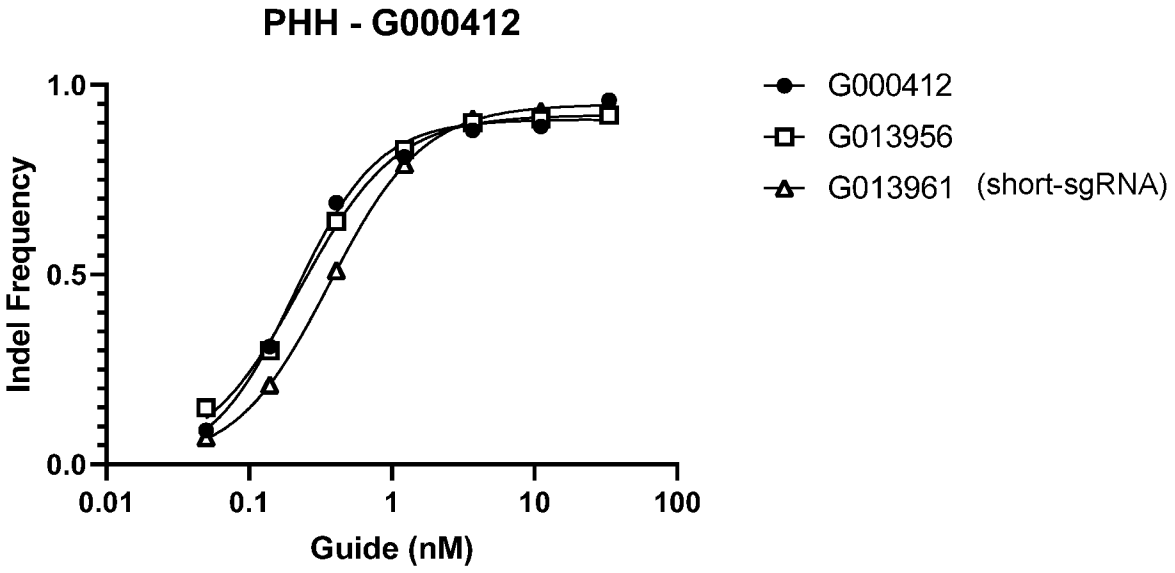


Fig. 25C

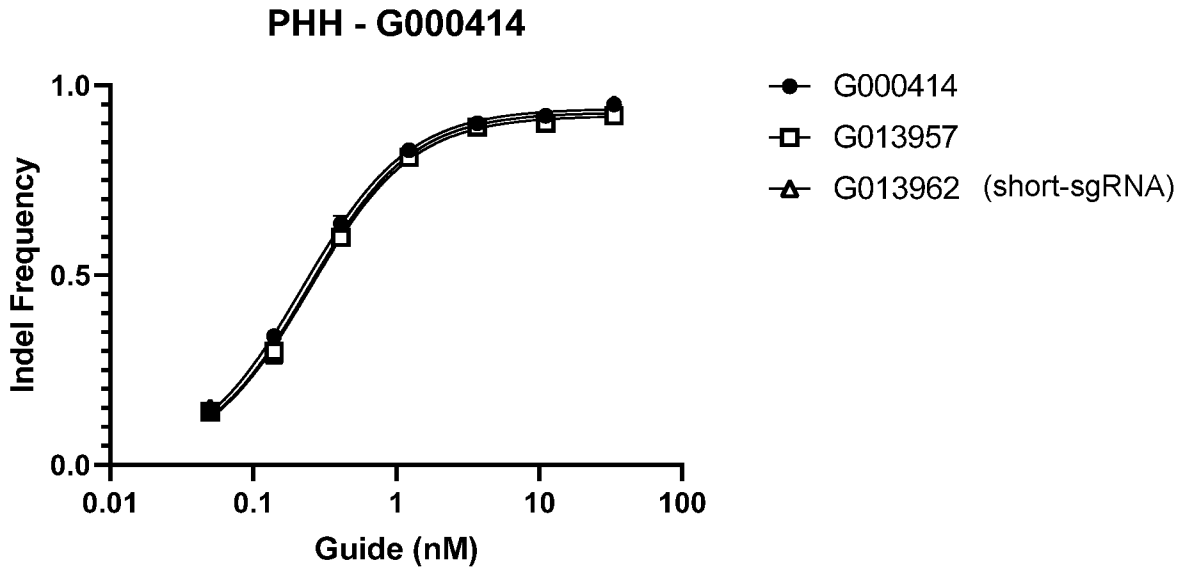


Fig. 25D

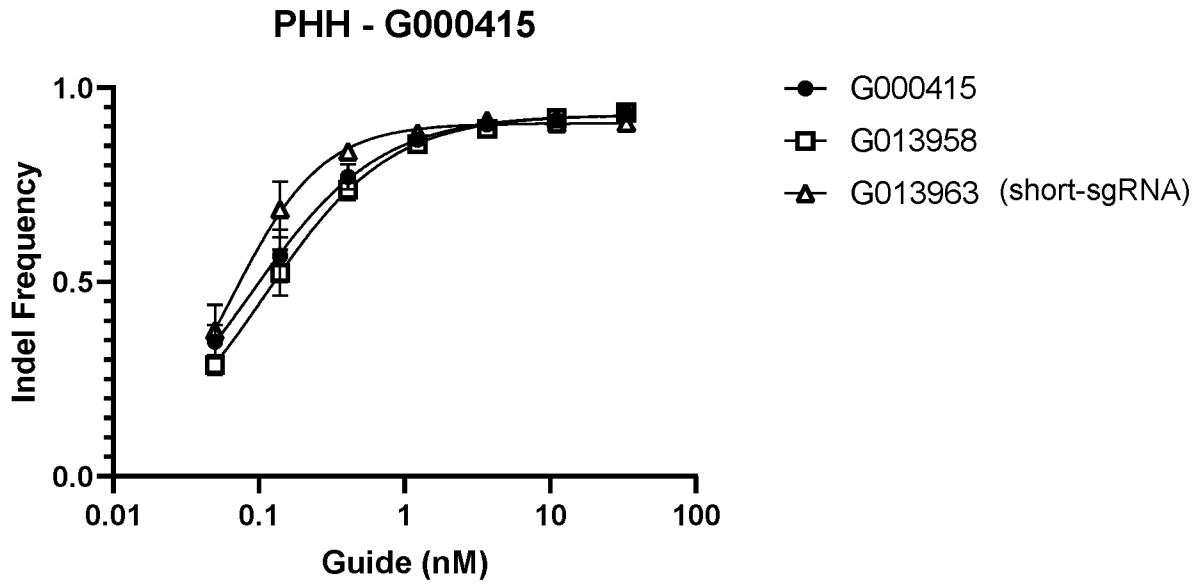


Fig. 25E

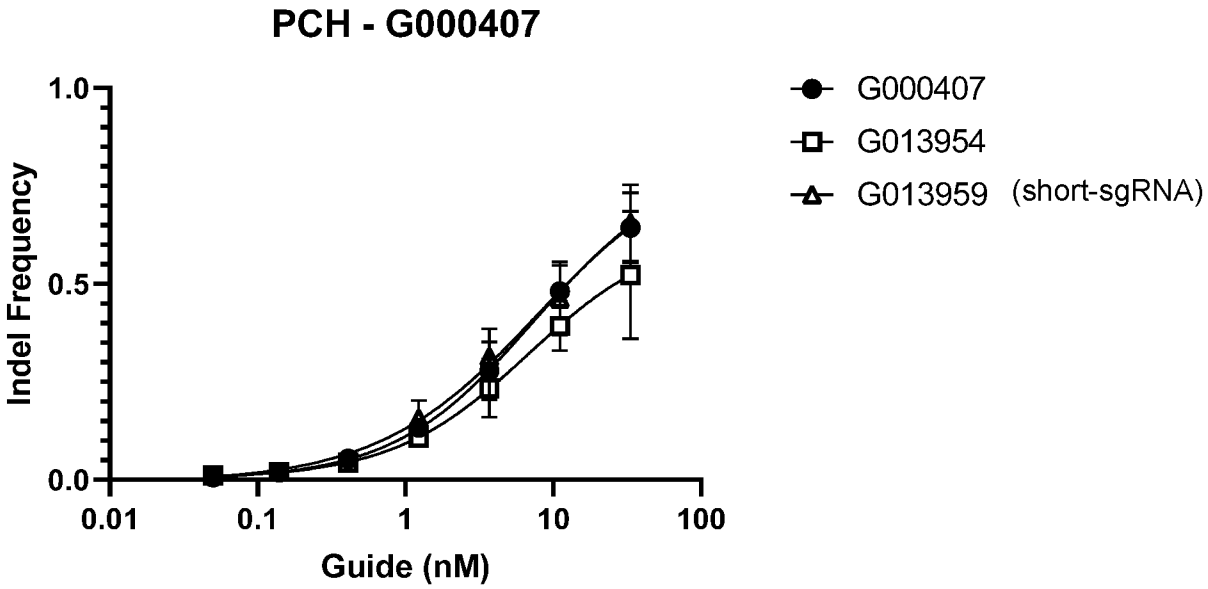


Fig. 26A

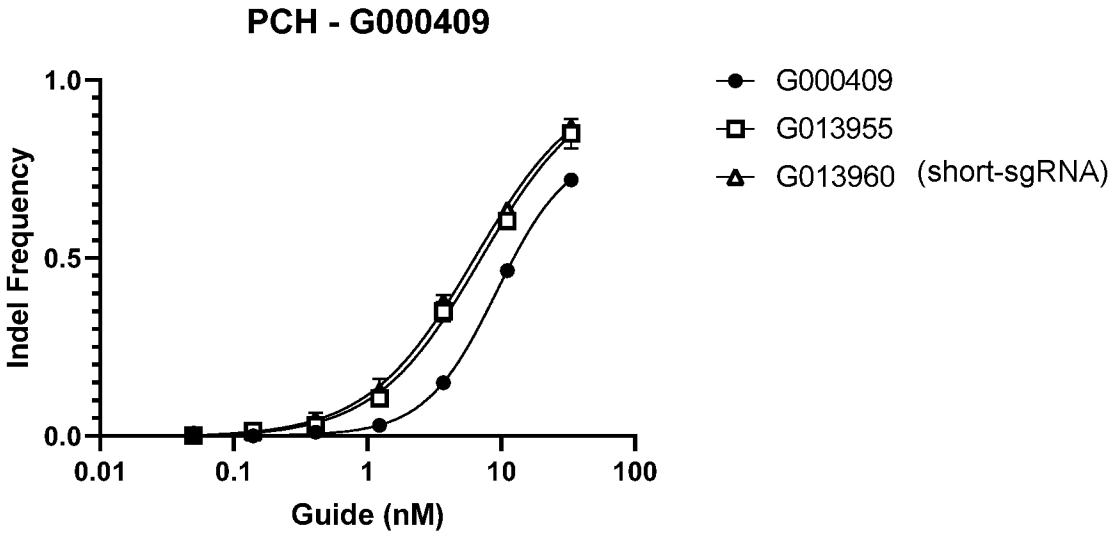


Fig. 26B

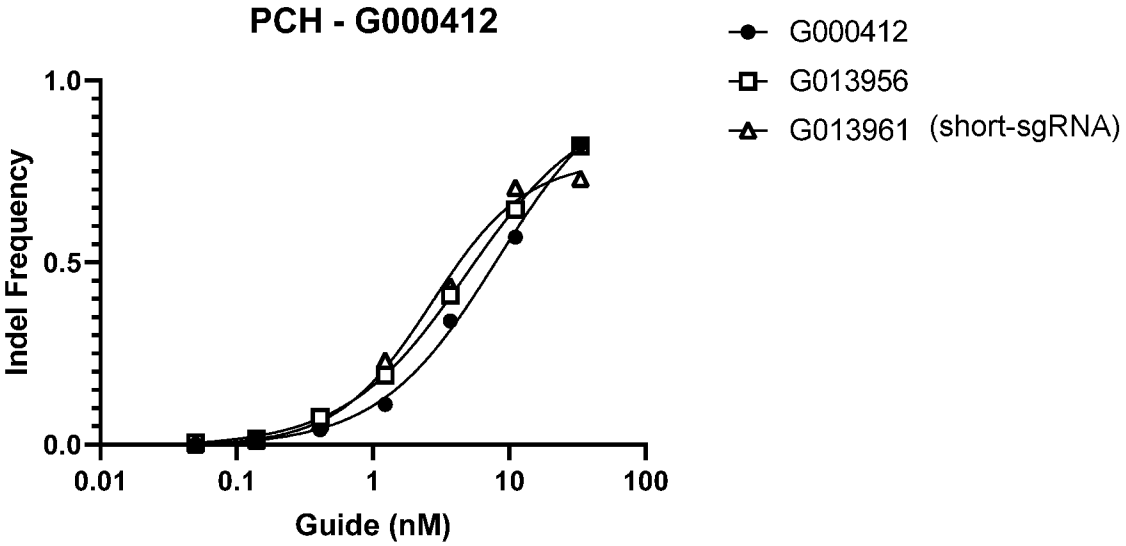


Fig. 26C

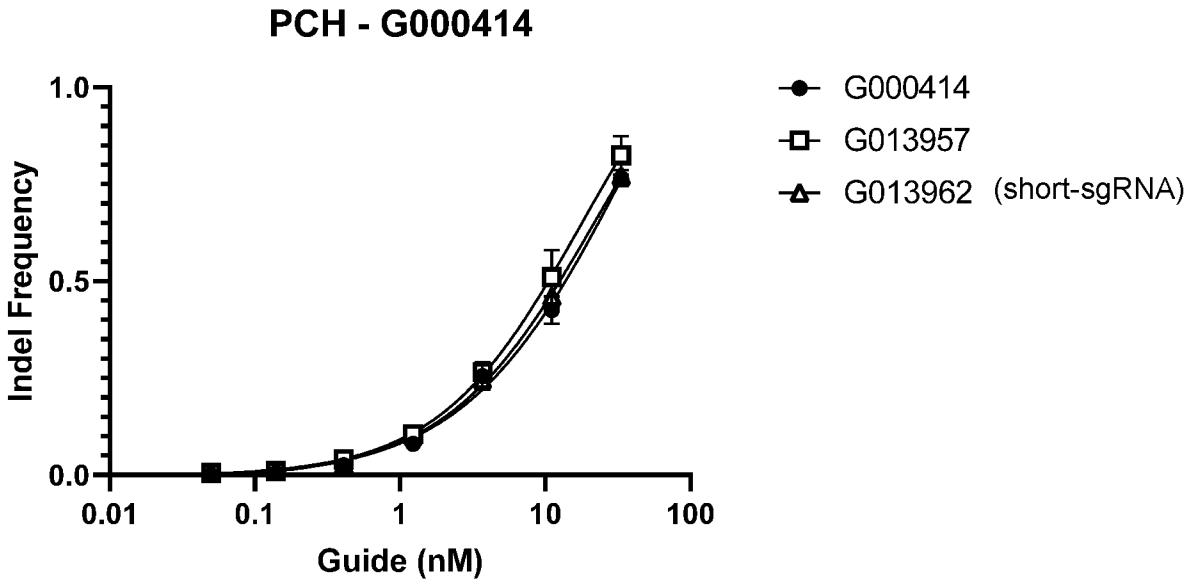


Fig. 26D

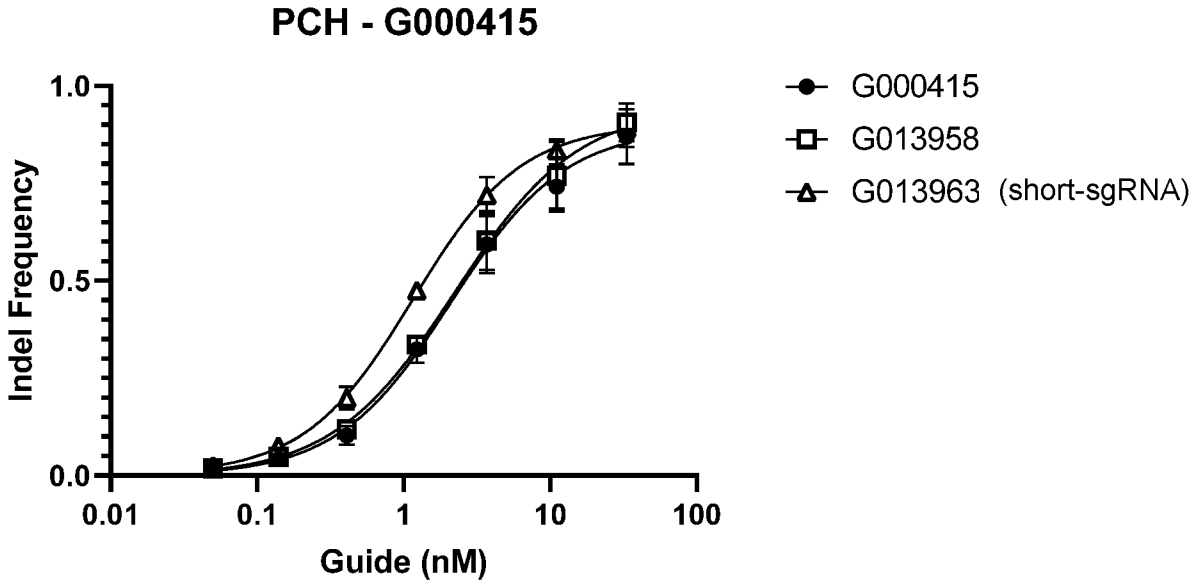


Fig. 26E

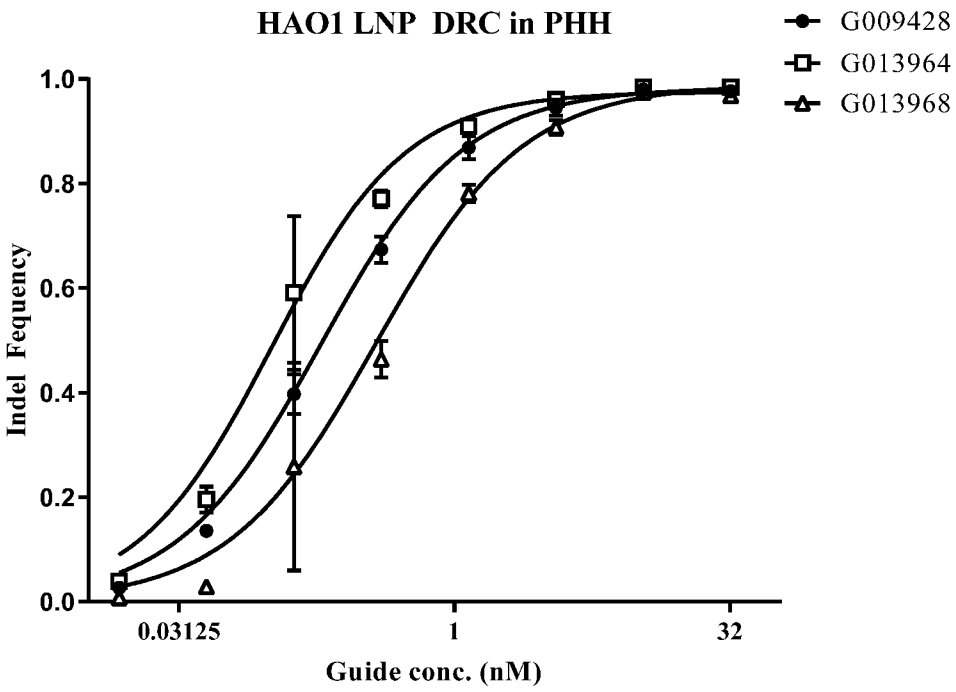


Fig. 27A

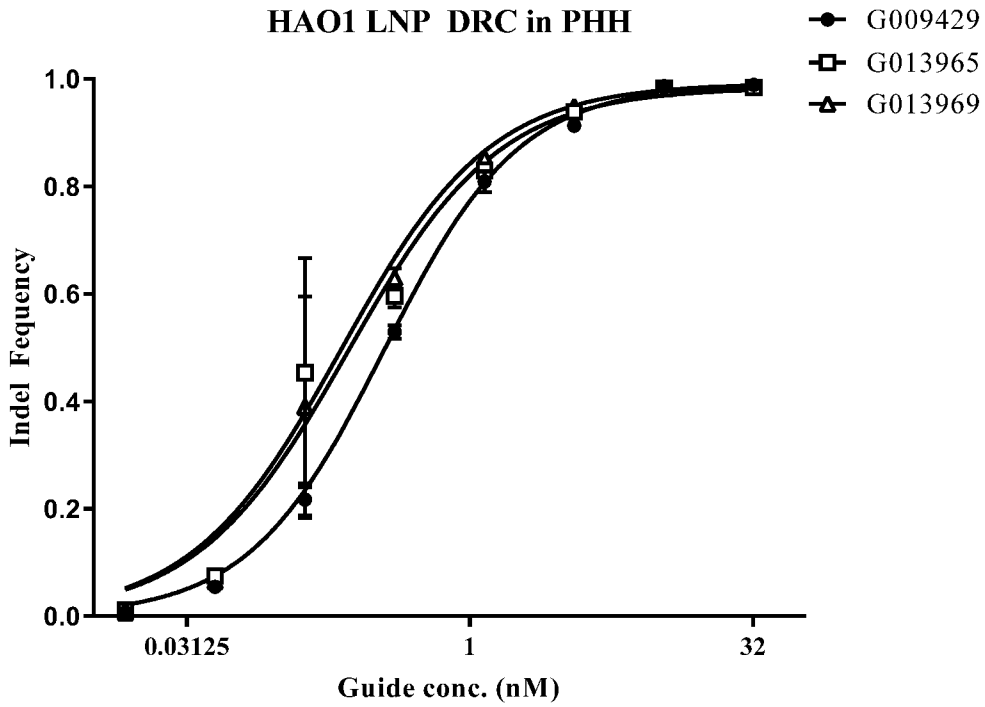


Fig. 27B

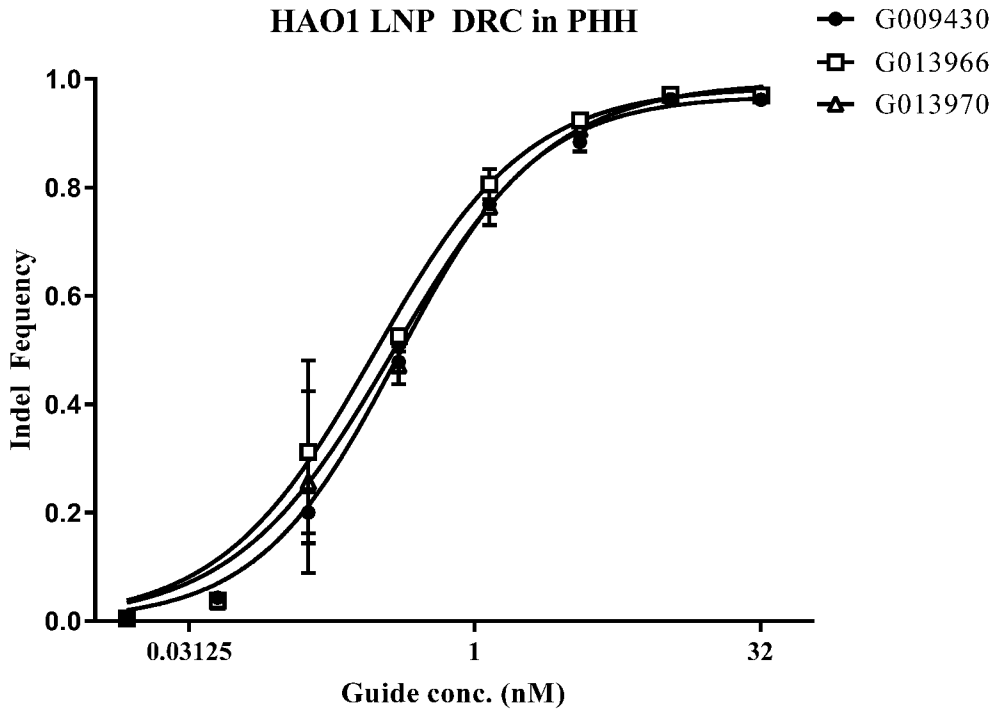


Fig. 27C

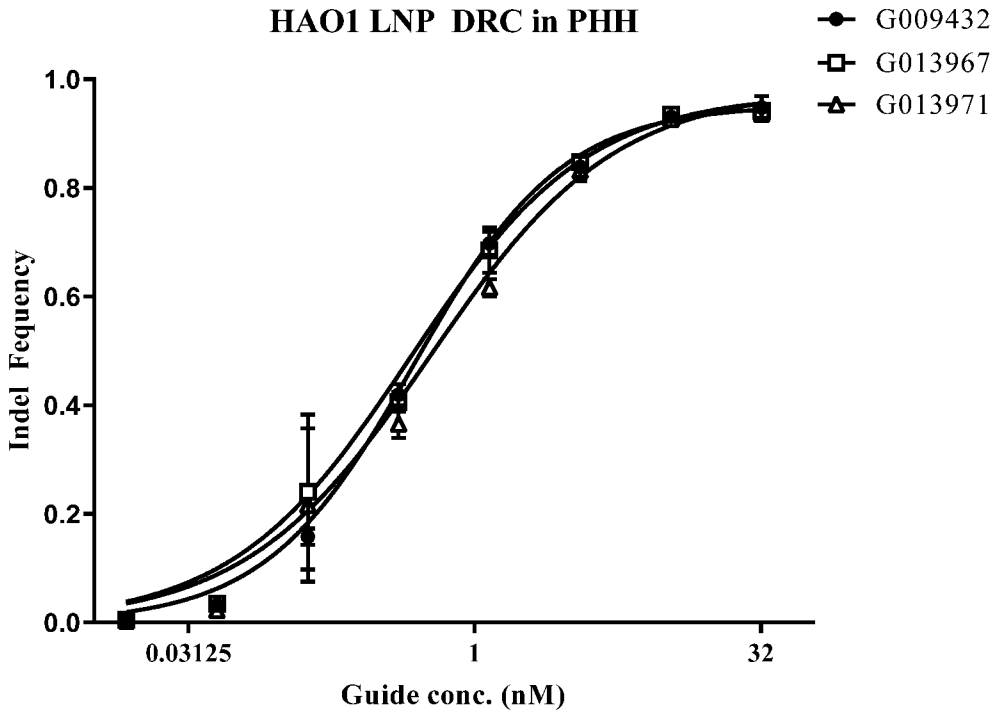


Fig. 27D

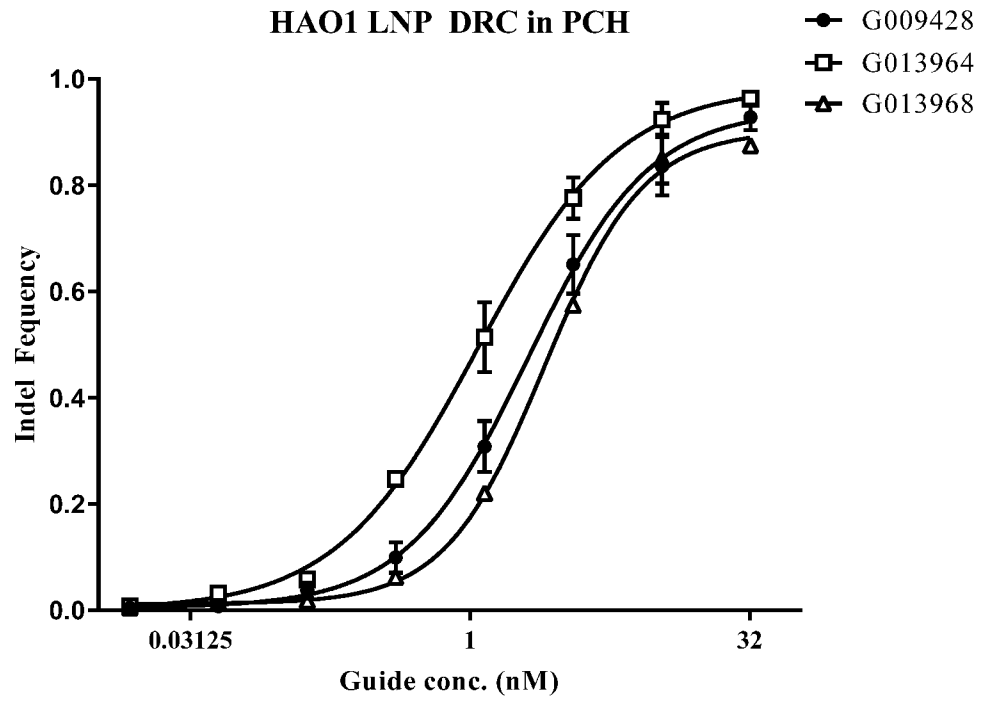


Fig. 28A

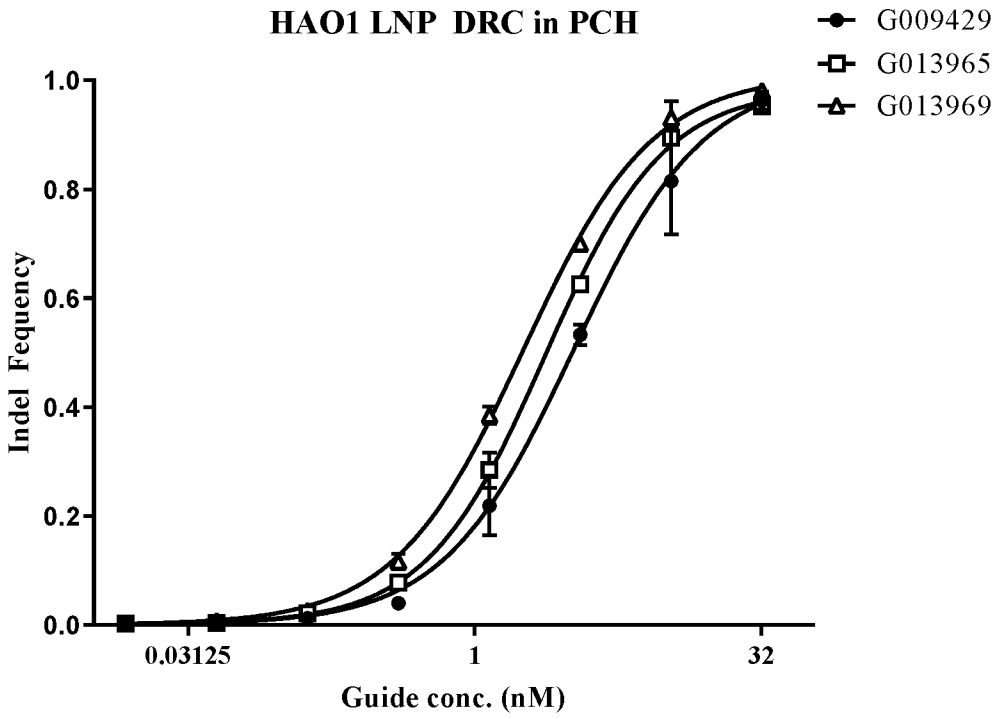


Fig. 28B

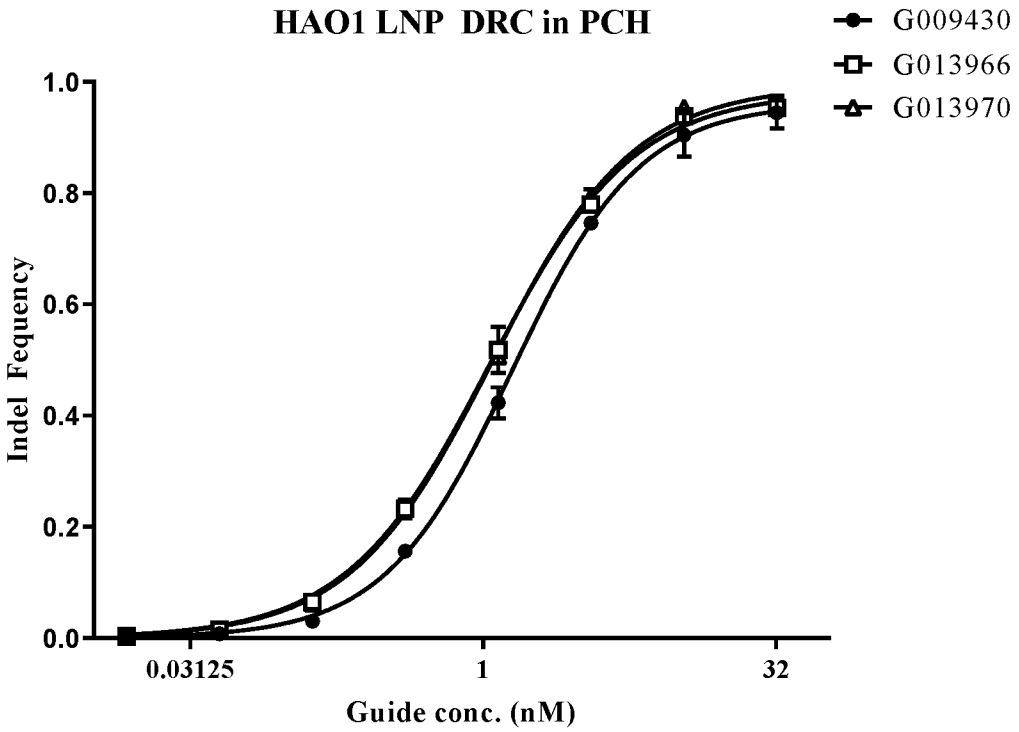


Fig. 28C

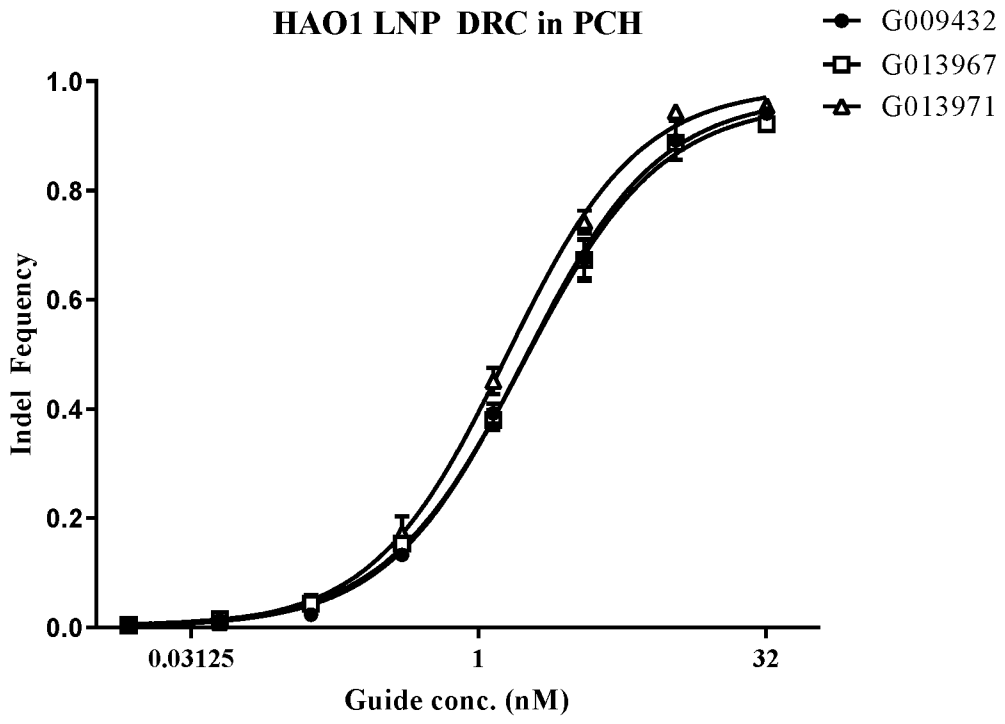


Fig. 28D

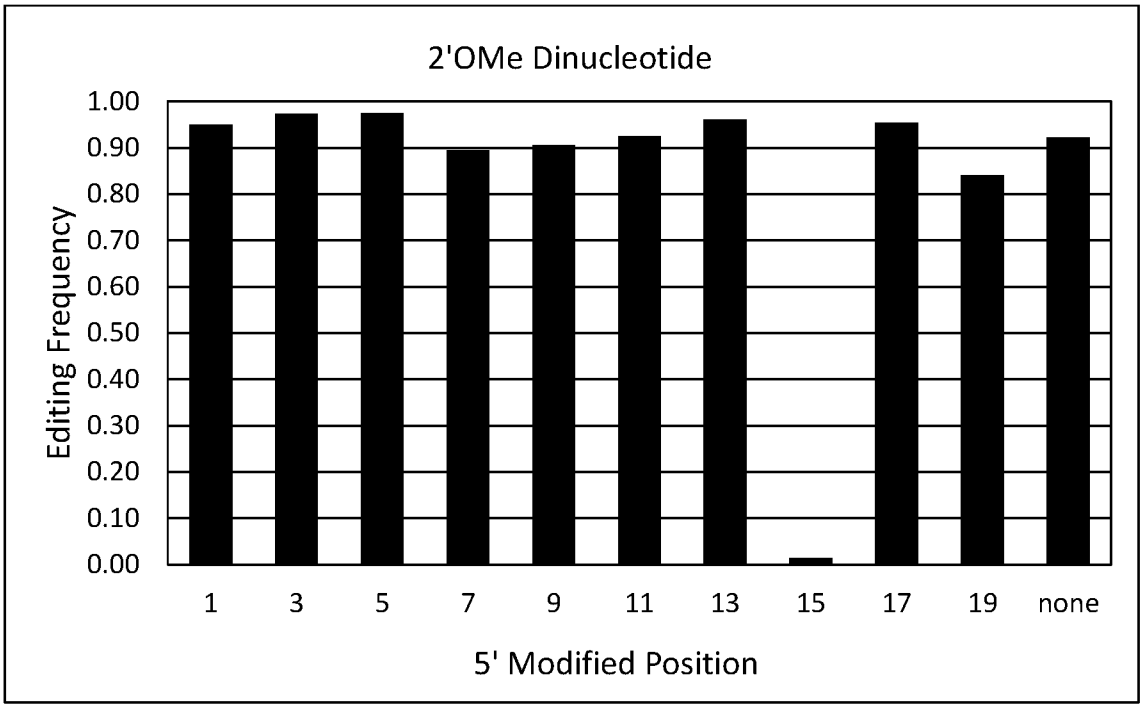


Fig. 29A

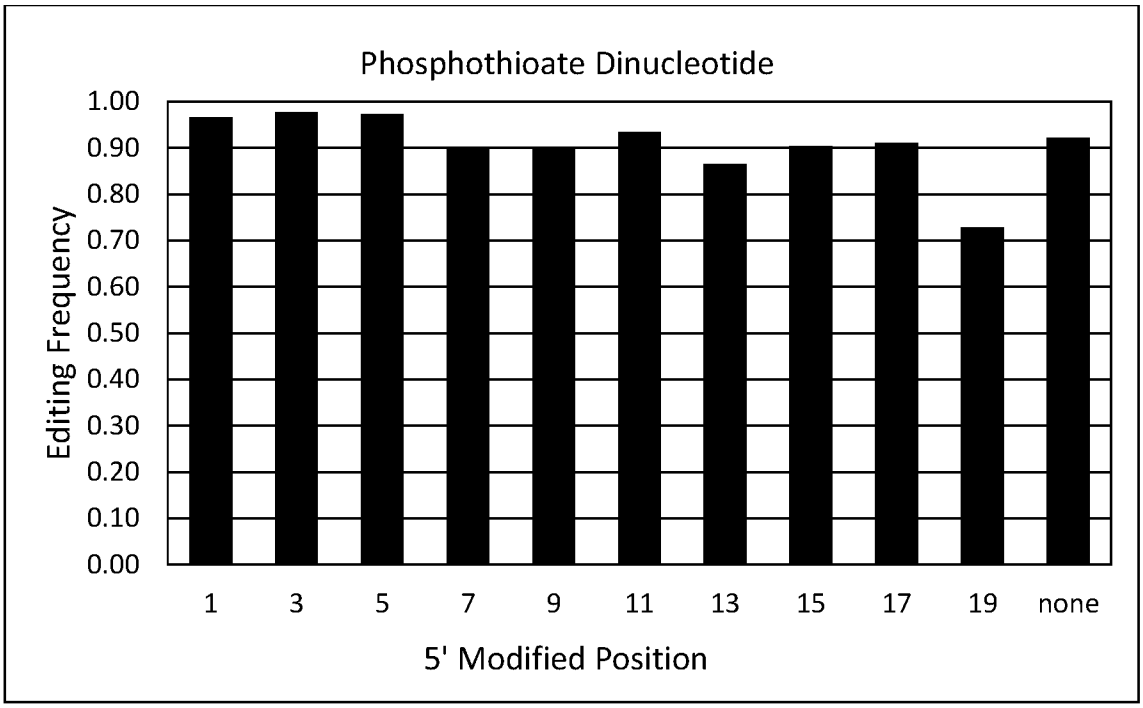


Fig. 29B

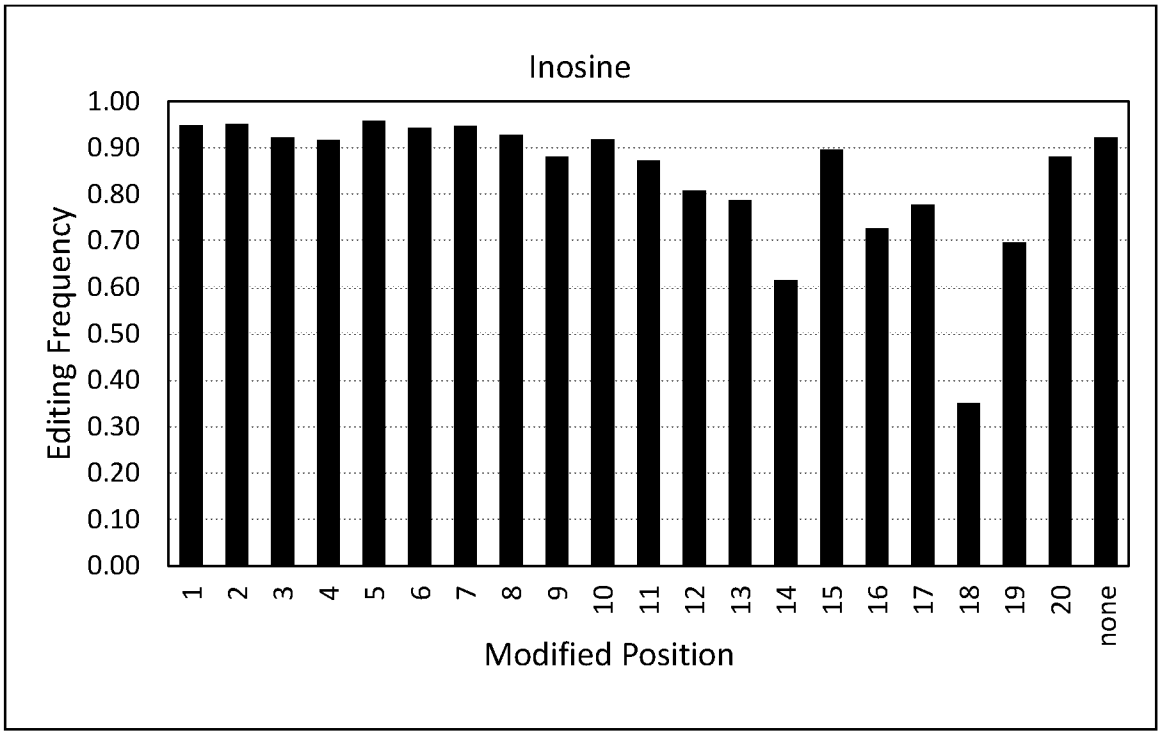


Fig. 29C

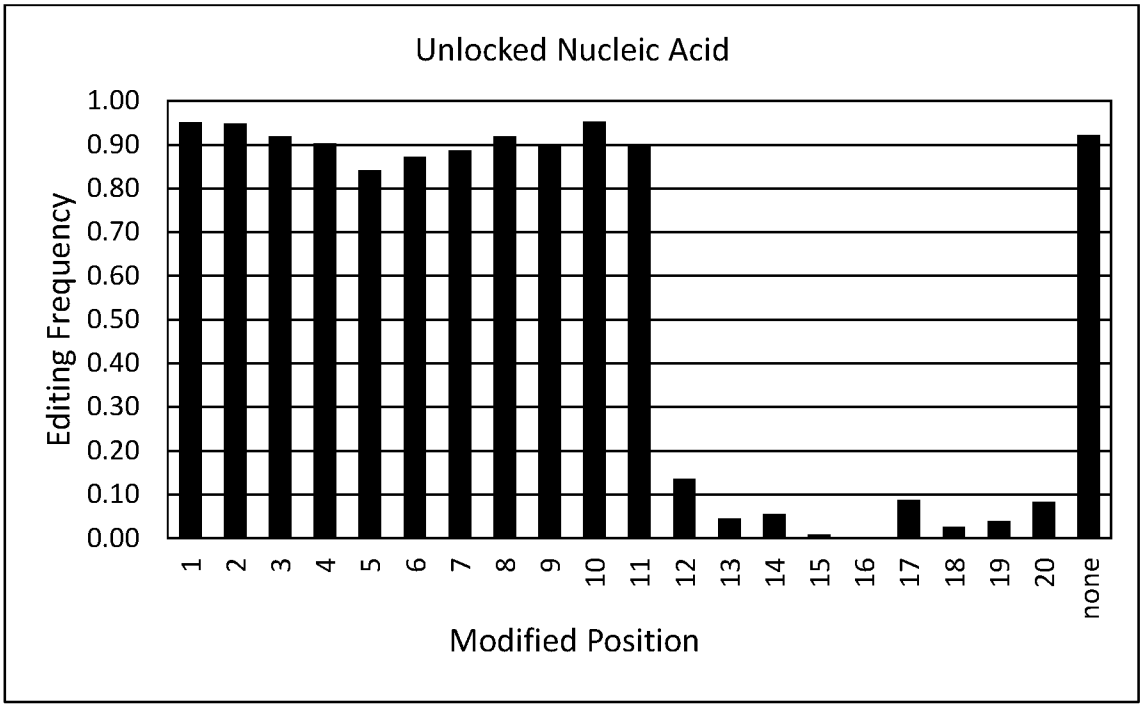


Fig. 29D

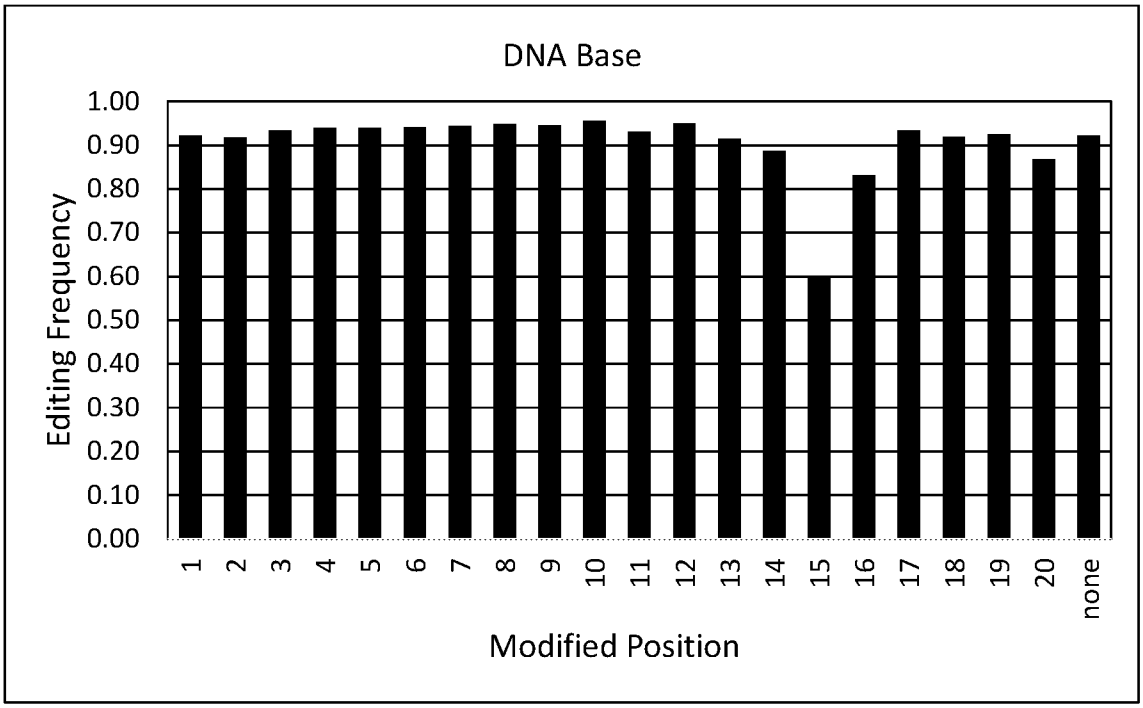


Fig. 29E

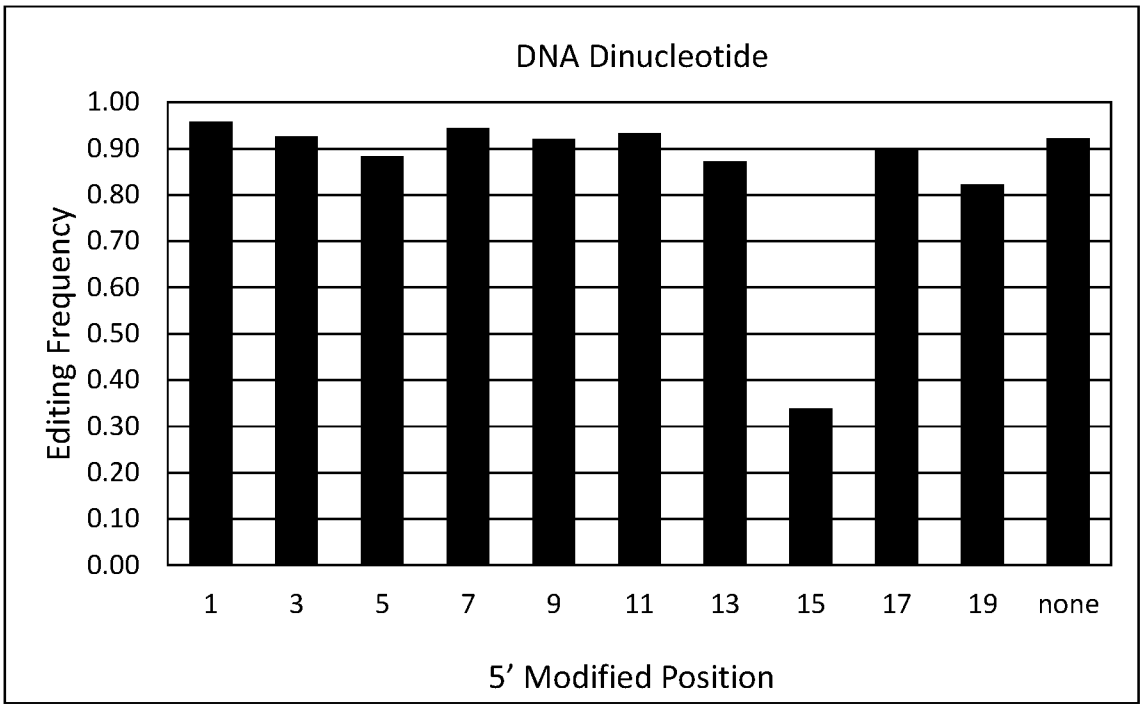


Fig. 29F

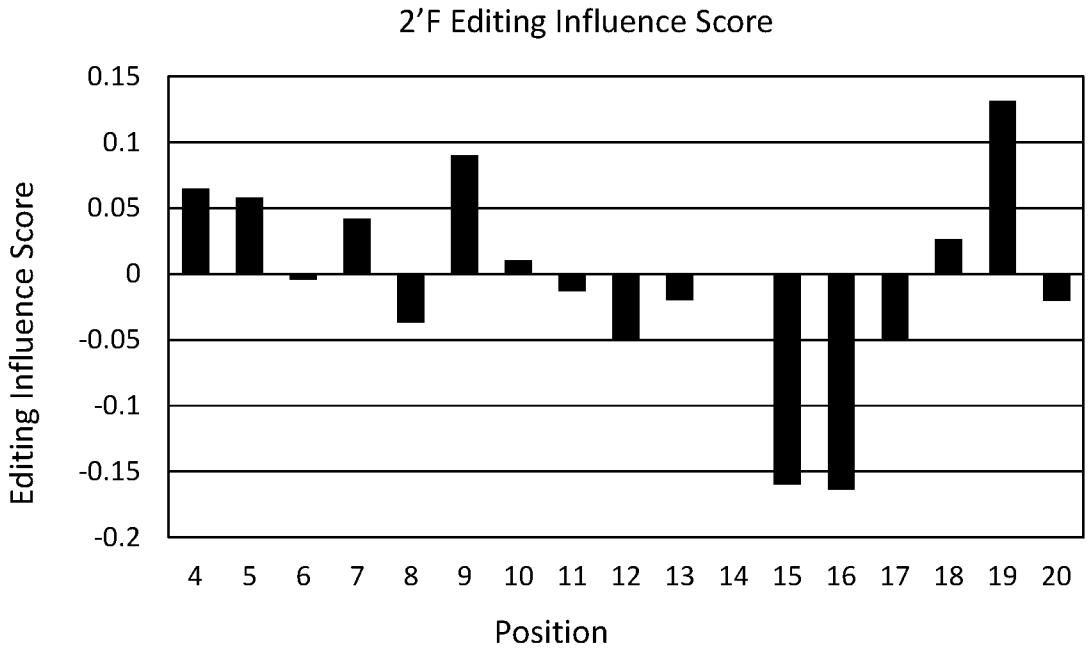


Fig. 30A

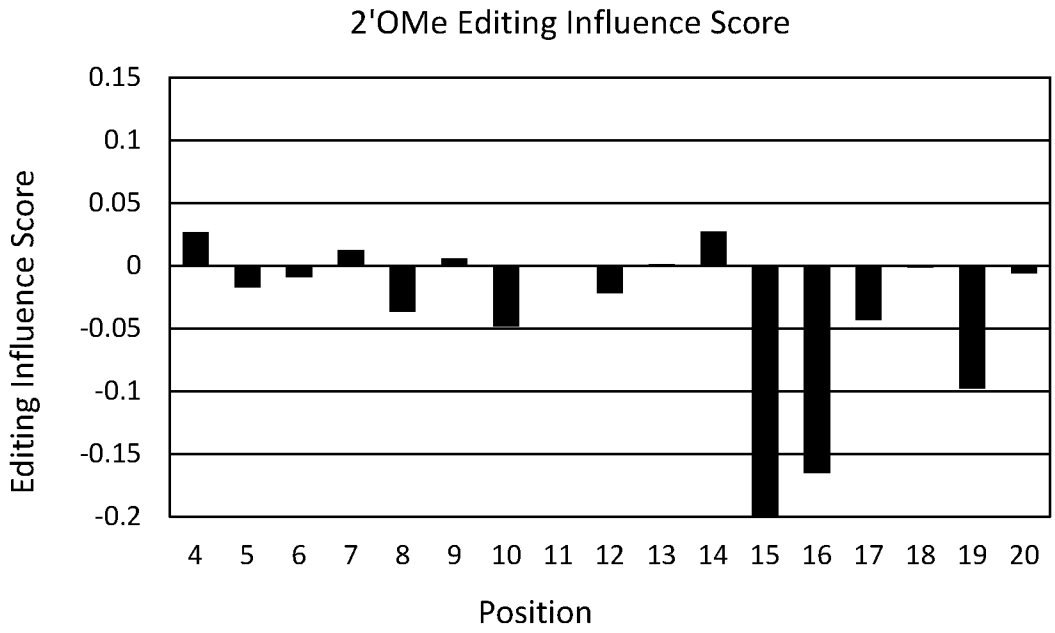


Fig. 30B

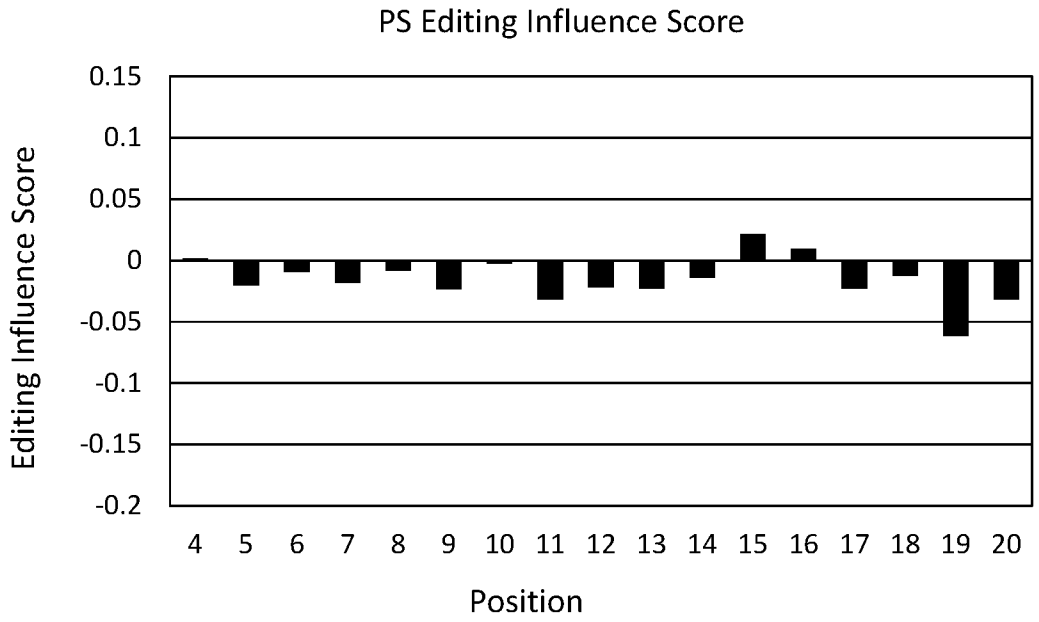

PS Editing Influence Score
Editing Influence Score
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0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Position

Fig. 30C

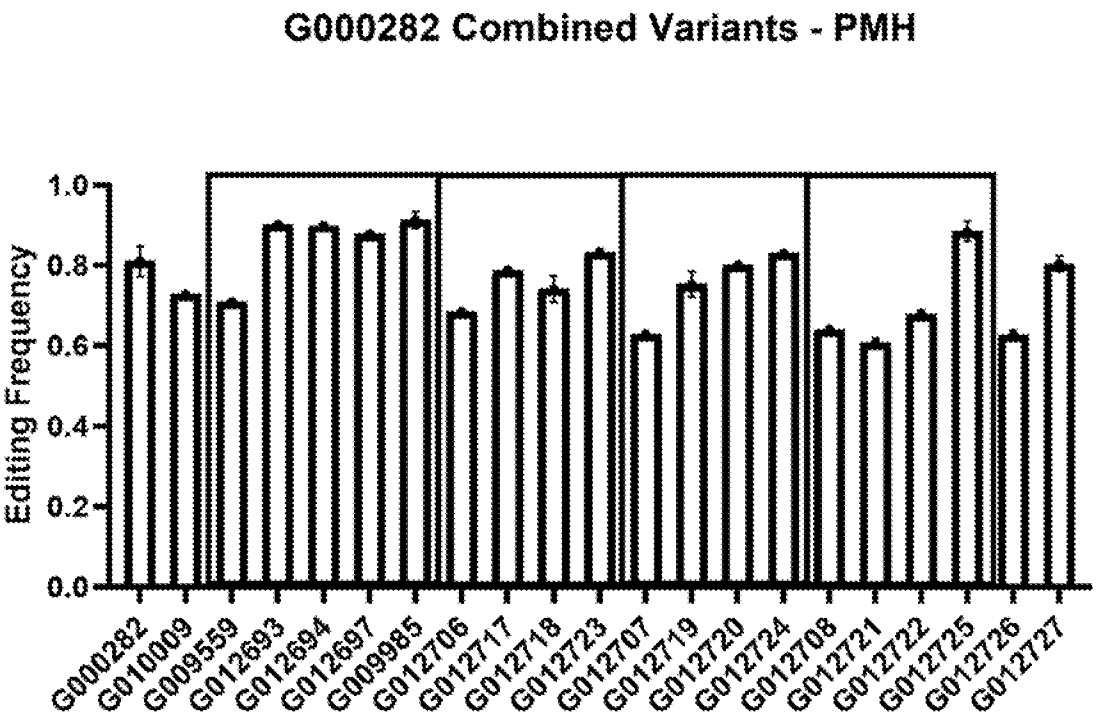


Fig. 31A

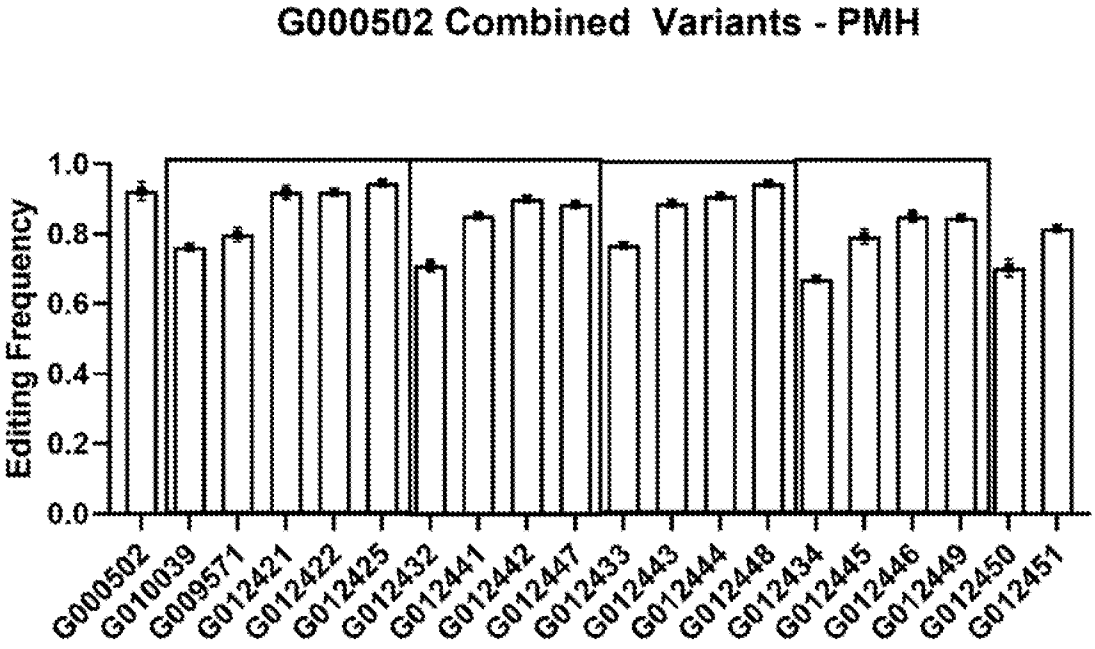


Fig. 31B

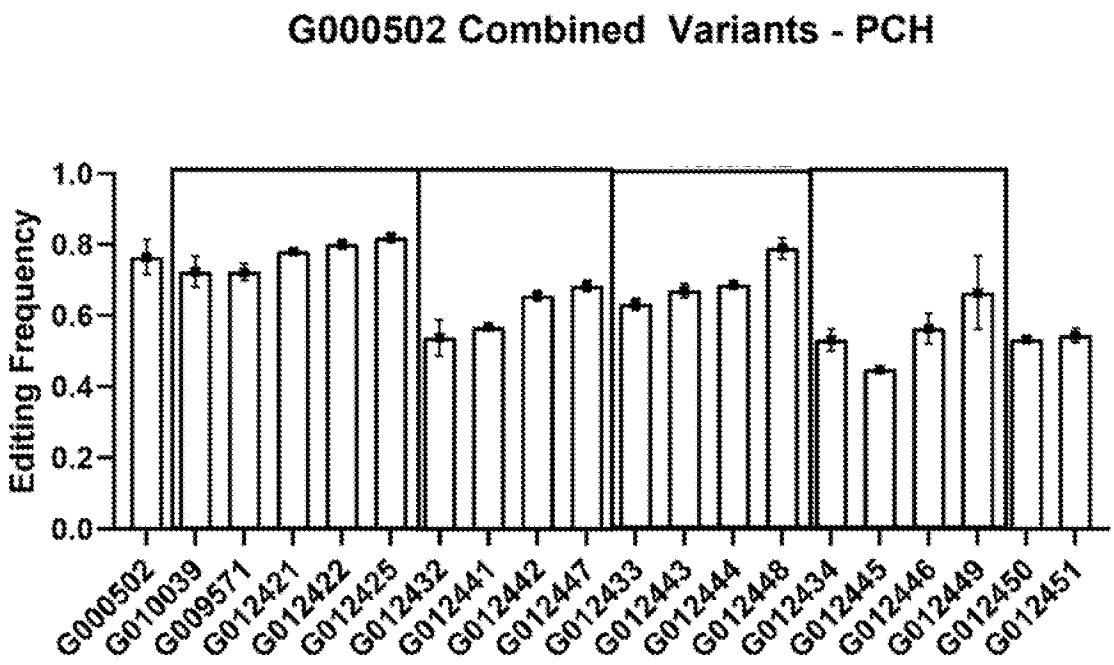

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G012445
G012446
G012449
G012450
G012451

Fig. 31C

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 19/36160

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12N 15/113; C12Q 1/68 (2019.01)
CPC - C12N 15/111; C12N 15/113; C12N 9/22; C12N 2310/20; C12N 2310/315; C12N 2310/321; C12N 2310/531; C07H 21/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	YIN et al. Structure-guided chemical modification of guide RNA enables potent non-viral in vivo genome editing. Nat Biotechnol December 2017, Vol 35, No 12, Pages 1179-1187. Especially pg 1181 fig 1C, pg 1182 fig 2A, pg 1183 fig 3.	152-165, 276-280, 283
X ---- Y	WO 2017/173054 A1 (INTELLIA THERAPEUTICS, INC.) 5 October 2017 (05.10.2017). Especially pg 103 Example 14 para [260], SEQ ID NO: 6	374, 375 ---------- 97, 98
Y	BRINER et al. Guide RNA functional modules direct Cas9 activity and orthogonality. Mol Cell, 23 October 2014, Vol 56, No 2, Pages 333-339. Especially pg 335 col 1 para 1, pg 334 Fig 1A.	1-3, 49-51, 86-88, 97, 98
Y	US 2016/0289675 A1 (AGILENT TECHNOLOGIES, INC.) 6 October 2016 (06.10.2016). Especially para [0021], [0045], [0062], [0067], [0074], [0075], [0076], [0271], sheet 13 fig 10.	1-3, 49-51, 86-88

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search
2 October 2019

Date of mailing of the international search report
28 OCT 2019

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Authorized officer:
Lee W. Young
PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 19/36160

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☒ forming part of the international application as filed:

      ☒ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:
GenCore ver 6.4.1 SEQ ID NO: 1 was searched

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 19/36160

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 4-48, 53-85, 89-96, 99-151, 162-275, 281, 282, 284-373, 376-468
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
-----Go to Extra Sheet for continuation-----

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
1-3, 49-51, 86-88, 97-98, limited to SEQ ID NO: 1 and claims 152-165, 276-280, 283, 374-375

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 19/36160

Continuation of Box III: Observations where Unity of Invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I+: Claims 1-3, 49-51, 86-88, 97, 98, drawn to a short-single guide (short-sgRNA) comprising a hairpin region that lacks at least 5-10 nucleotides. The short-sgRNA will be searched to the extent that it encompasses the first named short-sgRNA, SEQ ID NO: 1 (claims 97, 98). It is believed that claims 1-3, 49-51, 86-88, 97-98 read on this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 1. Additional short sg-RNAs will be searched upon payment of additional fees. Applicant must specify the claims that encompass any additional elected short sg-RNAs. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be: SEQ ID NO: 354 (claims 1-3, 49-51, 86-88, 97-98).

Group II: Claims 152-165, 276-280, 283, 374-375, drawn to a single guide RNA (sgRNA) comprising a YA [i.e. pyrimidine-adenine] modification.

The inventions listed as Groups I+ and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Technical Features:

Group I+ has the special technical features of a short-sgRNA comprising a hairpin region that lacks at least 5-10 nucleotides, not required by Group II.

Group II has the special technical feature of a sgRNA comprising full hairpin structures (i.e. hairpin-1 and hairpin-2 [see instant application sheet 19 fig 10A, for instance]), not required by Group I+.

Group II has the special technical feature of sgRNAs comprising at least one Y/A modification [i.e., see instant application sheet 20 fig 10B, for instance], not required by Group I+.

No technical features are shared between the polynucleotide sequences of Group I+ and, accordingly, these groups lack unity a priori.

Additionally, even if Groups I+ inventions and Group II were considered to share the technical features of:

1. Group I+ claims share the common technical features of claims 1, 49, 86, 97, 98.

2. Groups I and II share the common technical feature of a sgRNA having a chemical modification, e.g., in a hairpin or stem region.

these shared technical features are previously disclosed by the publication titled "Guide RNA functional modules direct Cas9 activity and orthogonality" by Briner et al. (hereinafter "Briner") [published 23 October 2014 in Mol Cell Vol 56 No 2 Pages 333-339], in view of US 2016/0289675 A1 to Agilent Technologies, Inc. (hereinafter "Agilent") and WO 2017/173054 A1 to Intellia Therapeutics, Inc. (hereinafter "Intellia").

As to claims 1, 49, 86, Briner discloses a guide RNA (gRNA) which is a short-single guide RNA (short-sgRNA) comprising a conserved portion of an sgRNA comprising a hairpin region, wherein the hairpin region lacks at least 5-10 nucleotides (pg 335 col 1 para 1; "Hairpin 1 can be removed from the sgRNA backbone as long as it is replaced by two nucleotides, presumably to enable appropriate spacing between the nexus and hairpin 2 (Figure S1, GVs 79-81)"; also see pg 334 Fig 1A for illustration of sgRNA structural modules). Briner does not disclose that the short-sgRNA comprises a 5' end modification or a 3' end modification. However, 3' and 5' end modifications where well-known in the art, as for example, disclosed by Agilent (para [0062]; "In certain embodiments, the modifications are located at the 5' end, at the 3' end"; para [0271]; The modifications that were tested and found to be tolerated at specific positions include 2'-O-methylribonucleotide (=2'OMe), 2'-deoxyribonucleotide, racemic phosphorothioate internucleotide linkage(s) (=P(S))",para [0021]; "This invention is based, at least in part, on an unexpected discovery that certain chemical modifications to gRNA are tolerated by the CRISPR-Cas system. In particular, certain chemical modifications believed to increase the stability of the gRNA, to alter the thermostability of a gRNA hybridization interaction, and/or to decrease the off-target effects of Cas:gRNA complexation do not substantially compromise the efficacy of Cas:gRNA binding to, nicking of, and/or cleavage of the target polynucleotide").

As to claim 49, Agilent further discloses one or more modification i. the upper stem region, or ii. The hairpin 1 region or iii. The hairpin 2 region (para [0175]; "the disclosed modifications are in the stem sequence of the crRNA... In certain embodiments, the disclosed modifications are in the stem sequence of the tracrRNA segment. [note: crRNA comprises left side of Briner Fig 1A lower and upper stem and the tracrRNA segment comprises the right side of Briner Fig 1A lower and upper stem).

----continued on next sheet------

continued from previous sheet

As to claim 86, Agilent further discloses one or more modifications in any one or more of:
i. at least one modification in the upper stem region; and ii. a 3' tail (para [0175]; "the disclosed modifications are in the stem sequence of the crRNA ... In certain embodiments, the disclosed modifications are in the stem sequence of the tracrRNA segment. [note: crRNA comprises left side of Briner Fig 1A lower and upper stem and the tracrRNA segment comprises the right side of Briner Fig 1A lower and upper stem).

As to claims 97 and 98, Briner, in view of Intellia discloses a guide RNA which is a short-sgRNA (Briner pg 335 col 1 para 1) comprising any of SEQ ID No: 1 (Intellia SEQ ID NO: 6; nt 1-100 100% sequence identity).

As the common technical features were known in the art at the time of the invention, they cannot be considered shared special technical features that would otherwise unify the groups. The inventions lack unity with one another.

Therefore, Groups I+ and II lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Note concerning claim 154: Claim 154 claim limitation (iii) omits the second YA site modification "a YA modification at one or more of conserved region YA sites 1 and [???]". For the purposes of the International Search & Opinion, the omitted YA site is interpreted to be YA site 8 ""a YA modification at one or more of conserved region YA sites 1 and 8", because numerous other independent claims 156-158 provide such an option.

Item 4 (continued): Claims 4-48, 53-85, 89-96, 99-151, 162-275, 281, 282, 284-373, 376-468 are multiple dependent claims and are not drafted according to the second and third sentences of PCT Rule 6.4(a).