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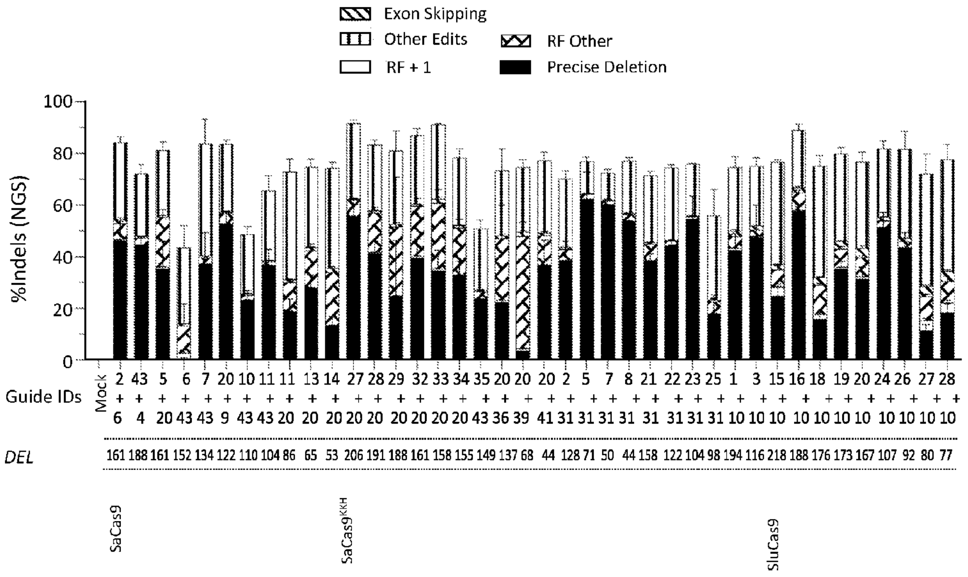

Fig. 1

(57) Abstract: Compositions and methods for treating Duchenne Muscular Dystrophy (DMD) and excising small portions of exons 44, 50, and 53 of the DMD gene are encompassed.

[Continued on next page]

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PRECISE EXCISIONS OF PORTIONS OF EXON 44, 50, AND 53 FOR TREATMENT OF DUCHENNE MUSCULAR DYSTROPHY

[0001] This application claims the benefit of priority to United States Provisional Application No. 63/317,818, filed March 8, 2022, and United States Provisional Application No. 63/374,887, filed September 7, 2022, both of which are incorporated herein by reference in their entirety.

[0002] The instant application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on March 6, 2023, is named 01245-0034-00PCT_Sequence_Listing and is 2,227,275 bytes in size.

INTRODUCTION AND SUMMARY

[0003] Muscular dystrophies (MD) are a group of more than 30 genetic diseases characterized by progressive weakness and degeneration of the skeletal muscles that control movement. Duchenne muscular dystrophy (DMD) is one of the most severe forms of MD that affects approximately 1 in 5000 boys and is characterized by progressive muscle weakness and premature death. Cardiomyopathy and heart failure are common, incurable and lethal features of DMD. The disease is caused by mutations in the gene encoding dystrophin (*DMD*), which result in loss of expression of dystrophin, causing muscle membrane fragility and progressive muscle wasting.

[0004] CRISPR-based genome editing can provide sequence-specific cleavage of genomic DNA using a Cas9 and a guide RNA. For example, a nucleic acid encoding the Cas9 enzyme and a nucleic acid encoding for the appropriate guide RNA can be provided on separate vectors or together on a single vector and administered *in vivo* or *in vitro* to knockout or correct a genetic mutation, for example. The approximately 20 nucleotides at the 5′ end of the guide RNA serves as the guide or spacer sequence that can be any sequence complementary to one strand of a genomic target location that has an adjacent protospacer adjacent motif (PAM). The PAM sequence is a short sequence adjacent to the Cas9 nuclease cut site that the Cas9 molecule requires for appropriate binding. The nucleotides 3' of the guide or spacer sequence of the guide RNA serve as a scaffold sequence for interacting with Cas9. When a guide RNA and a Cas9 are expressed, the guide RNA will bind to Cas9 and direct it to the sequence complementary to the guide sequence, where it will then initiate a double-stranded break (DSB). To repair these breaks, cells typically use an error prone mechanism of non-homologous end joining (NHEJ) which can lead to disruption of function in the target gene through insertions or deletion of codons, shifts in the reading frame, or result in a premature stop codon triggering nonsense-mediated decay. *See*, e.g., Kumar et al. (2018) Front. Mol. Neurosci. Vol. 11, Article 413.

[0005] While gene editing strategies using systems (e.g., CRISPR) for treating DMD have been previously explored, these strategies have focused primarily on either: a) cutting at multiple different sites to excise large portions (e.g., one or more exons) of the dystrophin gene (see, e.g., Ousterout et al., 2015, Nat Commun. 6:6244); or b) cutting in a single site to introduce indels that either result in a frame-shifting mutation and/or that destroy a splice acceptor/donor site in the dystrophin gene (see, e.g., Amoassi et al., 2018, Science, 362(6410):86-91). However, there remains a need for additional alternative and effective gene editing strategies for treating diseases like DMD.

[0006] Provided herein are compositions and methods for treating DMD utilizing Cas proteins such as *Staphylococcus aureus* (SaCas9) and *Staphylococcus lugdunensis* (SluCas9). In some embodiments, pairs of guide RNAs that excise small portions of the DMD gene are provided, where the nucleic acid encoding the pairs of guide RNAs may be on a single nucleic acid molecule.

[0007] Accordingly, the following non-limiting embodiments are provided.

Embodiment 1 is a composition comprising one or more guide RNAs or a nucleic acid encoding one or more guide RNAs, wherein the one or more guide RNAs comprise i) a guide sequence of **Table 6**; ii) at least 16, 17, 18, 19, or 20 contiguous nucleotides of a guide sequence of **Table 6**; iii) a guide sequence that is at least 90% identical to a guide sequence of **Table 6**; or iv) any one of the guide sequence pairs shown in **Tables 1B**, **1D**, **3B**, **3D**, **5B**, and **5D**, optionally further comprising a SaCas9 or a nucleic acid encoding a SaCas9 (for SEQ ID NOs: 1-159) or a SluCas9 or a nucleic acid encoding a SluCas9 (for SEQ ID NOs: 200-292, 924-938, or 950-955).

Embodiment 2 is a composition comprising a pair of guide RNAs or a nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprise or consist of a first and a second guide sequence, wherein the first and the second guide sequences are selected from any of the following pairs of guide sequences:

a. For exon 44 with SaCas9, SEQ ID NOs: 1 and 3; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and

122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; or 124 and 125;

b. For exon 44 with SluCas9, SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and 203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208;

c. For exon 50 with SaCas9, SEQ ID NOs: 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; or 158 and 159;

d. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232 and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and 239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; or 241 and 242;

e. For exon 53 with SaCas9, SEQ ID NOs: 16 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20; 17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 71 and 72; 71 and 73; 71 and 74; 71 and 75; 71 and 76; 71 and 77; 71 and 78; 71 and 84; 71 and 85; 71 and 86; 71 and 87; 71 and 88; 71 and 89; 71 and 90; 71 and 91; 71 and 92; 71 and 93; 71 and 94; 71 and 95; 71 and 96; 71 and 97; 71 and 98; 71 and 99; 71 and 100; 71 and 101; 71 and 102; 72 and 73; 72 and 74; 72 and 75; 72 and 76; 72 and 77; 72 and 78; 72 and 84; 72 and 85; 72 and 86; 72 and 87; 72 and 88; 72 and 89; 72 and 90; 72 and 91; 72 and 92; 72 and 93; 72 and 94; 72 and 95; 72 and 96; 72 and 97; 72 and 98; 72 and 99; 72 and 100; 72 and 101; 72 and 102; 73 and 74; 73 and 75; 73 and 76; 73 and 77; 73 and 78; 73 and 84; 73 and 85; 73 and 86; 73 and 87; 73 and 88; 73 and 89; 73 and 90; 73 and 91; 73 and 92; 73 and 93; 73 and 94; 73 and 95; 73 and 96; 73 and 97; 73 and 98; 73 and 99; 73 and 100; 73 and 101; 73 and 102; 74 and 75; 74 and 76; 74 and 77; 74 and 78; 74 and 84; 74 and 85; 74 and 86; 74 and 87; 74 and 88; 74 and 89; 74 and 90; 74 and 91; 74 and 92; 74 and 93; 74 and 94; 74 and 95; 74 and 96; 74 and 97; 74 and 98; 74 and 99; 74 and 100; 74 and 101; 74 and 102; 75 and 76; 75 and 77; 75 and 78; 75 and 84; 75 and 85; 75 and 86; 75 and 87; 75 and 88; 75 and 89; 75 and 90; 75 and 91; 75 and 92; 75 and 93; 75 and 94; 75 and 95; 75 and 96; 75 and 97; 75 and 98; 75 and 99; 75 and 100; 75 and 101; 75 and 102; 76 and 77; 76 and 78; 76 and 84; 76 and 85; 76 and 86; 76 and 87; 76 and 88; 76 and 89; 76 and 90; 76 and 91; 76 and 92; 76 and 93; 76 and 94; 76 and 95; 76 and 96; 76 and 97; 76 and 98; 76 and 99; 76 and 100; 76 and 101; 76 and 102; 77 and 78; 77 and 84; 77 and 85; 77 and 86; 77 and 87; 77 and 88; 77 and 89; 77 and 90; 77 and 91; 77 and 92; 77 and 93; 77 and 94; 77 and 95; 77 and 96; 77 and 97; 77 and 98; 77 and 99; 77 and 100; 77 and 101; 77 and 102; 78 and 84; 78 and 85; 78 and 86; 78 and 87; 78 and 88; 78 and 89; 78 and 90; 78 and 91; 78 and 92; 78 and 93; 78 and 94; 78 and 95; 78 and 96; 78 and 97; 78 and 98; 78 and 99; 78 and 100; 78 and 101; 78 and 102; 84 and 85; 84 and 86; 84 and 87; 84 and 88; 84 and 89; 84 and 90; 84 and 91; 84 and 92; 84 and 93; 84 and 94; 84 and 95; 84 and 96; 84 and 97; 84 and 98; 84 and 99; 84 and 100; 84 and 101; 84 and 102; 85 and 86; 85 and 87; 85 and 88; 85 and 89; 85 and 90; 85 and 91; 85 and 92; 85 and 93; 85 and 94; 85 and 95; 85 and 96; 85 and 97; 85 and 98; 85 and 99; 85 and 100; 85 and 101; 85 and 102; 86 and 87; 86 and 88; 86 and 89; 86 and 90; 86 and 91; 86 and 92;

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f. For exon 53 with SluCas9, SEQ ID NOs: 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and 277; 270 and 278; 270 and 279; 270 and 280; 270 and 281; 270 and 282; 270 and 283; 270 and 284; 270 and 285; 270 and 286; 270 and 287; 270 and 288; 270 and 289; 270 and 290; 270 and 291; 270 and 292; 271 and 272; 271 and 273; 271 and 274; 271 and 275; 271 and 276; 271 and 277; 271 and 278; 271 and 279; 271 and 280; 271 and 281; 271 and 282; 271 and 283; 271 and 284; 271 and 285; 271 and 286; 271 and 287; 271 and 288; 271 and 289; 271 and 290; 271 and 291; 271 and 292; 272 and 273; 272 and 274; 272 and 275; 272 and 276; 272 and 277; 272 and 278; 272 and 279; 272 and 280; 272 and 281; 272 and 282; 272 and 283; 272 and 284; 272 and 285; 272 and 286; 272 and 287; 272 and 288; 272 and 289; 272 and 290; 272 and 291; 272 and 292; 273 and 274; 273 and 275; 273 and 276; 273 and 277; 273 and 278; 273 and 279; 273 and 280; 273 and 281; 273 and 282; 273 and 283; 273 and 284; 273 and 285; 273 and 286; 273 and 287; 273 and 288; 273 and 289; 273 and 290; 273 and 291; 273 and 292; 274 and 275; 274 and 276; 274 and 277; 274 and 278; 274 and 279; 274 and 280; 274 and 281; 274 and 282; 274 and 283; 274 and 284; 274 and 285; 274 and 286; 274 and 287; 274 and 288; 274 and 289; 274 and 290; 274 and 291; 274 and 292; 275 and 276; 275 and 277; 275 and 278; 275 and 279; 275 and 280; 275 and

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g. For exon 44 with SluCas9, SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;

h. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;

i. For exon 53 with SaCas9, SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and

j. For exon 53 with SluCas9, SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

Embodiment 3 is a composition comprising: one or more nucleic acid molecules encoding

a. a SaCas9 or SluCas9; and

b. a first guide sequence and a second guide sequence, wherein the first and the second guide sequences are selected from any of the following pairs of guide sequences: SEQ ID NO: 1 and SEQ ID NO: 3; SEQ ID NO: 16 and SEQ ID NO: 17; SEQ ID NO: 16 and SEQ ID NO: 18; SEQ ID NO: 16 and SEQ ID NO: 19; SEQ ID NO: 16 and SEQ ID NO: 20; SEQ ID NO: 16 and SEQ ID NO: 21; SEQ ID NO: 16 and SEQ ID NO: 22; SEQ ID NO: 16 and SEQ ID NO: 23; SEQ ID NO: 16 and SEQ ID NO: 24; SEQ ID NO: 16 and SEQ ID NO: 25; SEQ ID NO: 16 and SEQ ID NO: 26; SEQ ID NO: 17 and SEQ ID NO: 18; SEQ ID NO: 17 and SEQ ID NO: 19; SEQ ID NO: 17 and SEQ ID NO: 20; SEQ ID NO: 17 and SEQ ID NO: 21; SEQ ID NO: 17 and SEQ ID NO: 22; SEQ ID NO: 17 and SEQ ID NO: 23; SEQ ID NO: 17 and SEQ ID NO: 24; SEQ ID NO: 17 and SEQ ID NO: 25; SEQ ID NO: 17 and SEQ ID NO: 26; SEQ ID NO: 18 and SEQ ID NO: 19; SEQ ID NO: 18 and SEQ ID NO: 20; SEQ ID NO: 18 and SEQ ID NO: 21; SEQ ID NO: 18 and SEQ ID NO: 22; SEQ ID NO: 18 and SEQ ID NO: 23; SEQ ID NO: 18 and SEQ ID NO: 24; SEQ ID NO: 18 and SEQ

ID NO: 25; SEQ ID NO: 18 and SEQ ID NO: 26; SEQ ID NO: 19 and SEQ ID NO: 20; SEQ ID NO: 19 and SEQ ID NO: 21; SEQ ID NO: 19 and SEQ ID NO: 22; SEQ ID NO: 19 and SEQ ID NO: 23; SEQ ID NO: 19 and SEQ ID NO: 24; SEQ ID NO: 19 and SEQ ID NO: 25; SEQ ID NO: 19 and SEQ ID NO: 26; SEQ ID NO: 20 and SEQ ID NO: 21; SEQ ID NO: 20 and SEQ ID NO: 22; SEQ ID NO: 20 and SEQ ID NO: 23; SEQ ID NO: 20 and SEQ ID NO: 24; SEQ ID NO: 20 and SEQ ID NO: 25; SEQ ID NO: 20 and SEQ ID NO: 26; SEQ ID NO: 21 and SEQ ID NO: 22; SEQ ID NO: 21 and SEQ ID NO: 23; SEQ ID NO: 21 and SEQ ID NO: 24; SEQ ID NO: 21 and SEQ ID NO: 25; SEQ ID NO: 21 and SEQ ID NO: 26; SEQ ID NO: 22 and SEQ ID NO: 23; SEQ ID NO: 22 and SEQ ID NO: 24; SEQ ID NO: 22 and SEQ ID NO: 25; SEQ ID NO: 22 and SEQ ID NO: 26; SEQ ID NO: 23 and SEQ ID NO: 24; SEQ ID NO: 23 and SEQ ID NO: 25; SEQ ID NO: 23 and SEQ ID NO: 26; SEQ ID NO: 24 and SEQ ID NO: 25; SEQ ID NO: 24 and SEQ ID NO: 26; SEQ ID NO: 25 and SEQ ID NO: 26; SEQ ID NO: 110 and SEQ ID NO: 120; SEQ ID NO: 110 and SEQ ID NO: 121; SEQ ID NO: 110 and SEQ ID NO: 122; SEQ ID NO: 110 and SEQ ID NO: 123; SEQ ID NO: 110 and SEQ ID NO: 124; SEQ ID NO: 110 and SEQ ID NO: 125; SEQ ID NO: 111 and SEQ ID NO: 112; SEQ ID NO: 111 and SEQ ID NO: 113; SEQ ID NO: 111 and SEQ ID NO: 114; SEQ ID NO: 111 and SEQ ID NO: 115; SEQ ID NO: 111 and SEQ ID NO: 116; SEQ ID NO: 111 and SEQ ID NO: 117; SEQ ID NO: 111 and SEQ ID NO: 118; SEQ ID NO: 111 and SEQ ID NO: 119; SEQ ID NO: 111 and SEQ ID NO: 120; SEQ ID NO: 111 and SEQ ID NO: 121; SEQ ID NO: 111 and SEQ ID NO: 122; SEQ ID NO: 111 and SEQ ID NO: 123; SEQ ID NO: 111 and SEQ ID NO: 124; SEQ ID NO: 111 and SEQ ID NO: 125; SEQ ID NO: 112 and SEQ ID NO: 113; SEQ ID NO: 112 and SEQ ID NO: 114; SEQ ID NO: 112 and SEQ ID NO: 115; SEQ ID NO: 112 and SEQ ID NO: 116; SEQ ID NO: 112 and SEQ ID NO: 117; SEQ ID NO: 112 and SEQ ID NO: 118; SEQ ID NO: 112 and SEQ ID NO: 119; SEQ ID NO: 112 and SEQ ID NO: 120; SEQ ID NO: 112 and SEQ ID NO: 121; SEQ ID NO: 112 and SEQ ID NO: 122; SEQ ID NO: 112 and SEQ ID NO: 123; SEQ ID NO: 112 and SEQ ID NO: 124; SEQ ID NO: 112 and SEQ ID NO: 125; SEQ ID NO: 113 and SEQ ID NO: 114; SEQ ID NO: 113 and SEQ ID NO: 115; SEQ ID NO: 113 and SEQ ID NO: 116; SEQ ID NO: 113 and SEQ ID NO: 117; SEQ ID NO: 113 and SEQ ID NO: 118; SEQ ID NO: 113 and SEQ ID NO: 119; SEQ ID NO: 113 and SEQ ID NO: 120; SEQ ID NO: 113 and SEQ ID NO: 121; SEQ ID NO: 113 and SEQ ID NO: 122; SEQ ID NO: 113 and SEQ ID NO: 123; SEQ ID NO: 113 and SEQ ID NO: 124; SEQ ID NO: 113 and SEQ ID NO: 125; SEQ ID NO: 114 and SEQ ID NO: 115; SEQ ID NO: 114 and SEQ ID NO: 116; SEQ ID NO: 114 and SEQ ID NO: 117;

SEQ ID NO: 114 and SEQ ID NO: 118; SEQ ID NO: 114 and SEQ ID NO: 119; SEQ ID NO: 114 and SEQ ID NO: 120; SEQ ID NO: 114 and SEQ ID NO: 121; SEQ ID NO: 114 and SEQ ID NO: 122; SEQ ID NO: 114 and SEQ ID NO: 123; SEQ ID NO: 114 and SEQ ID NO: 124; SEQ ID NO: 114 and SEQ ID NO: 125; SEQ ID NO: 115 and SEQ ID NO: 116; SEQ ID NO: 115 and SEQ ID NO: 117; SEQ ID NO: 115 and SEQ ID NO: 118; SEQ ID NO: 115 and SEQ ID NO: 119; SEQ ID NO: 115 and SEQ ID NO: 120; SEQ ID NO: 115 and SEQ ID NO: 121; SEQ ID NO: 115 and SEQ ID NO: 122; SEQ ID NO: 115 and SEQ ID NO: 123; SEQ ID NO: 115 and SEQ ID NO: 124; SEQ ID NO: 115 and SEQ ID NO: 125; SEQ ID NO: 116 and SEQ ID NO: 117; SEQ ID NO: 116 and SEQ ID NO: 118; SEQ ID NO: 116 and SEQ ID NO: 119; SEQ ID NO: 116 and SEQ ID NO: 120; SEQ ID NO: 116 and SEQ ID NO: 121; SEQ ID NO: 116 and SEQ ID NO: 122; SEQ ID NO: 116 and SEQ ID NO: 123; SEQ ID NO: 116 and SEQ ID NO: 124; SEQ ID NO: 116 and SEQ ID NO: 125; SEQ ID NO: 117 and SEQ ID NO: 118; SEQ ID NO: 117 and SEQ ID NO: 119; SEQ ID NO: 117 and SEQ ID NO: 120; SEQ ID NO: 117 and SEQ ID NO: 121; SEQ ID NO: 117 and SEQ ID NO: 122; SEQ ID NO: 117 and SEQ ID NO: 123; SEQ ID NO: 117 and SEQ ID NO: 124; SEQ ID NO: 117 and SEQ ID NO: 125; SEQ ID NO: 118 and SEQ ID NO: 119; SEQ ID NO: 118 and SEQ ID NO: 120; SEQ ID NO: 118 and SEQ ID NO: 121; SEQ ID NO: 118 and SEQ ID NO: 122; SEQ ID NO: 118 and SEQ ID NO: 123; SEQ ID NO: 118 and SEQ ID NO: 124; SEQ ID NO: 118 and SEQ ID NO: 125; SEQ ID NO: 119 and SEQ ID NO: 120; SEQ ID NO: 119 and SEQ ID NO: 121; SEQ ID NO: 119 and SEQ ID NO: 122; SEQ ID NO: 119 and SEQ ID NO: 123; SEQ ID NO: 119 and SEQ ID NO: 124; SEQ ID NO: 119 and SEQ ID NO: 125; SEQ ID NO: 120 and SEQ ID NO: 121; SEQ ID NO: 120 and SEQ ID NO: 122; SEQ ID NO: 120 and SEQ ID NO: 123; SEQ ID NO: 120 and SEQ ID NO: 124; SEQ ID NO: 120 and SEQ ID NO: 125; SEQ ID NO: 121 and SEQ ID NO: 122; SEQ ID NO: 121 and SEQ ID NO: 123; SEQ ID NO: 121 and SEQ ID NO: 124; SEQ ID NO: 121 and SEQ ID NO: 125; SEQ ID NO: 122 and SEQ ID NO: 123; SEQ ID NO: 122 and SEQ ID NO: 124; SEQ ID NO: 122 and SEQ ID NO: 125; SEQ ID NO: 123 and SEQ ID NO: 124; SEQ ID NO: 123 and SEQ ID NO: 125; SEQ ID NO: 124 and SEQ ID NO: 125; SEQ ID NO: 148 and SEQ ID NO: 149; SEQ ID NO: 148 and SEQ ID NO: 150; SEQ ID NO: 148 and SEQ ID NO: 151; SEQ ID NO: 148 and SEQ ID NO: 152; SEQ ID NO: 148 and SEQ ID NO: 153; SEQ ID NO: 148 and SEQ ID NO: 154; SEQ ID NO: 148 and SEQ ID NO: 155; SEQ ID NO: 148 and SEQ ID NO: 156; SEQ ID NO: 148 and SEQ ID NO: 157; SEQ ID NO: 148 and SEQ ID NO: 158; SEQ ID NO: 148 and SEQ ID NO: 159;

SEQ ID NO: 149 and SEQ ID NO: 150; SEQ ID NO: 149 and SEQ ID NO: 151; SEQ ID NO: 149 and SEQ ID NO: 152; SEQ ID NO: 149 and SEQ ID NO: 153; SEQ ID NO: 149 and SEQ ID NO: 154; SEQ ID NO: 149 and SEQ ID NO: 155; SEQ ID NO: 149 and SEQ ID NO: 156; SEQ ID NO: 149 and SEQ ID NO: 157; SEQ ID NO: 149 and SEQ ID NO: 158; SEQ ID NO: 149 and SEQ ID NO: 159; SEQ ID NO: 150 and SEQ ID NO: 151; SEQ ID NO: 150 and SEQ ID NO: 152; SEQ ID NO: 150 and SEQ ID NO: 153; SEQ ID NO: 150 and SEQ ID NO: 154; SEQ ID NO: 150 and SEQ ID NO: 155; SEQ ID NO: 150 and SEQ ID NO: 156; SEQ ID NO: 150 and SEQ ID NO: 157; SEQ ID NO: 150 and SEQ ID NO: 158; SEQ ID NO: 150 and SEQ ID NO: 159; SEQ ID NO: 151 and SEQ ID NO: 152; SEQ ID NO: 151 and SEQ ID NO: 153; SEQ ID NO: 151 and SEQ ID NO: 154; SEQ ID NO: 151 and SEQ ID NO: 155; SEQ ID NO: 151 and SEQ ID NO: 156; SEQ ID NO: 151 and SEQ ID NO: 157; SEQ ID NO: 151 and SEQ ID NO: 158; SEQ ID NO: 151 and SEQ ID NO: 159; SEQ ID NO: 152 and SEQ ID NO: 153; SEQ ID NO: 152 and SEQ ID NO: 154; SEQ ID NO: 152 and SEQ ID NO: 155; SEQ ID NO: 152 and SEQ ID NO: 156; SEQ ID NO: 152 and SEQ ID NO: 157; SEQ ID NO: 152 and SEQ ID NO: 158; SEQ ID NO: 152 and SEQ ID NO: 159; SEQ ID NO: 153 and SEQ ID NO: 154; SEQ ID NO: 153 and SEQ ID NO: 155; SEQ ID NO: 153 and SEQ ID NO: 156; SEQ ID NO: 153 and SEQ ID NO: 157; SEQ ID NO: 153 and SEQ ID NO: 158; SEQ ID NO: 153 and SEQ ID NO: 159; SEQ ID NO: 154 and SEQ ID NO: 155; SEQ ID NO: 154 and SEQ ID NO: 156; SEQ ID NO: 154 and SEQ ID NO: 157; SEQ ID NO: 154 and SEQ ID NO: 158; SEQ ID NO: 154 and SEQ ID NO: 159; SEQ ID NO: 155 and SEQ ID NO: 156; SEQ ID NO: 155 and SEQ ID NO: 157; SEQ ID NO: 155 and SEQ ID NO: 158; SEQ ID NO: 155 and SEQ ID NO: 159; SEQ ID NO: 156 and SEQ ID NO: 157; SEQ ID NO: 156 and SEQ ID NO: 158; SEQ ID NO: 156 and SEQ ID NO: 159; SEQ ID NO: 157 and SEQ ID NO: 158; SEQ ID NO: 157 and SEQ ID NO: 159; SEQ ID NO: 158 and SEQ ID NO: 159; SEQ ID NO: 71 and SEQ ID NO: 72; SEQ ID NO: 71 and SEQ ID NO: 73; SEQ ID NO: 71 and SEQ ID NO: 74; SEQ ID NO: 71 and SEQ ID NO: 75; SEQ ID NO: 71 and SEQ ID NO: 76; SEQ ID NO: 71 and SEQ ID NO: 77; SEQ ID NO: 71 and SEQ ID NO: 78; SEQ ID NO: 71 and SEQ ID NO: 84; SEQ ID NO: 71 and SEQ ID NO: 85; SEQ ID NO: 71 and SEQ ID NO: 86; SEQ ID NO: 71 and SEQ ID NO: 87; SEQ ID NO: 71 and SEQ ID NO: 88; SEQ ID NO: 71 and SEQ ID NO: 89; SEQ ID NO: 71 and SEQ ID NO: 90; SEQ ID NO: 71 and SEQ ID NO: 91; SEQ ID NO: 71 and SEQ ID NO: 92; SEQ ID NO: 71 and SEQ ID NO: 93; SEQ ID NO: 71 and SEQ ID NO: 94; SEQ ID NO: 71 and SEQ ID NO: 95; SEQ ID NO: 71 and SEQ ID NO: 96; SEQ ID NO: 71 and SEQ ID NO: 97; SEQ

ID NO: 71 and SEQ ID NO: 98; SEQ ID NO: 71 and SEQ ID NO: 99; SEQ ID NO: 71 and SEQ ID NO: 100; SEQ ID NO: 71 and SEQ ID NO: 101; SEQ ID NO: 71 and SEQ ID NO: 102; SEQ ID NO: 72 and SEQ ID NO: 73; SEQ ID NO: 72 and SEQ ID NO: 74; SEQ ID NO: 72 and SEQ ID NO: 75; SEQ ID NO: 72 and SEQ ID NO: 76; SEQ ID NO: 72 and SEQ ID NO: 77; SEQ ID NO: 72 and SEQ ID NO: 78; SEQ ID NO: 72 and SEQ ID NO: 84; SEQ ID NO: 72 and SEQ ID NO: 85; SEQ ID NO: 72 and SEQ ID NO: 86; SEQ ID NO: 72 and SEQ ID NO: 87; SEQ ID NO: 72 and SEQ ID NO: 88; SEQ ID NO: 72 and SEQ ID NO: 89; SEQ ID NO: 72 and SEQ ID NO: 90; SEQ ID NO: 72 and SEQ ID NO: 91; SEQ ID NO: 72 and SEQ ID NO: 92; SEQ ID NO: 72 and SEQ ID NO: 93; SEQ ID NO: 72 and SEQ ID NO: 94; SEQ ID NO: 72 and SEQ ID NO: 95; SEQ ID NO: 72 and SEQ ID NO: 96; SEQ ID NO: 72 and SEQ ID NO: 97; SEQ ID NO: 72 and SEQ ID NO: 98; SEQ ID NO: 72 and SEQ ID NO: 99; SEQ ID NO: 72 and SEQ ID NO: 100; SEQ ID NO: 72 and SEQ ID NO: 101; SEQ ID NO: 72 and SEQ ID NO: 102; SEQ ID NO: 73 and SEQ ID NO: 74; SEQ ID NO: 73 and SEQ ID NO: 75; SEQ ID NO: 73 and SEQ ID NO: 76; SEQ ID NO: 73 and SEQ ID NO: 77; SEQ ID NO: 73 and SEQ ID NO: 78; SEQ ID NO: 73 and SEQ ID NO: 84; SEQ ID NO: 73 and SEQ ID NO: 85; SEQ ID NO: 73 and SEQ ID NO: 86; SEQ ID NO: 73 and SEQ ID NO: 87; SEQ ID NO: 73 and SEQ ID NO: 88; SEQ ID NO: 73 and SEQ ID NO: 89; SEQ ID NO: 73 and SEQ ID NO: 90; SEQ ID NO: 73 and SEQ ID NO: 91; SEQ ID NO: 73 and SEQ ID NO: 92; SEQ ID NO: 73 and SEQ ID NO: 93; SEQ ID NO: 73 and SEQ ID NO: 94; SEQ ID NO: 73 and SEQ ID NO: 95; SEQ ID NO: 73 and SEQ ID NO: 96; SEQ ID NO: 73 and SEQ ID NO: 97; SEQ ID NO: 73 and SEQ ID NO: 98; SEQ ID NO: 73 and SEQ ID NO: 99; SEQ ID NO: 73 and SEQ ID NO: 100; SEQ ID NO: 73 and SEQ ID NO: 101; SEQ ID NO: 73 and SEQ ID NO: 102; SEQ ID NO: 74 and SEQ ID NO: 75; SEQ ID NO: 74 and SEQ ID NO: 76; SEQ ID NO: 74 and SEQ ID NO: 77; SEQ ID NO: 74 and SEQ ID NO: 78; SEQ ID NO: 74 and SEQ ID NO: 84; SEQ ID NO: 74 and SEQ ID NO: 85; SEQ ID NO: 74 and SEQ ID NO: 86; SEQ ID NO: 74 and SEQ ID NO: 87; SEQ ID NO: 74 and SEQ ID NO: 88; SEQ ID NO: 74 and SEQ ID NO: 89; SEQ ID NO: 74 and SEQ ID NO: 90; SEQ ID NO: 74 and SEQ ID NO: 91; SEQ ID NO: 74 and SEQ ID NO: 92; SEQ ID NO: 74 and SEQ ID NO: 93; SEQ ID NO: 74 and SEQ ID NO: 94; SEQ ID NO: 74 and SEQ ID NO: 95; SEQ ID NO: 74 and SEQ ID NO: 96; SEQ ID NO: 74 and SEQ ID NO: 97; SEQ ID NO: 74 and SEQ ID NO: 98; SEQ ID NO: 74 and SEQ ID NO: 99; SEQ ID NO: 74 and SEQ ID NO: 100; SEQ ID NO: 74 and SEQ ID NO: 101; SEQ ID NO: 74 and SEQ ID NO: 102; SEQ ID NO: 75 and SEQ ID NO: 76; SEQ ID NO: 75 and SEQ ID NO: 77; SEQ ID NO: 75 and SEQ ID NO: 78; SEQ ID NO: 75 and SEQ ID NO: 84; SEQ ID NO: 75 and SEQ ID NO: 85;

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Embodiment 4 is a composition comprising:

a. a single nucleic acid molecule comprising:

   i. a nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and at least one, at least two, or at least three guide RNAs; or

   ii. a nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or

   iii. a nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and 1, 2, or 3 guide RNAs;

wherein each guide RNA is selected from **Table 6**, optionally wherein the composition comprises at least one pair of guide RNAs, wherein the at least one pair is selected from the pairs shown in **Tables 1B, 1D, 3B, 3D, 5B,** or **5D**; or

b. two nucleic acid molecules comprising:

   i. a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9); and

      1. a second nucleic acid that does not encode a SaCas9 or SluCas9 and encodes any one of the following:

    2. at least one, at least two, at least three, at least four, at least five, or at least six guide RNAs; or
    3. from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or
    4. from one to six guide RNAs; or

ii. a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and

    1. at least one, at least two, or at least three guide RNAs; or
    2. from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or
    3. 1, 2, or 3 guide RNAs; and

a second nucleic acid that does not encode a SaCas9 or SluCas9, optionally wherein the second nucleic acid comprises any one of the following:

    1. at least one, at least two, at least three, at least four, at least five, or at least six guide RNAs; or
    2. from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or
    3. from one to six guide RNAs; or

iii. a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and at least one, at least two, or at least three guide RNAs; and

a second nucleic acid that does not encode a SaCas9 or SluCas9 and encodes from one to six guide RNAs; or

iv. a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and at least two guide RNAs, wherein a first guide RNA of the at least two guide RNAs binds upstream of a target sequence and a second guide RNA of the at least two guide RNAs binds downstream of the target sequence; and a second nucleic acid that does not encode a SaCas9 or SluCas9 and encodes at least one additional copy of each of the guide RNAs encoded in the first nucleic acid;

wherein each guide RNA is selected from **Table 6**, optionally wherein the composition comprises at least one pair of guide RNAs, wherein the at least one pair is selected from the pairs shown in **Tables 1B, 1D, 3B, 3D, 5B,** or **5D**.

Embodiment 5 is a composition of any one of embodiments 1-4, comprising a pair of guide RNAs, wherein the pair of guide RNAs is capable of excising a DNA fragment from the DMD gene; wherein the DNA fragment is between 5-250 nucleotides in length.

Embodiment 6 is a composition of embodiment 5, wherein the excised DNA fragment does not comprise an entire exon of the DMD gene.

Embodiment 7 is a composition comprising a single nucleic acid molecule encoding a pair of guide RNAs and a Cas9, wherein the single nucleic acid molecule comprises:

a. a first nucleic acid encoding the pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences: SEQ ID NOs: 1 and 3; 16 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20; 17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and

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b. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences: SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and 203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208; 231 and

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c. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences targeting exon 44: SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208; and a second nucleic acid encoding a *Staphylococcus lugdunensis* (SluCas9); or

d. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences targeting exon 50: SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241; and a second nucleic acid encoding a *Staphylococcus lugdunensis* (SluCas9); or

e. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences targeting exon 53: SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and a second nucleic acid encoding a *Staphylococcus aureus* Cas9 (SaCas9); or

f. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences targeting exon 53: SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292; and a second nucleic acid encoding a *Staphylococcus lugdunensis* (SluCas9).

Embodiment 8 is a composition comprising one or more nucleic acid molecules encoding a *Staphylococcus aureus* Cas9 (SaCas9) and a first and a second guide RNA, wherein the first and the second guide RNAs target different sequences in a DMD gene, and wherein the first and the second guide RNAs each comprise a sequence that is at least 90% identical to a first and a second guide sequence selected from any one of the following pairs of first and second guide sequences:

any one of the following pairs of first and second guide sequences targeting exon 53, SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73.

Embodiment 9 is a composition comprising one or more nucleic acid molecules encoding a *Staphylococcus lugdunensis* (SluCas9) and a first and a second guide RNA, wherein the first and the second guide RNAs target different sequences in a DMD gene, and wherein the first and the second guide RNAs each comprise a sequence that is at least 90% identical to a first and second guide sequence selected from any one of the following pairs of first and second guide sequences:

a. any one of the following pairs of first and second guide sequences targeting exon 44, SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;

b. any one of the following pairs of first and second guide sequences targeting exon 50, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;

c. any one of the following pairs of first and second guide sequences targeting exon 53, SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

Embodiment 10 is a composition comprising one or more nucleic acid molecules encoding an endonuclease and at least two guide RNAs, wherein the at least two guide RNAs each target a different sequence in a DMD gene, and wherein the at least two guide RNAs each comprise a sequence that is at least 90% identical to a first and second guide sequence selected from any one of the following pairs of first and second guide sequences:

a. for exon 44, SEQ ID NOs: 1 and 3; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; or 124 and 125;

b. for exon 50, SEQ ID NOs: 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; or 158 and 159;

c. for exon 53, SEQ ID NOs: 16 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20; 17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 71 and 72; 71 and 73; 71 and 74; 71 and 75; 71 and 76; 71 and 77; 71 and 78; 71 and 84; 71 and 85; 71 and 86; 71 and 87; 71 and 88; 71 and 89; 71 and 90; 71 and 91; 71 and 92; 71 and 93; 71 and 94; 71 and 95; 71 and 96; 71 and 97; 71 and 98; 71 and 99; 71 and 100; 71 and 101; 71 and 102; 72 and 73; 72 and 74; 72 and 75; 72 and 76; 72 and 77; 72 and 78; 72 and 84; 72 and 85; 72 and 86; 72 and 87; 72 and 88; 72 and 89; 72 and 90; 72 and 91; 72 and 92; 72 and 93; 72 and 94; 72 and 95; 72 and 96; 72 and 97; 72 and 98; 72 and 99; 72 and 100; 72 and 101; 72 and 102; 73 and 74; 73 and 75; 73 and 76; 73 and 77; 73 and 78; 73 and 84; 73 and 85; 73 and 86; 73 and 87; 73 and 88; 73 and 89; 73 and 90; 73 and 91; 73 and 92; 73 and 93; 73 and 94; 73 and 95; 73 and 96; 73 and 97; 73 and 98; 73 and 99; 73 and 100; 73 and 101; 73 and 102; 74 and 75; 74 and 76; 74 and 77; 74 and 78; 74 and 84; 74 and 85; 74 and 86; 74 and 87; 74 and 88; 74 and 89; 74 and 90; 74 and 91; 74 and 92; 74 and 93; 74 and 94; 74 and 95; 74 and 96; 74 and 97; 74 and 98; 74 and 99; 74 and 100; 74 and 101; 74 and 102; 75 and 76; 75 and 77; 75 and 78; 75 and 84; 75 and 85; 75 and 86; 75 and 87; 75 and 88; 75 and 89; 75 and 90; 75 and 91; 75 and 92; 75 and 93; 75 and 94; 75 and 95; 75 and 96; 75 and 97; 75 and 98; 75 and 99; 75 and 100; 75 and 101; 75 and 102; 76 and 77; 76 and 78; 76 and 84; 76 and 85; 76 and

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a second nucleic acid encoding a SaCas9.

Embodiment 11 is a composition comprising a first and a second nucleic acid molecule, wherein the first nucleic acid molecule encodes a *Staphylococcus aureus* Cas9 (SaCas9) endonuclease and optionally a first or a first and second guide RNA, and the second nucleic acid molecule comprises a first or a first and second guide RNA, wherein the first guide RNA comprises a first sequence and the second guide RNA comprises a second sequence from any one the following pairs of first and second sequences: SEQ ID NOs: 1 and 3; 16 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20; 17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; 124 and 125; 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; 158 and 159; 71 and 72; 71 and 73; 71 and 74; 71 and 75; 71 and 76; 71 and 77; 71 and 78; 71 and 84; 71 and 85; 71 and 86; 71 and 87; 71 and 88; 71 and 89; 71 and 90; 71 and 91; 71 and 92; 71 and 93; 71 and 94; 71 and 95; 71 and 96; 71 and 97; 71 and 98; 71 and 99; 71 and 100; 71 and 101; 71 and 102; 72 and 73; 72 and 74; 72 and 75; 72 and 76; 72 and 77; 72 and 78; 72

and 84; 72 and 85; 72 and 86; 72 and 87; 72 and 88; 72 and 89; 72 and 90; 72 and 91; 72 and 92; 72 and 93; 72 and 94; 72 and 95; 72 and 96; 72 and 97; 72 and 98; 72 and 99; 72 and 100; 72 and 101; 72 and 102; 73 and 74; 73 and 75; 73 and 76; 73 and 77; 73 and 78; 73 and 84; 73 and 85; 73 and 86; 73 and 87; 73 and 88; 73 and 89; 73 and 90; 73 and 91; 73 and 92; 73 and 93; 73 and 94; 73 and 95; 73 and 96; 73 and 97; 73 and 98; 73 and 99; 73 and 100; 73 and 101; 73 and 102; 74 and 75; 74 and 76; 74 and 77; 74 and 78; 74 and 84; 74 and 85; 74 and 86; 74 and 87; 74 and 88; 74 and 89; 74 and 90; 74 and 91; 74 and 92; 74 and 93; 74 and 94; 74 and 95; 74 and 96; 74 and 97; 74 and 98; 74 and 99; 74 and 100; 74 and 101; 74 and 102; 75 and 76; 75 and 77; 75 and 78; 75 and 84; 75 and 85; 75 and 86; 75 and 87; 75 and 88; 75 and 89; 75 and 90; 75 and 91; 75 and 92; 75 and 93; 75 and 94; 75 and 95; 75 and 96; 75 and 97; 75 and 98; 75 and 99; 75 and 100; 75 and 101; 75 and 102; 76 and 77; 76 and 78; 76 and 84; 76 and 85; 76 and 86; 76 and 87; 76 and 88; 76 and 89; 76 and 90; 76 and 91; 76 and 92; 76 and 93; 76 and 94; 76 and 95; 76 and 96; 76 and 97; 76 and 98; 76 and 99; 76 and 100; 76 and 101; 76 and 102; 77 and 78; 77 and 84; 77 and 85; 77 and 86; 77 and 87; 77 and 88; 77 and 89; 77 and 90; 77 and 91; 77 and 92; 77 and 93; 77 and 94; 77 and 95; 77 and 96; 77 and 97; 77 and 98; 77 and 99; 77 and 100; 77 and 101; 77 and 102; 78 and 84; 78 and 85; 78 and 86; 78 and 87; 78 and 88; 78 and 89; 78 and 90; 78 and 91; 78 and 92; 78 and 93; 78 and 94; 78 and 95; 78 and 96; 78 and 97; 78 and 98; 78 and 99; 78 and 100; 78 and 101; 78 and 102; 84 and 85; 84 and 86; 84 and 87; 84 and 88; 84 and 89; 84 and 90; 84 and 91; 84 and 92; 84 and 93; 84 and 94; 84 and 95; 84 and 96; 84 and 97; 84 and 98; 84 and 99; 84 and 100; 84 and 101; 84 and 102; 85 and 86; 85 and 87; 85 and 88; 85 and 89; 85 and 90; 85 and 91; 85 and 92; 85 and 93; 85 and 94; 85 and 95; 85 and 96; 85 and 97; 85 and 98; 85 and 99; 85 and 100; 85 and 101; 85 and 102; 86 and 87; 86 and 88; 86 and 89; 86 and 90; 86 and 91; 86 and 92; 86 and 93; 86 and 94; 86 and 95; 86 and 96; 86 and 97; 86 and 98; 86 and 99; 86 and 100; 86 and 101; 86 and 102; 87 and 88; 87 and 89; 87 and 90; 87 and 91; 87 and 92; 87 and 93; 87 and 94; 87 and 95; 87 and 96; 87 and 97; 87 and 98; 87 and 99; 87 and 100; 87 and 101; 87 and 102; 88 and 89; 88 and 90; 88 and 91; 88 and 92; 88 and 93; 88 and 94; 88 and 95; 88 and 96; 88 and 97; 88 and 98; 88 and 99; 88 and 100; 88 and 101; 88 and 102; 89 and 90; 89 and 91; 89 and 92; 89 and 93; 89 and 94; 89 and 95; 89 and 96; 89 and 97; 89 and 98; 89 and 99; 89 and 100; 89 and 101; 89 and 102; 90 and 91; 90 and 92; 90 and 93; 90 and 94; 90 and 95; 90 and 96; 90 and 97; 90 and 98; 90 and 99; 90 and 100; 90 and 101; 90 and 102; 91 and 92; 91 and 93; 91 and 94; 91 and 95; 91 and 96; 91 and 97; 91 and 98; 91 and 99; 91 and 100; 91 and 101; 91 and 102; 92 and 93; 92 and 94; 92 and 95; 92 and 96; 92 and 97; 92 and 98; 92 and 99; 92 and 100; 92 and 101; 92 and 102; 93 and 94; 93 and 95; 93 and 96; 93 and 97; 93 and 98; 93 and 99; 93 and 100; 93 and 101; 93 and 102; 94 and 95; 94 and 96; 94 and 97; 94 and 98; 94 and 99; 94 and 100; 94 and 101; 94 and 102; 95 and 96; 95 and 97; 95 and 98; 95 and 99; 95 and 100; 95 and 101; 95 and 102; 96 and 97; 96 and 98; 96 and 99; 96 and 100; 96 and 101; 96 and 102; 97 and 98; 97 and 99;

97 and 100; 97 and 101; 97 and 102; 98 and 99; 98 and 100; 98 and 101; 98 and 102; 99 and 100; 99 and 101; 99 and 102; 100 and 101; 100 and 102; or 101 and 102.

Embodiment 12 is a composition comprising a first and a second nucleic acid molecule, wherein the first nucleic acid molecule encodes a *Staphylococcus lugdunensis* (SluCas9) endonuclease and optionally a first or a first and second guide RNA, and the second nucleic acid molecule comprises a first or a first and second guide RNA, wherein the first guide RNA comprises a first sequence and the second guide RNAs comprises a second sequence from any one the following pairs of first and second sequences: SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and 203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208; 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232 and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and 239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; 241 and 242; 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and 277; 270 and 278; 270 and 279; 270 and 280; 270 and 281; 270 and 282; 270 and 283; 270 and 284; 270 and 285; 270 and 286; 270 and 287; 270 and 288; 270 and 289; 270 and 290; 270 and 291; 270 and 292; 271 and 272; 271 and 273; 271 and 274; 271 and 275; 271 and 276; 271 and 277; 271 and 278; 271 and 279; 271 and 280; 271 and 281; 271 and 282; 271 and 283; 271 and 284; 271 and 285; 271 and 286; 271 and 287; 271 and 288; 271 and 289; 271 and 290; 271 and 291; 271 and 292; 272 and 273; 272 and 274; 272 and 275; 272 and 276; 272 and 277; 272 and 278; 272 and 279; 272 and 280; 272 and 281; 272 and 282; 272 and 283; 272 and 284; 272 and 285; 272 and 286; 272 and 287; 272 and 288; 272 and 289; 272 and 290; 272 and 291; 272 and 292; 273 and 274; 273 and 275; 273 and 276; 273 and 277; 273 and 278; 273 and 279; 273 and 280; 273 and 281; 273 and 282; 273 and 283; 273 and 284; 273 and 285; 273 and 286; 273 and 287; 273 and 288; 273 and 289; 273 and 290; 273 and 291; 273 and 292; 274 and 275; 274 and 276; 274 and 277; 274 and 278; 274 and 279; 274 and 280; 274 and 281; 274 and 282; 274 and 283; 274 and 284; 274 and 285; 274 and 286; 274 and 287; 274 and 288; 274 and 289; 274

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Embodiment 13 is a composition comprising a first and a second nucleic acid molecule, wherein the first nucleic acid molecule encodes a sRGN endonuclease (e.g., sRGN3.1, sRGN3.3, or sRGN4) and optionally a first or a first and second guide RNA, and the second nucleic acid molecule comprises a first or a first and second guide RNA, wherein the first guide RNA comprises a first sequence and the second guide RNAs comprises a second sequence from any one the following pairs of first and second sequences: SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and 203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208; 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232 and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and 239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; 241 and 242; 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and 277; 270 and 278; 270 and 279; 270 and 280; 270 and 281; 270 and 282; 270 and 283; 270 and 284; 270 and 285; 270 and 286; 270 and 287; 270 and 288; 270 and 289; 270 and 290; 270 and 291; 270 and 292; 271 and 272; 271 and 273; 271 and 274; 271 and 275; 271 and 276; 271 and 277; 271 and 278; 271 and 279; 271 and 280; 271 and 281; 271 and 282; 271 and 283; 271 and 284; 271 and 285; 271 and 286; 271 and 287; 271 and 288; 271 and 289; 271 and 290; 271 and 291; 271 and 292; 272 and 273; 272 and 274; 272 and 275; 272 and 276; 272 and 277; 272 and 278; 272 and 279; 272 and 280; 272 and 281; 272 and 282; 272 and 283; 272 and 284; 272 and 285; 272 and 286; 272 and 287; 272 and 288; 272 and 289; 272 and 290; 272 and 291; 272 and 292; 273 and 274; 273 and 275; 273 and 276; 273 and 277; 273 and 278; 273 and 279; 273 and 280; 273 and 281; 273 and 282; 273 and 283; 273 and 284; 273 and 285; 273 and 286; 273 and 287; 273 and 288; 273 and 289; 273 and 290; 273 and 291; 273 and 292; 274 and 275; 274 and 276; 274 and 277; 274 and 278; 274 and 279; 274 and 280; 274 and 281; 274 and 282; 274 and 283; 274 and 284; 274 and 285; 274 and 286; 274 and 287; 274 and 288; 274 and 289; 274 and 290; 274 and 291; 274 and 292; 275 and 276; 275 and 277; 275 and 278; 275 and 279; 275 and 280; 275 and 281; 275 and 282; 275 and 283; 275 and 284; 275 and 285; 275 and 286; 275 and 287; 275 and 288; 275 and 289; 275 and 290; 275 and 291; 275 and 292; 276 and 277; 276 and 278; 276 and 279; 276 and 280; 276 and 281; 276 and 282; 276 and 283; 276 and 284; 276 and 285; 276 and 286; 276 and 287; 276 and 288; 276 and 289; 276 and 290; 276 and 291; 276

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Embodiment 14 is a composition of embodiment 13, wherein the sRGN endonuclease comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of any one of SEQ ID Nos: 7024, 7026, or 7027.

Embodiment 15 is a composition of embodiment 13 or 14, wherein the sRGN endonuclease is encoded by a nucleic acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of any one of SEQ ID Nos: 917, 919 or 920.

Embodiment 16 is a composition of any one of the preceding embodiments, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs facilitate a 3n+1 edit of exon 45, 51 or 53 of the dystrophin gene, wherein "n" is any negative whole number (e.g., any whole number between -10 and -75).

Embodiment 17 is a composition of any one of the preceding embodiments, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs target exon 45, 51 or 53 of the dystrophin gene and are capable of excising a nucleic acid that is at least 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62, 65, 68, 71, 74, 77, 80, 83, 86, 89, 92, 95, 98, 101, 104, 107, 110, 113, 116, 119, 122, 125, 128, 131, 134, 137, 140, 143, 146, 149, 152, 155, 158, 161, 164, 167, 170, 173, 176, 179, 182, 185, 188, 191, 194, 197, 200, 203, 206, 209, 212, 215, or 218 nucleotides in length.

Embodiment 18 is a composition of any one of the preceding embodiments, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs facilitate a 3n+2 edit of exon 44 or 50 of the dystrophin gene, wherein "n" is any negative whole number (e.g., any whole number between -10 and -75).

Embodiment 19 is a composition of any one of the preceding embodiments, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs target exon 44 or 50 of the dystrophin gene and are capable of excising a nucleic acid that is at least 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61, 64, 67, 70, 73, 76, 79, 82, 85, 88, 91, 94, 97, 100, 103, 106, 109, 112, 115, 118, 121, 124, 127, 130, 133, 136, 139, 142, 145, 148, 151, 154, 157, 160, 163, 166, 169, 172, 175, 178, 181, 184, 187, 190, 193, 196, 199, 202, 205, 208, 211, 214, or 217 nucleotides in length.

Embodiment 20 is a composition of any one of the preceding embodiments, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs excise a portion of an exon, wherein the size of the excised portion of the exon is between 5 and 250 nucleotides in length.

Embodiment 21 is a composition of any one of the preceding embodiments, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs excise a portion of an exon, wherein the size of the excised portion of the exon is between 5 and 250, 5 and 200, 5 and 150, 5 and 100, 5 and 75, 5 and 50, 5 and 25, 5 and 10, 20 and 250, 20 and 200, 20 and 150, 20 and 100, 20 and 75, 20 and 50, 20 and 25, 50 and 250, 50 and 200, 50 and 150, 50 and 100, and 50 and 75 nucleotides.

Embodiment 22 is a composition of any one of the preceding embodiments, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs excise a portion of the exon, wherein the size of the excised portion of the exon is between 8 and 167 nucleotides.

Embodiment 23 is a composition of any one of the preceding embodiments, wherein the one or more guide RNAs is an sgRNA.

Embodiment 24 is a composition of any one of the preceding embodiments, wherein the one or more guide RNAs is modified.

Embodiment 25 is a composition of any one of the preceding embodiments, wherein the one or more guide RNAs or nucleic acids are in a vector.

Embodiment 26 is a composition of embodiment 25, wherein the vector is a viral vector.

Embodiment 27 is a composition of embodiment 26, wherein the viral vector is an AAV vector.

Embodiment 28 is a composition of embodiment 27, wherein the AAV vector is an AAV9 vector.

Embodiment 29 is a composition of any one of the preceding embodiments, wherein the promoter for the one or more guide RNAs is hU6c.

Embodiment 30 is a composition of any one of the preceding embodiments, wherein the one or more guide RNAs is a guide RNA for SaCas9, and the one or more guide RNAs comprise a scaffold comprising the sequence of SEQ ID NO: 504.

Embodiment 31 is a composition of any one of the preceding embodiments, wherein the one or more guide RNAs is a guide RNA for SluCas9, and the one or more guide RNAs comprise a scaffold comprising the sequence of SEQ ID NO: 901.

Embodiment 32 is composition of any one of the preceding embodiments, wherein the one or more guide RNAs is in an AAV vector, wherein the vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first guide RNA scaffold sequence; the reverse complement of a nucleic acid encoding a first guide RNA sequence; the reverse complement of a promoter for expression of the nucleic acid encoding the first guide RNA sequence; a promoter (e.g., CK8e) for expression of a nucleic acid encoding SaCas9, SluCas9, or a sRGN; a nucleic acid encoding a SaCas9, SluCas9, or a sRGN (e.g., sRGN3.1, sRGN3,3, or sRGN4); a polyadenylation sequence; a promoter for expression of a second guide RNA sequence in the same direction as the promoter for SaCas9, SluCas9, or the sRGN; a second guide RNA guide sequence; and a second guide RNA scaffold sequence.

Embodiment 33 is a composition of embodiment 32, wherein:

i) the first guide RNA sequence comprises the sequence of SEQ ID NO: 271 or 281, and the second guide RNA sequence comprises the sequence of SEQ ID NO: 275; or

ii) the first guide RNA sequence comprises the sequence of SEQ ID NO: 283, and the second guide RNA sequence comprises the sequence of SEQ ID NO: 290.

Embodiment 34 is a composition of embodiment 32 or 33, wherein the promoter for expression of a nucleic acid encoding SaCas9, SluCas9, or a sRGN is a promoter for expression of a sRGN; wherein the nucleic acid encoding a SaCas9, SluCas9, or a sRGN encodes for a sRGN, and wherein the sRGN comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of any one of SEQ ID Nos: 7024, 7026, or 7027.

Embodiment 35 is a composition of embodiment 34, wherein the sRGN is encoded by a nucleic acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of any one of SEQ ID Nos: 917, 919 or 920.

Embodiment 36 is a composition of any one of embodiments 1-35, wherein the one or more guide RNA sequences, or the first and/or second guide RNA sequence of the pair of guide RNAs, is no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 nucleotides in length.

Embodiment 37 is a method of treating Duchenne Muscular Dystrophy (DMD), the method comprising delivering to a cell the composition of any one of embodiments 1-36.

Embodiment 38 is a method of excising a portion of the DMD gene, the method comprising delivering to a cell the composition of any one of embodiments 1-36, wherein the size of the excised portion is less than about 250 nucleotides.

DESCRIPTION OF FIGURES

[0008] **Figure 1** shows editing frequency and indel profiles of selected SaCas9, SaCas9-KKH and SluCas9 sgRNA pairs targeting Exon 51 of *DMD* gene in HEK293FT cells. Each stack bar represents a sgRNA pair and the bar height depicts the average frequency of the total edit. Different indel profiles for each pair of sgRNAs are represented by using distinct patterns as shown in the key. Error bar denotes the standard deviation for each indel group. The "Guide IDs" in the figure are shown as numbers only and generally correspond to the last digit in the "Guide RNA Name" column of **Table 6** for each provided Cas9 type. "RF +1" means a reframing edit by insertion of a single nucleotide. "RF Other" means other reframing edits. "Exon Skipping" means 1) indels overlap with the splice acceptor (AG) (5'-end of the target exon); 2) deletion with ≥ 9-nt overlap with the splicing window at one of the two guides; or 3) insertion at the exact GT/AG splicing sites and with length ≥ 9-nt at one of the two guides.

[0009] **Figures 2A and 2B** show editing frequency and indel profile of selected SaCas9 and SluCas9 sgRNA pairs targeting Exon 45 or Exon 51 of *DMD* gene in Human Skeletal Muscle Myoblasts (HsMM) cells. Each stack bar represents a sgRNA pair and the bar height depicts the average frequency of the total edit. Different indel profiles for each pair of sgRNAs are represented by using distinct patterns. **Figure 2A** shows editing frequency and profile as calculated by Inference of CRISPR Edit (ICE) via Sanger sequencing signal decomposition. **Figure 2B** shows editing frequency and profile as calculated by next generation sequencing (NGS). NA denotes data not available due to the failed QC at the step of analysis. Error bars denote the standard deviation for each indel group. The "Guide IDs" in the figure are shown as numbers only and generally correspond to the last digit in the "Guide RNA Name" column of **Table 6** for each provided Cas9 type. "RF +1" means a reframing edit by insertion of a single nucleotide. "RF Other" means other reframing edits. "Exon Skipping" means 1) indels overlap with the splice acceptor (AG) (5'-end of the target exon); 2) deletion with ≥ 9-nt overlap with the splicing window at one of the two guides; or 3) insertion at the exact GT/AG splicing sites and with length ≥ 9-nt at one of the two guides.

[0010] **Figure 3** shows editing frequency and indel profile of selected SaCas9, SaCas9-KKH and SluCas9 sgRNA pairs within exon 53 in HEK293FT cells. Each bar represents a sgRNA or sgRNA pair and the bar height depicts the average total indel frequency. Indel profiles are shown for each sgRNA using distinct patterns. Error bar = standard deviation for each indel group. The guide RNAs shown in the figure generally correspond to the "Guide RNA Name" column of **Table 6** (e.g., E53SL4 in Figure 3 corresponds to E53Slu4 in **Table 6**, E53SL23 in Figure 3 corresponds to E53Slu23). "+1 bp" means a reframing edit by insertion of a single nucleotide.

[0011] **Figures 4A-B** show the method of determining exemplary guide pairs for exons 44 and 50. **Figure 4A** shows the reframing for the respective exons (44 and 50) based on neighboring exons. **Figure 4B** shows the reframing window and last premature stop codon for exon 44 or 50.

[0012] **Figures 5A-B** are schematics showing six representative vector designs. White arrows indicate directionality of expression of the sgRNA(s), while the black arrows indicate directionality of the Cas9 protein. In a particular embodiment, the Cas9 promoter may be CK8e. "Pol III" refers to a representative promoter for the expression of sgRNAs, "g1" and "g2" each refer to a guide sequence, "scaffold" refers to the scaffold of a guide RNA, and "pa" refers to a polyadenylation sequence. **Figure 5A** shows Designs 1-4. **Figure 5B** shows Designs 5 and 6, which are specific variations of Design 2 (shown generically in **Figure 5A**), wherein the Cas9 is SluCas9, with specific guide sequences, promoters, scaffold, and NLS sequences. Design 5 and Design 6 differ only in the order in which the guide sequences are presented. Design 5 depicts the Slu7 guide sequence in the first guide position and the Slu3 guide in the second guide position. Design 6 depicts the Slu3 guide sequence in the first guide position and the Slu7 guide sequence in the second guide position.

[0013] **Figures 6A and 6B** show editing frequency and indel profile of selected SluCas9 sgRNA pairs targeting Exon 45 or Exon 51 of the *DMD* gene in HsMM cells. Each stack bar represents a sgRNA pair and the bar height depicts the average frequency of the total edit. Different indel profiles for each pair of sgRNAs are represented by using distinct patterns. **Figure 6A** shows editing frequency and profile as calculated by next generation sequencing (NGS) for the guide pairs, where E51Slu31 is targeting the reframing window of Exon 51 of the *DMD* gene. **Figure 6B** shows editing frequency and profile as calculated by next generation sequencing (NGS) for the guide pairs, where E51Slu10 is targeting the reframing window of Exon 51 of the *DMD* gene. Error bars denote the standard deviation for each indel group. The "Guide IDs" in the figure are shown as numbers only and generally correspond to the last digit in the "Guide RNA Name" column of Table 2 for each provided Cas9 type. "RF Other" means other reframing edits.

[0014] **Figures 7A and 7B** show editing frequency and indel profile of selected SluCas9 sgRNA pairs targeting various exons of the *DMD* gene in HsMM cells. **Figure 7A** shows editing frequency and indel profile of selected SluCas9 sgRNA pairs targeting Exon 51 of the *DMD* gene in HsMM cells. **Figure 7B** shows editing frequency and indel profile of selected SluCas9 sgRNA pairs targeting Exon 45 or Exon 51 of the *DMD* gene in HsMM cells. In Figures 7A and 7B, each stack bar represents a sgRNA pair and the bar height depicts the average frequency of the total edit. Different indel profiles for each pair of sgRNAs are represented by using distinct patterns. Editing frequencies and profiles are as calculated by next generation sequencing (NGS) for three guide pairs, in three doses of RNP; high (H), medium (M), and low (L). Error bars denote the standard deviation for each indel group. The "Guide IDs" in the figures are shown as numbers only and generally correspond to the last digit in the "Guide RNA Name" column of Table 2 for each provided Cas9 type. "RF Other" means other reframing edits.

[0015] **Figures 8A and 8B** show editing frequency and indel profile of selected SluCas9 sgRNA pairs targeting Exon 45 or Exon 51 of the *DMD* gene in HsMM cells. Each stack bar represents a sgRNA pair and the bar height depicts the average frequency of the total edit. Different indel profiles for each pair of sgRNAs are represented by using distinct patterns. **Figure 8A** shows editing frequency and profile as calculated by next generation sequencing (NGS) for the E51Slu10 and E51Slu16 guide pair, where ribonucleoprotein (RNP) stoichiometry varies across the sample set. **Figure 8B** shows editing frequency and profile as calculated by next generation sequencing (NGS) for the E51Slu10 and E51Slu26 guide pair, where ribonucleoprotein (RNP) stoichiometry varies across the sample set. Error bars denote the standard deviation for each indel group. The "Guide IDs" in the figure are shown as numbers only and generally correspond to the last digit in the "Guide RNA Name" column of Table 2 for each provided Cas9 type. "RF Other" means other reframing edits.

[0016] **Figure 9** shows the editing frequency of several nucleases (SluCas9, sRGNs 3.1, 3.3, 4) with various sgRNA pairs (Slu14/7, Slu16/23, Slu3/7) that target exon 53 of the DMD gene in human HEK293FT cells. One high-performing sgRNA for exon 45 of the *DMD* gene was included as a reference (E45Slu18/4). The Slu_v5 scaffold (SEQ ID NO: 901) was used for all samples, except for one triplicate of a E45Slu18/4 sample. Boxplot represents the average total indel frequency of each sgRNA pair. Data are the average of 2 - 3 replicates. In general, the "gRNAs" in the figure are shown as numbers only and generally correspond to the last digit in the "Guide RNA Name" column of Table 5C and 5D for each provided Cas9 type.

[0017] **Figure 10** shows the editing frequency and indel profile of several nucleases with various sgRNA pairs that target exon 53 of the *DMD* gene in human HEK293FT cells. One high-performing sgRNA for exon 45 of the *DMD* gene was included as a reference (E45Slu18/4). Each bar represents a sgRNA pair and the bar height depicts the average total indel frequency. Indel profiles are shown for each sgRNA as follows: black (precision deletion leading to reframing, sometimes referred to as "Precise Deletion"); vertical lines (indels other than precision deletion leading to reframing, sometimes referred to as "Other reframing"); white (all other indels, sometimes referred to as "Other indels"). Data are the average of 2 - 3 replicates. In general, the "gRNAs" in the figure are shown as numbers only and generally correspond to the last digit in the "Guide RNA Name" column of Table 5C and 5D for each provided Cas9 type.

[0018] **Figure 11** shows a bar graph representing the percentage of productive indels of several nucleases (SluCas9, sRGNs 3.1, 3.3, 4) with various sgRNA pairs that target exon 53 of the *DMD* gene in human HEK293FT cells. Y-axis represents the percentage of precision deletions over total indels. Data are the average of 2 - 3 replicates. In general, the "gRNAs" in the figure are shown as numbers only and generally correspond to the last digit in the "Guide RNA Name" column of Table 5C and 5D for each provided Cas9 type.

[0019] **Figure 12** shows a bar graph representing the editing frequency and indel profile of several nucleases (SluCas9, sRGNs 3.1, 3.3, 4) with two different sgRNA pairs (16+23, and 3+7) targeting exon 53 of the DMD gene in primary muscle skeletal myoblast (HsMM) cells. Each bar represents a sgRNA pair and the bar height depicts the average total indel frequency (%). Indel profiles are shown for each sgRNA as follows: black green (precision deletion leading to reframing, sometimes referred to as "Precise Deletion"); vertical lines (indels other than precision deletion leading to reframing, sometimes referred to as "Other reframing"); white (all other indels, sometimes referred to as "Other indels"). Data are the average of 3 replicates.

DETAILED DESCRIPTION

[0020] Reference will now be made in detail to certain embodiments of the invention, examples of which are illustrated in the accompanying drawings. While the invention is described in conjunction with the illustrated embodiments, it will be understood that they are not intended to limit the invention to those embodiments. On the contrary, the invention is intended to cover all alternatives, modifications, and equivalents, which may be included within the invention as defined by the appended claims and included embodiments.

[0021] Before describing the present teachings in detail, it is to be understood that the disclosure is not limited to specific compositions or process steps, as such may vary. It should be noted that, as used in this specification and the appended claims, the singular form “a”, “an”, and “the” include plural references unless the context clearly dictates otherwise. Thus, for example, reference to “a guide” includes a plurality of guides and reference to “a cell” includes a plurality of cells and the like.

[0022] Numeric ranges are inclusive of the numbers defining the range. Measured and measurable values are understood to be approximate, taking into account significant digits and the error associated with the measurement. Also, the use of “comprise”, “comprises”, “comprising”, “contain”, “contains”, “containing”, “include”, “includes”, and “including” are not intended to be limiting. It is to be understood that both the foregoing general description and detailed description are exemplary and explanatory only and are not restrictive of the teachings.

[0023] Unless specifically noted in the specification, embodiments in the specification that recite “comprising” various components are also contemplated as “consisting of” or “consisting essentially of” the recited components; embodiments in the specification that recite “consisting of” various components are also contemplated as “comprising” or “consisting essentially of” the recited components; and embodiments in the specification that recite “consisting essentially of” various components are also contemplated as “consisting of” or “comprising” the recited components (this interchangeability does not apply to the use of these terms in the claims). The term “or” is used in an inclusive sense, i.e., equivalent to “and/or,” unless the context clearly indicates otherwise.

[0024] The section headings used herein are for organizational purposes only and are not to be construed as limiting the desired subject matter in any way. In the event that any material incorporated by reference contradicts any term defined in this specification or any other express content of this specification, this specification controls. While the present teachings are described in conjunction with various embodiments, it is not intended that the present teachings be limited to such embodiments. On the contrary, the present teachings encompass various alternatives, modifications, and equivalents, as will be appreciated by those of skill in the art.

I. Definitions

[0025] Unless stated otherwise, the following terms and phrases as used herein are intended to have the following meanings:

[0026] “Polynucleotide,” “nucleic acid,” and “nucleic acid molecule,” are used herein to refer to a multimeric compound comprising nucleosides or nucleoside analogs which have nitrogenous heterocyclic bases or base analogs linked together along a backbone, including conventional RNA, DNA, mixed RNA-DNA, and polymers that are analogs thereof. A nucleic acid “backbone” can be made up of a variety of linkages, including one or more of sugar-phosphodiester linkages, peptide-nucleic acid bonds (“peptide nucleic acids” or PNA; PCT No. WO 95/32305), phosphorothioate linkages, methylphosphonate linkages, or combinations thereof. Sugar moieties of a nucleic acid can be ribose, deoxyribose, or similar compounds with substitutions, e.g., 2' methoxy or 2' halide substitutions. Nitrogenous bases can be conventional bases (A, G, C, T, U), analogs thereof (e.g., modified uridines such as 5-methoxyuridine, pseudouridine, or N1-methylpseudouridine, or others); inosine; derivatives of purines or pyrimidines (e.g., N^4-methyl deoxyguanosine, deaza- or aza-purines, deaza- or aza-pyrimidines, pyrimidine bases with substituent groups at the 5 or 6 position (e.g., 5-methylcytosine), purine bases with a substituent at the 2, 6, or 8 positions, 2-amino-6-methylaminopurine, O^6-methylguanine, 4-thio-pyrimidines, 4-amino-pyrimidines, 4-dimethylhydrazine-pyrimidines, and O^4-alkyl-pyrimidines; US Pat. No. 5,378,825 and PCT No. WO 93/13121). For general discussion see *The Biochemistry of the Nucleic Acids* 5-36, Adams et al., ed., 11th ed., 1992). Nucleic acids can include one or more "abasic" residues where the backbone includes no nitrogenous base for position(s) of the polymer (US Pat. No. 5,585,481). A nucleic acid can comprise only conventional RNA or DNA sugars, bases and linkages, or can include both conventional components and substitutions (e.g., conventional bases with 2' methoxy linkages, or polymers containing both conventional bases and one or more base analogs). Nucleic acid includes "locked nucleic acid" (LNA), an analogue containing one or more LNA nucleotide monomers with a bicyclic furanose unit locked in an RNA mimicking sugar conformation, which enhance hybridization affinity toward complementary RNA and DNA sequences (Vester and Wengel, 2004, *Biochemistry* 43(42):13233-41). RNA and DNA have different sugar moieties and can differ by the presence of uracil or analogs thereof in RNA and thymine or analogs thereof in DNA.

[0027] "Guide RNA" and simply "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" 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. For clarity, the terms "guide RNA" or "guide" as used herein, and unless specifically stated otherwise, may refer to an RNA molecule (comprising A, C, G, and U nucleotides) or to a DNA molecule encoding such an RNA molecule (comprising A, C, G, and T nucleotides) or complementary sequences thereof. In general, in the case of a DNA nucleic acid construct encoding a guide RNA, the U residues in any of the RNA sequences described herein may be replaced with T residues, and in the case of a guide RNA construct encoded by any of the DNA sequences described herein, the T residues may be replaced with U residues.

[0028] As used herein, a "spacer sequence," sometimes also referred to herein and in the literature as a "spacer," "protospacer," "guide sequence," or "targeting sequence" refers to a sequence within a guide RNA that is complementary to a target sequence and functions to direct a guide RNA to a target sequence for cleavage by a Cas9. For clarity, the terms "spacer sequence", "spacer," "protospacer," "guide sequence," or "targeting sequence" as used herein, and unless specifically stated otherwise, may refer to an RNA molecule (comprising A, C, G, and U nucleotides) or to a DNA molecule encoding such an RNA molecule (comprising A, C, G, and T nucleotides) or complementary sequences thereof. A guide sequence can be 24, 23, 22, 21, 20 or fewer base pairs in length, e.g., in the case of *Staphylococcus lugdunensis* (i.e., SluCas9) or *Staphylococcus aureus* (i.e., SaCas9) and related Cas9 homologs/orthologs. In preferred embodiments, a guide/spacer sequence in the case of SluCas9 or SaCas9 is at least 20 base pairs in length, or more specifically, within 20-25 base pairs in length (*see, e.g.*, Schmidt et al., 2021, Nature Communications, "Improved CRISPR genome editing using small highly active and specific engineered RNA-guided nucleases"). Shorter or longer sequences can also be used as guides, e.g., 15-, 16-, 17-, 18-, 19-, 20-, 21-, 22-, 23-, 24-, or 25-nucleotides in length. For example, in some embodiments, the guide sequence comprises at least 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous nucleotides of a sequence selected from SEQ ID NOs: 1-159 (for SaCas9, including SaCas9KKH), and 200-292, 924-938, or 950-955 (for SluCas9). In some embodiments, the guide sequence comprises a sequence selected from SEQ ID NOs: 1-159, 200-292, 924-938, or 950-955. In some embodiments, the target sequence is in a gene or on a chromosome, for example, and is complementary to the guide sequence. In some embodiments, the degree of complementarity or identity between a guide sequence and its corresponding target sequence may be about 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%. For example, in some embodiments, the guide sequence comprises a sequence with about 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to at least 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous nucleotides of a sequence selected from SEQ ID NOs: 1-159, 200-292, 924-938, or 950-955. In some embodiments, the guide sequence comprises a sequence with about 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence selected from SEQ ID NOs: 1-159, 200-292, 924-938, or 950-955. In preferred embodiments, a guide/spacer sequence in the case of SluCas9 or SaCas9 is at least 20 base pairs in length, or more specifically, within 20-25 base pairs in length (*see, e.g.*, Schmidt et al., 2021, Nature Communications, "Improved CRISPR genome editing using small highly active and specific engineered RNA-guided nucleases"). In some embodiments, the guide sequence and the target region may be 100% complementary or identical. In other embodiments, the guide sequence and the target region may contain at least one mismatch. For example, the guide sequence and the target sequence may contain 1, 2, 3, or 4 mismatches, where the total length of the target sequence is at least 16, 17, 18, 19, 20 or more base pairs. In some embodiments, the total length of the target sequence/guide is no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 22, no more than 23, or no more than 24 nucleotides in length. In some embodiments, the guide sequence and the target region may contain 1-4 mismatches where the guide sequence comprises at least 16, 17, 18, 19, 20 or more nucleotides. In some embodiments, the guide sequence and the target region may contain 1, 2, 3, or 4 mismatches where the guide sequence comprises 20 nucleotides. In some embodiments, the guide sequence and the target region do not contain any mismatches.

[0029] In some embodiments, the guide sequence comprises a sequence selected from SEQ ID NOs: 1-159, 200-292, 924-938, or 950-955, wherein if the 5' terminal nucleotide is not guanine, one or more guanine (g) is added to the sequence at its 5' end. In some embodiments, the 5' g or gg is included in some instances for transcription, for example, for expression by the RNA polymerase III-dependent U6 promoter or the T7 promoter. In some embodiments, a 5' guanine is added to any one of the guide sequences or pairs of guide sequences disclosed herein.

[0030] Target sequences for Cas9s include both the positive and negative strands of genomic DNA (i.e., the sequence given and the sequence's reverse compliment), as a nucleic acid substrate for a Cas9 is a double stranded nucleic acid. Accordingly, where a guide sequence is said to be "complementary to a target sequence", it is to be understood that the guide sequence may direct a guide RNA to bind to the reverse complement of a target sequence. Thus, in some embodiments, where the guide sequence binds the reverse complement of a target sequence, the guide sequence is identical to certain nucleotides of the target sequence (e.g., the target sequence not including the PAM) except for the substitution of U for T in the guide sequence.

[0031] As used herein, "ribonucleoprotein" (RNP) or "RNP complex" refers to a guide RNA together with a Cas9. In some embodiments, the guide RNA guides the Cas9, such as a SluCas9 or a SaCas9, to a target sequence, and the guide RNA hybridizes with and the agent binds to the target sequence, which can be followed by cleaving or nicking (in the context of a modified "nickase" Cas9).

[0032] 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.

[0033] "mRNA" is used herein to refer to a polynucleotide that is not DNA 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 an mRNA phosphate-sugar backbone consist essentially of ribose residues, 2'-methoxy ribose residues, or a combination thereof.

[0034] Guide sequences useful in the guide RNA compositions and methods described herein are shown, for example, in **Tables 1-6,** and throughout the specification.

[0035] As used herein, a "target sequence" refers to a sequence of nucleic acid in a target gene that has complementarity to at least a portion of the guide sequence of the guide RNA. The interaction of the target sequence and the guide sequence directs a Cas9 to bind, and potentially nick or cleave (depending on the activity of the agent), within or near the target sequence.

[0036] As used herein, "treatment" refers to any administration or application of a therapeutic for disease or disorder in a subject, and includes inhibiting the disease or development of the disease (which may occur before or after the disease is formally diagnosed, e.g., in cases where a subject has a genotype that has the potential or is likely to result in development of the disease), arresting its development, relieving one or more symptoms of the disease, curing the disease, or preventing reoccurrence of one or more symptoms of the disease. For example, treatment of DMD may comprise alleviating symptoms of DMD.

[0037] As used herein, "ameliorating" refers to any beneficial effect on a phenotype or symptom, such as reducing its severity, slowing or delaying its development, arresting its development, or partially or completely reversing or eliminating it. In the case of quantitative phenotypes such as expression levels, ameliorating encompasses changing the expression level so that it is closer to the expression level seen in healthy or unaffected cells or individuals.

[0038] A "pharmaceutically acceptable excipient" refers to an agent that is included in a pharmaceutical formulation that is not the active ingredient. Pharmaceutically acceptable excipients may e.g., aid in drug delivery or support or enhance stability or bioavailability.

[0039] The term "about" or "approximately" means an acceptable error for a particular value as determined by one of ordinary skill in the art, which depends in part on how the value is measured or determined.

[0040] As used herein, "*Staphylococcus aureus* Cas9" may also be referred to as SaCas9, and includes wild type SaCas9 (e.g., SEQ ID NO: 711) and variants thereof. A variant of SaCas9 comprises one or more amino acid changes as compared to SEQ ID NO: 711, including insertion, deletion, or substitution of one or more amino acids, or a chemical modification to one or more amino acids. For clarity, SaCas9KKH is a SaCas9 variant.

[0041] As used herein, "*Staphylococcus lugdunensis* Cas9" may also be referred to as SluCas9, and includes wild type SluCas9 (e.g., SEQ ID NO: 712) and variants thereof. A variant of SluCas9 comprises one or more amino acid changes as compared to SEQ ID NO: 712, including insertion, deletion, or substitution of one or more amino acids, or a chemical modification to one or more amino acids.

II. Compositions

[0042] Provided herein are compositions comprising guide RNAs and pairs of guide RNAs useful for treating Duchenne Muscular Dystrophy (DMD). The provided pairs of guide RNAs, when used with the correct endonuclease, function to precisely delete a small portion (e.g., less than about 250 nucleotides) of exon 44, 45, 50, 51, or 53 of the DMD gene. **Table 6** provides a listing of guide sequences of guide RNAs, and **Tables 1A-5D** provide detailed information regarding these sequences.

Guides and Guide Pairs

a) Exon 44:

(1) Table 1A. Exon 44 SaCas9 guides:

Seq ID No.	Guide ID or Guide RNA Name	Guide Sequence
1	E44Sa1	ATTTAGCATGTTCCCAATTCTC
2	E44Sa3	TCTCAGAAAGACACAAATTCCT
104	E44SaCas9KKH2	TACCATTTGTATTTAGCATGTT
105	E44SaCas9KKH3	ATTTAGCATGTTCCCAATTCTC
106	E44SaCas9KKH4	AACTGTTCAGCTTCTGTTAGCC
107	E44SaCas9KKH5	TTCAGCTTCTGTTAGCCACTGA
108	E44SaCas9KKH6	CACTGATTAAATATCTTTATAT
109	E44SaCas9KKH7	ATGAAAACGCCGCCATTTCTCA
110	E44SaCas9KKH8	CCGCCATTTCTCAACAGATCTG
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT
118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC
119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG

125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG

(2) *Table 1B. Exon 44 SaCas9 pairs:*

Guide 1 Seq ID No.	**Guide 1**	**Guide 1 Sequence**	**Guide 2 Seq ID No.**	**Guide 2**	**Guide 2 Sequence**
1	E44Sa1	ATTTAGCATGTTCCCAATTCTC	2	E44Sa3	TCTCAGAAAGACACAAATTCCT
110	E44SaCas9KKH8	CCGCCATTTCTCAACAGATCTG	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
110	E44SaCas9KKH8	CCGCCATTTCTCAACAGATCTG	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
110	E44SaCas9KKH8	CCGCCATTTCTCAACAGATCTG	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
110	E44SaCas9KKH8	CCGCCATTTCTCAACAGATCTG	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
110	E44SaCas9KKH8	CCGCCATTTCTCAACAGATCTG	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
110	E44SaCas9KKH8	CCGCCATTTCTCAACAGATCTG	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
111	E44SaCas9KKH9	CAACAGATCTGTCAAATCGCCT	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
112	E44SaCas9KKH14	TAAATACAAATGGTATCTTAAG	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
112	E44SaCas9K	TAAATACAAATGGTAT	125	E44SaCas9K	GCTTTTACCTGCAGGC

	KH14	CTTAAG		KH27	GATTTG
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
113	E44SaCas9KKH15	ATGCTAAATACAAATGGTATCT	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
114	E44SaCas9KKH16	AATTGGGAACATGCTAAATACA	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
115	E44SaCas9KKH17	GAGAATTGGGAACATGCTAAAT	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG	117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG	118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG	119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
116	E44SaCas9K	ATTCCTGAGAATTGGG	120	E44SaCas9K	CATTATGATATAAAGA

	KH18	AACATG		KH22	TATTTA
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
116	E44SaCas9KKH18	ATTCCTGAGAATTGGGAACATG	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT	118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT	119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
117	E44SaCas9KKH19	TCTCAGAAAGACACAAATTCCT	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC	119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG
118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
118	E44SaCas9KKH20	CTGAACAGTTTCTCAGAAAGAC	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG	120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA
119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
119	E44SaCas9KKH21	AATCAGTGGCTAACAGAAGCTG	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA	121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA
120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
120	E44SaCas9KKH22	CATTATGATATAAAGATATTTA	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA	122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT
121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
121	E44SaCas9KKH23	TTTTCATTATGATATAAAGATA	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT	123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT
122	E44SaCas9K	GGCGGCGTTTTCATTA	124	E44SaCas9K	AGGCGATTTGACAGAT

	KH24	TGATAT		KH26	CTGTTG
122	E44SaCas9KKH24	GGCGGCGTTTTCATTATGATAT	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT	124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG
123	E44SaCas9KKH25	TGAGAAATGGCGGCGTTTTCAT	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG
124	E44SaCas9KKH26	AGGCGATTTGACAGATCTGTTG	125	E44SaCas9KKH27	GCTTTTACCTGCAGGCGATTTG

(3) Table 1C. Exon 44 SluCas9 guides:

Seq ID No.	**Guide ID or Guide RNA Name**	**Guide Sequence**
200	E44Slu1	TATTTAGCATGTTCCCAATTCT
201	E44Slu2	AACAGATCTGTCAAATCGCCTG
202	E44Slu4	TGCTAAATACAAATGGTATCTT
203	E44Slu5	ATTGGGAACATGCTAAATACAA
204	E44Slu6	AAAGACACAAATTCCTGAGAAT
205	E44Slu7	GAAAGACACAAATTCCTGAGAA
206	E44Slu8	ATGATATAAAGATATTTAATCA
207	E44Slu9	TTGACAGATCTGTTGAGAAATG
208	E44Slu10	GATTTGACAGATCTGTTGAGAA

(4) Table 1D. Exon 44 SluCas9 pairs:

Guide 1 Seq ID No.	**Guide 1**	**Guide 1 Sequence**	**Guide 2 Seq ID No.**	**Guide 2**	**Guide 2 Sequence**
200	E44SL1	TATTTAGCATGTTCCCAATTCT	201	E44SL2	AACAGATCTGTCAAATCGCCTG
200	E44SL1	TATTTAGCATGTTCCCAATTCT	202	E44SL4	TGCTAAATACAAATGGTATCTT
200	E44SL1	TATTTAGCATGTTCCCAATTCT	203	E44SL5	ATTGGGAACATGCTAAATACAA
200	E44SL1	TATTTAGCATGTTCCCAATTCT	204	E44SL6	AAAGACACAAATTCCTGAGAAT
200	E44SL1	TATTTAGCATGTTCCCAATTCT	205	E44SL7	GAAAGACACAAATTCCTGAGAA
200	E44SL1	TATTTAGCATGTTCCCAATTCT	206	E44SL8	ATGATATAAAGATATTTAATCA
200	E44SL1	TATTTAGCATGTTCCCAATTCT	207	E44SL9	TTGACAGATCTGTTGAGAAATG
200	E44SL1	TATTTAGCATGTTCCCAATTCT	208	E44SL10	GATTTGACAGATCTGTTGAGAA
201	E44SL2	AACAGATCTGTCAAATCGCCTG	202	E44SL4	TGCTAAATACAAATGGTATCTT
201	E44SL2	AACAGATCTGTCAAATCGCCTG	203	E44SL5	ATTGGGAACATGCTAAATACAA
201	E44SL2	AACAGATCTGTCAAATCGCCTG	204	E44SL6	AAAGACACAAATTCCTGAGAAT
201	E44SL2	AACAGATCTGTCAAATCGCCTG	205	E44SL7	GAAAGACACAAATTCCTGAGAA
201	E44SL2	AACAGATCTGTCAAATCGCCTG	206	E44SL8	ATGATATAAAGATATTTAATCA
201	E44SL2	AACAGATCTGTCAAATCGCCTG	207	E44SL9	TTGACAGATCTGTTGAGAAATG
201	E44SL2	AACAGATCTGTCAAATCGCCTG	208	E44SL10	GATTTGACAGATCTGTTGAGAA
202	E44SL4	TGCTAAATACAAATGGTATCTT	203	E44SL5	ATTGGGAACATGCTAAATACAA
202	E44SL4	TGCTAAATACAAATGGTATCTT	204	E44SL6	AAAGACACAAATTCCTGAGAAT
202	E44SL4	TGCTAAATACAAATGGTATCTT	205	E44SL7	GAAAGACACAAATTCCTGAGAA
202	E44SL4	TGCTAAATACAAATGGTATCTT	206	E44SL8	ATGATATAAAGATATTTAATCA
202	E44SL4	TGCTAAATACAAATGGTATCTT	207	E44SL9	TTGACAGATCTGTTGAGAAATG
202	E44SL4	TGCTAAATACAAATGGTATCTT	208	E44SL10	GATTTGACAGATCTGTTGAGAA
203	E44SL5	ATTGGGAACATGCTAAATACAA	204	E44SL6	AAAGACACAAATTCCTGAGAAT
203	E44SL5	ATTGGGAACATGCTAAATACAA	205	E44SL7	GAAAGACACAAATTCCTGAGAA

203	E44SL5	ATTGGGAACATGCTAAATACAA	206	E44SL8	ATGATATAAAGATATTTAATCA
203	E44SL5	ATTGGGAACATGCTAAATACAA	207	E44SL9	TTGACAGATCTGTTGAGAAATG
203	E44SL5	ATTGGGAACATGCTAAATACAA	208	E44SL10	GATTTGACAGATCTGTTGAGAA
204	E44SL6	AAAGACACAAATTCCTGAGAAT	205	E44SL7	GAAAGACACAAATTCCTGAGAA
204	E44SL6	AAAGACACAAATTCCTGAGAAT	206	E44SL8	ATGATATAAAGATATTTAATCA
204	E44SL6	AAAGACACAAATTCCTGAGAAT	207	E44SL9	TTGACAGATCTGTTGAGAAATG
204	E44SL6	AAAGACACAAATTCCTGAGAAT	208	E44SL10	GATTTGACAGATCTGTTGAGAA
205	E44SL7	GAAAGACACAAATTCCTGAGAA	206	E44SL8	ATGATATAAAGATATTTAATCA
205	E44SL7	GAAAGACACAAATTCCTGAGAA	207	E44SL9	TTGACAGATCTGTTGAGAAATG
205	E44SL7	GAAAGACACAAATTCCTGAGAA	208	E44SL10	GATTTGACAGATCTGTTGAGAA
206	E44SL8	ATGATATAAAGATATTTAATCA	207	E44SL9	TTGACAGATCTGTTGAGAAATG
206	E44SL8	ATGATATAAAGATATTTAATCA	208	E44SL10	GATTTGACAGATCTGTTGAGAA
207	E44SL9	TTGACAGATCTGTTGAGAAATG	208	E44SL10	GATTTGACAGATCTGTTGAGAA

b) Exon 45:

(1) Table 2A. Exon 45 SaCas9 guides:

Seq ID No.	**Guide ID or Guide RNA Name**	**Guide Sequence**
3	E45Sa1	TCAGGCTTCCCAATTTTTCCTG
4	E45Sa2	TAGAATACTGGCATCTGTTTTT
5	E45Sa3	TGGCATCTGTTTTTGAGGATTG
6	E45Sa4	TTGCCGCTGCCCAATGCCATCC
7	E45Sa6	TCTACAGGAAAAATTGGGAAGC
8	E45Sa7	GCGGCAAACTGTTGTCAGAACA
9	E45Sa8	TTTTGGTATCTTACAGGAACTC
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC
127	E45SaCas9KKH2	CTGCCACCGCAGATTCAGGCTT
128	E45SaCas9KKH3	TCAGGCTTCCCAATTTTTCCTG
129	E45SaCas9KKH4	TAGAATACTGGCATCTGTTTTT
130	E45SaCas9KKH5	TGGCATCTGTTTTTGAGGATTG
131	E45SaCas9KKH6	AGGATTGCTGAATTATTTCTTC
132	E45SaCas9KKH7	AATTATTTCTTCCCCAGTTGCA
133	E45SaCas9KKH8	CAGTTGCATTCAATGTTCTGAC
134	E45SaCas9KKH9	TTCTCACAACACTTTCCCCCTG
135	E45SaCas9KKH10	TTGCCGCTGCCCAATGCCATCC
136	E45SaCas9KKH16	AAACAGCTGTCAGACAGAAAAA
137	E45SaCas9KKH17	GAAGCCTGAATCTGCGGTGGCA
138	E45SaCas9KKH18	GAAAAATTGGGAAGCCTGAATC
139	E45SaCas9KKH19	TCTACAGGAAAAATTGGGAAGC
140	E45SaCas9KKH20	ACACATCCCACTATTCTACACC
141	E45SaCas9KKH21	TCAGCAATCCTCAAAAACAGAT
142	E45SaCas9KKH22	AATAATTCAGCAATCCTCAAAA
143	E45SaCas9KKH23	GCAACTGGGGAAGAAATAATTC

144	E45SaCas9KKH24	CATTGAATGCAACTGGGGAAGA
145	E45SaCas9KKH25	GAACATTGAATGCAACTGGGGA
146	E45SaCas9KKH26	GCGGCAAACTGTTGTCAGAACA
147	E45SaCas9KKH27	TTTTGGTATCTTACAGGAACTC

(2) Table 2B. Exon 45 SaCas9 pairs:

Guide 1 Seq ID No.	Guide 1	Guide 1 Sequence	Guide 2 Seq ID No.	Guide 2	Guide 2 Sequence
3	E45Sa1	TCAGGCTTCCCAATTTTTCCTG	4	E45Sa2	TAGAATACTGGCATCTGTTTTT
3	E45Sa1	TCAGGCTTCCCAATTTTTCCTG	5	E45Sa3	TGGCATCTGTTTTTGAGGATTG
3	E45Sa1	TCAGGCTTCCCAATTTTTCCTG	6	E45Sa4	TTGCCGCTGCCCAATGCCATCC
3	E45Sa1	TCAGGCTTCCCAATTTTTCCTG	7	E45Sa6	TCTACAGGAAAAATTGGGAAGC
3	E45Sa1	TCAGGCTTCCCAATTTTTCCTG	8	E45Sa7	GCGGCAAACTGTTGTCAGAACA
3	E45Sa1	TCAGGCTTCCCAATTTTTCCTG	9	E45Sa8	TTTTGGTATCTTACAGGAACTC
4	E45Sa2	TAGAATACTGGCATCTGTTTTT	5	E45Sa3	TGGCATCTGTTTTTGAGGATTG
4	E45Sa2	TAGAATACTGGCATCTGTTTTT	6	E45Sa4	TTGCCGCTGCCCAATGCCATCC
4	E45Sa2	TAGAATACTGGCATCTGTTTTT	7	E45Sa6	TCTACAGGAAAAATTGGGAAGC
4	E45Sa2	TAGAATACTGGCATCTGTTTTT	8	E45Sa7	GCGGCAAACTGTTGTCAGAACA
4	E45Sa2	TAGAATACTGGCATCTGTTTTT	9	E45Sa8	TTTTGGTATCTTACAGGAACTC
5	E45Sa3	TGGCATCTGTTTTTGAGGATTG	6	E45Sa4	TTGCCGCTGCCCAATGCCATCC
5	E45Sa3	TGGCATCTGTTTTTGAGGATTG	7	E45Sa6	TCTACAGGAAAAATTGGGAAGC
5	E45Sa3	TGGCATCTGTTTTTGAGGATTG	8	E45Sa7	GCGGCAAACTGTTGTCAGAACA
5	E45Sa3	TGGCATCTGTTTTTGAGGATTG	9	E45Sa8	TTTTGGTATCTTACAGGAACTC
6	E45Sa4	TTGCCGCTGCCCAATGCCATCC	7	E45Sa6	TCTACAGGAAAAATTGGGAAGC
6	E45Sa4	TTGCCGCTGCCCAATGCCATCC	8	E45Sa7	GCGGCAAACTGTTGTCAGAACA
6	E45Sa4	TTGCCGCTGCCCAATGCCATCC	9	E45Sa8	TTTTGGTATCTTACAGGAACTC
7	E45Sa6	TCTACAGGAAAAATTGGGAAGC	8	E45Sa7	GCGGCAAACTGTTGTCAGAACA
7	E45Sa6	TCTACAGGAAAAATTGGGAAGC	9	E45Sa8	TTTTGGTATCTTACAGGAACTC
8	E45Sa7	GCGGCAAACTGTTGTCAGAACA	9	E45Sa8	TTTTGGTATCTTACAGGAACTC
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	127	E45SaCas9KKH2	CTGCCACCGCAGATTCAGGCTT
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	128	E45SaCas9KKH3	TCAGGCTTCCCAATTTTTCCTG
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	129	E45SaCas9KKH4	TAGAATACTGGCATCTGTTTTT
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	130	E45SaCas9KKH5	TGGCATCTGTTTTTGAGGATTG
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	131	E45SaCas9KKH6	AGGATTGCTGAATTATTTCTTC
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	132	E45SaCas9KKH7	AATTATTTCTTCCCCAGTTGCA
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	133	E45SaCas9KKH8	CAGTTGCATTCAATGTTCTGAC
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	134	E45SaCas9KKH9	TTCTGACAACAGTTTGCCGCTG
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	135	E45SaCas9KKH10	TTGCCGCTGCCCAATGCCATCC
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	136	E45SaCas9KKH16	AAACAGCTGTCAGACAGAAAAA
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126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	139	E45SaCas9KKH19	TCTACAGGAAAAATTGGGAAGC
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126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	141	E45SaCas9KKH21	TCAGCAATCCTCAAAAACAGAT
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126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	143	E45SaCas9KKH23	GCAACTGGGGAAGAAATAATTC
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126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	145	E45SaCas9KKH25	GAACATTGAATGCAACTGGGGA
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	146	E45SaCas9KKH26	GCGGCAAACTGTTGTCAGAACA
126	E45SaCas9KKH1	TGTTTGCAGACCTCCTGCCACC	147	E45SaCas9KKH27	TTTTGGTATCTTACAGGAACTC
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127	E45SaCas9KKH2	CTGCCACCGCAGATTCAGGCTT	129	E45SaCas9KKH4	TAGAATACTGGCATCTGTTTTT
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127	E45SaCas9KKH2	CTGCCACCGCAGATTCAGGCTT	132	E45SaCas9KKH7	AATTATTTCTTCCCCAGTTGCA
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127	E45SaCas9KKH2	CTGCCACCGCAGATTCAGGCTT	136	E45SaCas9KKH16	AAACAGCTGTCAGACAGAAAAA
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127	E45SaCas9KKH2	CTGCCACCGCAGATTCAGGCTT	143	E45SaCas9KKH23	GCAACTGGGGAAGAAATAATTC
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127	E45SaCas9KKH2	CTGCCACCGCAGATTCAGGCTT	145	E45SaCas9KKH25	GAACATTGAATGCAACTGGGGA
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137	E45SaCas9KKH17	GAAGCCTGAATCTGCGGTGGCA	142	E45SaCas9KKH22	AATAATTCAGCAATCCTCAAAA
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138	E45SaCas9KKH 18	GAAAAATTGGGAAGCCTGAATC	140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG
138	E45SaCas9KKH 18	GAAAAATTGGGAAGCCTGAATC	141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT
138	E45SaCas9KKH 18	GAAAAATTGGGAAGCCTGAATC	142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA
138	E45SaCas9KKH 18	GAAAAATTGGGAAGCCTGAATC	143	E45SaCas9KKH 23	GCAACTGGGGAAGAAATAATTC
138	E45SaCas9KKH 18	GAAAAATTGGGAAGCCTGAATC	144	E45SaCas9KKH 24	CATTGAATGCAACTGGGGAAGA
138	E45SaCas9KKH 18	GAAAAATTGGGAAGCCTGAATC	145	E45SaCas9KKH 25	GAACATTGAATGCAACTGGGGA
138	E45SaCas9KKH 18	GAAAAATTGGGAAGCCTGAATC	146	E45SaCas9KKH 26	GCGGCAAACTGTTGTCAGAACA
138	E45SaCas9KKH 18	GAAAAATTGGGAAGCCTGAATC	147	E45SaCas9KKH 27	TTTTGGTATCTTACAGGAACTC
139	E45SaCas9KKH 19	TCTACAGGAAAAATTGGGAAGC	140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG
139	E45SaCas9KKH 19	TCTACAGGAAAAATTGGGAAGC	141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT
139	E45SaCas9KKH 19	TCTACAGGAAAAATTGGGAAGC	142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA
139	E45SaCas9KKH 19	TCTACAGGAAAAATTGGGAAGC	143	E45SaCas9KKH 23	GCAACTGGGGAAGAAATAATTC
139	E45SaCas9KKH 19	TCTACAGGAAAAATTGGGAAGC	144	E45SaCas9KKH 24	CATTGAATGCAACTGGGGAAGA
139	E45SaCas9KKH 19	TCTACAGGAAAAATTGGGAAGC	145	E45SaCas9KKH 25	GAACATTGAATGCAACTGGGGA
139	E45SaCas9KKH 19	TCTACAGGAAAAATTGGGAAGC	146	E45SaCas9KKH 26	GCGGCAAACTGTTGTCAGAACA
139	E45SaCas9KKH 19	TCTACAGGAAAAATTGGGAAGC	147	E45SaCas9KKH 27	TTTTGGTATCTTACAGGAACTC
140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG	141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT
140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG	142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA
140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG	143	E45SaCas9KKH 23	GCAACTGGGGAAGAAATAATTC
140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG	144	E45SaCas9KKH 24	CATTGAATGCAACTGGGGAAGA
140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG	145	E45SaCas9KKH 25	GAACATTGAATGCAACTGGGGA
140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG	146	E45SaCas9KKH 26	GCGGCAAACTGTTGTCAGAACA
140	E45SaCas9KKH 20	ACAGATGCCAGTATTCTACAGG	147	E45SaCas9KKH 27	TTTTGGTATCTTACAGGAACTC
141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT	142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA
141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT	143	E45SaCas9KKH 23	GCAACTGGGGAAGAAATAATTC
141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT	144	E45SaCas9KKH 24	CATTGAATGCAACTGGGGAAGA
141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT	145	E45SaCas9KKH 25	GAACATTGAATGCAACTGGGGA
141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT	146	E45SaCas9KKH 26	GCGGCAAACTGTTGTCAGAACA
141	E45SaCas9KKH 21	TCAGCAATCCTCAAAAACAGAT	147	E45SaCas9KKH 27	TTTTGGTATCTTACAGGAACTC
142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA	143	E45SaCas9KKH 23	GCAACTGGGGAAGAAATAATTC
142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA	144	E45SaCas9KKH 24	CATTGAATGCAACTGGGGAAGA
142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA	145	E45SaCas9KKH 25	GAACATTGAATGCAACTGGGGA
142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA	146	E45SaCas9KKH 26	GCGGCAAACTGTTGTCAGAACA
142	E45SaCas9KKH 22	AATAATTCAGCAATCCTCAAAA	147	E45SaCas9KKH 27	TTTTGGTATCTTACAGGAACTC
143	E45SaCas9KKH 23	GCAACTGGGGAAGAAATAATTC	144	E45SaCas9KKH 24	CATTGAATGCAACTGGGGAAGA
143	E45SaCas9KKH 23	GCAACTGGGGAAGAAATAATTC	145	E45SaCas9KKH 25	GAACATTGAATGCAACTGGGGA
143	E45SaCas9KKH 23	GCAACTGGGGAAGAAATAATTC	146	E45SaCas9KKH 26	GCGGCAAACTGTTGTCAGAACA

143	E45SaCas9KKH23	GCAACTGGGGAAGAAATAATTC	147	E45SaCas9KKH27	TTTTGGTATCTTACAGGAACTC
144	E45SaCas9KKH24	CATTGAATGCAACTGGGGAAGA	145	E45SaCas9KKH25	GAACATTGAATGCAACTGGGGA
144	E45SaCas9KKH24	CATTGAATGCAACTGGGGAAGA	146	E45SaCas9KKH26	GCGGCAAACTGTTGTCAGAACA
144	E45SaCas9KKH24	CATTGAATGCAACTGGGGAAGA	147	E45SaCas9KKH27	TTTTGGTATCTTACAGGAACTC
145	E45SaCas9KKH25	GAACATTGAATGCAACTGGGGA	146	E45SaCas9KKH26	GCGGCAAACTGTTGTCAGAACA
145	E45SaCas9KKH25	GAACATTGAATGCAACTGGGGA	147	E45SaCas9KKH27	TTTTGGTATCTTACAGGAACTC
146	E45SaCas9KKH26	GCGGCAAACTGTTGTCAGAACA	147	E45SaCas9KKH27	TTTTGGTATCTTACAGGAACTC

(3) Table 2C. Exon 45 SluCas9 guides:

Seq ID No.	**Guide ID or Guide RNA Name**	**Guide Sequence**
209	E45Slu1	AGACCTCCTGCCACCGCAGATT
210	E45Slu2	TCCCAATTTTTCCTGTAGAATA
211	E45Slu3	TAGAATACTGGCATCTGTTTTT
212	E45Slu4	TTTGCCGCTGCCCAATGCCATC
213	E45Slu7	CTGTCAGACAGAAAAAAGAGGT
214	E45Slu8	GCTGTCAGACAGAAAAAAGAGG
215	E45Slu9	AACAGCTGTCAGACAGAAAAAA
216	E45Slu10	AAGCCTGAATCTGCGGTGGCAG
217	E45Slu11	GGGAAGCCTGAATCTGCGGTGG
218	E45Slu12	AATTGGGAAGCCTGAATCTGCG
219	E45Slu13	AAAAATTGGGAAGCCTGAATCT
220	E45Slu14	GCCAGTATTCTACAGGAAAAAT
221	E45Slu15	TGCCAGTATTCTACAGGAAAAA
222	E45Slu16	AAAAACAGATGCCAGTATTCTA
223	E45Slu17	TGTCAGAACATTGAATGCAACT
224	E45Slu18	TTGTCAGAACATTGAATGCAAC
225	E45Slu19	GTTGTCAGAACATTGAATGCAA
226	E45Slu20	AACTCCAGGATGGCATTGGGCA
227	E45Slu21	TACAGGAACTCCAGGATGGCAT
228	E45Slu22	TTACAGGAACTCCAGGATGGCA
229	E45Slu23	GGTATCTTACAGGAACTCCAGG
230	E45Slu24	TTTTGGTATCTTACAGGAACTC

(4) Table 2D. Exon 45 SluCas9 pairs:

Guide 1 Seq ID No.	**Guide 1**	**Guide 1 Sequence**	**Guide 2 Seq ID No.**	**Guide 2**	**Guide 2 Sequence**
209	E45SL1	AGACCTCCTGCCACCGCAGATT	210	E45SL2	TCCCAATTTTTCCTGTAGAATA
209	E45SL1	AGACCTCCTGCCACCGCAGATT	211	E45SL3	TAGAATACTGGCATCTGTTTTT
209	E45SL1	AGACCTCCTGCCACCGCAGATT	212	E45SL4	TTTGCCGCTGCCCAATGCCATC
209	E45SL1	AGACCTCCTGCCACCGCAGATT	213	E45SL7	CTGTCAGACAGAAAAAAGAGGT
209	E45SL1	AGACCTCCTGCCACCGCAGATT	214	E45SL8	GCTGTCAGACAGAAAAAAGAGG
209	E45SL1	AGACCTCCTGCCACCGCAGATT	215	E45SL9	AACAGCTGTCAGACAGAAAAAA
209	E45SL1	AGACCTCCTGCCACCGCAGATT	216	E45SL10	AAGCCTGAATCTGCGGTGGCAG
209	E45SL1	AGACCTCCTGCCACCGCAGATT	217	E45SL11	GGGAAGCCTGAATCTGCGGTGG

209	E45SL1	AGACCTCCTGCCACCGCAGATT	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
209	E45SL1	AGACCTCCTGCCACCGCAGATT	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
209	E45SL1	AGACCTCCTGCCACCGCAGATT	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
209	E45SL1	AGACCTCCTGCCACCGCAGATT	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
209	E45SL1	AGACCTCCTGCCACCGCAGATT	222	E45SL16	AAAAACAGATGCCAGTATTCTA
209	E45SL1	AGACCTCCTGCCACCGCAGATT	223	E45SL17	TGTCAGAACATTGAATGCAACT
209	E45SL1	AGACCTCCTGCCACCGCAGATT	224	E45SL18	TTGTCAGAACATTGAATGCAAC
209	E45SL1	AGACCTCCTGCCACCGCAGATT	225	E45SL19	GTTGTCAGAACATTGAATGCAA
209	E45SL1	AGACCTCCTGCCACCGCAGATT	226	E45SL20	AACTCCAGGATGGCATTGGGCA
209	E45SL1	AGACCTCCTGCCACCGCAGATT	227	E45SL21	TACAGGAACTCCAGGATGGCAT
209	E45SL1	AGACCTCCTGCCACCGCAGATT	228	E45SL22	TTACAGGAACTCCAGGATGGCA
209	E45SL1	AGACCTCCTGCCACCGCAGATT	229	E45SL23	GGTATCTTACAGGAACTCCAGG
209	E45SL1	AGACCTCCTGCCACCGCAGATT	230	E45SL24	TTTTGGTATCTTACAGGAACTC
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	211	E45SL3	TAGAATACTGGCATCTGTTTTT
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	212	E45SL4	TTTGCCGCTGCCCAATGCCATC
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	213	E45SL7	CTGTCAGACAGAAAAAAGAGGT
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	214	E45SL8	GCTGTCAGACAGAAAAAAGAGG
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	215	E45SL9	AACAGCTGTCAGACAGAAAAAA
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	216	E45SL10	AAGCCTGAATCTGCGGTGGCAG
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	217	E45SL11	GGGAAGCCTGAATCTGCGGTGG
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	222	E45SL16	AAAAACAGATGCCAGTATTCTA
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	223	E45SL17	TGTCAGAACATTGAATGCAACT
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	224	E45SL18	TTGTCAGAACATTGAATGCAAC
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	225	E45SL19	GTTGTCAGAACATTGAATGCAA
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	226	E45SL20	AACTCCAGGATGGCATTGGGCA
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	227	E45SL21	TACAGGAACTCCAGGATGGCAT
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	228	E45SL22	TTACAGGAACTCCAGGATGGCA
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	229	E45SL23	GGTATCTTACAGGAACTCCAGG
210	E45SL2	TCCCAATTTTTCCTGTAGAATA	230	E45SL24	TTTTGGTATCTTACAGGAACTC
211	E45SL3	TAGAATACTGGCATCTGTTTTT	212	E45SL4	TTTGCCGCTGCCCAATGCCATC
211	E45SL3	TAGAATACTGGCATCTGTTTTT	213	E45SL7	CTGTCAGACAGAAAAAAGAGGT
211	E45SL3	TAGAATACTGGCATCTGTTTTT	214	E45SL8	GCTGTCAGACAGAAAAAAGAGG
211	E45SL3	TAGAATACTGGCATCTGTTTTT	215	E45SL9	AACAGCTGTCAGACAGAAAAAA
211	E45SL3	TAGAATACTGGCATCTGTTTTT	216	E45SL10	AAGCCTGAATCTGCGGTGGCAG
211	E45SL3	TAGAATACTGGCATCTGTTTTT	217	E45SL11	GGGAAGCCTGAATCTGCGGTGG
211	E45SL3	TAGAATACTGGCATCTGTTTTT	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
211	E45SL3	TAGAATACTGGCATCTGTTTTT	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
211	E45SL3	TAGAATACTGGCATCTGTTTTT	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
211	E45SL3	TAGAATACTGGCATCTGTTTTT	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
211	E45SL3	TAGAATACTGGCATCTGTTTTT	222	E45SL16	AAAAACAGATGCCAGTATTCTA

211	E45SL3	TAGAATACTGGCATCTGTTTTT	223	E45SL17	TGTCAGAACATTGAATGCAACT
211	E45SL3	TAGAATACTGGCATCTGTTTTT	224	E45SL18	TTGTCAGAACATTGAATGCAAC
211	E45SL3	TAGAATACTGGCATCTGTTTTT	225	E45SL19	GTTGTCAGAACATTGAATGCAA
211	E45SL3	TAGAATACTGGCATCTGTTTTT	226	E45SL20	AACTCCAGGATGGCATTGGGCA
211	E45SL3	TAGAATACTGGCATCTGTTTTT	227	E45SL21	TACAGGAACTCCAGGATGGCAT
211	E45SL3	TAGAATACTGGCATCTGTTTTT	228	E45SL22	TTACAGGAACTCCAGGATGGCA
211	E45SL3	TAGAATACTGGCATCTGTTTTT	229	E45SL23	GGTATCTTACAGGAACTCCAGG
211	E45SL3	TAGAATACTGGCATCTGTTTTT	230	E45SL24	TTTTGGTATCTTACAGGAACTC
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	213	E45SL7	CTGTCAGACAGAAAAAAGAGGT
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	214	E45SL8	GCTGTCAGACAGAAAAAAGAGG
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	215	E45SL9	AACAGCTGTCAGACAGAAAAAA
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	216	E45SL10	AAGCCTGAATCTGCGGTGGCAG
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	217	E45SL11	GGGAAGCCTGAATCTGCGGTGG
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	222	E45SL16	AAAAACAGATGCCAGTATTCTA
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	223	E45SL17	TGTCAGAACATTGAATGCAACT
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	224	E45SL18	TTGTCAGAACATTGAATGCAAC
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	225	E45SL19	GTTGTCAGAACATTGAATGCAA
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	226	E45SL20	AACTCCAGGATGGCATTGGGCA
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	227	E45SL21	TACAGGAACTCCAGGATGGCAT
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	228	E45SL22	TTACAGGAACTCCAGGATGGCA
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	229	E45SL23	GGTATCTTACAGGAACTCCAGG
212	E45SL4	TTTGCCGCTGCCCAATGCCATC	230	E45SL24	TTTTGGTATCTTACAGGAACTC
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	214	E45SL8	GCTGTCAGACAGAAAAAAGAGG
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	215	E45SL9	AACAGCTGTCAGACAGAAAAAA
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	216	E45SL10	AAGCCTGAATCTGCGGTGGCAG
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	217	E45SL11	GGGAAGCCTGAATCTGCGGTGG
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	222	E45SL16	AAAAACAGATGCCAGTATTCTA
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	223	E45SL17	TGTCAGAACATTGAATGCAACT
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	224	E45SL18	TTGTCAGAACATTGAATGCAAC
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	225	E45SL19	GTTGTCAGAACATTGAATGCAA
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	226	E45SL20	AACTCCAGGATGGCATTGGGCA
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	227	E45SL21	TACAGGAACTCCAGGATGGCAT
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	228	E45SL22	TTACAGGAACTCCAGGATGGCA
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	229	E45SL23	GGTATCTTACAGGAACTCCAGG
213	E45SL7	CTGTCAGACAGAAAAAAGAGGT	230	E45SL24	TTTTGGTATCTTACAGGAACTC
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	215	E45SL9	AACAGCTGTCAGACAGAAAAAA

214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	216	E45SL10	AAGCCTGAATCTGCGGTGGCAG
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	217	E45SL11	GGGAAGCCTGAATCTGCGGTGG
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	222	E45SL16	AAAAACAGATGCCAGTATTCTA
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	223	E45SL17	TGTCAGAACATTGAATGCAACT
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	224	E45SL18	TTGTCAGAACATTGAATGCAAC
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	225	E45SL19	GTTGTCAGAACATTGAATGCAA
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	226	E45SL20	AACTCCAGGATGGCATTGGGCA
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	227	E45SL21	TACAGGAACTCCAGGATGGCAT
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	228	E45SL22	TTACAGGAACTCCAGGATGGCA
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	229	E45SL23	GGTATCTTACAGGAACTCCAGG
214	E45SL8	GCTGTCAGACAGAAAAAAGAGG	230	E45SL24	TTTTGGTATCTTACAGGAACTC
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	216	E45SL10	AAGCCTGAATCTGCGGTGGCAG
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	217	E45SL11	GGGAAGCCTGAATCTGCGGTGG
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	222	E45SL16	AAAAACAGATGCCAGTATTCTA
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	223	E45SL17	TGTCAGAACATTGAATGCAACT
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	224	E45SL18	TTGTCAGAACATTGAATGCAAC
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	225	E45SL19	GTTGTCAGAACATTGAATGCAA
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	226	E45SL20	AACTCCAGGATGGCATTGGGCA
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	227	E45SL21	TACAGGAACTCCAGGATGGCAT
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	228	E45SL22	TTACAGGAACTCCAGGATGGCA
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	229	E45SL23	GGTATCTTACAGGAACTCCAGG
215	E45SL9	AACAGCTGTCAGACAGAAAAAA	230	E45SL24	TTTTGGTATCTTACAGGAACTC
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	217	E45SL11	GGGAAGCCTGAATCTGCGGTGG
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	222	E45SL16	AAAAACAGATGCCAGTATTCTA
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	223	E45SL17	TGTCAGAACATTGAATGCAACT
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	224	E45SL18	TTGTCAGAACATTGAATGCAAC
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	225	E45SL19	GTTGTCAGAACATTGAATGCAA
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	226	E45SL20	AACTCCAGGATGGCATTGGGCA
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	227	E45SL21	TACAGGAACTCCAGGATGGCAT
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	228	E45SL22	TTACAGGAACTCCAGGATGGCA
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	229	E45SL23	GGTATCTTACAGGAACTCCAGG
216	E45SL10	AAGCCTGAATCTGCGGTGGCAG	230	E45SL24	TTTTGGTATCTTACAGGAACTC

217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	218	E45SL12	AATTGGGAAGCCTGAATCTGCG
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	222	E45SL16	AAAAACAGATGCCAGTATTCTA
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	223	E45SL17	TGTCAGAACATTGAATGCAACT
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	224	E45SL18	TTGTCAGAACATTGAATGCAAC
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	225	E45SL19	GTTGTCAGAACATTGAATGCAA
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	226	E45SL20	AACTCCAGGATGGCATTGGGCA
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	227	E45SL21	TACAGGAACTCCAGGATGGCAT
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	228	E45SL22	TTACAGGAACTCCAGGATGGCA
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	229	E45SL23	GGTATCTTACAGGAACTCCAGG
217	E45SL11	GGGAAGCCTGAATCTGCGGTGG	230	E45SL24	TTTTGGTATCTTACAGGAACTC
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	219	E45SL13	AAAAATTGGGAAGCCTGAATCT
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	222	E45SL16	AAAAACAGATGCCAGTATTCTA
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	223	E45SL17	TGTCAGAACATTGAATGCAACT
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	224	E45SL18	TTGTCAGAACATTGAATGCAAC
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	225	E45SL19	GTTGTCAGAACATTGAATGCAA
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	226	E45SL20	AACTCCAGGATGGCATTGGGCA
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	227	E45SL21	TACAGGAACTCCAGGATGGCAT
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	228	E45SL22	TTACAGGAACTCCAGGATGGCA
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	229	E45SL23	GGTATCTTACAGGAACTCCAGG
218	E45SL12	AATTGGGAAGCCTGAATCTGCG	230	E45SL24	TTTTGGTATCTTACAGGAACTC
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	220	E45SL14	GCCAGTATTCTACAGGAAAAAT
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	222	E45SL16	AAAAACAGATGCCAGTATTCTA
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	223	E45SL17	TGTCAGAACATTGAATGCAACT
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	224	E45SL18	TTGTCAGAACATTGAATGCAAC
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	225	E45SL19	GTTGTCAGAACATTGAATGCAA
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	226	E45SL20	AACTCCAGGATGGCATTGGGCA
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	227	E45SL21	TACAGGAACTCCAGGATGGCAT
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	228	E45SL22	TTACAGGAACTCCAGGATGGCA
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	229	E45SL23	GGTATCTTACAGGAACTCCAGG
219	E45SL13	AAAAATTGGGAAGCCTGAATCT	230	E45SL24	TTTTGGTATCTTACAGGAACTC
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	221	E45SL15	TGCCAGTATTCTACAGGAAAAA
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	222	E45SL16	AAAAACAGATGCCAGTATTCTA
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	223	E45SL17	TGTCAGAACATTGAATGCAACT
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	224	E45SL18	TTGTCAGAACATTGAATGCAAC
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	225	E45SL19	GTTGTCAGAACATTGAATGCAA
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	226	E45SL20	AACTCCAGGATGGCATTGGGCA
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	227	E45SL21	TACAGGAACTCCAGGATGGCAT
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	228	E45SL22	TTACAGGAACTCCAGGATGGCA

220	E45SL14	GCCAGTATTCTACAGGAAAAAT	229	E45SL23	GGTATCTTACAGGAACTCCAGG
220	E45SL14	GCCAGTATTCTACAGGAAAAAT	230	E45SL24	TTTTGGTATCTTACAGGAACTC
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	222	E45SL16	AAAAACAGATGCCAGTATTCTA
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	223	E45SL17	TGTCAGAACATTGAATGCAACT
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	224	E45SL18	TTGTCAGAACATTGAATGCAAC
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	225	E45SL19	GTTGTCAGAACATTGAATGCAA
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	226	E45SL20	AACTCCAGGATGGCATTGGGCA
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	227	E45SL21	TACAGGAACTCCAGGATGGCAT
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	228	E45SL22	TTACAGGAACTCCAGGATGGCA
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	229	E45SL23	GGTATCTTACAGGAACTCCAGG
221	E45SL15	TGCCAGTATTCTACAGGAAAAA	230	E45SL24	TTTTGGTATCTTACAGGAACTC
222	E45SL16	AAAAACAGATGCCAGTATTCTA	223	E45SL17	TGTCAGAACATTGAATGCAACT
222	E45SL16	AAAAACAGATGCCAGTATTCTA	224	E45SL18	TTGTCAGAACATTGAATGCAAC
222	E45SL16	AAAAACAGATGCCAGTATTCTA	225	E45SL19	GTTGTCAGAACATTGAATGCAA
222	E45SL16	AAAAACAGATGCCAGTATTCTA	226	E45SL20	AACTCCAGGATGGCATTGGGCA
222	E45SL16	AAAAACAGATGCCAGTATTCTA	227	E45SL21	TACAGGAACTCCAGGATGGCAT
222	E45SL16	AAAAACAGATGCCAGTATTCTA	228	E45SL22	TTACAGGAACTCCAGGATGGCA
222	E45SL16	AAAAACAGATGCCAGTATTCTA	229	E45SL23	GGTATCTTACAGGAACTCCAGG
222	E45SL16	AAAAACAGATGCCAGTATTCTA	230	E45SL24	TTTTGGTATCTTACAGGAACTC
223	E45SL17	TGTCAGAACATTGAATGCAACT	224	E45SL18	TTGTCAGAACATTGAATGCAAC
223	E45SL17	TGTCAGAACATTGAATGCAACT	225	E45SL19	GTTGTCAGAACATTGAATGCAA
223	E45SL17	TGTCAGAACATTGAATGCAACT	226	E45SL20	AACTCCAGGATGGCATTGGGCA
223	E45SL17	TGTCAGAACATTGAATGCAACT	227	E45SL21	TACAGGAACTCCAGGATGGCAT
223	E45SL17	TGTCAGAACATTGAATGCAACT	228	E45SL22	TTACAGGAACTCCAGGATGGCA
223	E45SL17	TGTCAGAACATTGAATGCAACT	229	E45SL23	GGTATCTTACAGGAACTCCAGG
223	E45SL17	TGTCAGAACATTGAATGCAACT	230	E45SL24	TTTTGGTATCTTACAGGAACTC
224	E45SL18	TTGTCAGAACATTGAATGCAAC	225	E45SL19	GTTGTCAGAACATTGAATGCAA
224	E45SL18	TTGTCAGAACATTGAATGCAAC	226	E45SL20	AACTCCAGGATGGCATTGGGCA
224	E45SL18	TTGTCAGAACATTGAATGCAAC	227	E45SL21	TACAGGAACTCCAGGATGGCAT
224	E45SL18	TTGTCAGAACATTGAATGCAAC	228	E45SL22	TTACAGGAACTCCAGGATGGCA
224	E45SL18	TTGTCAGAACATTGAATGCAAC	229	E45SL23	GGTATCTTACAGGAACTCCAGG
224	E45SL18	TTGTCAGAACATTGAATGCAAC	230	E45SL24	TTTTGGTATCTTACAGGAACTC
225	E45SL19	GTTGTCAGAACATTGAATGCAA	226	E45SL20	AACTCCAGGATGGCATTGGGCA
225	E45SL19	GTTGTCAGAACATTGAATGCAA	227	E45SL21	TACAGGAACTCCAGGATGGCAT
225	E45SL19	GTTGTCAGAACATTGAATGCAA	228	E45SL22	TTACAGGAACTCCAGGATGGCA
225	E45SL19	GTTGTCAGAACATTGAATGCAA	229	E45SL23	GGTATCTTACAGGAACTCCAGG
225	E45SL19	GTTGTCAGAACATTGAATGCAA	230	E45SL24	TTTTGGTATCTTACAGGAACTC
226	E45SL20	AACTCCAGGATGGCATTGGGCA	227	E45SL21	TACAGGAACTCCAGGATGGCAT
226	E45SL20	AACTCCAGGATGGCATTGGGCA	228	E45SL22	TTACAGGAACTCCAGGATGGCA
226	E45SL20	AACTCCAGGATGGCATTGGGCA	229	E45SL23	GGTATCTTACAGGAACTCCAGG
226	E45SL20	AACTCCAGGATGGCATTGGGCA	230	E45SL24	TTTTGGTATCTTACAGGAACTC
227	E45SL21	TACAGGAACTCCAGGATGGCAT	228	E45SL22	TTACAGGAACTCCAGGATGGCA
227	E45SL21	TACAGGAACTCCAGGATGGCAT	229	E45SL23	GGTATCTTACAGGAACTCCAGG
227	E45SL21	TACAGGAACTCCAGGATGGCAT	230	E45SL24	TTTTGGTATCTTACAGGAACTC

228	E45SL22	TTACAGGAACTCCAGGATGGCA	229	E45SL23	GGTATCTTACAGGAACTCCAGG
228	E45SL22	TTACAGGAACTCCAGGATGGCA	230	E45SL24	TTTTGGTATCTTACAGGAACTC
229	E45SL23	GGTATCTTACAGGAACTCCAGG	230	E45SL24	TTTTGGTATCTTACAGGAACTC

c) Exon 50:

(1) Table 3A. Exon 50 SaCas9 guides:

Seq ID No.	**Guide ID or Guide RNA Name**	**Guide Sequence**
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG
152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG
153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT
154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA
155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC
156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA
158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA

(2) Table 3B. Exon 50 SaCas9 pairs:

Guide 1 Seq ID No.	**Guide 1**	**Guide 1 Sequence**	**Guide 2 Seq ID No.**	**Guide 2**	**Guide 2 Sequence**
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
148	E50SaCas9KKH1	GGGATCCAGTATACTTACAGGC	159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA

149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
149	E50SaCas9KKH2	ATCCAGTATACTTACAGGCTCC	159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
150	E50SaCas9KKH3	CAGTATACTTACAGGCTCCAAT	159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG	152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG	153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG	154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG	155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG	156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG	158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
151	E50SaCas9KKH4	ATACTTACAGGCTCCAATAGTG	159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA
152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG	153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT
152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG	154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA
152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG	155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC
152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG	156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA
152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG	158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
152	E50SaCas9KKH5	CCAATAGTGGTCAGTCCAGGAG	159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA
153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT	154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA
153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT	155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC
153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT	156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA
153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT	158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
153	E50SaCas9KKH6	AGGCTGCTTTGCCCTCAGCTCT	159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA
154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA	155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC
154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA	156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA
154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA	158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
154	E50SaCas9KKH7	TTTGCCCTCAGCTCTTGAAGTA	159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA
155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC	156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT
155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA
155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC	158	E50SaCas9KKH12	AGGAAGTTAGAAGATCTGAGCT
155	E50SaCas9KKH8	TTTACCGCCTTCCACTCAGAGC	159	E50SaCas9KKH13	TTTTCTGTTAAAGAGGAAGTTA
156	E50SaCas9KKH10	GGACTGACCACTATTGGAGCCT	157	E50SaCas9KKH11	AAGATCTGAGCTCTGAGTGGAA

156	E50SaCas9KKH 10	GGACTGACCACTATTGGAGCCT	158	E50SaCas9KKH 12	AGGAAGTTAGAAGATCTGAGCT
156	E50SaCas9KKH 10	GGACTGACCACTATTGGAGCCT	159	E50SaCas9KKH 13	TTTTCTGTTAAAGAGGAAGTTA
157	E50SaCas9KKH 11	AAGATCTGAGCTCTGAGTGGAA	158	E50SaCas9KKH 12	AGGAAGTTAGAAGATCTGAGCT
157	E50SaCas9KKH 11	AAGATCTGAGCTCTGAGTGGAA	159	E50SaCas9KKH 13	TTTTCTGTTAAAGAGGAAGTTA
158	E50SaCas9KKH 12	AGGAAGTTAGAAGATCTGAGCT	159	E50SaCas9KKH 13	TTTTCTGTTAAAGAGGAAGTTA

(3) Table 3C. Exon 50 SluCas9 guides:

Seq ID No.	**Guide ID or Guide RNA Name**	**Sequence**
231	E50Slu2	AGTATACTTACAGGCTCCAATA
232	E50Slu3	CAGGCTCCAATAGTGGTCAGTC
233	E50Slu4	CAATAGTGGTCAGTCCAGGAGC
234	E50Slu5	GTGGTCAGTCCAGGAGCTAGGT
235	E50Slu6	TTGCCCTCAGCTCTTGAAGTAA
236	E50Slu9	CTAGCTCCTGGACTGACCACTA
237	E50Slu10	GCAAAGCAGCCTGACCTAGCTC
238	E50Slu11	AAACCGTTTACTTCAAGAGCTG
239	E50Slu12	TAAACCGTTTACTTCAAGAGCT
240	E50Slu13	AGATCTGAGCTCTGAGTGGAAG
241	E50Slu14	AGAAGATCTGAGCTCTGAGTGG
242	E50Slu15	AGTTAGAAGATCTGAGCTCTGA

(4) Table 3D. Exon 50 SluCas9 pairs:

Guide 1 Seq ID No.	**Guide 1**	**Guide 1 Sequence**	**Guide 2 Seq ID No.**	**Guide 2**	**Guide 2 Sequence**
231	E50SL2	AGTATACTTACAGGCTCCAATA	232	E50SL3	CAGGCTCCAATAGTGGTCAGTC
231	E50SL2	AGTATACTTACAGGCTCCAATA	233	E50SL4	CAATAGTGGTCAGTCCAGGAGC
231	E50SL2	AGTATACTTACAGGCTCCAATA	234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT
231	E50SL2	AGTATACTTACAGGCTCCAATA	235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA
231	E50SL2	AGTATACTTACAGGCTCCAATA	236	E50SL9	CTAGCTCCTGGACTGACCACTA
231	E50SL2	AGTATACTTACAGGCTCCAATA	237	E50SL10	GCAAAGCAGCCTGACCTAGCTC
231	E50SL2	AGTATACTTACAGGCTCCAATA	238	E50SL11	AAACCGTTTACTTCAAGAGCTG
231	E50SL2	AGTATACTTACAGGCTCCAATA	239	E50SL12	TAAACCGTTTACTTCAAGAGCT
231	E50SL2	AGTATACTTACAGGCTCCAATA	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
231	E50SL2	AGTATACTTACAGGCTCCAATA	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
231	E50SL2	AGTATACTTACAGGCTCCAATA	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	233	E50SL4	CAATAGTGGTCAGTCCAGGAGC
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	236	E50SL9	CTAGCTCCTGGACTGACCACTA
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	237	E50SL10	GCAAAGCAGCCTGACCTAGCTC
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	238	E50SL11	AAACCGTTTACTTCAAGAGCTG
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	239	E50SL12	TAAACCGTTTACTTCAAGAGCT
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
232	E50SL3	CAGGCTCCAATAGTGGTCAGTC	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA

233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT
233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA
233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	236	E50SL9	CTAGCTCCTGGACTGACCACTA
233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	237	E50SL10	GCAAAGCAGCCTGACCTAGCTC
233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	238	E50SL11	AAACCGTTTACTTCAAGAGCTG
233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	239	E50SL12	TAAACCGTTTACTTCAAGAGCT
233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
233	E50SL4	CAATAGTGGTCAGTCCAGGAGC	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA
234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT	235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA
234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT	236	E50SL9	CTAGCTCCTGGACTGACCACTA
234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT	237	E50SL10	GCAAAGCAGCCTGACCTAGCTC
234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT	238	E50SL11	AAACCGTTTACTTCAAGAGCTG
234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT	239	E50SL12	TAAACCGTTTACTTCAAGAGCT
234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
234	E50SL5	GTGGTCAGTCCAGGAGCTAGGT	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA
235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA	236	E50SL9	CTAGCTCCTGGACTGACCACTA
235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA	237	E50SL10	GCAAAGCAGCCTGACCTAGCTC
235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA	238	E50SL11	AAACCGTTTACTTCAAGAGCTG
235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA	239	E50SL12	TAAACCGTTTACTTCAAGAGCT
235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
235	E50SL6	TTGCCCTCAGCTCTTGAAGTAA	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA
236	E50SL9	CTAGCTCCTGGACTGACCACTA	237	E50SL10	GCAAAGCAGCCTGACCTAGCTC
236	E50SL9	CTAGCTCCTGGACTGACCACTA	238	E50SL11	AAACCGTTTACTTCAAGAGCTG
236	E50SL9	CTAGCTCCTGGACTGACCACTA	239	E50SL12	TAAACCGTTTACTTCAAGAGCT
236	E50SL9	CTAGCTCCTGGACTGACCACTA	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
236	E50SL9	CTAGCTCCTGGACTGACCACTA	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
236	E50SL9	CTAGCTCCTGGACTGACCACTA	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA
237	E50SL10	GCAAAGCAGCCTGACCTAGCTC	238	E50SL11	AAACCGTTTACTTCAAGAGCTG
237	E50SL10	GCAAAGCAGCCTGACCTAGCTC	239	E50SL12	TAAACCGTTTACTTCAAGAGCT
237	E50SL10	GCAAAGCAGCCTGACCTAGCTC	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
237	E50SL10	GCAAAGCAGCCTGACCTAGCTC	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
237	E50SL10	GCAAAGCAGCCTGACCTAGCTC	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA
238	E50SL11	AAACCGTTTACTTCAAGAGCTG	239	E50SL12	TAAACCGTTTACTTCAAGAGCT
238	E50SL11	AAACCGTTTACTTCAAGAGCTG	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
238	E50SL11	AAACCGTTTACTTCAAGAGCTG	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
238	E50SL11	AAACCGTTTACTTCAAGAGCTG	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA
239	E50SL12	TAAACCGTTTACTTCAAGAGCT	240	E50SL13	AGATCTGAGCTCTGAGTGGAAG
239	E50SL12	TAAACCGTTTACTTCAAGAGCT	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
239	E50SL12	TAAACCGTTTACTTCAAGAGCT	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA
240	E50SL13	AGATCTGAGCTCTGAGTGGAAG	241	E50SL14	AGAAGATCTGAGCTCTGAGTGG
240	E50SL13	AGATCTGAGCTCTGAGTGGAAG	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA

241	E50SL14	AGAAGATCTGAGCTCTGAGTGG	242	E50SL15	AGTTAGAAGATCTGAGCTCTGA

d) Exon 51:

(1) *Table 4A. Exon 51 SaCas9 guides:*

Seq ID No.	Guide ID or Guide RNA Name	Guide Sequence
11	E51Sa1	TAGTAACCACAGGTTGTGTCAC
12	E51Sa2	GTTGTGTCACCAGAGTAACAGT
13	E51Sa4	GAGGGTGATGGTGGGTGACCTT
14	E51Sa5	TATAAAATCACAGAGGGTGATG
15	E51Sa6	TTGATCAAGTTATAAAATCACA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT
29	E51SaCas9KKH3	CCTTCTGCTTGATGATCATCTC
30	E51SaCas9KKH4	ATGATCATCTCGTTGATATCCT
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC
32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA
33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA
34	E51SaCas9KKH8	CTTGATCAAGCAGAGAAAGCCA
35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG
36	E51SaCas9KKH10	CAGTCGGTAAGTTCTGTCCAAG
37	E51SaCas9KKH11	GTAAGTTCTGTCCAAGCCCGGT
38	E51SaCas9KKH12	AGCCCGGTTGAAATCTGCCAGA
39	E51SaCas9KKH13	AGCAGGTACCTCCAACATCAAG
40	E51SaCas9KKH14	CAACATCAAGGAAGATGGCATT
41	E51SaCas9KKH15	AGGAAGATGGCATTTCTAGTTT
42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC
45	E51SaCas9KKH19	TAGTAACCACAGGTTGTGTCAC
46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT
48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC
49	E51SaCas9KKH23	TCTGAGTAGGAGCTAAAATATT
50	E51SaCas9KKH24	AGAAGGTATGAGAAAAAATGAT
51	E51SaCas9KKH25	TCAAGCAGAAGGTATGAGAAAA
52	E51SaCas9KKH26	TCATCAAGCAGAAGGTATGAGA
53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA
55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA

61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC

(2) Table 4B. Exon 51 SaCas9 pairs:

Guide 1 Seq ID No.	Guide 1	Guide 1 Sequence	Guide 2 Seq ID No.	Guide 2	Guide 2 Sequence
11	E51Sa1	TAGTAACCACAGGTTGTGTCAC	12	E51Sa2	GTTGTGTCACCAGAGTAACAGT
11	E51Sa1	TAGTAACCACAGGTTGTGTCAC	13	E51Sa4	GAGGGTGATGGTGGGTGACCTT
11	E51Sa1	TAGTAACCACAGGTTGTGTCAC	14	E51Sa5	TATAAAATCACAGAGGGTGATG
11	E51Sa1	TAGTAACCACAGGTTGTGTCAC	15	E51Sa6	TTGATCAAGTTATAAAATCACA
12	E51Sa2	GTTGTGTCACCAGAGTAACAGT	13	E51Sa4	GAGGGTGATGGTGGGTGACCTT
12	E51Sa2	GTTGTGTCACCAGAGTAACAGT	14	E51Sa5	TATAAAATCACAGAGGGTGATG
12	E51Sa2	GTTGTGTCACCAGAGTAACAGT	15	E51Sa6	TTGATCAAGTTATAAAATCACA
13	E51Sa4	GAGGGTGATGGTGGGTGACCTT	14	E51Sa5	TATAAAATCACAGAGGGTGATG
13	E51Sa4	GAGGGTGATGGTGGGTGACCTT	15	E51Sa6	TTGATCAAGTTATAAAATCACA
14	E51Sa5	TATAAAATCACAGAGGGTGATG	15	E51Sa6	TTGATCAAGTTATAAAATCACA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	29	E51SaCas9KKH3	CCTTCTGCTTGATGATCATCTC
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	30	E51SaCas9KKH4	ATGATCATCTCGTTGATATCCT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	34	E51SaCas9KKH8	CTTGATCAAGCAGAGAAAGCCA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	36	E51SaCas9KKH10	CAGTCGGTAAGTTCTGTCCAAG
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	37	E51SaCas9KKH11	GTAAGTTCTGTCCAAGCCCGGT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	38	E51SaCas9KKH12	AGCCCGGTTGAAATCTGCCAGA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	39	E51SaCas9KKH13	AGCAGGTACCTCCAACATCAAG
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	40	E51SaCas9KKH14	CAACATCAAGGAAGATGGCATT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	41	E51SaCas9KKH15	AGGAAGATGGCATTTCTAGTTT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	45	E51SaCas9KKH19	TAGTAACCACAGGTTGTGTCAC
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT

27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
27	E51SaCas9KKH1	TCATTTTTTCTCATACCTTCTG	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	29	E51SaCas9KKH3	CCTTCTGCTTGATGATCATCTC
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	30	E51SaCas9KKH4	ATGATCATCTCGTTGATATCCT
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	34	E51SaCas9KKH8	CTTGATCAAGCAGAGAAAGCCA
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	36	E51SaCas9KKH10	CAGTCGGTAAGTTCTGTCCAAG
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	37	E51SaCas9KKH11	GTAAGTTCTGTCCAAGCCCGGT
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	38	E51SaCas9KKH12	AGCCCGGTTGAAATCTGCCAGA
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	39	E51SaCas9KKH13	AGCAGGTACCTCCAACATCAAG
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	40	E51SaCas9KKH14	CAACATCAAGGAAGATGGCATT
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	41	E51SaCas9KKH15	AGGAAGATGGCATTTCTAGTTT
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	45	E51SaCas9KKH19	TAGTAACCACAGGTTGTGTCAC
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
28	E51SaCas9KKH2	TTTTTTCTCATACCTTCTGCTT	56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT

28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	57	E51SaCas9KKH 31	TATAAAATCACAGAGGGTGATG
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	58	E51SaCas9KKH 32	AAGTTATAAAATCACAGAGGGT
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	59	E51SaCas9KKH 33	ATCAAGTTATAAAATCACAGAG
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	60	E51SaCas9KKH 34	TTGATCAAGTTATAAAATCACA
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	61	E51SaCas9KKH 35	CTTTCTCTGCTTGATCAAGTTA
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	62	E51SaCas9KKH 36	CCGACTGGCTTTCTCTGCTTGA
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	63	E51SaCas9KKH 37	ACTTACCGACTGGCTTTCTCTG
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	64	E51SaCas9KKH 38	GATGTTGGAGGTACCTGCTCTG
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	65	E51SaCas9KKH 39	AAATGCCATCTTCCTTGATGTT
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	66	E51SaCas9KKH 40	CCAAACTAGAAATGCCATCTTC
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	67	E51SaCas9KKH 41	AGGAAACTGCCATCTCCAAACT
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	68	E51SaCas9KKH 42	CTGTTACTCTGGTGACACAACC
28	E51SaCas9KKH 2	TTTTTTCTCATACCTTCTGCTT	69	E51SaCas9KKH 43	TAGCTCCTACTCAGACTGTTAC
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	31	E51SaCas9KKH 5	AAGGTCACCCACCATCACCCTC
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	32	E51SaCas9KKH 6	ATCACCCTCTGTGATTTTATAA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	33	E51SaCas9KKH 7	ATAACTTGATCAAGCAGAGAAA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	34	E51SaCas9KKH 8	CTTGATCAAGCAGAGAAAGCCA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	35	E51SaCas9KKH 9	ATCAAGCAGAGAAAGCCAGTCG
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	36	E51SaCas9KKH 10	CAGTCGGTAAGTTCTGTCCAAG
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	37	E51SaCas9KKH 11	GTAAGTTCTGTCCAAGCCCGGT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	38	E51SaCas9KKH 12	AGCCCGGTTGAAATCTGCCAGA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	39	E51SaCas9KKH 13	AGCAGGTACCTCCAACATCAAG
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	40	E51SaCas9KKH 14	CAACATCAAGGAAGATGGCATT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	41	E51SaCas9KKH 15	AGGAAGATGGCATTTCTAGTTT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	42	E51SaCas9KKH 16	ATGGCATTTCTAGTTTGGAGAT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	43	E51SaCas9KKH 17	CTAGTTTGGAGATGGCAGTTTC
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	47	E51SaCas9KKH 21	GTTGTGTCACCAGAGTAACAGT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	48	E51SaCas9KKH 22	GAGTAACAGTCTGAGTAGGAGC
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	53	E51SaCas9KKH 27	TCAACGAGATGATCATCAAGCA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	54	E51SaCas9KKH 28	GTGACCTTGAGGATATCAACGA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	55	E51SaCas9KKH 29	TGGGTGACCTTGAGGATATCAA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	56	E51SaCas9KKH 30	GAGGGTGATGGTGGGTGACCTT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	57	E51SaCas9KKH 31	TATAAAATCACAGAGGGTGATG
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	58	E51SaCas9KKH 32	AAGTTATAAAATCACAGAGGGT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	59	E51SaCas9KKH 33	ATCAAGTTATAAAATCACAGAG
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	60	E51SaCas9KKH 34	TTGATCAAGTTATAAAATCACA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	61	E51SaCas9KKH 35	CTTTCTCTGCTTGATCAAGTTA
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	62	E51SaCas9KKH 36	CCGACTGGCTTTCTCTGCTTGA

29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	63	E51SaCas9KKH 37	ACTTACCGACTGGCTTTCTCTG
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	64	E51SaCas9KKH 38	GATGTTGGAGGTACCTGCTCTG
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	65	E51SaCas9KKH 39	AAATGCCATCTTCCTTGATGTT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	66	E51SaCas9KKH 40	CCAAACTAGAAATGCCATCTTC
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	67	E51SaCas9KKH 41	AGGAAACTGCCATCTCCAAACT
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	68	E51SaCas9KKH 42	CTGTTACTCTGGTGACACAACC
29	E51SaCas9KKH 3	CCTTCTGCTTGATGATCATCTC	69	E51SaCas9KKH 43	TAGCTCCTACTCAGACTGTTAC
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	31	E51SaCas9KKH 5	AAGGTCACCCACCATCACCCTC
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	32	E51SaCas9KKH 6	ATCACCCTCTGTGATTTTATAA
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	33	E51SaCas9KKH 7	ATAACTTGATCAAGCAGAGAAA
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	34	E51SaCas9KKH 8	CTTGATCAAGCAGAGAAAGCCA
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	35	E51SaCas9KKH 9	ATCAAGCAGAGAAAGCCAGTCG
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	36	E51SaCas9KKH 10	CAGTCGGTAAGTTCTGTCCAAG
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	37	E51SaCas9KKH 11	GTAAGTTCTGTCCAAGCCCGGT
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	38	E51SaCas9KKH 12	AGCCCGGTTGAAATCTGCCAGA
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	39	E51SaCas9KKH 13	AGCAGGTACCTCCAACATCAAG
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	40	E51SaCas9KKH 14	CAACATCAAGGAAGATGGCATT
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	41	E51SaCas9KKH 15	AGGAAGATGGCATTTCTAGTTT
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	42	E51SaCas9KKH 16	ATGGCATTTCTAGTTTGGAGAT
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	43	E51SaCas9KKH 17	CTAGTTTGGAGATGGCAGTTTC
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	47	E51SaCas9KKH 21	GTTGTGTCACCAGAGTAACAGT
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	48	E51SaCas9KKH 22	GAGTAACAGTCTGAGTAGGAGC
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	53	E51SaCas9KKH 27	TCAACGAGATGATCATCAAGCA
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	54	E51SaCas9KKH 28	GTGACCTTGAGGATATCAACGA
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	55	E51SaCas9KKH 29	TGGGTGACCTTGAGGATATCAA
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	56	E51SaCas9KKH 30	GAGGGTGATGGTGGGTGACCTT
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	57	E51SaCas9KKH 31	TATAAAATCACAGAGGGTGATG
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30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	63	E51SaCas9KKH 37	ACTTACCGACTGGCTTTCTCTG
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	64	E51SaCas9KKH 38	GATGTTGGAGGTACCTGCTCTG
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	65	E51SaCas9KKH 39	AAATGCCATCTTCCTTGATGTT
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30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	67	E51SaCas9KKH 41	AGGAAACTGCCATCTCCAAACT
30	E51SaCas9KKH 4	ATGATCATCTCGTTGATATCCT	68	E51SaCas9KKH 42	CTGTTACTCTGGTGACACAACC
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31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	34	E51SaCas9KKH8	CTTGATCAAGCAGAGAAAGCCA
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	36	E51SaCas9KKH10	CAGTCGGTAAGTTCTGTCCAAG
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	37	E51SaCas9KKH11	GTAAGTTCTGTCCAAGCCCGGT
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	38	E51SaCas9KKH12	AGCCCGGTTGAAATCTGCCAGA
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	39	E51SaCas9KKH13	AGCAGGTACCTCCAACATCAAG
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	40	E51SaCas9KKH14	CAACATCAAGGAAGATGGCATT
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	41	E51SaCas9KKH15	AGGAAGATGGCATTTCTAGTTT
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	45	E51SaCas9KKH19	TAGTAACCACAGGTTGTGTCAC
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACACT
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC
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31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
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31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
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31	E51SaCas9KKH5	AAGGTCACCCACCATCACCCTC	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
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32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA
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32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	39	E51SaCas9KKH13	AGCAGGTACCTCCAACATCAAG
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32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	41	E51SaCas9KKH15	AGGAAGATGGCATTTCTAGTTT
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32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC
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32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT
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32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC
32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
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32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
32	E51SaCas9KKH6	ATCACCCTCTGTGATTTTATAA	56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT
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33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA	34	E51SaCas9KKH8	CTTGATCAAGCAGAGAAAGCCA
33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA	35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG
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33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA	53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
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33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
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33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
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33	E51SaCas9KKH7	ATAACTTGATCAAGCAGAGAAA	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
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34	E51SaCas9KKH8	CTTGATCAAGCAGAGAAAGCCA	35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCC
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35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG	55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
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35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
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35	E51SaCas9KKH9	ATCAAGCAGAGAAAGCCAGTCG	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
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36	E51SaCas9KKH 10	CAGTCGGTAAGTTCTGTCCAAG	55	E51SaCas9KKH 29	TGGGTGACCTTGAGGATATCAA
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42	E51SaCas9KKH 16	ATGGCATTTCTAGTTTGGA GAT	63	E51SaCas9KKH 37	ACTTACCGACTGGCTTTCT CTG

42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
42	E51SaCas9KKH16	ATGGCATTTCTAGTTTGGAGAT	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	45	E51SaCas9KKH19	TAGTAACCACAGGTTGTGTCAC
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
43	E51SaCas9KKH17	CTAGTTTGGAGATGGCAGTTTC	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	45	E51SaCas9KKH19	TAGTAACCACAGGTTGTGTCAC
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
44	E51SaCas9KKH18	GATGGCAGTTTCCTTAGTAACC	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA

44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC	63	E51SaCas9KKH 37	ACTTACCGACTGGCTTTCTCTG
44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC	64	E51SaCas9KKH 38	GATGTTGGAGGTACCTGCTCTG
44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC	65	E51SaCas9KKH 39	AAATGCCATCTTCCTTGATGTT
44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC	66	E51SaCas9KKH 40	CCAAACTAGAAATGCCATCTTC
44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC	67	E51SaCas9KKH 41	AGGAAACTGCCATCTCCAAACT
44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC	68	E51SaCas9KKH 42	CTGTTACTCTGGTGACACAACC
44	E51SaCas9KKH 18	GATGGCAGTTTCCTTAGTAACC	69	E51SaCas9KKH 43	TAGCTCCTACTCAGACTGTTAC
45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT
45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	47	E51SaCas9KKH 21	GTTGTGTCACCAGAGTAACAGT
45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	48	E51SaCas9KKH 22	GAGTAACAGTCTGAGTAGGAGC
45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	53	E51SaCas9KKH 27	TCAACGAGATGATCATCAAGCA
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45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	55	E51SaCas9KKH 29	TGGGTGACCTTGAGGATATCAA
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45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	59	E51SaCas9KKH 33	ATCAAGTTATAAAATCACAGAG
45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	60	E51SaCas9KKH 34	TTGATCAAGTTATAAAATCACA
45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	61	E51SaCas9KKH 35	CTTTCTCTGCTTGATCAAGTTA
45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	62	E51SaCas9KKH 36	CCGACTGGCTTTCTCTGCTTGA
45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	63	E51SaCas9KKH 37	ACTTACCGACTGGCTTTCTCTG
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45	E51SaCas9KKH 19	TAGTAACCACAGGTTGTGTCAC	69	E51SaCas9KKH 43	TAGCTCCTACTCAGACTGTTAC
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	47	E51SaCas9KKH 21	GTTGTGTCACCAGAGTAACAGT
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	48	E51SaCas9KKH 22	GAGTAACAGTCTGAGTAGGAGC
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46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	55	E51SaCas9KKH 29	TGGGTGACCTTGAGGATATCAA
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	56	E51SaCas9KKH 30	GAGGGTGATGGTGGGTGACCTT
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	57	E51SaCas9KKH 31	TATAAAATCACAGAGGGTGATG
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	58	E51SaCas9KKH 32	AAGTTATAAAATCACAGAGGGT
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	59	E51SaCas9KKH 33	ATCAAGTTATAAAATCACAGAG
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	60	E51SaCas9KKH 34	TTGATCAAGTTATAAAATCACA
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	61	E51SaCas9KKH 35	CTTTCTCTGCTTGATCAAGTTA
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	62	E51SaCas9KKH 36	CCGACTGGCTTTCTCTGCTTGA
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	63	E51SaCas9KKH 37	ACTTACCGACTGGCTTTCTCTG
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	64	E51SaCas9KKH 38	GATGTTGGAGGTACCTGCTCTG
46	E51SaCas9KKH 20	CCACAGGTTGTGTCACCAGAGT	65	E51SaCas9KKH 39	AAATGCCATCTTCCTTGATGTT

46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
46	E51SaCas9KKH20	CCACAGGTTGTGTCACCAGAGT	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG
47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
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47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
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47	E51SaCas9KKH21	GTTGTGTCACCAGAGTAACAGT	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
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48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC	53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA
48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC	54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA
48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC	55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA
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48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC	58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT
48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC	59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG
48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
48	E51SaCas9KKH22	GAGTAACAGTCTGAGTAGGAGC	61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
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53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA	54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA
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53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
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53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
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53	E51SaCas9KKH27	TCAACGAGATGATCATCAAGCA	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
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54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
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54	E51SaCas9KKH28	GTGACCTTGAGGATATCAACGA	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
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55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA	58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT
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55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
55	E51SaCas9KKH29	TGGGTGACCTTGAGGATATCAA	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC

56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG
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56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
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56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
56	E51SaCas9KKH30	GAGGGTGATGGTGGGTGACCTT	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
57	E51SaCas9KKH31	TATAAAATCACAGAGGGTGATG	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
58	E51SaCas9KKH32	AAGTTATAAAATCACAGAGGGT	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT

59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
59	E51SaCas9KKH33	ATCAAGTTATAAAATCACAGAG	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
60	E51SaCas9KKH34	TTGATCAAGTTATAAAATCACA	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA	62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA
61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
61	E51SaCas9KKH35	CTTTCTCTGCTTGATCAAGTTA	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA	63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG
62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
62	E51SaCas9KKH36	CCGACTGGCTTTCTCTGCTTGA	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG	64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG
63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
63	E51SaCas9KKH37	ACTTACCGACTGGCTTTCTCTG	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG	65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT
64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
64	E51SaCas9KKH38	GATGTTGGAGGTACCTGCTCTG	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT	66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC
65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC

65	E51SaCas9KKH39	AAATGCCATCTTCCTTGATGTT	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC	67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT
66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
66	E51SaCas9KKH40	CCAAACTAGAAATGCCATCTTC	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT	68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC
67	E51SaCas9KKH41	AGGAAACTGCCATCTCCAAACT	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC
68	E51SaCas9KKH42	CTGTTACTCTGGTGACACAACC	69	E51SaCas9KKH43	TAGCTCCTACTCAGACTGTTAC

(3) Table 4C. Exon 51 SluCas9 guides:

Seq ID No.	**Guide ID or Guide RNA Name**	**Guide Sequence**
243	E51Slu1	TGATCATCTCGTTGATATCCTC
244	E51Slu2	TTGATCAAGCAGAGAAAGCCAG
245	E51Slu3	AGTCGGTAAGTTCTGTCCAAGC
246	E51Slu4	GCCCGGTTGAAATCTGCCAGAG
247	E51Slu5	CAGAGCAGGTACCTCCAACATC
248	E51Slu6	GGTACCTCCAACATCAAGGAAG
249	E51Slu7	CAAGGAAGATGGCATTTCTAGT
250	E51Slu8	AGATGGCATTTCTAGTTTGGAG
251	E51Slu9	ATGGCAGTTTCCTTAGTAACCA
252	E51Slu10	GTCACCAGAGTAACAGTCTGAG
253	E51Slu15	CAACGAGATGATCATCAAGCAG
254	E51Slu16	GAGGGTGATGGTGGGTGACCTT
255	E51Slu17	ATAAAATCACAGAGGGTGATGG
256	E51Slu18	TATAAAATCACAGAGGGTGATG
257	E51Slu19	AGTTATAAAATCACAGAGGGTG
258	E51Slu20	TGATCAAGTTATAAAATCACAG
259	E51Slu21	TTGATCAAGTTATAAAATCACA
260	E51Slu22	GGGCTTGGACAGAACTTACCGA
261	E51Slu23	CTCTGGCAGATTTCAACCGGGC
262	E51Slu24	ACCTGCTCTGGCAGATTTCAAC
263	E51Slu25	TACCTGCTCTGGCAGATTTCAA
264	E51Slu26	CTTGATGTTGGAGGTACCTGCT
265	E51Slu27	AATGCCATCTTCCTTGATGTTG
266	E51Slu28	AGAAATGCCATCTTCCTTGATG
267	E51Slu29	GGTGACACAACCTGTGGTTACT
268	E51Slu30	TGTTACTCTGGTGACACAACCT
269	E51Slu31	AGCTCCTACTCAGACTGTTACT

(4) Table 4D. Exon 51 SluCas9 pairs:

Guide 1 Seq ID No.	**Guide 1**	**Guide 1 Sequence**	**Guide 2 Seq ID No.**	**Guide 2**	**Guide 2 Sequence**
243	E51SL1	TGATCATCTCGTTGATATCCTC	244	E51SL2	TTGATCAAGCAGAGAAAGCCAG
243	E51SL1	TGATCATCTCGTTGATATCCTC	245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC
243	E51SL1	TGATCATCTCGTTGATATCCTC	246	E51SL4	GCCCGGTTGAAATCTGCCAGAG

243	E51SL1	TGATCATCTCGTTGATATCCTC	247	E51SL5	CAGAGCAGGTACCTCCAACATC
243	E51SL1	TGATCATCTCGTTGATATCCTC	248	E51SL6	GGTACCTCCAACATCAAGGAAG
243	E51SL1	TGATCATCTCGTTGATATCCTC	249	E51SL7	CAAGGAAGATGGCATTTCTAGT
243	E51SL1	TGATCATCTCGTTGATATCCTC	250	E51SL8	AGATGGCATTTCTAGTTTGGAG
243	E51SL1	TGATCATCTCGTTGATATCCTC	251	E51SL9	ATGGCAGTTTCCTTAGTAACCA
243	E51SL1	TGATCATCTCGTTGATATCCTC	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
243	E51SL1	TGATCATCTCGTTGATATCCTC	253	E51SL15	CAACGAGATGATCATCAAGCAG
243	E51SL1	TGATCATCTCGTTGATATCCTC	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
243	E51SL1	TGATCATCTCGTTGATATCCTC	255	E51SL17	ATAAAATCACAGAGGGTGATGG
243	E51SL1	TGATCATCTCGTTGATATCCTC	256	E51SL18	TATAAAATCACAGAGGGTGATG
243	E51SL1	TGATCATCTCGTTGATATCCTC	257	E51SL19	AGTTATAAAATCACAGAGGGTG
243	E51SL1	TGATCATCTCGTTGATATCCTC	258	E51SL20	TGATCAAGTTATAAAATCACAG
243	E51SL1	TGATCATCTCGTTGATATCCTC	259	E51SL21	TTGATCAAGTTATAAAATCACA
243	E51SL1	TGATCATCTCGTTGATATCCTC	260	E51SL22	GGGCTTGGACAGAACTTACCGA
243	E51SL1	TGATCATCTCGTTGATATCCTC	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
243	E51SL1	TGATCATCTCGTTGATATCCTC	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
243	E51SL1	TGATCATCTCGTTGATATCCTC	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
243	E51SL1	TGATCATCTCGTTGATATCCTC	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
243	E51SL1	TGATCATCTCGTTGATATCCTC	265	E51SL27	AATGCCATCTTCCTTGATGTTG
243	E51SL1	TGATCATCTCGTTGATATCCTC	266	E51SL28	AGAAATGCCATCTTCCTTGATG
243	E51SL1	TGATCATCTCGTTGATATCCTC	267	E51SL29	GGTGACACAACCTGTGGTTACT
243	E51SL1	TGATCATCTCGTTGATATCCTC	268	E51SL30	TGTTACTCTGGTGACACAACCT
243	E51SL1	TGATCATCTCGTTGATATCCTC	269	E51SL31	AGCTCCTACTCAGACTGTTACT
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	246	E51SL4	GCCCGGTTGAAATCTGCCAGAG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	247	E51SL5	CAGAGCAGGTACCTCCAACATC
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	248	E51SL6	GGTACCTCCAACATCAAGGAAG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	249	E51SL7	CAAGGAAGATGGCATTTCTAGT
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	250	E51SL8	AGATGGCATTTCTAGTTTGGAG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	251	E51SL9	ATGGCAGTTTCCTTAGTAACCA
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	253	E51SL15	CAACGAGATGATCATCAAGCAG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	255	E51SL17	ATAAAATCACAGAGGGTGATGG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	256	E51SL18	TATAAAATCACAGAGGGTGATG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	257	E51SL19	AGTTATAAAATCACAGAGGGTG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	258	E51SL20	TGATCAAGTTATAAAATCACAG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	259	E51SL21	TTGATCAAGTTATAAAATCACA
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	265	E51SL27	AATGCCATCTTCCTTGATGTTG

244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	267	E51SL29	GGTGACACAACCTGTGGTTACT
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	268	E51SL30	TGTTACTCTGGTGACACAACCT
244	E51SL2	TTGATCAAGCAGAGAAAGCCAG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	246	E51SL4	GCCCGGTTGAAATCTGCCAGAG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	247	E51SL5	CAGAGCAGGTACCTCCAACATC
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	248	E51SL6	GGTACCTCCAACATCAAGGAAG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	249	E51SL7	CAAGGAAGATGGCATTTCTAGT
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	250	E51SL8	AGATGGCATTTCTAGTTTGGAG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	251	E51SL9	ATGGCAGTTTCCTTAGTAACCA
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	253	E51SL15	CAACGAGATGATCATCAAGCAG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	255	E51SL17	ATAAAATCACAGAGGGTGATGG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	256	E51SL18	TATAAAATCACAGAGGGTGATG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	257	E51SL19	AGTTATAAAATCACAGAGGGTG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	258	E51SL20	TGATCAAGTTATAAAATCACAG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	259	E51SL21	TTGATCAAGTTATAAAATCACA
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	260	E51SL22	GGGCTTGGACAGAACTTACCGA
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	265	E51SL27	AATGCCATCTTCCTTGATGTTG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	266	E51SL28	AGAAATGCCATCTTCCTTGATG
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	267	E51SL29	GGTGACACAACCTGTGGTTACT
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	268	E51SL30	TGTTACTCTGGTGACACAACCT
245	E51SL3	AGTCGGTAAGTTCTGTCCAAGC	269	E51SL31	AGCTCCTACTCAGACTGTTACT
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	247	E51SL5	CAGAGCAGGTACCTCCAACATC
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	248	E51SL6	GGTACCTCCAACATCAAGGAAG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	249	E51SL7	CAAGGAAGATGGCATTTCTAGT
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	250	E51SL8	AGATGGCATTTCTAGTTTGGAG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	251	E51SL9	ATGGCAGTTTCCTTAGTAACCA
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	253	E51SL15	CAACGAGATGATCATCAAGCAG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	255	E51SL17	ATAAAATCACAGAGGGTGATGG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	256	E51SL18	TATAAAATCACAGAGGGTGATG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	257	E51SL19	AGTTATAAAATCACAGAGGGTG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	258	E51SL20	TGATCAAGTTATAAAATCACAG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	259	E51SL21	TTGATCAAGTTATAAAATCACA
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC

246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	267	E51SL29	GGTGACACAACCTGTGGTTACT
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	268	E51SL30	TGTTACTCTGGTGACACAACCT
246	E51SL4	GCCCGGTTGAAATCTGCCAGAG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
247	E51SL5	CAGAGCAGGTACCTCCAACATC	248	E51SL6	GGTACCTCCAACATCAAGGAAG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	249	E51SL7	CAAGGAAGATGGCATTTCTAGT
247	E51SL5	CAGAGCAGGTACCTCCAACATC	250	E51SL8	AGATGGCATTTCTAGTTTGGAG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	251	E51SL9	ATGGCAGTTTCCTTAGTAACCA
247	E51SL5	CAGAGCAGGTACCTCCAACATC	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	253	E51SL15	CAACGAGATGATCATCAAGCAG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
247	E51SL5	CAGAGCAGGTACCTCCAACATC	255	E51SL17	ATAAAATCACAGAGGGTGATGG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	256	E51SL18	TATAAAATCACAGAGGGTGATG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	257	E51SL19	AGTTATAAAATCACAGAGGGTG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	258	E51SL20	TGATCAAGTTATAAAATCACAG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	259	E51SL21	TTGATCAAGTTATAAAATCACA
247	E51SL5	CAGAGCAGGTACCTCCAACATC	260	E51SL22	GGGCTTGGACAGAACTTACCGA
247	E51SL5	CAGAGCAGGTACCTCCAACATC	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
247	E51SL5	CAGAGCAGGTACCTCCAACATC	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
247	E51SL5	CAGAGCAGGTACCTCCAACATC	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
247	E51SL5	CAGAGCAGGTACCTCCAACATC	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
247	E51SL5	CAGAGCAGGTACCTCCAACATC	265	E51SL27	AATGCCATCTTCCTTGATGTTG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	266	E51SL28	AGAAATGCCATCTTCCTTGATG
247	E51SL5	CAGAGCAGGTACCTCCAACATC	267	E51SL29	GGTGACACAACCTGTGGTTACT
247	E51SL5	CAGAGCAGGTACCTCCAACATC	268	E51SL30	TGTTACTCTGGTGACACAACCT
247	E51SL5	CAGAGCAGGTACCTCCAACATC	269	E51SL31	AGCTCCTACTCAGACTGTTACT
248	E51SL6	GGTACCTCCAACATCAAGGAAG	249	E51SL7	CAAGGAAGATGGCATTTCTAGT
248	E51SL6	GGTACCTCCAACATCAAGGAAG	250	E51SL8	AGATGGCATTTCTAGTTTGGAG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	251	E51SL9	ATGGCAGTTTCCTTAGTAACCA
248	E51SL6	GGTACCTCCAACATCAAGGAAG	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	253	E51SL15	CAACGAGATGATCATCAAGCAG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
248	E51SL6	GGTACCTCCAACATCAAGGAAG	255	E51SL17	ATAAAATCACAGAGGGTGATGG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	256	E51SL18	TATAAAATCACAGAGGGTGATG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	257	E51SL19	AGTTATAAAATCACAGAGGGTG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	258	E51SL20	TGATCAAGTTATAAAATCACAG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	259	E51SL21	TTGATCAAGTTATAAAATCACA
248	E51SL6	GGTACCTCCAACATCAAGGAAG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
248	E51SL6	GGTACCTCCAACATCAAGGAAG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
248	E51SL6	GGTACCTCCAACATCAAGGAAG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
248	E51SL6	GGTACCTCCAACATCAAGGAAG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA

248	E51SL6	GGTACCTCCAACATCAAGGAAG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
248	E51SL6	GGTACCTCCAACATCAAGGAAG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
248	E51SL6	GGTACCTCCAACATCAAGGAAG	267	E51SL29	GGTGACACAACCTGTGGTTACT
248	E51SL6	GGTACCTCCAACATCAAGGAAG	268	E51SL30	TGTTACTCTGGTGACACAACCT
248	E51SL6	GGTACCTCCAACATCAAGGAAG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	250	E51SL8	AGATGGCATTTCTAGTTTGGAG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	251	E51SL9	ATGGCAGTTTCCTTAGTAACCA
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	253	E51SL15	CAACGAGATGATCATCAAGCAG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	255	E51SL17	ATAAAATCACAGAGGGTGATGG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	256	E51SL18	TATAAAATCACAGAGGGTGATG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	257	E51SL19	AGTTATAAAATCACAGAGGGTG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	258	E51SL20	TGATCAAGTTATAAAATCACAG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	259	E51SL21	TTGATCAAGTTATAAAATCACA
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	260	E51SL22	GGGCTTGGACAGAACTTACCGA
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	265	E51SL27	AATGCCATCTTCCTTGATGTTG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	266	E51SL28	AGAAATGCCATCTTCCTTGATG
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	267	E51SL29	GGTGACACAACCTGTGGTTACT
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	268	E51SL30	TGTTACTCTGGTGACACAACCT
249	E51SL7	CAAGGAAGATGGCATTTCTAGT	269	E51SL31	AGCTCCTACTCAGACTGTTACT
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	251	E51SL9	ATGGCAGTTTCCTTAGTAACCA
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	253	E51SL15	CAACGAGATGATCATCAAGCAG
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	255	E51SL17	ATAAAATCACAGAGGGTGATGG
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	256	E51SL18	TATAAAATCACAGAGGGTGATG
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	257	E51SL19	AGTTATAAAATCACAGAGGGTG
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	258	E51SL20	TGATCAAGTTATAAAATCACAG
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	259	E51SL21	TTGATCAAGTTATAAAATCACA
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	267	E51SL29	GGTGACACAACCTGTGGTTACT
250	E51SL8	AGATGGCATTTCTAGTTTGGAG	268	E51SL30	TGTTACTCTGGTGACACAACCT

250	E51SL8	AGATGGCATTTCTAGTTTGGAG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	252	E51SL10	GTCACCAGAGTAACAGTCTGAG
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	253	E51SL15	CAACGAGATGATCATCAAGCAG
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	255	E51SL17	ATAAAATCACAGAGGGTGATGG
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	256	E51SL18	TATAAAATCACAGAGGGTGATG
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	257	E51SL19	AGTTATAAAATCACAGAGGGTG
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	258	E51SL20	TGATCAAGTTATAAAATCACAG
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	259	E51SL21	TTGATCAAGTTATAAAATCACA
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	260	E51SL22	GGGCTTGGACAGAACTTACCGA
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	265	E51SL27	AATGCCATCTTCCTTGATGTTG
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	266	E51SL28	AGAAATGCCATCTTCCTTGATG
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	267	E51SL29	GGTGACACAACCTGTGGTTACT
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	268	E51SL30	TGTTACTCTGGTGACACAACCT
251	E51SL9	ATGGCAGTTTCCTTAGTAACCA	269	E51SL31	AGCTCCTACTCAGACTGTTACT
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	253	E51SL15	CAACGAGATGATCATCAAGCAG
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	255	E51SL17	ATAAAATCACAGAGGGTGATGG
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	256	E51SL18	TATAAAATCACAGAGGGTGATG
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	257	E51SL19	AGTTATAAAATCACAGAGGGTG
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	258	E51SL20	TGATCAAGTTATAAAATCACAG
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	259	E51SL21	TTGATCAAGTTATAAAATCACA
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	267	E51SL29	GGTGACACAACCTGTGGTTACT
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	268	E51SL30	TGTTACTCTGGTGACACAACCT
252	E51SL10	GTCACCAGAGTAACAGTCTGAG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
253	E51SL15	CAACGAGATGATCATCAAGCAG	254	E51SL16	GAGGGTGATGGTGGGTGACCTT
253	E51SL15	CAACGAGATGATCATCAAGCAG	255	E51SL17	ATAAAATCACAGAGGGTGATGG
253	E51SL15	CAACGAGATGATCATCAAGCAG	256	E51SL18	TATAAAATCACAGAGGGTGATG
253	E51SL15	CAACGAGATGATCATCAAGCAG	257	E51SL19	AGTTATAAAATCACAGAGGGTG
253	E51SL15	CAACGAGATGATCATCAAGCAG	258	E51SL20	TGATCAAGTTATAAAATCACAG
253	E51SL15	CAACGAGATGATCATCAAGCAG	259	E51SL21	TTGATCAAGTTATAAAATCACA
253	E51SL15	CAACGAGATGATCATCAAGCAG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
253	E51SL15	CAACGAGATGATCATCAAGCAG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC

253	E51SL15	CAACGAGATGATCATCAAGCAG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
253	E51SL15	CAACGAGATGATCATCAAGCAG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
253	E51SL15	CAACGAGATGATCATCAAGCAG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
253	E51SL15	CAACGAGATGATCATCAAGCAG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
253	E51SL15	CAACGAGATGATCATCAAGCAG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
253	E51SL15	CAACGAGATGATCATCAAGCAG	267	E51SL29	GGTGACACAACCTGTGGTTACT
253	E51SL15	CAACGAGATGATCATCAAGCAG	268	E51SL30	TGTTACTCTGGTGACACAACCT
253	E51SL15	CAACGAGATGATCATCAAGCAG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	255	E51SL17	ATAAAATCACAGAGGGTGATGG
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	256	E51SL18	TATAAAATCACAGAGGGTGATG
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	257	E51SL19	AGTTATAAAATCACAGAGGGTG
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	258	E51SL20	TGATCAAGTTATAAAATCACAG
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	259	E51SL21	TTGATCAAGTTATAAAATCACA
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	260	E51SL22	GGGCTTGGACAGAACTTACCGA
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	265	E51SL27	AATGCCATCTTCCTTGATGTTG
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	266	E51SL28	AGAAATGCCATCTTCCTTGATG
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	267	E51SL29	GGTGACACAACCTGTGGTTACT
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	268	E51SL30	TGTTACTCTGGTGACACAACCT
254	E51SL16	GAGGGTGATGGTGGGTGACCTT	269	E51SL31	AGCTCCTACTCAGACTGTTACT
255	E51SL17	ATAAAATCACAGAGGGTGATGG	256	E51SL18	TATAAAATCACAGAGGGTGATG
255	E51SL17	ATAAAATCACAGAGGGTGATGG	257	E51SL19	AGTTATAAAATCACAGAGGGTG
255	E51SL17	ATAAAATCACAGAGGGTGATGG	258	E51SL20	TGATCAAGTTATAAAATCACAG
255	E51SL17	ATAAAATCACAGAGGGTGATGG	259	E51SL21	TTGATCAAGTTATAAAATCACA
255	E51SL17	ATAAAATCACAGAGGGTGATGG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
255	E51SL17	ATAAAATCACAGAGGGTGATGG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
255	E51SL17	ATAAAATCACAGAGGGTGATGG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
255	E51SL17	ATAAAATCACAGAGGGTGATGG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
255	E51SL17	ATAAAATCACAGAGGGTGATGG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
255	E51SL17	ATAAAATCACAGAGGGTGATGG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
255	E51SL17	ATAAAATCACAGAGGGTGATGG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
255	E51SL17	ATAAAATCACAGAGGGTGATGG	267	E51SL29	GGTGACACAACCTGTGGTTACT
255	E51SL17	ATAAAATCACAGAGGGTGATGG	268	E51SL30	TGTTACTCTGGTGACACAACCT
255	E51SL17	ATAAAATCACAGAGGGTGATGG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
256	E51SL18	TATAAAATCACAGAGGGTGATG	257	E51SL19	AGTTATAAAATCACAGAGGGTG
256	E51SL18	TATAAAATCACAGAGGGTGATG	258	E51SL20	TGATCAAGTTATAAAATCACAG
256	E51SL18	TATAAAATCACAGAGGGTGATG	259	E51SL21	TTGATCAAGTTATAAAATCACA
256	E51SL18	TATAAAATCACAGAGGGTGATG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
256	E51SL18	TATAAAATCACAGAGGGTGATG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
256	E51SL18	TATAAAATCACAGAGGGTGATG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
256	E51SL18	TATAAAATCACAGAGGGTGATG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA

256	E51SL18	TATAAAATCACAGAGGGTGATG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
256	E51SL18	TATAAAATCACAGAGGGTGATG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
256	E51SL18	TATAAAATCACAGAGGGTGATG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
256	E51SL18	TATAAAATCACAGAGGGTGATG	267	E51SL29	GGTGACACAACCTGTGGTTACT
256	E51SL18	TATAAAATCACAGAGGGTGATG	268	E51SL30	TGTTACTCTGGTGACACAACCT
256	E51SL18	TATAAAATCACAGAGGGTGATG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
257	E51SL19	AGTTATAAAATCACAGAGGGTG	258	E51SL20	TGATCAAGTTATAAAATCACAG
257	E51SL19	AGTTATAAAATCACAGAGGGTG	259	E51SL21	TTGATCAAGTTATAAAATCACA
257	E51SL19	AGTTATAAAATCACAGAGGGTG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
257	E51SL19	AGTTATAAAATCACAGAGGGTG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
257	E51SL19	AGTTATAAAATCACAGAGGGTG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
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257	E51SL19	AGTTATAAAATCACAGAGGGTG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
257	E51SL19	AGTTATAAAATCACAGAGGGTG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
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257	E51SL19	AGTTATAAAATCACAGAGGGTG	267	E51SL29	GGTGACACAACCTGTGGTTACT
257	E51SL19	AGTTATAAAATCACAGAGGGTG	268	E51SL30	TGTTACTCTGGTGACACAACCT
257	E51SL19	AGTTATAAAATCACAGAGGGTG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
258	E51SL20	TGATCAAGTTATAAAATCACAG	259	E51SL21	TTGATCAAGTTATAAAATCACA
258	E51SL20	TGATCAAGTTATAAAATCACAG	260	E51SL22	GGGCTTGGACAGAACTTACCGA
258	E51SL20	TGATCAAGTTATAAAATCACAG	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
258	E51SL20	TGATCAAGTTATAAAATCACAG	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
258	E51SL20	TGATCAAGTTATAAAATCACAG	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
258	E51SL20	TGATCAAGTTATAAAATCACAG	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
258	E51SL20	TGATCAAGTTATAAAATCACAG	265	E51SL27	AATGCCATCTTCCTTGATGTTG
258	E51SL20	TGATCAAGTTATAAAATCACAG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
258	E51SL20	TGATCAAGTTATAAAATCACAG	267	E51SL29	GGTGACACAACCTGTGGTTACT
258	E51SL20	TGATCAAGTTATAAAATCACAG	268	E51SL30	TGTTACTCTGGTGACACAACCT
258	E51SL20	TGATCAAGTTATAAAATCACAG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
259	E51SL21	TTGATCAAGTTATAAAATCACA	260	E51SL22	GGGCTTGGACAGAACTTACCGA
259	E51SL21	TTGATCAAGTTATAAAATCACA	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
259	E51SL21	TTGATCAAGTTATAAAATCACA	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
259	E51SL21	TTGATCAAGTTATAAAATCACA	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
259	E51SL21	TTGATCAAGTTATAAAATCACA	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
259	E51SL21	TTGATCAAGTTATAAAATCACA	265	E51SL27	AATGCCATCTTCCTTGATGTTG
259	E51SL21	TTGATCAAGTTATAAAATCACA	266	E51SL28	AGAAATGCCATCTTCCTTGATG
259	E51SL21	TTGATCAAGTTATAAAATCACA	267	E51SL29	GGTGACACAACCTGTGGTTACT
259	E51SL21	TTGATCAAGTTATAAAATCACA	268	E51SL30	TGTTACTCTGGTGACACAACCT
259	E51SL21	TTGATCAAGTTATAAAATCACA	269	E51SL31	AGCTCCTACTCAGACTGTTACT
260	E51SL22	GGGCTTGGACAGAACTTACCGA	261	E51SL23	CTCTGGCAGATTTCAACCGGGC
260	E51SL22	GGGCTTGGACAGAACTTACCGA	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
260	E51SL22	GGGCTTGGACAGAACTTACCGA	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
260	E51SL22	GGGCTTGGACAGAACTTACCGA	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
260	E51SL22	GGGCTTGGACAGAACTTACCGA	265	E51SL27	AATGCCATCTTCCTTGATGTTG

260	E51SL22	GGGCTTGGACAGAACTTACCGA	266	E51SL28	AGAAATGCCATCTTCCTTGATG
260	E51SL22	GGGCTTGGACAGAACTTACCGA	267	E51SL29	GGTGACACAACCTGTGGTTACT
260	E51SL22	GGGCTTGGACAGAACTTACCGA	268	E51SL30	TGTTACTCTGGTGACACAACCT
260	E51SL22	GGGCTTGGACAGAACTTACCGA	269	E51SL31	AGCTCCTACTCAGACTGTTACT
261	E51SL23	CTCTGGCAGATTTCAACCGGGC	262	E51SL24	ACCTGCTCTGGCAGATTTCAAC
261	E51SL23	CTCTGGCAGATTTCAACCGGGC	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
261	E51SL23	CTCTGGCAGATTTCAACCGGGC	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
261	E51SL23	CTCTGGCAGATTTCAACCGGGC	265	E51SL27	AATGCCATCTTCCTTGATGTTG
261	E51SL23	CTCTGGCAGATTTCAACCGGGC	266	E51SL28	AGAAATGCCATCTTCCTTGATG
261	E51SL23	CTCTGGCAGATTTCAACCGGGC	267	E51SL29	GGTGACACAACCTGTGGTTACT
261	E51SL23	CTCTGGCAGATTTCAACCGGGC	268	E51SL30	TGTTACTCTGGTGACACAACCT
261	E51SL23	CTCTGGCAGATTTCAACCGGGC	269	E51SL31	AGCTCCTACTCAGACTGTTACT
262	E51SL24	ACCTGCTCTGGCAGATTTCAAC	263	E51SL25	TACCTGCTCTGGCAGATTTCAA
262	E51SL24	ACCTGCTCTGGCAGATTTCAAC	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
262	E51SL24	ACCTGCTCTGGCAGATTTCAAC	265	E51SL27	AATGCCATCTTCCTTGATGTTG
262	E51SL24	ACCTGCTCTGGCAGATTTCAAC	266	E51SL28	AGAAATGCCATCTTCCTTGATG
262	E51SL24	ACCTGCTCTGGCAGATTTCAAC	267	E51SL29	GGTGACACAACCTGTGGTTACT
262	E51SL24	ACCTGCTCTGGCAGATTTCAAC	268	E51SL30	TGTTACTCTGGTGACACAACCT
262	E51SL24	ACCTGCTCTGGCAGATTTCAAC	269	E51SL31	AGCTCCTACTCAGACTGTTACT
263	E51SL25	TACCTGCTCTGGCAGATTTCAA	264	E51SL26	CTTGATGTTGGAGGTACCTGCT
263	E51SL25	TACCTGCTCTGGCAGATTTCAA	265	E51SL27	AATGCCATCTTCCTTGATGTTG
263	E51SL25	TACCTGCTCTGGCAGATTTCAA	266	E51SL28	AGAAATGCCATCTTCCTTGATG
263	E51SL25	TACCTGCTCTGGCAGATTTCAA	267	E51SL29	GGTGACACAACCTGTGGTTACT
263	E51SL25	TACCTGCTCTGGCAGATTTCAA	268	E51SL30	TGTTACTCTGGTGACACAACCT
263	E51SL25	TACCTGCTCTGGCAGATTTCAA	269	E51SL31	AGCTCCTACTCAGACTGTTACT
264	E51SL26	CTTGATGTTGGAGGTACCTGCT	265	E51SL27	AATGCCATCTTCCTTGATGTTG
264	E51SL26	CTTGATGTTGGAGGTACCTGCT	266	E51SL28	AGAAATGCCATCTTCCTTGATG
264	E51SL26	CTTGATGTTGGAGGTACCTGCT	267	E51SL29	GGTGACACAACCTGTGGTTACT
264	E51SL26	CTTGATGTTGGAGGTACCTGCT	268	E51SL30	TGTTACTCTGGTGACACAACCT
264	E51SL26	CTTGATGTTGGAGGTACCTGCT	269	E51SL31	AGCTCCTACTCAGACTGTTACT
265	E51SL27	AATGCCATCTTCCTTGATGTTG	266	E51SL28	AGAAATGCCATCTTCCTTGATG
265	E51SL27	AATGCCATCTTCCTTGATGTTG	267	E51SL29	GGTGACACAACCTGTGGTTACT
265	E51SL27	AATGCCATCTTCCTTGATGTTG	268	E51SL30	TGTTACTCTGGTGACACAACCT
265	E51SL27	AATGCCATCTTCCTTGATGTTG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
266	E51SL28	AGAAATGCCATCTTCCTTGATG	267	E51SL29	GGTGACACAACCTGTGGTTACT
266	E51SL28	AGAAATGCCATCTTCCTTGATG	268	E51SL30	TGTTACTCTGGTGACACAACCT
266	E51SL28	AGAAATGCCATCTTCCTTGATG	269	E51SL31	AGCTCCTACTCAGACTGTTACT
267	E51SL29	GGTGACACAACCTGTGGTTACT	268	E51SL30	TGTTACTCTGGTGACACAACCT
267	E51SL29	GGTGACACAACCTGTGGTTACT	269	E51SL31	AGCTCCTACTCAGACTGTTACT
268	E51SL30	TGTTACTCTGGTGACACAACCT	269	E51SL31	AGCTCCTACTCAGACTGTTACT

e) Exon 53:

(1) Table 5A. Exon 53 SaCas9 guides:

Seq ID No.	Guide ID or Guide RNA Name	Guide Sequence

16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG
18	E53Sa3	CTTGTACTTCATCCCACTGATT
19	E53Sa4	ACTGATTCTGAATTCTTTCAAC
20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG
21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC
22	E53Sa7	GCAACAGTTGAATGAAATGTTA
23	E53Sa8	CCTTCAGAACCGGAGGCAACAG
24	E53Sa9	AGTTGAAAGAATTCAGAATCAG
25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
70	E53SaCas9KKH1	AAAAGGTATCTTTGATACTAAC
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC
75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT
76	E53SaCas9KKH7	AGGTGTTCTTGTACTTCATCCC
77	E53SaCas9KKH8	CTTGTACTTCATCCCACTGATT
78	E53SaCas9KKH9	ACTGATTCTGAATTCTTTCAAC
79	E53SaCas9KKH10	TTCTTTCAACTAGAATAAAAGG
80	E53SaCas9KKH11	TTCAACTAGAATAAAAGGAAAA
81	E53SaCas9KKH12	AGAATAAAAGGAAAAATAAATA
82	E53SaCas9KKH13	GTTAGTATCAAAGATACCTTTT
83	E53SaCas9KKH14	CACAGAAACCAAGGTTAGTATC
84	E53SaCas9KKH15	AAAGAAAATCACAGAAACCAAG
85	E53SaCas9KKH16	TCCAAAAGAAAATCACAGAAAC
86	E53SaCas9KKH17	ATACAGTAGATGCAATCCAAAA
87	E53SaCas9KKH18	AGGAGGGTCCCTATACAGTAGA
88	E53SaCas9KKH19	ATGGAAGGAGGGTCCCTATACA
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA
94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA
95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA

103	E53SaCas9KKH34	ATATATTTATTTTTCCTTTTAT

(2) Table 5B. Exon 53 SaCas9 pairs:

Guide 1 Seq ID No.	Guide 1	Guide 1 Sequence	Guide 2 Seq ID No.	Guide 2	Guide 2 Sequence
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	18	E53Sa3	CTTGTACTTCATCCCACTGATT
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	19	E53Sa4	ACTGATTCTGAATTCTTTCAAC
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	22	E53Sa7	GCAACAGTTGAATGAAATGTTA
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	23	E53Sa8	CCTTCAGAACCGGAGGCAACAG
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	24	E53Sa9	AGTTGAAAGAATTCAGAATCAG
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
16	E53Sa1	CCTTGGTTTCTGTGATTTTCTT	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	18	E53Sa3	CTTGTACTTCATCCCACTGATT
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	19	E53Sa4	ACTGATTCTGAATTCTTTCAAC
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	22	E53Sa7	GCAACAGTTGAATGAAATGTTA
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	23	E53Sa8	CCTTCAGAACCGGAGGCAACAG
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	24	E53Sa9	AGTTGAAAGAATTCAGAATCAG
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
17	E53Sa2	TCCTTAGCTTCCAGCCATTGTG	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
18	E53Sa3	CTTGTACTTCATCCCACTGATT	19	E53Sa4	ACTGATTCTGAATTCTTTCAAC
18	E53Sa3	CTTGTACTTCATCCCACTGATT	20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG
18	E53Sa3	CTTGTACTTCATCCCACTGATT	21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC
18	E53Sa3	CTTGTACTTCATCCCACTGATT	22	E53Sa7	GCAACAGTTGAATGAAATGTTA
18	E53Sa3	CTTGTACTTCATCCCACTGATT	23	E53Sa8	CCTTCAGAACCGGAGGCAACAG
18	E53Sa3	CTTGTACTTCATCCCACTGATT	24	E53Sa9	AGTTGAAAGAATTCAGAATCAG
18	E53Sa3	CTTGTACTTCATCCCACTGATT	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
18	E53Sa3	CTTGTACTTCATCCCACTGATT	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
19	E53Sa4	ACTGATTCTGAATTCTTTCAAC	20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG
19	E53Sa4	ACTGATTCTGAATTCTTTCAAC	21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC
19	E53Sa4	ACTGATTCTGAATTCTTTCAAC	22	E53Sa7	GCAACAGTTGAATGAAATGTTA
19	E53Sa4	ACTGATTCTGAATTCTTTCAAC	23	E53Sa8	CCTTCAGAACCGGAGGCAACAG
19	E53Sa4	ACTGATTCTGAATTCTTTCAAC	24	E53Sa9	AGTTGAAAGAATTCAGAATCAG
19	E53Sa4	ACTGATTCTGAATTCTTTCAAC	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
19	E53Sa4	ACTGATTCTGAATTCTTTCAAC	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG	21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC
20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG	22	E53Sa7	GCAACAGTTGAATGAAATGTTA
20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG	23	E53Sa8	CCTTCAGAACCGGAGGCAACAG
20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG	24	E53Sa9	AGTTGAAAGAATTCAGAATCAG

20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
20	E53Sa5	AGCCAAGCTTGAGTCATGGAAG	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC	22	E53Sa7	GCAACAGTTGAATGAAATGTTA
21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC	23	E53Sa8	CCTTCAGAACCGGAGGCAACAG
21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC	24	E53Sa9	AGTTGAAAGAATTCAGAATCAG
21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
21	E53Sa6	TTAGGACAGGCCAGAGCCAAGC	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
22	E53Sa7	GCAACAGTTGAATGAAATGTTA	23	E53Sa8	CCTTCAGAACCGGAGGCAACAG
22	E53Sa7	GCAACAGTTGAATGAAATGTTA	24	E53Sa9	AGTTGAAAGAATTCAGAATCAG
22	E53Sa7	GCAACAGTTGAATGAAATGTTA	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
22	E53Sa7	GCAACAGTTGAATGAAATGTTA	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
23	E53Sa8	CCTTCAGAACCGGAGGCAACAG	24	E53Sa9	AGTTGAAAGAATTCAGAATCAG
23	E53Sa8	CCTTCAGAACCGGAGGCAACAG	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
23	E53Sa8	CCTTCAGAACCGGAGGCAACAG	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
24	E53Sa9	AGTTGAAAGAATTCAGAATCAG	25	E53Sa10	TTTTATTCTAGTTGAAAGAATT
24	E53Sa9	AGTTGAAAGAATTCAGAATCAG	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
25	E53Sa10	TTTTATTCTAGTTGAAAGAATT	26	E53Sa11	TTTTTCCTTTTATTCTAGTTGA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	76	E53SaCas9KKH7	AGGTGTTCTTGTACTTCATCCC
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	77	E53SaCas9KKH8	CTTGTACTTCATCCCACTGATT
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	78	E53SaCas9KKH9	ACTGATTCTGAATTCTTTCAAC
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	84	E53SaCas9KKH15	AAAGAAAATCACAGAAACCAAG
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	85	E53SaCas9KKH16	TCCAAAAGAAAATCACAGAAAC
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	86	E53SaCas9KKH17	ATACAGTAGATGCAATCCAAAA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	87	E53SaCas9KKH18	AGGAGGGTCCCTATACAGTAGA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	88	E53SaCas9KKH19	ATGGAAGGAGGGTCCCTATACA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT

71	E53SaCas9KKH2	CTTTGATACTAACCTTGGTTTC	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	76	E53SaCas9KKH7	AGGTGTTCTTGTACTTCATCCC
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	77	E53SaCas9KKH8	CTTGTACTTCATCCCACTGATT
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	78	E53SaCas9KKH9	ACTGATTCTGAATTCTTTCAAC
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	84	E53SaCas9KKH15	AAAGAAAATCACAGAAACCAAG
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	85	E53SaCas9KKH16	TCCAAAAGAAAATCACAGAAAC
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	86	E53SaCas9KKH17	ATACAGTAGATGCAATCCAAAA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	87	E53SaCas9KKH18	AGGAGGGTCCCTATACAGTAGA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	88	E53SaCas9KKH19	ATGGAAGGAGGGTCCCTATACA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
72	E53SaCas9KKH3	CCTTGGTTTCTGTGATTTTCTT	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	76	E53SaCas9KKH7	AGGTGTTCTTGTACTTCATCCC
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	77	E53SaCas9KKH8	CTTGTACTTCATCCCACTGATT
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	78	E53SaCas9KKH9	ACTGATTCTGAATTCTTTCAAC
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	84	E53SaCas9KKH15	AAAGAAAATCACAGAAACCAAG
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	85	E53SaCas9KKH16	TCCAAAAGAAAATCACAGAAAC
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	86	E53SaCas9KKH17	ATACAGTAGATGCAATCCAAAA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	87	E53SaCas9KKH18	AGGAGGGTCCCTATACAGTAGA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	88	E53SaCas9KKH19	ATGGAAGGAGGGTCCCTATACA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA

73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
73	E53SaCas9KKH4	TCCTTAGCTTCCAGCCATTGTG	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	76	E53SaCas9KKH7	AGGTGTTCTTGTACTTCATCCC
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	77	E53SaCas9KKH8	CTTGTACTTCATCCCACTGATT
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	78	E53SaCas9KKH9	ACTGATTCTGAATTCTTTCAAC
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	84	E53SaCas9KKH15	AAAGAAAATCACAGAAACCAAG
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	85	E53SaCas9KKH16	TCCAAAAGAAAATCACAGAAAC
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	86	E53SaCas9KKH17	ATACAGTAGATGCAATCCAAAA
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	87	E53SaCas9KKH18	AGGAGGGTCCCTATACAGTACA
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	88	E53SaCas9KKH19	ATGGAAGGAGGGTCCCTATACA
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG
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74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA
74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
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74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
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74	E53SaCas9KKH5	AACATTTCATTCAACTGTTGCC	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
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75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT	84	E53SaCas9KKH15	AAAGAAAATCACAGAAACCAAG
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75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT	90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG
75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT	91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC

75	E53SaCas9KKH6	TTCAACTGTTGCCTCCGGTTCT	92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA
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89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
89	E53SaCas9KKH20	AGTCATGGAAGGAGGGTCCCTA	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA

90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
90	E53SaCas9KKH21	AGCCAAGCTTGAGTCATGGAAG	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
91	E53SaCas9KKH22	TTAGGACAGGCCAGAGCCAAGC	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
92	E53SaCas9KKH23	TGGAAGCTAAGGAAGAAGCTGA	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
93	E53SaCas9KKH24	AATGAAATGTTAAAGGATTCAA	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA	95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA
94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA

94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
94	E53SaCas9KKH25	GCAACAGTTGAATGAAATGTTA	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA	96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG
95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
95	E53SaCas9KKH26	AGAACCGGAGGCAACAGTTGAA	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG	97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC
96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
96	E53SaCas9KKH27	CCTTCAGAACCGGAGGCAACAG	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC	98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA
97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
97	E53SaCas9KKH28	GAACACCTTCAGAACCGGAGGC	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA	99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG
98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
98	E53SaCas9KKH29	AAAGAATTCAGAATCAGTGGGA	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG	100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA
99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
99	E53SaCas9KKH30	AGTTGAAAGAATTCAGAATCAG	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA	101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT
100	E53SaCas9KKH31	ATTCTAGTTGAAAGAATTCAGA	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA
101	E53SaCas9KKH32	TTTTATTCTAGTTGAAAGAATT	102	E53SaCas9KKH33	TTTTTCCTTTTATTCTAGTTGA

(3) Table 5C. Exon 53 SluCas9 guides:

Seq ID No.	**Guide ID or Guide RNA Name**	**Guide Sequence**
270	E53Slu2	CCTTGGTTTCTGTGATTTTCTT
271	E53Slu3	CTTTTGGATTGCATCTACTGTA
272	E53Slu4	TTTTGGATTGCATCTACTGTAT
273	E53Slu5	ACCCTCCTTCCATGACTCAAGC
274	E53Slu6	CTTCCATGACTCAAGCTTGGCT
275	E53Slu7	ACATTTCATTCAACTGTTGCCT
276	E53Slu8	TCAACTGTTGCCTCCGGTTCTG

277	E53Slu10	CCAAAAGAAAATCACAGAAACC
278	E53Slu11	GCCAAGCTTGAGTCATGGAAGG
279	E53Slu12	AGCCAAGCTTGAGTCATGGAAG
280	E53Slu13	CAGAGCCAAGCTTGAGTCATGG
281	E53Slu14	AGGCCAGAGCCAAGCTTGAGTC
282	E53Slu15	AGAAGCTGAGCAGGTCTTAGGA
283	E53Slu16	AAGGAAGAAGCTGAGCAGGTCT
284	E53Slu17	GGAAGCTAAGGAAGAAGCTGAG
285	E53Slu18	TTCAACACAATGGCTGGAAGCT
286	E53Slu19	GTTAAAGGATTCAACACAATGG
287	E53Slu20	AAATGTTAAAGGATTCAACACA
288	E53Slu21	GCAACAGTTGAATGAAATGTTA
289	E53Slu22	TACAAGAACACCTTCAGAACCG
290	E53Slu23	AAGTACAAGAACACCTTCAGAA
291	E53Slu24	AGTTGAAAGAATTCAGAATCAG
292	E53Slu25	TAGTTGAAAGAATTCAGAATCA
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA
926	E53Sl3.1G-Cv5	CGTTTGGATTGCATCTACTGTA
927	E53Sl3.2A-Cv5	CTATTGGATTGCATCTACTGTA
928	E53Sl3.2C-Cv5	CTCTTGGATTGCATCTACTGTA
929	E53Sl3.2G-Cv5	CTGTTGGATTGCATCTACTGTA
930	E53Sl3.3A-Cv5	CTTATGGATTGCATCTACTGTA
931	E53Sl3.3C-Cv5	CTTCTGGATTGCATCTACTGTA
932	E53Sl3.3G-Cv5	CTTGTGGATTGCATCTACTGTA
933	E53Sl3.4A-Cv5	CTTTAGGATTGCATCTACTGTA
934	E53Sl3.4C-Cv5	CTTTCGGATTGCATCTACTGTA
935	E53Sl3.4G-Cv5	CTTTGGGATTGCATCTACTGTA
936	E53Sl3.del2-Cv5	TTTGGATTGCATCTACTGTA
937	E53Sl3.delT-Cv5	CTTTGGATTGCATCTACTGTA
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA
950	E53SL3-21	TTTTGGATTGCATCTACTGTA
951	E53SL3-20	TTTGGATTGCATCTACTGTA
952	E53SL3-19	TTGGATTGCATCTACTGTA
953	E53SL3-18	TGGATTGCATCTACTGTA
954	E53SL3-17	GGATTGCATCTACTGTA
955	E53SL3-16	GATTGCATCTACTGTA

(4) Table 5D. Exon 53 SluCas9 pairs:

Guide 1 Seq ID No.	Guide 1	Guide 1 Sequence	Guide 2 Seq ID No.	Guide 2	Guide 2 Sequence
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	271	E53SL3	CTTTTGGATTGCATCTACTGTA
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	272	E53SL4	TTTTGGATTGCATCTACTGTAT
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	275	E53SL7	ACATTTCATTCAACTGTTGCCT
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	277	E53SL10	CCAAAAGAAAATCACAGAAACC
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	285	E53SL18	TTCAACACAATGGCTGGAAGCT
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	286	E53SL19	GTTAAAGGATTCAACACAATGG
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	287	E53SL20	AAATGTTAAAGGATTCAACACA
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	288	E53SL21	GCAACAGTTGAATGAAATGTTA
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	289	E53SL22	TACAAGAACACCTTCAGAACCG
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	290	E53SL23	AAGTACAAGAACACCTTCAGAA
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
270	E53SL2	CCTTGGTTTCTGTGATTTTCTT	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
271	E53SL3	CTTTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
271	E53SL3	CTTTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
271	E53SL3	CTTTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
271	E53SL3	CTTTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
271	E53SL3	CTTTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
271	E53SL3	CTTTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
271	E53SL3	CTTTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
271	E53SL3	CTTTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
271	E53SL3	CTTTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
271	E53SL3	CTTTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
271	E53SL3	CTTTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
271	E53SL3	CTTTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
271	E53SL3	CTTTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
271	E53SL3	CTTTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
271	E53SL3	CTTTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
271	E53SL3	CTTTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
271	E53SL3	CTTTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
271	E53SL3	CTTTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
271	E53SL3	CTTTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
271	E53SL3	CTTTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
271	E53SL3	CTTTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
272	E53SL4	TTTTGGATTGCATCTACTGTAT	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
272	E53SL4	TTTTGGATTGCATCTACTGTAT	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
272	E53SL4	TTTTGGATTGCATCTACTGTAT	275	E53SL7	ACATTTCATTCAACTGTTGCCT

272	E53SL4	TTTTGGATTGCATCTACTGTAT	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
272	E53SL4	TTTTGGATTGCATCTACTGTAT	277	E53SL10	CCAAAAGAAAATCACAGAAACC
272	E53SL4	TTTTGGATTGCATCTACTGTAT	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
272	E53SL4	TTTTGGATTGCATCTACTGTAT	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
272	E53SL4	TTTTGGATTGCATCTACTGTAT	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
272	E53SL4	TTTTGGATTGCATCTACTGTAT	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
272	E53SL4	TTTTGGATTGCATCTACTGTAT	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
272	E53SL4	TTTTGGATTGCATCTACTGTAT	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
272	E53SL4	TTTTGGATTGCATCTACTGTAT	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
272	E53SL4	TTTTGGATTGCATCTACTGTAT	285	E53SL18	TTCAACACAATGGCTGGAAGCT
272	E53SL4	TTTTGGATTGCATCTACTGTAT	286	E53SL19	GTTAAAGGATTCAACACAATGG
272	E53SL4	TTTTGGATTGCATCTACTGTAT	287	E53SL20	AAATGTTAAAGGATTCAACACA
272	E53SL4	TTTTGGATTGCATCTACTGTAT	288	E53SL21	GCAACAGTTGAATGAAATGTTA
272	E53SL4	TTTTGGATTGCATCTACTGTAT	289	E53SL22	TACAAGAACACCTTCAGAACCG
272	E53SL4	TTTTGGATTGCATCTACTGTAT	290	E53SL23	AAGTACAAGAACACCTTCAGAA
272	E53SL4	TTTTGGATTGCATCTACTGTAT	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
272	E53SL4	TTTTGGATTGCATCTACTGTAT	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	275	E53SL7	ACATTTCATTCAACTGTTGCCT
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	277	E53SL10	CCAAAAGAAAATCACAGAAACC
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	285	E53SL18	TTCAACACAATGGCTGGAAGCT
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	286	E53SL19	GTTAAAGGATTCAACACAATGG
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	287	E53SL20	AAATGTTAAAGGATTCAACACA
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	288	E53SL21	GCAACAGTTGAATGAAATGTTA
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	289	E53SL22	TACAAGAACACCTTCAGAACCG
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	290	E53SL23	AAGTACAAGAACACCTTCAGAA
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
273	E53SL5	ACCCTCCTTCCATGACTCAAGC	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	275	E53SL7	ACATTTCATTCAACTGTTGCCT
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	277	E53SL10	CCAAAAGAAAATCACAGAAACC
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG

274	E53SL6	CTTCCATGACTCAAGCTTGGCT	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	285	E53SL18	TTCAACACAATGGCTGGAAGCT
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	286	E53SL19	GTTAAAGGATTCAACACAATGG
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	287	E53SL20	AAATGTTAAAGGATTCAACACA
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	288	E53SL21	GCAACAGTTGAATGAAATGTTA
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	289	E53SL22	TACAAGAACACCTTCAGAACCG
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	290	E53SL23	AAGTACAAGAACACCTTCAGAA
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
274	E53SL6	CTTCCATGACTCAAGCTTGGCT	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
275	E53SL7	ACATTTCATTCAACTGTTGCCT	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
275	E53SL7	ACATTTCATTCAACTGTTGCCT	277	E53SL10	CCAAAAGAAAATCACAGAAACC
275	E53SL7	ACATTTCATTCAACTGTTGCCT	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
275	E53SL7	ACATTTCATTCAACTGTTGCCT	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
275	E53SL7	ACATTTCATTCAACTGTTGCCT	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
275	E53SL7	ACATTTCATTCAACTGTTGCCT	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
275	E53SL7	ACATTTCATTCAACTGTTGCCT	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
275	E53SL7	ACATTTCATTCAACTGTTGCCT	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
275	E53SL7	ACATTTCATTCAACTGTTGCCT	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
275	E53SL7	ACATTTCATTCAACTGTTGCCT	285	E53SL18	TTCAACACAATGGCTGGAAGCT
275	E53SL7	ACATTTCATTCAACTGTTGCCT	286	E53SL19	GTTAAAGGATTCAACACAATGG
275	E53SL7	ACATTTCATTCAACTGTTGCCT	287	E53SL20	AAATGTTAAAGGATTCAACACA
275	E53SL7	ACATTTCATTCAACTGTTGCCT	288	E53SL21	GCAACAGTTGAATGAAATGTTA
275	E53SL7	ACATTTCATTCAACTGTTGCCT	289	E53SL22	TACAAGAACACCTTCAGAACCG
275	E53SL7	ACATTTCATTCAACTGTTGCCT	290	E53SL23	AAGTACAAGAACACCTTCAGAA
275	E53SL7	ACATTTCATTCAACTGTTGCCT	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
275	E53SL7	ACATTTCATTCAACTGTTGCCT	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	277	E53SL10	CCAAAAGAAAATCACAGAAACC
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	285	E53SL18	TTCAACACAATGGCTGGAAGCT
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	286	E53SL19	GTTAAAGGATTCAACACAATGG
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	287	E53SL20	AAATGTTAAAGGATTCAACACA
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	288	E53SL21	GCAACAGTTGAATGAAATGTTA
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	289	E53SL22	TACAAGAACACCTTCAGAACCG

276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	290	E53SL23	AAGTACAAGAACACCTTCAGAA
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
276	E53SL8	TCAACTGTTGCCTCCGGTTCTG	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
277	E53SL10	CCAAAAGAAAATCACAGAAACC	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
277	E53SL10	CCAAAAGAAAATCACAGAAACC	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
277	E53SL10	CCAAAAGAAAATCACAGAAACC	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
277	E53SL10	CCAAAAGAAAATCACAGAAACC	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
277	E53SL10	CCAAAAGAAAATCACAGAAACC	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
277	E53SL10	CCAAAAGAAAATCACAGAAACC	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
277	E53SL10	CCAAAAGAAAATCACAGAAACC	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
277	E53SL10	CCAAAAGAAAATCACAGAAACC	285	E53SL18	TTCAACACAATGGCTGGAAGCT
277	E53SL10	CCAAAAGAAAATCACAGAAACC	286	E53SL19	GTTAAAGGATTCAACACAATGG
277	E53SL10	CCAAAAGAAAATCACAGAAACC	287	E53SL20	AAATGTTAAAGGATTCAACACA
277	E53SL10	CCAAAAGAAAATCACAGAAACC	288	E53SL21	GCAACAGTTGAATGAAATGTTA
277	E53SL10	CCAAAAGAAAATCACAGAAACC	289	E53SL22	TACAAGAACACCTTCAGAACCG
277	E53SL10	CCAAAAGAAAATCACAGAAACC	290	E53SL23	AAGTACAAGAACACCTTCAGAA
277	E53SL10	CCAAAAGAAAATCACAGAAACC	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
277	E53SL10	CCAAAAGAAAATCACAGAAACC	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	285	E53SL18	TTCAACACAATGGCTGGAAGCT
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	286	E53SL19	GTTAAAGGATTCAACACAATGG
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	287	E53SL20	AAATGTTAAAGGATTCAACACA
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	288	E53SL21	GCAACAGTTGAATGAAATGTTA
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	289	E53SL22	TACAAGAACACCTTCAGAACCG
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	290	E53SL23	AAGTACAAGAACACCTTCAGAA
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
278	E53SL11	GCCAAGCTTGAGTCATGGAAGG	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	285	E53SL18	TTCAACACAATGGCTGGAAGCT
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	286	E53SL19	GTTAAAGGATTCAACACAATGG
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	287	E53SL20	AAATGTTAAAGGATTCAACACA
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	288	E53SL21	GCAACAGTTGAATGAAATGTTA
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	289	E53SL22	TACAAGAACACCTTCAGAACCG

279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	290	E53SL23	AAGTACAAGAACACCTTCAGAA
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
279	E53SL12	AGCCAAGCTTGAGTCATGGAAG	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	285	E53SL18	TTCAACACAATGGCTGGAAGCT
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	286	E53SL19	GTTAAAGGATTCAACACAATGG
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	287	E53SL20	AAATGTTAAAGGATTCAACACA
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	288	E53SL21	GCAACAGTTGAATGAAATGTTA
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	289	E53SL22	TACAAGAACACCTTCAGAACCG
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	290	E53SL23	AAGTACAAGAACACCTTCAGAA
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
280	E53SL13	CAGAGCCAAGCTTGAGTCATGG	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	285	E53SL18	TTCAACACAATGGCTGGAAGCT
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	286	E53SL19	GTTAAAGGATTCAACACAATGG
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	287	E53SL20	AAATGTTAAAGGATTCAACACA
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	288	E53SL21	GCAACAGTTGAATGAAATGTTA
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	289	E53SL22	TACAAGAACACCTTCAGAACCG
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	290	E53SL23	AAGTACAAGAACACCTTCAGAA
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	286	E53SL19	GTTAAAGGATTCAACACAATGG
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	287	E53SL20	AAATGTTAAAGGATTCAACACA
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	289	E53SL22	TACAAGAACACCTTCAGAACCG
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	285	E53SL18	TTCAACACAATGGCTGGAAGCT
283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	286	E53SL19	GTTAAAGGATTCAACACAATGG
283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	287	E53SL20	AAATGTTAAAGGATTCAACACA
283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	288	E53SL21	GCAACAGTTGAATGAAATGTTA
283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	289	E53SL22	TACAAGAACACCTTCAGAACCG

283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	290	E53SL23	AAGTACAAGAACACCTTCAGAA
283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG	285	E53SL18	TTCAACACAATGGCTGGAAGCT
284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG	286	E53SL19	GTTAAAGGATTCAACACAATGG
284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG	287	E53SL20	AAATGTTAAAGGATTCAACACA
284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG	288	E53SL21	GCAACAGTTGAATGAAATGTTA
284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG	289	E53SL22	TACAAGAACACCTTCAGAACCG
284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG	290	E53SL23	AAGTACAAGAACACCTTCAGAA
284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
285	E53SL18	TTCAACACAATGGCTGGAAGCT	286	E53SL19	GTTAAAGGATTCAACACAATGG
285	E53SL18	TTCAACACAATGGCTGGAAGCT	287	E53SL20	AAATGTTAAAGGATTCAACACA
285	E53SL18	TTCAACACAATGGCTGGAAGCT	288	E53SL21	GCAACAGTTGAATGAAATGTTA
285	E53SL18	TTCAACACAATGGCTGGAAGCT	289	E53SL22	TACAAGAACACCTTCAGAACCG
285	E53SL18	TTCAACACAATGGCTGGAAGCT	290	E53SL23	AAGTACAAGAACACCTTCAGAA
285	E53SL18	TTCAACACAATGGCTGGAAGCT	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
285	E53SL18	TTCAACACAATGGCTGGAAGCT	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
286	E53SL19	GTTAAAGGATTCAACACAATGG	287	E53SL20	AAATGTTAAAGGATTCAACACA
286	E53SL19	GTTAAAGGATTCAACACAATGG	288	E53SL21	GCAACAGTTGAATGAAATGTTA
286	E53SL19	GTTAAAGGATTCAACACAATGG	289	E53SL22	TACAAGAACACCTTCAGAACCG
286	E53SL19	GTTAAAGGATTCAACACAATGG	290	E53SL23	AAGTACAAGAACACCTTCAGAA
286	E53SL19	GTTAAAGGATTCAACACAATGG	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
286	E53SL19	GTTAAAGGATTCAACACAATGG	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
287	E53SL20	AAATGTTAAAGGATTCAACACA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
287	E53SL20	AAATGTTAAAGGATTCAACACA	289	E53SL22	TACAAGAACACCTTCAGAACCG
287	E53SL20	AAATGTTAAAGGATTCAACACA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
287	E53SL20	AAATGTTAAAGGATTCAACACA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
287	E53SL20	AAATGTTAAAGGATTCAACACA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
288	E53SL21	GCAACAGTTGAATGAAATGTTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
288	E53SL21	GCAACAGTTGAATGAAATGTTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
288	E53SL21	GCAACAGTTGAATGAAATGTTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
288	E53SL21	GCAACAGTTGAATGAAATGTTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
289	E53SL22	TACAAGAACACCTTCAGAACCG	290	E53SL23	AAGTACAAGAACACCTTCAGAA
289	E53SL22	TACAAGAACACCTTCAGAACCG	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
289	E53SL22	TACAAGAACACCTTCAGAACCG	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
290	E53SL23	AAGTACAAGAACACCTTCAGAA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
290	E53SL23	AAGTACAAGAACACCTTCAGAA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
291	E53SL24	AGTTGAAAGAATTCAGAATCAG	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
924	E53SL3.1A-Cv5	CATTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
925	E53SL3.1C-Cv5	CCTTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
926	E53Sl3.1G-Cv5	CGTTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
926	E53Sl3.1G-Cv5	CGTTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
926	E53Sl3.1G-Cv5	CGTTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
926	E53S13.1G-Cv5	CGTTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
927	E53S13.2A-Cv5	CTATTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
928	E53S13.2C-Cv5	CTCTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
929	E53S13.2G-Cv5	CTGTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
930	E53S13.3A-Cv5	CTTATGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
931	E53S13.3C-Cv5	CTTCTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
932	E53S13.3G-Cv5	CTTGTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
933	E53S13.4A-Cv5	CTTTAGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
934	E53S13.4C-Cv5	CTTTCGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
935	E53S13.4G-Cv5	CTTTGGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
936	E53S13.del2-Cv5	TTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCAGAA
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
937	E53S13.delT-Cv5	CTTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
938	E53S13.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	272	E53SL4	TTTTGGATTGCATCTACTGTAT
938	E53S13.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	273	E53SL5	ACCCTCCTTCCATGACTCAAGC
938	E53S13.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	274	E53SL6	CTTCCATGACTCAAGCTTGGCT

938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	276	E53SL8	TCAACTGTTGCCTCCGGTTCTG
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	277	E53SL10	CCAAAAGAAAATCACAGAAACC
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	278	E53SL11	GCCAAGCTTGAGTCATGGAAGG
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	279	E53SL12	AGCCAAGCTTGAGTCATGGAAG
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	280	E53SL13	CAGAGCCAAGCTTGAGTCATGG
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	281	E53SL14	AGGCCAGAGCCAAGCTTGAGTC
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	282	E53SL15	AGAAGCTGAGCAGGTCTTAGGA
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	283	E53SL16	AAGGAAGAAGCTGAGCAGGTCT
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	284	E53SL17	GGAAGCTAAGGAAGAAGCTGAG
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	285	E53SL18	TTCAACACAATGGCTGGAAGCT
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	286	E53SL19	GTTAAAGGATTCAACACAATGG
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	287	E53SL20	AAATGTTAAAGGATTCAACACA
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	288	E53SL21	GCAACAGTTGAATGAAATGTTA
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	289	E53SL22	TACAAGAACACCTTCAGAACCG
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	290	E53SL23	AAGTACAAGAACACCTTCACAA
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	291	E53SL24	AGTTGAAAGAATTCAGAATCAG
938	E53Sl3.delT+A.-Cv5	ACTTTGGATTGCATCTACTGTA	292	E53SL25	TAGTTGAAAGAATTCAGAATCA
950	E53SL3-21	TTTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
951	E53SL3-20	TTTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
952	E53SL3-19	TTGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
953	E53SL3-18	TGGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
954	E53SL3-17	GGATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT
955	E53SL3-16	GATTGCATCTACTGTA	275	E53SL7	ACATTTCATTCAACTGTTGCCT

f) Table 6: All guide sequences (human-hg38.12)

Seq ID No.	Guide RNA Name or Guide ID name	exon_id	enzyme	strand	Guide Sequence	pam
1	E44Sa1	44	SaCas9	+	ATTTAGCATGTTCCCAATTCTC	AGGAAT
2	E44Sa3	44	SaCas9	-	TCTCAGAAAGACACAAATTCCT	GAGAAT
3	E45Sa1	45	SaCas9	+	TCAGGCTTCCCAATTTTTCCTG	TAGAAT
4	E45Sa2	45	SaCas9	+	TAGAATACTGGCATCTGTTTTT	GAGGAT
5	E45Sa3	45	SaCas9	+	TGGCATCTGTTTTTGAGGATTG	CTGAAT
6	E45Sa4	45	SaCas9	+	TTGCCGCTGCCCAATGCCATCC	TGGAGT
7	E45Sa6	45	SaCas9	-	TCTACAGGAAAAATTGGGAAGC	CTGAAT
8	E45Sa7	45	SaCas9	-	GCGGCAAACTGTTGTCAGAACA	TTGAAT
9	E45Sa8	45	SaCas9	-	TTTTGGTATCTTACAGGAACTC	CAGGAT
10	E50Sa2	50	SaCas9	-	AGGAAGTTAGAAGATCTGAGCT	CTGAGT
11	E51Sa1	51	SaCas9	+	TAGTAACCACAGGTTGTGTCAC	CAGAGT
12	E51Sa2	51	SaCas9	+	GTTGTGTCACCAGAGTAACAGT	CTGAGT

13	E51Sa4	51	SaCas9	-	GAGGGTGATGGTGGGTGACCTT	GAGGAT
14	E51Sa5	51	SaCas9	-	TATAAAATCACAGAGGGTGATG	GTGGGT
15	E51Sa6	51	SaCas9	-	TTGATCAAGTTATAAAATCACA	GAGGGT
16	E53Sa1	53	SaCas9	+	CCTTGGTTTCTGTGATTTTCTT	TTGGAT
17	E53Sa2	53	SaCas9	+	TCCTTAGCTTCCAGCCATTGTG	TTGAAT
18	E53Sa3	53	SaCas9	+	CTTGTACTTCATCCCACTGATT	CTGAAT
19	E53Sa4	53	SaCas9	+	ACTGATTCTGAATTCTTTCAAC	TAGAAT
20	E53Sa5	53	SaCas9	-	AGCCAAGCTTGAGTCATGGAAG	GAGGGT
21	E53Sa6	53	SaCas9	-	TTAGGACAGGCCAGAGCCAAGC	TTGAGT
22	E53Sa7	53	SaCas9	-	GCAACAGTTGAATGAAATGTTA	AAGGAT
23	E53Sa8	53	SaCas9	-	CCTTCAGAACCGGAGGCAACAG	TTGAAT
24	E53Sa9	53	SaCas9	-	AGTTGAAAGAATTCAGAATCAG	TGGGAT
25	E53Sa10	53	SaCas9	-	TTTTATTCTAGTTGAAAGAATT	CAGAAT
26	E53Sa11	53	SaCas9	-	TTTTTCCTTTTATTCTAGTTGA	AAGAAT
27	E51SaCas9KKH1	51	SACAS9 KKH	+	TCATTTTTTCTCATACCTTCTG	CTTGAT
28	E51SaCas9KKH2	51	SACAS9 KKH	+	TTTTTTCTCATACCTTCTGCTT	GATGAT
29	E51SaCas9KKH3	51	SACAS9 KKH	+	CCTTCTGCTTGATGATCATCTC	GTTGAT
30	E51SaCas9KKH4	51	SACAS9 KKH	+	ATGATCATCTCGTTGATATCCT	CAAGGT
31	E51SaCas9KKH5	51	SACAS9 KKH	+	AAGGTCACCCACCATCACCCTC	TGTGAT
32	E51SaCas9KKH6	51	SACAS9 KKH	+	ATCACCCTCTGTGATTTTATAA	CTTGAT
33	E51SaCas9KKH7	51	SACAS9 KKH	+	ATAACTTGATCAAGCAGAGAAA	GCCAGT
34	E51SaCas9KKH8	51	SACAS9 KKH	+	CTTGATCAAGCAGAGAAAGCCA	GTCGGT
35	E51SaCas9KKH9	51	SACAS9 KKH	+	ATCAAGCAGAGAAAGCCAGTCG	GTAAGT
36	E51SaCas9KKH10	51	SACAS9 KKH	+	CAGTCGGTAAGTTCTGTCCAAG	CCCGGT
37	E51SaCas9KKH11	51	SACAS9 KKH	+	GTAAGTTCTGTCCAAGCCCGGT	TGAAAT
38	E51SaCas9KKH12	51	SACAS9 KKH	+	AGCCCGGTTGAAATCTGCCAGA	GCAGGT
39	E51SaCas9KKH13	51	SACAS9 KKH	+	AGCAGGTACCTCCAACATCAAG	GAAGAT
40	E51SaCas9KKH14	51	SACAS9 KKH	+	CAACATCAAGGAAGATGGCATT	TCTAGT
41	E51SaCas9KKH15	51	SACAS9 KKH	+	AGGAAGATGGCATTTCTAGTTT	GGAGAT
42	E51SaCas9KKH16	51	SACAS9 KKH	+	ATGGCATTTCTAGTTTGGAGAT	GGCAGT
43	E51SaCas9KKH17	51	SACAS9 KKH	+	CTAGTTTGGAGATGGCAGTTTC	CTTAGT
44	E51SaCas9KKH18	51	SACAS9 KKH	+	GATGGCAGTTTCCTTAGTAACC	ACAGGT
45	E51SaCas9KKH19	51	SACAS9 KKH	+	TAGTAACCACAGGTTGTGTCAC	CAGAGT
46	E51SaCas9KKH20	51	SACAS9 KKH	+	CCACAGGTTGTGTCACCAGAGT	AACAGT
47	E51SaCas9KKH21	51	SACAS9 KKH	+	GTTGTGTCACCAGAGTAACAGT	CTGAGT
48	E51SaCas9KKH22	51	SACAS9 KKH	+	GAGTAACAGTCTGAGTAGGAGC	TAAAAT
49	E51SaCas9KKH23	51	SACAS9 KKH	+	TCTGAGTAGGAGCTAAAATATT	TTGGGT

50	E51SaCas9KKH24	51	SACAS9 KKH	-	AGAAGGTATGAGAAAAAATGAT	AAAAGT
51	E51SaCas9KKH25	51	SACAS9 KKH	-	TCAAGCAGAAGGTATGAGAAAA	AATGAT
52	E51SaCas9KKH26	51	SACAS9 KKH	-	TCATCAAGCAGAAGGTATGAGA	AAAAAT
53	E51SaCas9KKH27	51	SACAS9 KKH	-	TCAACGAGATGATCATCAAGCA	GAAGGT
54	E51SaCas9KKH28	51	SACAS9 KKH	-	GTGACCTTGAGGATATCAACGA	GATGAT
55	E51SaCas9KKH29	51	SACAS9 KKH	-	TGGGTGACCTTGAGGATATCAA	CGAGAT
56	E51SaCas9KKH30	51	SACAS9 KKH	-	GAGGGTGATGGTGGGTGACCTT	GAGGAT
57	E51SaCas9KKH31	51	SACAS9 KKH	-	TATAAAATCACAGAGGGTGATG	GTGGGT
58	E51SaCas9KKH32	51	SACAS9 KKH	-	AAGTTATAAAATCACAGAGGGT	GATGGT
59	E51SaCas9KKH33	51	SACAS9 KKH	-	ATCAAGTTATAAAATCACAGAG	GGTGAT
60	E51SaCas9KKH34	51	SACAS9 KKH	-	TTGATCAAGTTATAAAATCACA	GAGGGT
61	E51SaCas9KKH35	51	SACAS9 KKH	-	CTTTCTCTGCTTGATCAAGTTA	TAAAAT
62	E51SaCas9KKH36	51	SACAS9 KKH	-	CCGACTGGCTTTCTCTGCTTGA	TCAAGT
63	E51SaCas9KKH37	51	SACAS9 KKH	-	ACTTACCGACTGGCTTTCTCTG	CTTGAT
64	E51SaCas9KKH38	51	SACAS9 KKH	-	GATGTTGGAGGTACCTGCTCTG	GCAGAT
65	E51SaCas9KKH39	51	SACAS9 KKH	-	AAATGCCATCTTCCTTGATGTT	GGAGGT
66	E51SaCas9KKH40	51	SACAS9 KKH	-	CCAAACTAGAAATGCCATCTTC	CTTGAT
67	E51SaCas9KKH41	51	SACAS9 KKH	-	AGGAAACTGCCATCTCCAAACT	AGAAAT
68	E51SaCas9KKH42	51	SACAS9 KKH	-	CTGTTACTCTGGTGACACAACC	TGTGGT
69	E51SaCas9KKH43	51	SACAS9 KKH	-	TAGCTCCTACTCAGACTGTTAC	TCTGGT
70	E53SaCas9KKH1	53	SACAS9 KKH	+	AAAAGGTATCTTTGATACTAAC	CTTGGT
71	E53SaCas9KKH2	53	SACAS9 KKH	+	CTTTGATACTAACCTTGGTTTC	TGTGAT
72	E53SaCas9KKH3	53	SACAS9 KKH	+	CCTTGGTTTCTGTGATTTTCTT	TTGGAT
73	E53SaCas9KKH4	53	SACAS9 KKH	+	TCCTTAGCTTCCAGCCATTGTG	TTGAAT
74	E53SaCas9KKH5	53	SACAS9 KKH	+	AACATTTCATTCAACTGTTGCC	TCCGGT
75	E53SaCas9KKH6	53	SACAS9 KKH	+	TTCAACTGTTGCCTCCGGTTCT	GAAGGT
76	E53SaCas9KKH7	53	SACAS9 KKH	+	AGGTGTTCTTGTACTTCATCCC	ACTGAT
77	E53SaCas9KKH8	53	SACAS9 KKH	+	CTTGTACTTCATCCCACTGATT	CTGAAT
78	E53SaCas9KKH9	53	SACAS9 KKH	+	ACTGATTCTGAATTCTTTCAAC	TAGAAT
79	E53SaCas9KKH10	53	SACAS9 KKH	+	TTCTTTCAACTAGAATAAAAGG	AAAAAT
80	E53SaCas9KKH11	53	SACAS9 KKH	+	TTCAACTAGAATAAAAGGAAAA	ATAAAT
81	E53SaCas9KKH12	53	SACAS9 KKH	+	AGAATAAAAGGAAAAATAAATA	TATAGT
82	E53SaCas9KKH13	53	SACAS9 KKH	-	GTTAGTATCAAAGATACCTTTT	TAAAAT
83	E53SaCas9KKH14	53	SACAS9 KKH	-	CACAGAAACCAAGGTTAGTATC	AAAGAT
84	E53SaCas9KKH15	53	SACAS9 KKH	-	AAAGAAAATCACAGAAACCAAG	GTTAGT
85	E53SaCas9KKH16	53	SACAS9 KKH	-	TCCAAAAGAAAATCACAGAAAC	CAAGGT
86	E53SaCas9KKH17	53	SACAS9 KKH	-	ATACAGTAGATGCAATCCAAAA	GAAAAT

87	E53SaCas9KKH18	53	SACAS9 KKH	-	AGGAGGGTCCCTATACAGTAGA	TGCAAT
88	E53SaCas9KKH19	53	SACAS9 KKH	-	ATGGAAGGAGGGTCCCTATACA	GTAGAT
89	E53SaCas9KKH20	53	SACAS9 KKH	-	AGTCATGGAAGGAGGGTCCCTA	TACAGT
90	E53SaCas9KKH21	53	SACAS9 KKH	-	AGCCAAGCTTGAGTCATGGAAG	GAGGGT
91	E53SaCas9KKH22	53	SACAS9 KKH	-	TTAGGACAGGCCAGAGCCAAGC	TTGAGT
92	E53SaCas9KKH23	53	SACAS9 KKH	-	TGGAAGCTAAGGAAGAAGCTGA	GCAGGT
93	E53SaCas9KKH24	53	SACAS9 KKH	-	AATGAAATGTTAAAGGATTCAA	CACAAT
94	E53SaCas9KKH25	53	SACAS9 KKH	-	GCAACAGTTGAATGAAATGTTA	AAGGAT
95	E53SaCas9KKH26	53	SACAS9 KKH	-	AGAACCGGAGGCAACAGTTGAA	TGAAAT
96	E53SaCas9KKH27	53	SACAS9 KKH	-	CCTTCAGAACCGGAGGCAACAG	TTGAAT
97	E53SaCas9KKH28	53	SACAS9 KKH	-	GAACACCTTCAGAACCGGAGGC	AACAGT
98	E53SaCas9KKH29	53	SACAS9 KKH	-	AAAGAATTCAGAATCAGTGGGA	TGAAGT
99	E53SaCas9KKH30	53	SACAS9 KKH	-	AGTTGAAAGAATTCAGAATCAG	TGGGAT
100	E53SaCas9KKH31	53	SACAS9 KKH	-	ATTCTAGTTGAAAGAATTCAGA	ATCAGT
101	E53SaCas9KKH32	53	SACAS9 KKH	-	TTTTATTCTAGTTGAAAGAATT	CAGAAT
102	E53SaCas9KKH33	53	SACAS9 KKH	-	TTTTTCCTTTTATTCTAGTTGA	AAGAAT
103	E53SaCas9KKH34	53	SACAS9 KKH	-	ATATATTTATTTTTCCTTTTAT	TCTAGT
200	E44Slu1	44	SluCas9	+	TATTTAGCATGTTCCCAATTCT	CAGG
201	E44Slu2	44	SluCas9	+	AACAGATCTGTCAAATCGCCTG	CAGG
202	E44Slu4	44	SluCas9	-	TGCTAAATACAAATGGTATCTT	AAGG
203	E44Slu5	44	SluCas9	-	ATTGGGAACATGCTAAATACAA	ATGG
204	E44Slu6	44	SluCas9	-	AAAGACACAAATTCCTGAGAAT	TGGG
205	E44Slu7	44	SluCas9	-	GAAAGACACAAATTCCTGAGAA	TTGG
206	E44Slu8	44	SluCas9	-	ATGATATAAAGATATTTAATCA	GTGG
207	E44Slu9	44	SluCas9	-	TTGACAGATCTGTTGAGAAATG	GCGG
208	E44Slu10	44	SluCas9	-	GATTTGACAGATCTGTTGAGAA	ATGG
209	E45Slu1	45	SluCas9	+	AGACCTCCTGCCACCGCAGATT	CAGG
210	E45Slu2	45	SluCas9	+	TCCCAATTTTTCCTGTAGAATA	CTGG
211	E45Slu3	45	SluCas9	+	TAGAATACTGGCATCTGTTTTT	GAGG
212	E45Slu4	45	SluCas9	+	TTTGCCGCTGCCCAATGCCATC	CTGG
213	E45Slu7	45	SluCas9	-	CTGTCAGACAGAAAAAAGAGGT	AGGG
214	E45Slu8	45	SluCas9	-	GCTGTCAGACAGAAAAAAGAGG	TAGG
215	E45Slu9	45	SluCas9	-	AACAGCTGTCAGACAGAAAAAA	GAGG
216	E45Slu10	45	SluCas9	-	AAGCCTGAATCTGCGGTGGCAG	GAGG
217	E45Slu11	45	SluCas9	-	GGGAAGCCTGAATCTGCGGTGG	CAGG
218	E45Slu12	45	SluCas9	-	AATTGGGAAGCCTGAATCTGCG	GTGG
219	E45Slu13	45	SluCas9	-	AAAAATTGGGAAGCCTGAATCT	GCGG

220	E45Slu14	45	SluCas9	-	GCCAGTATTCTACAGGAAAAAT	TGGG
221	E45Slu15	45	SluCas9	-	TGCCAGTATTCTACAGGAAAAA	TTGG
222	E45Slu16	45	SluCas9	-	AAAAACAGATGCCAGTATTCTA	CAGG
223	E45Slu17	45	SluCas9	-	TGTCAGAACATTGAATGCAACT	GGGG
224	E45Slu18	45	SluCas9	-	TTGTCAGAACATTGAATGCAAC	TGGG
225	E45Slu19	45	SluCas9	-	GTTGTCAGAACATTGAATGCAA	CTGG
226	E45Slu20	45	SluCas9	-	AACTCCAGGATGGCATTGGGCA	GCGG
227	E45Slu21	45	SluCas9	-	TACAGGAACTCCAGGATGGCAT	TGGG
228	E45Slu22	45	SluCas9	-	TTACAGGAACTCCAGGATGGCA	TTGG
229	E45Slu23	45	SluCas9	-	GGTATCTTACAGGAACTCCAGG	ATGG
230	E45Slu24	45	SluCas9	-	TTTTGGTATCTTACAGGAACTC	CAGG
231	E50Slu2	50	SluCas9	+	AGTATACTTACAGGCTCCAATA	GTGG
232	E50Slu3	50	SluCas9	+	CAGGCTCCAATAGTGGTCAGTC	CAGG
233	E50Slu4	50	SluCas9	+	CAATAGTGGTCAGTCCAGGAGC	TAGG
234	E50Slu5	50	SluCas9	+	GTGGTCAGTCCAGGAGCTAGGT	CAGG
235	E50Slu6	50	SluCas9	+	TTGCCCTCAGCTCTTGAAGTAA	ACGG
236	E50Slu9	50	SluCas9	-	CTAGCTCCTGGACTGACCACTA	TTGG
237	E50Slu10	50	SluCas9	-	GCAAAGCAGCCTGACCTAGCTC	CTGG
238	E50Slu11	50	SluCas9	-	AAACCGTTTACTTCAAGAGCTG	AGGG
239	E50Slu12	50	SluCas9	-	TAAACCGTTTACTTCAAGAGCT	GAGG
240	E50Slu13	50	SluCas9	-	AGATCTGAGCTCTGAGTGGAAG	GCGG
241	E50Slu14	50	SluCas9	-	AGAAGATCTGAGCTCTGAGTGG	AAGG
242	E50Slu15	50	SluCas9	-	AGTTAGAAGATCTGAGCTCTGA	GTGG
243	E51Slu1	51	SluCas9	+	TGATCATCTCGTTGATATCCTC	AAGG
244	E51Slu2	51	SluCas9	+	TTGATCAAGCAGAGAAAGCCAG	TCGG
245	E51Slu3	51	SluCas9	+	AGTCGGTAAGTTCTGTCCAAGC	CCGG
246	E51Slu4	51	SluCas9	+	GCCCGGTTGAAATCTGCCAGAG	CAGG
247	E51Slu5	51	SluCas9	+	CAGAGCAGGTACCTCCAACATC	AAGG
248	E51Slu6	51	SluCas9	+	GGTACCTCCAACATCAAGGAAG	ATGG
249	E51Slu7	51	SluCas9	+	CAAGGAAGATGGCATTTCTAGT	TTGG
250	E51Slu8	51	SluCas9	+	AGATGGCATTTCTAGTTTGGAG	ATGG
251	E51Slu9	51	SluCas9	+	ATGGCAGTTTCCTTAGTAACCA	CAGG
252	E51Slu10	51	SluCas9	+	GTCACCAGAGTAACAGTCTGAG	TAGG
253	E51Slu15	51	SluCas9	-	CAACGAGATGATCATCAAGCAG	AAGG
254	E51Slu16	51	SluCas9	-	GAGGGTGATGGTGGGTGACCTT	GAGG
255	E51Slu17	51	SluCas9	-	ATAAAATCACAGAGGGTGATGG	TGGG
256	E51Slu18	51	SluCas9	-	TATAAAATCACAGAGGGTGATG	GTGG

257	E51Slu19	51	SluCas9	-	AGTTATAAAATCACAGAGGGTG	ATGG
258	E51Slu20	51	SluCas9	-	TGATCAAGTTATAAAATCACAG	AGGG
259	E51Slu21	51	SluCas9	-	TTGATCAAGTTATAAAATCACA	GAGG
260	E51Slu22	51	SluCas9	-	GGGCTTGGACAGAACTTACCGA	CTGG
261	E51Slu23	51	SluCas9	-	CTCTGGCAGATTTCAACCGGGC	TTGG
262	E51Slu24	51	SluCas9	-	ACCTGCTCTGGCAGATTTCAAC	CGGG
263	E51Slu25	51	SluCas9	-	TACCTGCTCTGGCAGATTTCAA	CCGG
264	E51Slu26	51	SluCas9	-	CTTGATGTTGGAGGTACCTGCT	CTGG
265	E51Slu27	51	SluCas9	-	AATGCCATCTTCCTTGATGTTG	GAGG
266	E51Slu28	51	SluCas9	-	AGAAATGCCATCTTCCTTGATG	TTGG
267	E51Slu29	51	SluCas9	-	GGTGACACAACCTGTGGTTACT	AAGG
268	E51Slu30	51	SluCas9	-	TGTTACTCTGGTGACACAACCT	GTGG
269	E51Slu31	51	SluCas9	-	AGCTCCTACTCAGACTGTTACT	CTGG
270	E53Slu2	53	SluCas9	+	CCTTGGTTTCTGTGATTTTCTT	TTGG
271	E53Slu3	53	SluCas9	+	CTTTTGGATTGCATCTACTGTA	TAGG
272	E53Slu4	53	SluCas9	+	TTTTGGATTGCATCTACTGTAT	AGGG
273	E53Slu5	53	SluCas9	+	ACCCTCCTTCCATGACTCAAGC	TTGG
274	E53Slu6	53	SluCas9	+	CTTCCATGACTCAAGCTTGGCT	CTGG
275	E53Slu7	53	SluCas9	+	ACATTTCATTCAACTGTTGCCT	CCGG
276	E53Slu8	53	SluCas9	+	TCAACTGTTGCCTCCGGTTCTG	AAGG
277	E53Slu10	53	SluCas9	-	CCAAAAGAAAATCACAGAAACC	AAGG
278	E53Slu11	53	SluCas9	-	GCCAAGCTTGAGTCATGGAAGG	AGGG
279	E53Slu12	53	SluCas9	-	AGCCAAGCTTGAGTCATGGAAG	GAGG
280	E53Slu13	53	SluCas9	-	CAGAGCCAAGCTTGAGTCATGG	AAGG
281	E53Slu14	53	SluCas9	-	AGGCCAGAGCCAAGCTTGAGTC	ATGG
282	E53Slu15	53	SluCas9	-	AGAAGCTGAGCAGGTCTTAGGA	CAGG
283	E53Slu16	53	SluCas9	-	AAGGAAGAAGCTGAGCAGGTCT	TAGG
284	E53Slu17	53	SluCas9	-	GGAAGCTAAGGAAGAAGCTGAG	CAGG
285	E53Slu18	53	SluCas9	-	TTCAACACAATGGCTGGAAGCT	AAGG
286	E53Slu19	53	SluCas9	-	GTTAAAGGATTCAACACAATGG	CTGG
287	E53Slu20	53	SluCas9	-	AAATGTTAAAGGATTCAACACA	ATGG
288	E53Slu21	53	SluCas9	-	GCAACAGTTGAATGAAATGTTA	AAGG
289	E53Slu22	53	SluCas9	-	TACAAGAACACCTTCAGAACCG	GAGG
290	E53Slu23	53	SluCas9	-	AAGTACAAGAACACCTTCAGAA	CCGG
291	E53Slu24	53	SluCas9	-	AGTTGAAAGAATTCAGAATCAG	TGGG
292	E53Slu25	53	SluCas9	-	TAGTTGAAAGAATTCAGAATCA	GTGG
104	E44SaCas9KKH2	44	SaCas9 KKH	+	TACCATTTGTATTTAGCATGTT	CCCAAT

105	E44SaCas9KKH3	44	SaCas9 KKH	+	ATTTAGCATGTTCCCAATTCTC	AGGAAT
106	E44SaCas9KKH4	44	SaCas9 KKH	+	AACTGTTCAGCTTCTGTTAGCC	ACTGAT
107	E44SaCas9KKH5	44	SaCas9 KKH	+	TTCAGCTTCTGTTAGCCACTGA	TTAAAT
108	E44SaCas9KKH6	44	SaCas9 KKH	+	CACTGATTAAATATCTTTATAT	CATAAT
109	E44SaCas9KKH7	44	SaCas9 KKH	+	ATGAAAACGCCGCCATTTCTCA	ACAGAT
110	E44SaCas9KKH8	44	SaCas9 KKH	+	CCGCCATTTCTCAACAGATCTG	TCAAAT
111	E44SaCas9KKH9	44	SaCas9 KKH	+	CAACAGATCTGTCAAATCGCCT	GCAGGT
112	E44SaCas9KKH14	44	SaCas9 KKH	-	TAAATACAAATGGTATCTTAAG	GTAAGT
113	E44SaCas9KKH15	44	SaCas9 KKH	-	ATGCTAAATACAAATGGTATCT	TAAGGT
114	E44SaCas9KKH16	44	SaCas9 KKH	-	AATTGGGAACATGCTAAATACA	AATGGT
115	E44SaCas9KKH17	44	SaCas9 KKH	-	GAGAATTGGGAACATGCTAAAT	ACAAAT
116	E44SaCas9KKH18	44	SaCas9 KKH	-	ATTCCTGAGAATTGGGAACATG	CTAAAT
117	E44SaCas9KKH19	44	SaCas9 KKH	-	TCTCAGAAAGACACAAATTCCT	GAGAAT
118	E44SaCas9KKH20	44	SaCas9 KKH	-	CTGAACAGTTTCTCAGAAAGAC	ACAAAT
119	E44SaCas9KKH21	44	SaCas9 KKH	-	AATCAGTGGCTAACAGAAGCTG	AACAGT
120	E44SaCas9KKH22	44	SaCas9 KKH	-	CATTATGATATAAAGATATTTA	ATCAGT
121	E44SaCas9KKH23	44	SaCas9 KKH	-	TTTTCATTATGATATAAAGATA	TTTAAT
122	E44SaCas9KKH24	44	SaCas9 KKH	-	GGCGGCGTTTTCATTATGATAT	AAAGAT
123	E44SaCas9KKH25	44	SaCas9 KKH	-	TGAGAAATGGCGGCGTTTTCAT	TATGAT
124	E44SaCas9KKH26	44	SaCas9 KKH	-	AGGCGATTTGACAGATCTGTTG	AGAAAT
125	E44SaCas9KKH27	44	SaCas9 KKH	-	GCTTTTACCTGCAGGCGATTTG	ACAGAT
126	E45SaCas9KKH1	45	SaCas9 KKH	+	TGTTTGCAGACCTCCTGCCACC	GCAGAT
127	E45SaCas9KKH2	45	SaCas9 KKH	+	CTGCCACCGCAGATTCAGGCTT	CCCAAT
128	E45SaCas9KKH3	45	SaCas9 KKH	+	TCAGGCTTCCCAATTTTTCCTG	TAGAAT
129	E45SaCas9KKH4	45	SaCas9 KKH	+	TAGAATACTGGCATCTGTTTTT	GAGGAT
130	E45SaCas9KKH5	45	SaCas9 KKH	+	TGGCATCTGTTTTTGAGGATTG	CTGAAT
131	E45SaCas9KKH6	45	SaCas9 KKH	+	AGGATTGCTGAATTATTTCTTC	CCCAGT
132	E45SaCas9KKH7	45	SaCas9 KKH	+	AATTATTTCTTCCCCAGTTGCA	TTCAAT
133	E45SaCas9KKH8	45	SaCas9 KKH	+	CAGTTGCATTCAATGTTCTGAC	AACAGT
134	E45SaCas9KKH9	45	SaCas9 KKH	+	TTCTGACAACAGTTTGCCGCTG	CCCAAT
135	E45SaCas9KKH10	45	SaCas9 KKH	+	TTGCCGCTGCCCAATGCCATCC	TGGAGT
136	E45SaCas9KKH16	45	SaCas9 KKH	-	AAACAGCTGTCAGACAGAAAAA	AGAGGT
137	E45SaCas9KKH17	45	SaCas9 KKH	-	GAAGCCTGAATCTGCGGTGGCA	GGAGGT
138	E45SaCas9KKH18	45	SaCas9 KKH	-	GAAAAATTGGGAAGCCTGAATC	TGCGGT
139	E45SaCas9KKH19	45	SaCas9 KKH	-	TCTACAGGAAAAATTGGGAAGC	CTGAAT
140	E45SaCas9KKH20	45	SaCas9 KKH	-	ACAGATGCCAGTATTCTACAGG	AAAAAT
141	E45SaCas9KKH21	45	SaCas9 KKH	-	TCAGCAATCCTCAAAAACAGAT	GCCAGT

142	E45SaCas9KKH22	45	SaCas9 KKH	-	AATAATTCAGCAATCCTCAAAA	ACAGAT
143	E45SaCas9KKH23	45	SaCas9 KKH	-	GCAACTGGGGAAGAAATAATTC	AGCAAT
144	E45SaCas9KKH24	45	SaCas9 KKH	-	CATTGAATGCAACTGGGGAAGA	AATAAT
145	E45SaCas9KKH25	45	SaCas9 KKH	-	GAACATTGAATGCAACTGGGGA	AGAAAT
146	E45SaCas9KKH26	45	SaCas9 KKH	-	GCGGCAAACTGTTGTCAGAACA	TTGAAT
147	E45SaCas9KKH27	45	SaCas9 KKH	-	TTTTGGTATCTTACAGGAACTC	CAGGAT
148	E50SaCas9KKH1	50	SaCas9 KKH	+	GGGATCCAGTATACTTACAGGC	TCCAAT
149	E50SaCas9KKH2	50	SaCas9 KKH	+	ATCCAGTATACTTACAGGCTCC	AATAGT
150	E50SaCas9KKH3	50	SaCas9 KKH	+	CAGTATACTTACAGGCTCCAAT	AGTGGT
151	E50SaCas9KKH4	50	SaCas9 KKH	+	ATACTTACAGGCTCCAATAGTG	GTCAGT
152	E50SaCas9KKH5	50	SaCas9 KKH	+	CCAATAGTGGTCAGTCCAGGAG	CTAGGT
153	E50SaCas9KKH6	50	SaCas9 KKH	+	AGGCTGCTTTGCCCTCAGCTCT	TGAAGT
154	E50SaCas9KKH7	50	SaCas9 KKH	+	TTTGCCCTCAGCTCTTGAAGTA	AACGGT
155	E50SaCas9KKH8	50	SaCas9 KKH	+	TTTACCGCCTTCCACTCAGAGC	TCAGAT
156	E50SaCas9KKH10	50	SaCas9 KKH	-	GGACTGACCACTATTGGAGCCT	GTAAGT
157	E50SaCas9KKH11	50	SaCas9 KKH	-	AAGATCTGAGCTCTGAGTGGAA	GGCGGT
158	E50SaCas9KKH12	50	SaCas9 KKH	-	AGGAAGTTAGAAGATCTGAGCT	CTGAGT
159	E50SaCas9KKH13	50	SaCas9 KKH	-	TTTTCTGTTAAAGAGGAAGTTA	GAAGAT
924	E53SL3.1A-Cv5	53	SluCas9		CATTTGGATTGCATCTACTGTA	
925	E53SL3.1C-Cv5	53	SluCas9		CCTTTGGATTGCATCTACTGTA	
926	E53S13.1G-Cv5	53	SluCas9		CGTTTGGATTGCATCTACTGTA	
927	E53S13.2A-Cv5	53	SluCas9		CTATTGGATTGCATCTACTGTA	
928	E53S13.2C-Cv5	53	SluCas9		CTCTTGGATTGCATCTACTGTA	
929	E53S13.2G-Cv5	53	SluCas9		CTGTTGGATTGCATCTACTGTA	
930	E53S13.3A-Cv5	53	SluCas9		CTTATGGATTGCATCTACTGTA	
931	E53S13.3C-Cv5	53	SluCas9		CTTCTGGATTGCATCTACTGTA	
932	E53S13.3G-Cv5	53	SluCas9		CTTGTGGATTGCATCTACTGTA	
933	E53S13.4A-Cv5	53	SluCas9		CTTTAGGATTGCATCTACTGTA	
934	E53S13.4C-Cv5	53	SluCas9		CTTTCGGATTGCATCTACTGTA	
935	E53S13.4G-Cv5	53	SluCas9		CTTTGGGATTGCATCTACTGTA	
936	E53S13.del2-Cv5	53	SluCas9		TTTGGATTGCATCTACTGTA	
937	E53S13.delT-Cv5	53	SluCas9		CTTTGGATTGCATCTACTGTA	
938	E53S13.delT+A.-Cv5	53	SluCas9		ACTTTGGATTGCATCTACTGTA	
950	E53SL3-21	53	SluCas9		TTTTGGATTGCATCTACTGTA	
951	E53SL3-20	53	SluCas9		TTTGGATTGCATCTACTGTA	
952	E53SL3-19	53	SluCas9		TTGGATTGCATCTACTGTA	
953	E53SL3-18	53	SluCas9		TGGATTGCATCTACTGTA	

954	E53SL3-17	53	SluCas9		GGATTGCATCTACTGTA	
955	E53SL3-16	53	SluCas9		GATTGCATCTACTGTA	

Compositions

[0043] In some embodiments, a composition is provided comprising one or more guide RNAs, or one or more nucleic acids encoding one or more guide RNAs, comprising or consisting of one or more guide sequence of **Table 6** (SEQ ID NOs: 1-159 for SaCas9 and 200-292, 924-938, 950- and 955 for SluCas9). **Table 6** provides the endonuclease associated with each guide sequence such that for each guide sequence described herein the type of endonuclease to be paired with the guide (for compositions) or used with the guide (for methods/uses) can be determined.

[0044] In some embodiments, a composition is provided comprising one or more guide RNAs, or one or more nucleic acids encoding one or more guide RNAs, wherein the guide RNA comprises at least 16, 17, 18, 19, or 20 contiguous nucleotides of a guide sequence of **Table 6,** or is at least 70%, at least 75%, at least 80%, at least 85%, or at least 90% identical to a guide sequence comprising at least 16, 17, 18, 19, or 20 nucleotides of a guide sequence of **Table 6**. In particular embodiments, a composition is provided comprising one or more guide RNAs, or one or more nucleic acids encoding one or more guide RNAs, wherein the guide RNA comprises at least 20 contiguous nucleotides of a guide sequence of **Table 6,** or is at least 70%, at least 75%, at least 80%, at least 85%, or at least 90% identical to guide sequence comprising at least 20 nucleotides of a guide sequence of **Table 6**. In other particular embodiments, a composition is provided comprising one or more guide RNAs, or one or more nucleic acids encoding one or more guide RNAs, wherein the guide RNA comprises no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 contiguous nucleotides of a guide sequence of **Table 6,** or is at least 70%, at least 75%, at least 80%, at least 85%, or at least 90% identical to guide sequence comprising no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 contiguous nucleotides of a guide sequence of **Table 6**.

[0045] In some embodiments, a composition is provided comprising two or more guide RNAs, or nucleic acid encoding two or more guide RNAs, wherein each guide RNA comprises a guide sequence of **Table 6**, or at least 16, 17, 18, 19, or 20 contiguous nucleotides of a guide sequence of **Table 6,** or is at least 70%, at least 75%, at least 80%, at least 85%, or at least 90% identical to a guide sequence comprising at least 16, 17, 18, 19, or 20 nucleotides of a guide sequence selected from **Table 6**. In particular embodiments, a composition is provided comprising two or more guide RNAs, or nucleic acid encoding two or more guide RNAs, wherein each guide RNA comprises at least 20 contiguous nucleotides of a guide sequence of **Table 6,** or is at least 70%, at least 75%, at least 80%, at least 85%, or at least 90% identical to a guide sequence comprising at least 20 nucleotides of a guide sequence selected from **Table 6**. In other particular embodiments, a composition is provided comprising two or more guide RNAs, or nucleic acid encoding two or more guide RNAs, wherein at least one of the two or more guide RNAs, optionally each guide RNA, comprises no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 contiguous nucleotides of a guide sequence of **Table 6,** or is at least 70%, at least 75%, at least 80%, at least 85%, or at least 90% identical to a guide sequence comprising no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 nucleotides of a guide sequence selected from **Table 6**.

[0046] In some embodiments, a composition is provided comprising a pair of guide RNAs, or nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises sequences from any of the pairs disclosed in **Tables 1B, 1D, 2B, 2D, 3B, 3D, 4B, 4D, 5B,** and **5D.** In some embodiments, a composition is provided comprising any of the pairs of guide RNA sequences disclosed in **Tables 1B, 1D, 2B, 2D, 3B, 3D, 4B, 4D, 5B,** and **5D**.

[0047] In some embodiments, a composition is provided comprising one or more nucleic acid molecules, wherein at least one of the molecules comprises nucleic acid encoding: a) a SaCas9 or SluCas9; and b) a first and a second guide RNA comprising a first and a second guide sequence, wherein the first and second guide sequence are selected from any one of the guide sequence pairs of **Tables 1B, 1D, 2B, 2D, 3B, 3D, 4B, 4D, 5B,** and **5D**.

[0048] In some embodiments, a composition is provided comprising two nucleic acid molecules, wherein at least one of the molecules comprises a nucleic acid encoding a first and a second guide RNA comprising a first and a second guide sequence, wherein the first and second guide sequence are selected from any one of the guide sequence pairs of **Tables 1B, 1D, 2B, 2D, 3B, 3D, 4B, 4D, 5B,** and **5D**, optionally wherein the nucleic acid does not comprise a nucleic acid encoding an endonuclease.

[0049] In some embodiments, a composition is provided comprising a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 1B or 1D** for exon 44. In some embodiments, a composition is provided comprising a pair of guide RNAs, or nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 2B or 2D** for exon 45. In some embodiments, a composition is provided comprising a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 3B or 3D** for exon 50. In some embodiments, a composition is provided comprising a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 4B or 4D** for exon 51. In some embodiments, a composition is provided comprising a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 5B or 5D** for exon 53. In some embodiments, a composition is provided comprising one or more nucleic acid molecules encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 1B or 1D** for exon 44. In some embodiments, a composition is provided comprising one or more nucleic acid molecules encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 2B or 2D** for exon 45. In some embodiments, a composition is provided comprising one or more nucleic acid molecules encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 3B or 3D** for exon 50. In some embodiments, a composition is provided comprising one or more nucleic acid molecules encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 4B or 4D** for exon 51. In some embodiments, a composition is provided comprising one or more nucleic acid molecules encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises or consists of any one of the pairs of guide sequences of any one of **Tables 5B or 5D** for exon 53.

[0050] In some embodiments, a composition is provided comprising a pair of guide RNAs or a nucleic acid encoding a pair of guide RNAs, wherein the guide RNAs comprise or consist of any one of the following pairs of guide sequences:

a. For exon 44 (e.g., with SluCas9): SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;
b. For exon 45 (e.g., with SluCas9), SEQ ID NOs: 223 and 230; or 224 and 212.
c. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;
d. For exon 51 (e.g., with SaCas9), SEQ ID NOs: 28 and 57; 31 and 57; 31 and 46; 32 and 69; 33 and 57; 33 and 69; 34 and 57; 36 and 69; 37 and 69; 37 and 46; 39 and 46; 40 and 46; 46 and 35; 46 and 62; 46 and 65; 46 and 67; 47 and 57; 48 and 57; 49 and 57; 51 and 57; 53 and 46; 54 and 46; 55 and 46; 58 and 46; 59 and 46; 60 and 46; 61 and 69; or 69 and 30;
e. For exon 51 (e.g., with SluCas9), SEQ ID NOs: 243 and 252; 245 and 252; 252 and 253; 252 and 254; 252 and 256; 252 and 257; 252 and 258; 252 and 262; 252 and 264; 252 and 265; or 252 and 266;
f. For exon 53 (e.g., with SaCas9), SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and
g. For exon 53 (e.g., with SluCas9), SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and

291; 272 and 292; 950 and 275; 951 and 275; 952 and 275; 953 and 275; 954 and 275; or 955 and 275.

[0051] In some embodiments, a composition is provided comprising: i) an SaCas9-KKH or a nucleic acid encoding a SaCas9-KKH, and ii) a first and a second guide RNA, or a nucleic acid encoding a first and a second guide RNA, wherein the first guide RNA comprises the nucleotide sequence of SEQ ID NO: 88, and wherein the second guide RNA comprises the nucleotide sequence of SEQ ID NO: 97. In some embodiments, a composition is provided comprising: i) a SluCas9 or a nucleic acid encoding a SluCas9, and ii) a first and a second guide RNA, or a nucleic acid encoding a first and a second guide RNA, wherein the first guide RNA comprises the nucleotide sequence of SEQ ID NO: 283, and wherein the second guide RNA comprises the nucleotide sequence of SEQ ID NO: 290. In some embodiments, a composition is provided comprising: i) a SluCas9 or a nucleic acid encoding a SluCas9, and ii) a first and a second guide RNA, or a nucleic acid encoding a first and a second guide RNA, wherein the first guide RNA comprises the nucleotide sequence of SEQ ID NO: 283, and wherein the second guide RNA comprises the nucleotide sequence of SEQ ID NO: 292.

[0052] In some embodiments, the disclosure provides for one or more nucleic acid molecules encoding a pair of guide RNAs comprising a first guide RNA and a second guide RNA, wherein the first guide RNA and the second guide RNA target exon 53. In some embodiments, the guide RNAs are for use with an SaCas9 endonuclease. In some embodiments, the one or more nucleic acid molecules also encode for an SaCas9 endonuclease. In some embodiments, the one or more nucleic acid molecules are in a composition further comprising an SaCas9 endonuclease. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 86 and the second guide RNA comprises the sequence of SEQ ID NO: 96. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 87 and the second guide RNA comprises the sequence of SEQ ID NO: 96. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 88 and the second guide RNA comprises the sequence of SEQ ID NO: 97. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 89 and the second guide RNA comprises the sequence of SEQ ID NO: 96. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 90 and the second guide RNA comprises the sequence of SEQ ID NO: 97. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 92 and the second guide RNA comprises the sequence of SEQ ID NO: 77. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 92 and the second guide RNA comprises the sequence of SEQ ID NO: 78. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 92 and the second guide RNA comprises the sequence of SEQ ID NO: 96. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 92 and the second guide RNA comprises the sequence of SEQ ID NO: 99. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 93 and the second guide RNA comprises the sequence of SEQ ID NO: 98. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 93 and the second guide

RNA comprises the sequence of SEQ ID NO: 102. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 94 and the second guide RNA comprises the sequence of SEQ ID NO: 100. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 95 and the second guide RNA comprises the sequence of SEQ ID NO: 77. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 95 and the second guide RNA comprises the sequence of SEQ ID NO: 78. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 95 and the second guide RNA comprises the sequence of SEQ ID NO: 99. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 96 and the second guide RNA comprises the sequence of SEQ ID NO: 100. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 97 and the second guide RNA comprises the sequence of SEQ ID NO: 98. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 97 and the second guide RNA comprises the sequence of SEQ ID NO: 102. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 98 and the second guide RNA comprises the sequence of SEQ ID NO: 73. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 102 and the second guide RNA comprises the sequence of SEQ ID NO: 73. In some embodiments the guide RNAs each comprise a scaffold sequence comprising the sequence of SEQ ID NO: 504.

[0053] In some embodiments, the disclosure provides for one or more nucleic acid molecules encoding a pair of guide RNAs comprising a first guide RNA and a second guide RNA, wherein the first guide RNA and the second guide RNA target exon 53. In some embodiments, the guide RNAs are for use with an SluCas9 endonuclease. In some embodiments, the one or more nucleic acid molecules also encode for an SluCas9 endonuclease. In some embodiments, the one or more nucleic acid molecules are in a composition further comprising an SluCas9 endonuclease. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 278 and the second guide RNA comprises the sequence of SEQ ID NO: 290. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 278 and the second guide RNA comprises the sequence of SEQ ID NO: 292. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 281 and the second guide RNA comprises the sequence of SEQ ID NO: 291. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 283 and the second guide RNA comprises the sequence of SEQ ID NO: 290. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 283 and the second guide RNA comprises the sequence of SEQ ID NO: 292. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 287 and the second guide RNA comprises the sequence of SEQ ID NO: 291. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 272 and the second guide RNA comprises the sequence of SEQ ID NO: 290. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 291 and the second guide RNA comprises the sequence of

SEQ ID NO: 290. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 278 and the second guide RNA comprises the sequence of SEQ ID NO: 290. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 272 and the second guide RNA comprises the sequence of SEQ ID NO: 292. In some embodiments the guide RNAs each comprise a scaffold sequence comprising the sequence of SEQ ID NO: 901.

[0054] In some embodiments, the disclosure provides for one or more nucleic acid molecules encoding a pair of guide RNAs comprising a first guide RNA and a second guide RNA , wherein the first guide RNA and the second guide RNA target exon 44. In some embodiments, the guide RNAs are for use with an SluCas9 endonuclease. In some embodiments, the one or more nucleic acid molecules also encode for an SluCas9 endonuclease. In some embodiments, the one or more nucleic acid molecules are in a composition further comprising an SluCas9 endonuclease. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 200 and the second guide RNA comprises the sequence of SEQ ID NO: 203. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 200 and the second guide RNA comprises the sequence of SEQ ID NO: 204. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 202 and the second guide RNA comprises the sequence of SEQ ID NO: 203. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 202 and the second guide RNA comprises the sequence of SEQ ID NO: 205. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 202 and the second guide RNA comprises the sequence of SEQ ID NO: 206. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 202 and the second guide RNA comprises the sequence of SEQ ID NO: 207. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 204 and the second guide RNA comprises the sequence of SEQ ID NO: 208. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 204 and the second guide RNA comprises the sequence of SEQ ID NO: 205. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 204 and the second guide RNA comprises the sequence of SEQ ID NO: 206. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 204 and the second guide RNA comprises the sequence of SEQ ID NO: 207. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 204 and the second guide RNA comprises the sequence of SEQ ID NO: 208. In some embodiments the guide RNAs each comprise a scaffold sequence comprising the sequence of SEQ ID NO: 901.

[0055] In some embodiments, the disclosure provides for one or more nucleic acid molecules encoding a pair of guide RNAs comprising a first guide RNA and a second guide RNA, wherein the first guide RNA and the second guide RNA target exon 50. In some embodiments, the guide RNAs are for use with an SluCas9 endonuclease. In some embodiments, the one or more nucleic acid molecules also encode for an SluCas9 endonuclease. In some embodiments, the one or more nucleic acid molecules are in a composition further comprising an SluCas9 endonuclease. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 231 and the second guide RNA comprises the sequence of SEQ ID NO: 232. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 231 and the second guide RNA comprises the sequence of SEQ ID NO: 234. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 231 and the second guide RNA comprises the sequence of SEQ ID NO: 236. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 231 and the second guide RNA comprises the sequence of SEQ ID NO: 237. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 236 and the second guide RNA comprises the sequence of SEQ ID NO: 233. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 236 and the second guide RNA comprises the sequence of SEQ ID NO: 235. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 236 and the second guide RNA comprises the sequence of SEQ ID NO: 238. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 236 and the second guide RNA comprises the sequence of SEQ ID NO: 240. In some embodiments, the first guide RNA comprises the sequence of SEQ ID NOs: 236 and the second guide RNA comprises the sequence of SEQ ID NO: 241. In some embodiments the guide RNAs each comprise a scaffold sequence comprising the sequence of SEQ ID NO: 901.

[0056] In some embodiments, the composition further comprises an endonuclease or a nucleic acid encoding an endonuclease. An exemplary endonuclease for use with each of the guide RNAs or pairs of guide RNAs is provided herein, for example, in **Table 6**, at column "enzyme," or in the "Guide ID" name as "Sa" for SaCas9, "SaCas9KKH" for SaCas9, or "SL" for SluCas9.

[0057] In some embodiments, a composition is provided comprising a single nucleic acid molecule comprising a nucleic acid encoding any of the guide RNAs disclosed herein, or any of the pairs of guide RNAs disclosed herein, and optionally a nucleic acid encoding an endonuclease.

[0058] In some embodiments, a composition is provided comprising at least two nucleic acid molecules comprising a nucleic acid encoding any of the guide RNAs disclosed herein, or any of the pairs of guide RNAs disclosed herein, and optionally a nucleic acid encoding an endonuclease, wherein at least one nucleic acid molecule does not comprise a nucleic acid encoding an endonuclease.

[0059] In some embodiments, a composition is provided comprising or consisting of a single nucleic acid molecule comprising: i) a nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and at least one, at least two, or at least three guide RNAs; or ii) a nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or iii) a nucleic acid encoding Staphylococcus aureus Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and one to three guide RNAs, wherein in each instance, the single nucleic acid molecule comprises a nucleic acid encoding at least one, at least two, or two guide sequence(s) of **Table 6**. In some embodiments, the single nucleic acid molecule comprises nucleic acid encoding any one of the following pairs of guide sequences:

a. For exon 44 (with e.g., SaCas9), SEQ ID NOs: 1 and 3; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; 124 and 125;

b. For exon 44 (with, e.g., SluCas9), SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and 203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208;

c. For exon 45 (with, e.g., SaCas9), SEQ ID NOs: 3 and 4; 3 and 5; 3 and 6; 3 and 7; 3 and 8; 3 and 9; 4 and 5; 4 and 6; 4 and 7; 4 and 8; 4 and 9; 5 and 6; 5 and 7; 5 and 8; 5 and 9; 6 and 7; 6 and 8; 6 and 9; 7 and 8; 7 and 9; 8 and 9;

126 and 127; 126 and 128; 126 and 129; 126 and 130; 126 and 131; 126 and 132; 126 and 133; 126 and 134; 126 and 135; 126 and 136; 126 and 137; 126 and 138; 126 and 139; 126 and 140; 126 and 141; 126 and 142; 126 and 143; 126 and 144; 126 and 145; 126 and 146; 126 and 147; 127 and 128; 127 and 129; 127 and 130; 127 and 131; 127 and 132; 127 and 133; 127 and 134; 127 and 135; 127 and 136; 127 and 137; 127 and 138; 127 and 139; 127 and 140; 127 and 141; 127 and 142; 127 and 143; 127 and 144; 127 and 145; 127 and 146; 127 and 147; 128 and 129; 128 and 130; 128 and 131; 128 and 132; 128 and 133; 128 and 134; 128 and 135; 128 and 136; 128 and 137; 128 and 138; 128 and 139; 128 and 140; 128 and 141; 128 and 142; 128 and 143; 128 and 144; 128 and 145; 128 and 146; 128 and 147; 129 and 130; 129 and 131; 129 and 132; 129 and 133; 129 and 134; 129 and 135; 129 and 136; 129 and 137; 129 and 138; 129 and 139; 129 and 140; 129 and 141; 129 and 142; 129 and 143; 129 and 144; 129 and 145; 129 and 146; 129 and 147; 130 and 131; 130 and 132; 130 and 133; 130 and 134; 130 and 135; 130 and 136; 130 and 137; 130 and 138; 130 and 139; 130 and 140; 130 and 141; 130 and 142; 130 and 143; 130 and 144; 130 and 145; 130 and 146; 130 and 147; 131 and 132; 131 and 133; 131 and 134; 131 and 135; 131 and 136; 131 and 137; 131 and 138; 131 and 139; 131 and 140; 131 and 141; 131 and 142; 131 and 143; 131 and 144; 131 and 145; 131 and 146; 131 and 147; 132 and 133; 132 and 134; 132 and 135; 132 and 136; 132 and 137; 132 and 138; 132 and 139; 132 and 140; 132 and 141; 132 and 142; 132 and 143; 132 and 144; 132 and 145; 132 and 146; 132 and 147; 133 and 134; 133 and 135; 133 and 136; 133 and 137; 133 and 138; 133 and 139; 133 and 140; 133 and 141; 133 and 142; 133 and 143; 133 and 144; 133 and 145; 133 and 146; 133 and 147; 134 and 135; 134 and 136; 134 and 137; 134 and 138; 134 and 139; 134 and 140; 134 and 141; 134 and 142; 134 and 143; 134 and 144; 134 and 145; 134 and 146; 134 and 147; 135 and 136; 135 and 137; 135 and 138; 135 and 139; 135 and 140; 135 and 141; 135 and 142; 135 and 143; 135 and 144; 135 and 145; 135 and 146; 135 and 147; 136 and 137; 136 and 138; 136 and 139; 136 and 140; 136 and 141; 136 and 142; 136 and 143; 136 and 144; 136 and 145; 136 and 146; 136 and 147; 137 and 138; 137 and 139; 137 and 140; 137 and 141; 137 and 142; 137 and 143; 137 and 144; 137 and 145; 137 and 146;

137 and 147; 138 and 139; 138 and 140; 138 and 141; 138 and 142; 138 and 143; 138 and 144; 138 and 145; 138 and 146; 138 and 147; 139 and 140; 139 and 141; 139 and 142; 139 and 143; 139 and 144; 139 and 145; 139 and 146; 139 and 147; 140 and 141; 140 and 142; 140 and 143; 140 and 144; 140 and 145; 140 and 146; 140 and 147; 141 and 142; 141 and 143; 141 and 144; 141 and 145; 141 and 146; 141 and 147; 142 and 143; 142 and 144; 142 and 145; 142 and 146; 142 and 147; 143 and 144; 143 and 145; 143 and 146; 143 and 147; 144 and 145; 144 and 146; 144 and 147; 145 and 146; 145 and 147; 146 and 147;

d. For exon 45 (with, e.g., SluCas9), SEQ ID NOs: 209 and 210; 209 and 211; 209 and 212; 209 and 213; 209 and 214; 209 and 215; 209 and 216; 209 and 217; 209 and 218; 209 and 219; 209 and 220; 209 and 221; 209 and 222; 209 and 223; 209 and 224; 209 and 225; 209 and 226; 209 and 227; 209 and 228; 209 and 229; 209 and 230; 210 and 211; 210 and 212; 210 and 213; 210 and 214; 210 and 215; 210 and 216; 210 and 217; 210 and 218; 210 and 219; 210 and 220; 210 and 221; 210 and 222; 210 and 223; 210 and 224; 210 and 225; 210 and 226; 210 and 227; 210 and 228; 210 and 229; 210 and 230; 211 and 212; 211 and 213; 211 and 214; 211 and 215; 211 and 216; 211 and 217; 211 and 218; 211 and 219; 211 and 220; 211 and 221; 211 and 222; 211 and 223; 211 and 224; 211 and 225; 211 and 226; 211 and 227; 211 and 228; 211 and 229; 211 and 230; 212 and 213; 212 and 214; 212 and 215; 212 and 216; 212 and 217; 212 and 218; 212 and 219; 212 and 220; 212 and 221; 212 and 222; 212 and 223; 212 and 224; 212 and 225; 212 and 226; 212 and 227; 212 and 228; 212 and 229; 212 and 230; 213 and 214; 213 and 215; 213 and 216; 213 and 217; 213 and 218; 213 and 219; 213 and 220; 213 and 221; 213 and 222; 213 and 223; 213 and 224; 213 and 225; 213 and 226; 213 and 227; 213 and 228; 213 and 229; 213 and 230; 214 and 215; 214 and 216; 214 and 217; 214 and 218; 214 and 219; 214 and 220; 214 and 221; 214 and 222; 214 and 223; 214 and 224; 214 and 225; 214 and 226; 214 and 227; 214 and 228; 214 and 229; 214 and 230; 215 and 216; 215 and 217; 215 and 218; 215 and 219; 215 and 220; 215 and 221; 215 and 222; 215 and 223; 215 and 224; 215 and 225; 215 and 226; 215 and 227; 215 and 228; 215 and 229; 215 and 230; 216 and 217; 216 and 218; 216 and 219; 216 and 220; 216 and 221; 216 and 222; 216 and 223; 216 and 224; 216 and 225; 216 and 226; 216 and 227; 216 and 228; 216 and 229; 216 and 230; 217 and 218; 217 and 219; 217 and 220; 217 and 221; 217 and 222; 217 and 223; 217 and 224; 217 and 225; 217 and 226; 217

and 227; 217 and 228; 217 and 229; 217 and 230; 218 and 219; 218 and 220; 218 and 221; 218 and 222; 218 and 223; 218 and 224; 218 and 225; 218 and 226; 218 and 227; 218 and 228; 218 and 229; 218 and 230; 219 and 220; 219 and 221; 219 and 222; 219 and 223; 219 and 224; 219 and 225; 219 and 226; 219 and 227; 219 and 228; 219 and 229; 219 and 230; 220 and 221; 220 and 222; 220 and 223; 220 and 224; 220 and 225; 220 and 226; 220 and 227; 220 and 228; 220 and 229; 220 and 230; 221 and 222; 221 and 223; 221 and 224; 221 and 225; 221 and 226; 221 and 227; 221 and 228; 221 and 229; 221 and 230; 222 and 223; 222 and 224; 222 and 225; 222 and 226; 222 and 227; 222 and 228; 222 and 229; 222 and 230; 223 and 224; 223 and 225; 223 and 226; 223 and 227; 223 and 228; 223 and 229; 223 and 230; 224 and 225; 224 and 226; 224 and 227; 224 and 228; 224 and 229; 224 and 230; 225 and 226; 225 and 227; 225 and 228; 225 and 229; 225 and 230; 226 and 227; 226 and 228; 226 and 229; 226 and 230; 227 and 228; 227 and 229; 227 and 230; 228 and 229; 228 and 230; 229 and 230;

e. For exon 50 (with, e.g., SaCas9), SEQ ID NOs: 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; 158 and 159;

f. For exon 50 (with, e.g., SluCas9), SEQ ID NOs: 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232 and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and

239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; 241 and 242;

g. For exon 51 (with, e.g., SaCas9), SEQ ID NOs: 11 and 12; 11 and 13; 11 and 14; 11 and 15; 12 and 13; 12 and 14; 12 and 15; 13 and 14; 13 and 15; 14 and 15; 27 and 28; 27 and 29; 27 and 30; 27 and 31; 27 and 32; 27 and 33; 27 and 34; 27 and 35; 27 and 36; 27 and 37; 27 and 38; 27 and 39; 27 and 40; 27 and 41; 27 and 42; 27 and 43; 27 and 44; 27 and 45; 27 and 46; 27 and 47; 27 and 48; 27 and 53; 27 and 54; 27 and 55; 27 and 56; 27 and 57; 27 and 58; 27 and 59; 27 and 60; 27 and 61; 27 and 62; 27 and 63; 27 and 64; 27 and 65; 27 and 66; 27 and 67; 27 and 68; 27 and 69; 28 and 29; 28 and 30; 28 and 31; 28 and 32; 28 and 33; 28 and 34; 28 and 35; 28 and 36; 28 and 37; 28 and 38; 28 and 39; 28 and 40; 28 and 41; 28 and 42; 28 and 43; 28 and 44; 28 and 45; 28 and 46; 28 and 47; 28 and 48; 28 and 53; 28 and 54; 28 and 55; 28 and 56; 28 and 57; 28 and 58; 28 and 59; 28 and 60; 28 and 61; 28 and 62; 28 and 63; 28 and 64; 28 and 65; 28 and 66; 28 and 67; 28 and 68; 28 and 69; 29 and 30; 29 and 31; 29 and 32; 29 and 33; 29 and 34; 29 and 35; 29 and 36; 29 and 37; 29 and 38; 29 and 39; 29 and 40; 29 and 41; 29 and 42; 29 and 43; 29 and 44; 29 and 45; 29 and 46; 29 and 47; 29 and 48; 29 and 53; 29 and 54; 29 and 55; 29 and 56; 29 and 57; 29 and 58; 29 and 59; 29 and 60; 29 and 61; 29 and 62; 29 and 63; 29 and 64; 29 and 65; 29 and 66; 29 and 67; 29 and 68; 29 and 69; 30 and 31; 30 and 32; 30 and 33; 30 and 34; 30 and 35; 30 and 36; 30 and 37; 30 and 38; 30 and 39; 30 and 40; 30 and 41; 30 and 42; 30 and 43; 30 and 44; 30 and 45; 30 and 46; 30 and 47; 30 and 48; 30 and 53; 30 and 54; 30 and 55; 30 and 56; 30 and 57; 30 and 58; 30 and 59; 30 and 60; 30 and 61; 30 and 62; 30 and 63; 30 and 64; 30 and 65; 30 and 66; 30 and 67; 30 and 68; 30 and 69; 31 and 32; 31 and 33; 31 and 34; 31 and 35; 31 and 36; 31 and 37; 31 and 38; 31 and 39; 31 and 40; 31 and 41; 31 and 42; 31 and 43; 31 and 44; 31 and 45; 31 and 46; 31 and 47; 31 and 48; 31 and 53; 31 and 54; 31 and 55; 31 and 56; 31 and 57; 31 and 58; 31 and 59; 31 and 60; 31 and 61; 31 and 62; 31 and 63; 31 and 64; 31 and 65; 31 and 66; 31 and 67; 31 and 68; 31 and 69; 32 and 33; 32 and 34; 32 and 35; 32 and 36; 32 and 37; 32 and 38; 32 and 39; 32 and 40; 32 and 41; 32 and 42; 32 and 43; 32 and 44; 32 and 45; 32 and 46; 32 and 47; 32 and 48; 32 and 53; 32 and 54; 32 and 55; 32 and 56; 32 and 57; 32 and 58; 32 and 59; 32 and 60; 32 and 61; 32 and 62; 32 and 63; 32 and 64; 32 and 65; 32 and

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i. For exon 53 (with, e.g., SaCas9), SEQ ID NOs: 16 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20; 17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 71 and 72; 71 and 73; 71 and 74; 71 and

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j. For exon 53 (with, e.g., SluCas9), SEQ ID NOs: 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and 277; 270 and 278; 270 and 279; 270 and 280; 270 and 281; 270 and 282; 270 and 283; 270 and 284; 270 and 285; 270 and 286; 270 and 287; 270 and 288; 270 and 289; 270 and 290; 270 and 291; 270 and 292; 271 and 272; 271 and 273; 271 and 274; 271 and 275; 271 and 276; 271 and 277; 271 and 278; 271 and 279; 271 and 280; 271 and 281; 271 and 282; 271 and 283; 271 and 284; 271 and 285; 271 and 286; 271 and 287; 271 and 288; 271 and 289; 271 and 290; 271 and 291; 271 and 292; 272 and 273; 272 and 274; 272 and 275; 272 and 276; 272 and 277; 272 and 278; 272 and 279; 272 and 280; 272 and 281; 272 and 282; 272 and 283; 272 and 284; 272 and 285; 272 and 286; 272 and 287; 272 and 288; 272 and 289; 272 and 290; 272 and 291; 272 and 292; 273 and 274; 273 and 275; 273 and 276; 273 and 277; 273 and 278; 273 and 279; 273 and 280; 273 and 281; 273 and 282; 273 and 283; 273 and 284; 273 and 285; 273 and 286; 273 and 287; 273 and 288; 273 and 289; 273 and 290; 273 and 291; 273 and 292; 274 and 275; 274 and 276; 274 and 277; 274 and 278; 274 and 279; 274 and 280; 274 and 281; 274 and 282; 274 and 283; 274 and 284; 274 and 285; 274 and 286; 274 and 287; 274 and 288; 274 and 289; 274 and 290; 274 and 291; 274 and 292; 275 and 276; 275 and 277; 275 and 278; 275 and 279; 275 and 280; 275 and 281; 275 and 282; 275 and 283; 275 and 284; 275 and 285; 275 and 286; 275 and 287; 275 and 288; 275 and 289; 275 and 290; 275 and 291; 275 and 292; 276 and 277; 276 and 278; 276 and 279; 276 and 280;

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and 272; 937 and 273; 937 and 274; 937 and 275; 937 and 276; 937 and 277; 937 and 278; 937 and 279; 937 and 280; 937 and 281; 937 and 282; 937 and 283; 937 and 284; 937 and 285; 937 and 286; 937 and 287; 937 and 288; 937 and 289; 937 and 290; 937 and 291; 937 and 292; 938 and 270; 938 and 272; 938 and 273; 938 and 274; 938 and 275; 938 and 276; 938 and 277; 938 and 278; 938 and 279; 938 and 280; 938 and 281; 938 and 282; 938 and 283; 938 and 284; 938 and 285; 938 and 286; 938 and 287; 938 and 288; 938 and 289; 938 and 290; 938 and 291; 938 and 292; 950 and 275; 951 and 275; 952 and 275; 953 and 275; 954 and 275; or 955 and 275;

k. For exon 44 (with, e.g., SluCas9), SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;

l. For exon 45 (with, e.g., SluCas9), SEQ ID NOs: 223 and 230; or 224 and 212.

m. For exon 50 (with, e.g., SluCas9), SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;

n. For exon 51 (with, e.g., SaCas9), SEQ ID NOs: 28 and 57; 31 and 57; 31 and 46; 32 and 69; 33 and 57; 33 and 69; 34 and 57; 36 and 69; 37 and 69; 37 and 46; 39 and 46; 40 and 46; 46 and 35; 46 and 62; 46 and 65; 46 and 67; 47 and 57; 48 and 57; 49 and 57; 51 and 57; 53 and 46; 54 and 46; 55 and 46; 58 and 46; 59 and 46; 60 and 46; 61 and 69; or 69 and 30;

o. For exon 51 (with, e.g., SluCas9), SEQ ID NOs: 243 and 252; 245 and 252; 252 and 253; 252 and 254; 252 and 256; 252 and 257; 252 and 258; 252 and 262; 252 and 264; 252 and 265; or 252 and 266;

p. For exon 53 (with, e.g., SaCas9), SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and

q. For exon 53 (e.g., with SluCas9), SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

[0060] In some embodiments, a composition is provided comprising or consisting of at least two nucleic acid molecules comprising a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and i) a nucleic acid encoding at least one, at least two, or at least three guide RNAs; or ii) a nucleic acid encoding from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or iii) a nucleic acid encoding one to three guide RNAs; and a second nucleic acid that does not encode a SaCas9 or SluCas9, optionally wherein the second nucleic acid comprises any one of i) at least one, at least two, at least three, at least four, at least five, or at least six guide RNAs; or ii) from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or iii) from one to six guide RNAs, wherein in each instance, the guide RNAs comprises nucleic acid encoding at least one, at least two, or two guide sequence of **Table 6**. In some embodiments, at least one of the two nucleic acid molecules comprise nucleic acid encoding any one of the following pairs of guide sequences:

a. For exon 44 (e.g., with SaCas9), SEQ ID NOs: 1 and 3; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; 124 and 125;

b. For exon 44 (e.g., with SluCas9), SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and 203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and

207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208;

c. For exon 45 (e.g., with SaCas9), SEQ ID NOs: 3 and 4; 3 and 5; 3 and 6; 3 and 7; 3 and 8; 3 and 9; 4 and 5; 4 and 6; 4 and 7; 4 and 8; 4 and 9; 5 and 6; 5 and 7; 5 and 8; 5 and 9; 6 and 7; 6 and 8; 6 and 9; 7 and 8; 7 and 9; 8 and 9; 126 and 127; 126 and 128; 126 and 129; 126 and 130; 126 and 131; 126 and 132; 126 and 133; 126 and 134; 126 and 135; 126 and 136; 126 and 137; 126 and 138; 126 and 139; 126 and 140; 126 and 141; 126 and 142; 126 and 143; 126 and 144; 126 and 145; 126 and 146; 126 and 147; 127 and 128; 127 and 129; 127 and 130; 127 and 131; 127 and 132; 127 and 133; 127 and 134; 127 and 135; 127 and 136; 127 and 137; 127 and 138; 127 and 139; 127 and 140; 127 and 141; 127 and 142; 127 and 143; 127 and 144; 127 and 145; 127 and 146; 127 and 147; 128 and 129; 128 and 130; 128 and 131; 128 and 132; 128 and 133; 128 and 134; 128 and 135; 128 and 136; 128 and 137; 128 and 138; 128 and 139; 128 and 140; 128 and 141; 128 and 142; 128 and 143; 128 and 144; 128 and 145; 128 and 146; 128 and 147; 129 and 130; 129 and 131; 129 and 132; 129 and 133; 129 and 134; 129 and 135; 129 and 136; 129 and 137; 129 and 138; 129 and 139; 129 and 140; 129 and 141; 129 and 142; 129 and 143; 129 and 144; 129 and 145; 129 and 146; 129 and 147; 130 and 131; 130 and 132; 130 and 133; 130 and 134; 130 and 135; 130 and 136; 130 and 137; 130 and 138; 130 and 139; 130 and 140; 130 and 141; 130 and 142; 130 and 143; 130 and 144; 130 and 145; 130 and 146; 130 and 147; 131 and 132; 131 and 133; 131 and 134; 131 and 135; 131 and 136; 131 and 137; 131 and 138; 131 and 139; 131 and 140; 131 and 141; 131 and 142; 131 and 143; 131 and 144; 131 and 145; 131 and 146; 131 and 147; 132 and 133; 132 and 134; 132 and 135; 132 and 136; 132 and 137; 132 and 138; 132 and 139; 132 and 140; 132 and 141; 132 and 142; 132 and 143; 132 and 144; 132 and 145; 132 and 146; 132 and 147; 133 and 134; 133 and 135; 133 and 136; 133 and 137; 133 and 138; 133 and 139; 133 and 140; 133 and 141; 133 and 142; 133 and 143; 133 and 144; 133 and 145; 133 and 146; 133 and 147; 134 and 135; 134 and 136; 134 and 137; 134 and 138; 134 and 139; 134 and 140; 134 and 141; 134 and 142; 134 and 143; 134 and 144; 134 and 145; 134 and 146; 134 and 147; 135 and 136; 135 and 137; 135 and 138; 135 and 139; 135 and 140; 135 and 141; 135 and 142;

135 and 143; 135 and 144; 135 and 145; 135 and 146; 135 and 147; 136 and 137; 136 and 138; 136 and 139; 136 and 140; 136 and 141; 136 and 142; 136 and 143; 136 and 144; 136 and 145; 136 and 146; 136 and 147; 137 and 138; 137 and 139; 137 and 140; 137 and 141; 137 and 142; 137 and 143; 137 and 144; 137 and 145; 137 and 146; 137 and 147; 138 and 139; 138 and 140; 138 and 141; 138 and 142; 138 and 143; 138 and 144; 138 and 145; 138 and 146; 138 and 147; 139 and 140; 139 and 141; 139 and 142; 139 and 143; 139 and 144; 139 and 145; 139 and 146; 139 and 147; 140 and 141; 140 and 142; 140 and 143; 140 and 144; 140 and 145; 140 and 146; 140 and 147; 141 and 142; 141 and 143; 141 and 144; 141 and 145; 141 and 146; 141 and 147; 142 and 143; 142 and 144; 142 and 145; 142 and 146; 142 and 147; 143 and 144; 143 and 145; 143 and 146; 143 and 147; 144 and 145; 144 and 146; 144 and 147; 145 and 146; 145 and 147; 146 and 147;

d. For exon 45 (e.g., with SluCas9), SEQ ID NOs: 209 and 210; 209 and 211; 209 and 212; 209 and 213; 209 and 214; 209 and 215; 209 and 216; 209 and 217; 209 and 218; 209 and 219; 209 and 220; 209 and 221; 209 and 222; 209 and 223; 209 and 224; 209 and 225; 209 and 226; 209 and 227; 209 and 228; 209 and 229; 209 and 230; 210 and 211; 210 and 212; 210 and 213; 210 and 214; 210 and 215; 210 and 216; 210 and 217; 210 and 218; 210 and 219; 210 and 220; 210 and 221; 210 and 222; 210 and 223; 210 and 224; 210 and 225; 210 and 226; 210 and 227; 210 and 228; 210 and 229; 210 and 230; 211 and 212; 211 and 213; 211 and 214; 211 and 215; 211 and 216; 211 and 217; 211 and 218; 211 and 219; 211 and 220; 211 and 221; 211 and 222; 211 and 223; 211 and 224; 211 and 225; 211 and 226; 211 and 227; 211 and 228; 211 and 229; 211 and 230; 212 and 213; 212 and 214; 212 and 215; 212 and 216; 212 and 217; 212 and 218; 212 and 219; 212 and 220; 212 and 221; 212 and 222; 212 and 223; 212 and 224; 212 and 225; 212 and 226; 212 and 227; 212 and 228; 212 and 229; 212 and 230; 213 and 214; 213 and 215; 213 and 216; 213 and 217; 213 and 218; 213 and 219; 213 and 220; 213 and 221; 213 and 222; 213 and 223; 213 and 224; 213 and 225; 213 and 226; 213 and 227; 213 and 228; 213 and 229; 213 and 230; 214 and 215; 214 and 216; 214 and 217; 214 and 218; 214 and 219; 214 and 220; 214 and 221; 214 and 222; 214 and 223; 214 and 224; 214 and 225; 214 and 226; 214 and 227; 214 and 228; 214 and 229; 214 and 230; 215 and 216; 215 and 217; 215 and 218; 215 and 219; 215 and 220; 215 and 221; 215 and 222; 215 and 223; 215 and 224; 215 and 225;

215 and 226; 215 and 227; 215 and 228; 215 and 229; 215 and 230; 216 and 217; 216 and 218; 216 and 219; 216 and 220; 216 and 221; 216 and 222; 216 and 223; 216 and 224; 216 and 225; 216 and 226; 216 and 227; 216 and 228; 216 and 229; 216 and 230; 217 and 218; 217 and 219; 217 and 220; 217 and 221; 217 and 222; 217 and 223; 217 and 224; 217 and 225; 217 and 226; 217 and 227; 217 and 228; 217 and 229; 217 and 230; 218 and 219; 218 and 220; 218 and 221; 218 and 222; 218 and 223; 218 and 224; 218 and 225; 218 and 226; 218 and 227; 218 and 228; 218 and 229; 218 and 230; 219 and 220; 219 and 221; 219 and 222; 219 and 223; 219 and 224; 219 and 225; 219 and 226; 219 and 227; 219 and 228; 219 and 229; 219 and 230; 220 and 221; 220 and 222; 220 and 223; 220 and 224; 220 and 225; 220 and 226; 220 and 227; 220 and 228; 220 and 229; 220 and 230; 221 and 222; 221 and 223; 221 and 224; 221 and 225; 221 and 226; 221 and 227; 221 and 228; 221 and 229; 221 and 230; 222 and 223; 222 and 224; 222 and 225; 222 and 226; 222 and 227; 222 and 228; 222 and 229; 222 and 230; 223 and 224; 223 and 225; 223 and 226; 223 and 227; 223 and 228; 223 and 229; 223 and 230; 224 and 225; 224 and 226; 224 and 227; 224 and 228; 224 and 229; 224 and 230; 225 and 226; 225 and 227; 225 and 228; 225 and 229; 225 and 230; 226 and 227; 226 and 228; 226 and 229; 226 and 230; 227 and 228; 227 and 229; 227 and 230; 228 and 229; 228 and 230; 229 and 230;

e. For exon 50 (e.g., with SaCas9), SEQ ID NOs: 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; 158 and 159;

f. For exon 50 (e.g., with SluCas9), SEQ ID NOs: 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232

and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and 239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; 241 and 242;

g. For exon 51 (e.g., with SaCas9), SEQ ID NOs: 11 and 12; 11 and 13; 11 and 14; 11 and 15; 12 and 13; 12 and 14; 12 and 15; 13 and 14; 13 and 15; 14 and 15; 27 and 28; 27 and 29; 27 and 30; 27 and 31; 27 and 32; 27 and 33; 27 and 34; 27 and 35; 27 and 36; 27 and 37; 27 and 38; 27 and 39; 27 and 40; 27 and 41; 27 and 42; 27 and 43; 27 and 44; 27 and 45; 27 and 46; 27 and 47; 27 and 48; 27 and 53; 27 and 54; 27 and 55; 27 and 56; 27 and 57; 27 and 58; 27 and 59; 27 and 60; 27 and 61; 27 and 62; 27 and 63; 27 and 64; 27 and 65; 27 and 66; 27 and 67; 27 and 68; 27 and 69; 28 and 29; 28 and 30; 28 and 31; 28 and 32; 28 and 33; 28 and 34; 28 and 35; 28 and 36; 28 and 37; 28 and 38; 28 and 39; 28 and 40; 28 and 41; 28 and 42; 28 and 43; 28 and 44; 28 and 45; 28 and 46; 28 and 47; 28 and 48; 28 and 53; 28 and 54; 28 and 55; 28 and 56; 28 and 57; 28 and 58; 28 and 59; 28 and 60; 28 and 61; 28 and 62; 28 and 63; 28 and 64; 28 and 65; 28 and 66; 28 and 67; 28 and 68; 28 and 69; 29 and 30; 29 and 31; 29 and 32; 29 and 33; 29 and 34; 29 and 35; 29 and 36; 29 and 37; 29 and 38; 29 and 39; 29 and 40; 29 and 41; 29 and 42; 29 and 43; 29 and 44; 29 and 45; 29 and 46; 29 and 47; 29 and 48; 29 and 53; 29 and 54; 29 and 55; 29 and 56; 29 and 57; 29 and 58; 29 and 59; 29 and 60; 29 and 61; 29 and 62; 29 and 63; 29 and 64; 29 and 65; 29 and 66; 29 and 67; 29 and 68; 29 and 69; 30 and 31; 30 and 32; 30 and 33; 30 and 34; 30 and 35; 30 and 36; 30 and 37; 30 and 38; 30 and 39; 30 and 40; 30 and 41; 30 and 42; 30 and 43; 30 and 44; 30 and 45; 30 and 46; 30 and 47; 30 and 48; 30 and 53; 30 and 54; 30 and 55; 30 and 56; 30 and 57; 30 and 58; 30 and 59; 30 and 60; 30 and 61; 30 and 62; 30 and 63; 30 and 64; 30 and 65; 30 and 66; 30 and 67; 30 and 68; 30 and 69; 31 and 32; 31 and 33; 31 and 34; 31 and 35; 31 and 36; 31 and 37; 31 and 38; 31 and 39; 31 and 40; 31 and 41; 31 and 42; 31 and 43; 31 and 44; 31 and 45; 31 and 46; 31 and 47; 31 and 48; 31 and 53; 31 and 54; 31 and 55; 31 and 56; 31 and 57; 31 and 58; 31 and 59; 31 and 60; 31 and 61; 31 and 62; 31 and 63; 31 and

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j. For exon 53 (e.g., with SluCas9), SEQ ID NOs: 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and 277; 270 and 278; 270 and 279; 270 and 280; 270 and 281; 270 and 282; 270 and 283; 270 and 284; 270 and 285; 270 and 286; 270 and 287; 270 and 288; 270 and 289; 270 and 290; 270 and 291; 270 and 292; 271 and 272; 271 and 273; 271 and 274; 271 and 275; 271 and 276; 271 and 277; 271 and 278; 271 and 279; 271 and 280; 271 and 281; 271 and 282; 271 and 283; 271 and 284; 271 and 285; 271 and 286; 271 and 287; 271 and 288; 271 and 289; 271 and 290; 271 and 291; 271 and 292; 272 and 273; 272 and 274; 272 and 275; 272 and 276; 272 and 277; 272 and 278; 272 and 279; 272 and 280; 272 and 281; 272 and 282; 272 and 283; 272 and 284; 272 and 285; 272 and 286; 272 and 287; 272 and 288; 272 and 289; 272 and 290; 272 and 291; 272 and 292; 273 and 274; 273 and 275; 273 and 276; 273 and 277; 273 and 278; 273 and 279; 273 and 280; 273 and 281; 273 and 282; 273 and 283; 273 and 284; 273 and 285; 273 and 286; 273 and 287; 273 and 288; 273 and 289; 273 and 290; 273 and 291; 273 and 292; 274 and 275; 274 and 276; 274 and 277; 274 and 278; 274 and 279; 274 and 280; 274 and 281; 274 and 282; 274 and 283; 274 and 284; 274 and

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and 276; 926 and 277; 926 and 278; 926 and 279; 926 and 280; 926 and 281; 926 and 282; 926 and 283; 926 and 284; 926 and 285; 926 and 286; 926 and 287; 926 and 288; 926 and 289; 926 and 290; 926 and 291; 926 and 292; 927 and 270; 927 and 272; 927 and 273; 927 and 274; 927 and 275; 927 and 276; 927 and 277; 927 and 278; 927 and 279; 927 and 280; 927 and 281; 927 and 282; 927 and 283; 927 and 284; 927 and 285; 927 and 286; 927 and 287; 927 and 288; 927 and 289; 927 and 290; 927 and 291; 927 and 292; 928 and 270; 928 and 272; 928 and 273; 928 and 274; 928 and 275; 928 and 276; 928 and 277; 928 and 278; 928 and 279; 928 and 280; 928 and 281; 928 and 282; 928 and 283; 928 and 284; 928 and 285; 928 and 286; 928 and 287; 928 and 288; 928 and 289; 928 and 290; 928 and 291; 928 and 292; 929 and 270; 929 and 272; 929 and 273; 929 and 274; 929 and 275; 929 and 276; 929 and 277; 929 and 278; 929 and 279; 929 and 280; 929 and 281; 929 and 282; 929 and 283; 929 and 284; 929 and 285; 929 and 286; 929 and 287; 929 and 288; 929 and 289; 929 and 290; 929 and 291; 929 and 292; 930 and 270; 930 and 272; 930 and 273; 930 and 274; 930 and 275; 930 and 276; 930 and 277; 930 and 278; 930 and 279; 930 and 280; 930 and 281; 930 and 282; 930 and 283; 930 and 284; 930 and 285; 930 and 286; 930 and 287; 930 and 288; 930 and 289; 930 and 290; 930 and 291; 930 and 292; 931 and 270; 931 and 272; 931 and 273; 931 and 274; 931 and 275; 931 and 276; 931 and 277; 931 and 278; 931 and 279; 931 and 280; 931 and 281; 931 and 282; 931 and 283; 931 and 284; 931 and 285; 931 and 286; 931 and 287; 931 and 288; 931 and 289; 931 and 290; 931 and 291; 931 and 292; 932 and 270; 932 and 272; 932 and 273; 932 and 274; 932 and 275; 932 and 276; 932 and 277; 932 and 278; 932 and 279; 932 and 280; 932 and 281; 932 and 282; 932 and 283; 932 and 284; 932 and 285; 932 and 286; 932 and 287; 932 and 288; 932 and 289; 932 and 290; 932 and 291; 932 and 292; 933 and 270; 933 and 272; 933 and 273; 933 and 274; 933 and 275; 933 and 276; 933 and 277; 933 and 278; 933 and 279; 933 and 280; 933 and 281; 933 and 282; 933 and 283; 933 and 284; 933 and 285; 933 and 286; 933 and 287; 933 and 288; 933 and 289; 933 and 290; 933 and 291; 933 and 292; 934 and 270; 934 and 272; 934 and 273; 934 and 274; 934 and 275; 934 and 276; 934 and 277; 934 and 278; 934 and 279; 934 and 280; 934 and 281; 934 and 282; 934 and 283; 934 and 284; 934 and 285; 934 and 286; 934 and 287; 934 and 288; 934 and 289; 934 and 290; 934 and 291; 934 and 292; 935 and 270; 935 and 272; 935 and 273; 935 and 274; 935 and 275; 935 and 276; 935 and 277; 935 and 278; 935 and 279; 935 and 280; 935 and 281; 935 and 282; 935 and 283; 935 and 284; 935 and 285; 935 and 286; 935 and 287;

935 and 288; 935 and 289; 935 and 290; 935 and 291; 935 and 292; 936 and 270; 936 and 272; 936 and 273; 936 and 274; 936 and 275; 936 and 276; 936 and 277; 936 and 278; 936 and 279; 936 and 280; 936 and 281; 936 and 282; 936 and 283; 936 and 284; 936 and 285; 936 and 286; 936 and 287; 936 and 288; 936 and 289; 936 and 290; 936 and 291; 936 and 292; 937 and 270; 937 and 272; 937 and 273; 937 and 274; 937 and 275; 937 and 276; 937 and 277; 937 and 278; 937 and 279; 937 and 280; 937 and 281; 937 and 282; 937 and 283; 937 and 284; 937 and 285; 937 and 286; 937 and 287; 937 and 288; 937 and 289; 937 and 290; 937 and 291; 937 and 292; 938 and 270; 938 and 272; 938 and 273; 938 and 274; 938 and 275; 938 and 276; 938 and 277; 938 and 278; 938 and 279; 938 and 280; 938 and 281; 938 and 282; 938 and 283; 938 and 284; 938 and 285; 938 and 286; 938 and 287; 938 and 288; 938 and 289; 938 and 290; 938 and 291; 938 and 292; 950 and 275; 951 and 275; 952 and 275; 953 and 275; 954 and 275; or 955 and 275;

k. For exon 44 (e.g., with SluCas9), SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;
l. For exon 45 (e.g., with SluCas9), SEQ ID NOs: 223 and 230; or 224 and 212.
m. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;
n. For exon 51 (e.g., with SaCas9), SEQ ID NOs: 28 and 57; 31 and 57; 31 and 46; 32 and 69; 33 and 57; 33 and 69; 34 and 57; 36 and 69; 37 and 69; 37 and 46; 39 and 46; 40 and 46; 46 and 35; 46 and 62; 46 and 65; 46 and 67; 47 and 57; 48 and 57; 49 and 57; 51 and 57; 53 and 46; 54 and 46; 55 and 46; 58 and 46; 59 and 46; 60 and 46; 61 and 69; or 69 and 30;
o. For exon 51 (e.g., with SluCas9), SEQ ID NOs: 243 and 252; 245 and 252; 252 and 253; 252 and 254; 252 and 256; 252 and 257; 252 and 258; 252 and 262; 252 and 264; 252 and 265; or 252 and 266;
p. For exon 53 (e.g., with SaCas9), SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and
q. For exon 53 (e.g., with SluCas9), SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

[0061] The disclosure herein may reference a “first and a second spacer” or a “first and a second guide RNA, gRNA, or sgRNA” followed by one or more pairs of specific sequences. It should be noted that the order of the sequences in the pair is not intended to be restricted to the order in which they are presented/described. For example, the phrase “the first sgRNA and the second sgRNA comprise the sequences of SEQ ID NOs: 10 and 15” could mean that the first sgRNA comprises the sequence of SEQ ID NO: 10 and the second sgRNA sequence comprises the sequence of SEQ ID NO: 15, or this phrase could mean that the first sgRNA comprises the sequence of SEQ ID NO: 15 and the second sgRNA sequence comprises the sequence of SEQ ID NO: 10.

[0062] In some embodiments, the first and/or the second nucleic acid, if present, comprises at least two guide RNAs. In some embodiments, the first and/or the second nucleic acid, if present, comprises at least three guide RNAs. In some embodiments, the first and/or the second nucleic acid, if present, comprises at least four guide RNAs. In some embodiments, the first and/or the second nucleic acid, if present, comprises at least five guide RNAs. In some embodiments, the first and/or the second nucleic acid, if present, comprises at least six guide RNAs. In some embodiments, the first nucleic acid encodes an endonuclease and at least one, at least two, or at least three guide RNAs. In some embodiments, the first nucleic acid comprises an endonuclease and from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid. In some embodiments, the first nucleic acid encodes an endonuclease and from one to three guide RNAs. In some embodiments, the first nucleic acid comprises 1, 2, 3, 4, 5, or 6 guide RNAs, but does not encode an endonuclease.

[0063] In some embodiments, the second nucleic acid, if present, encodes at least one, at least two, at least three, at least four, at least five, or at least six guide RNAs. In some embodiments, the second nucleic acid, if present, encodes from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid In some embodiments, the second nucleic acid, if present, encodes from one to six guide RNAs. In some embodiments, the second nucleic acid, if present, encodes 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, or 2-3 guide RNAs. In some embodiments, the second nucleic acid, if present, encodes 2, 3, 4, 5, or 6 guide RNAs. In some embodiments, the second nucleic acid comprises 1, 2, 3, 4, 5, or 6 guide RNAs, but does not encode an endonuclease.

[0064] In some embodiments, the disclosure provides for a composition comprising at least two nucleic acid molecules, wherein the first nucleic acid comprises a guide RNA and the second nucleic acid comprises a guide RNA, wherein the guide RNA encoded by the first nucleic acid and the second nucleic acid are the same. In some embodiments, the disclosure provides for a composition comprising at least two nucleic acid molecules, wherein the first nucleic acid comprises a guide RNA and the second nucleic acid comprises a guide RNA, wherein the guide RNA encoded by the first nucleic acid and the second nucleic acid are different. In some embodiments, the disclosure provides for a composition comprising at least two nucleic acid molecules, wherein the first nucleic acid comprises a guide RNA and the second nucleic acid comprises a guide RNA, wherein at least one guide RNA binds to a target sequence within an exon in the DMD gene that is upstream of a premature stop codon, and wherein at least one guide RNA binds to a target sequence within an exon in the DMD gene that is downstream of a premature stop codon. In some embodiments, the disclosure provides for a composition comprising at least two nucleic acid molecules, wherein the first nucleic acid comprises a guide RNA and the second nucleic acid comprises a guide RNA, wherein the same guide RNA is encoded by the nucleic acid of the first and second nucleic acid molecule. In some embodiments, the disclosure provides for a composition comprising at least two nucleic acid molecules, wherein the first nucleic acid comprises a guide RNA and the second nucleic acid comprises a guide RNA, wherein the second nucleic acid molecule encodes a guide RNA that binds to the same target sequence as the guide RNA in the first nucleic acid molecule. In some embodiments, the disclosure provides for a composition comprising at least two nucleic acid molecules, wherein the second nucleic acid molecule encodes at least 2, at least 3, at least 4, at least 5, or at least 6 guide RNAs, wherein the guide RNAs in the second nucleic acid molecule bind to the same target sequence as the guide RNA in the first nucleic acid molecule.

[0065] In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, i) each guide RNA targets the same genomic target sequence; ii) each guide RNA targets a different target sequence; or iii) at least one guide RNA targets one sequence and at least one guide RNA targets a different sequence.

[0066] In some embodiments, the disclosure provides for a composition comprising a guide RNA that binds to an exon of the DMD gene, wherein the exon is selected from exon 44, 45, 50, 51, and 53.

[0067] In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs that bind to an exon of the DMD gene, wherein at least one guide RNA binds to a target sequence within an exon in the DMD gene, and wherein at least one guide RNA binds to a different target sequence within the same exon in the DMD gene.

[0068] In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein at least one guide RNA binds to a target sequence within an exon that is upstream of a premature stop codon, and wherein at least one guide RNA binds to a target sequence within an exon that is downstream of a premature stop codon.

[0069] In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein at least one guide RNA binds to a target sequence within an exon in the DMD gene, and wherein at least one guide RNA binds to a different target sequence within the same exon in the DMD gene, wherein when expressed in vitro or in vivo in the presence of an appropriate endonuclease (e.g., SaCas9 or SluCas9), a portion of the exon is excised. In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in the presence of an appropriate endonuclease (e.g., SaCas9 or SluCas9), the endonuclease excises a portion of the exon.

[0070] In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in the presence of an appropriate endonuclease (e.g., SaCas9 or SluCas9), the endonuclease excises a portion of the exon, and wherein the portion of the exon remaining after excision are rejoined with a one nucleotide insertion. In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in the presence of an appropriate endonuclease (e.g., SaCas9 or SluCas9), the endonuclease excises a portion of the exon, wherein the portion of the exon remaining after excision is rejoined without a nucleotide insertion.

[0071] In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in the presence of an appropriate endonuclease (e.g., SaCas9 or SluCas9), the endonuclease excises a portion of a dystrophin gene (*e.g.*, an exon). In some embodiments, the portions of the gene remaining after excision are rejoined with a one nucleotide insertion or a two nucleotide insertion. In some embodiments, the portions of the exon remaining after excision are rejoined without any nucleotide insertion. "Precise segmental deletion" or "precise deletion" means that the dual cut process takes out a specific deletion. This precise deletion can lead to exon reframing. In some embodiments, the size of the excised portion is between 5 and 250, 5 and 225, 5 and 200, 5 and 190, 5 and 180, 5 and 170, 5 and 160, 5 and 150, 5 and 125, 5 and 120, 5 and 115, 5 and 110, 5 and 100, 5 and 95, 5 and 90, 5 and 85, 5 and 80, 5 and 75, 5 and 70, 5 and 65, 5 and 60, 5 and 55, 5 and 50, 5 and 45, 5 and 40, 5 and 35, 5 and 30, 5 and 25, 5 and 20, 5 and 15, and 5-10 nucleotides. In some embodiments, the size of excised portion is between 20 and 250, 20 and 225, 20 and 200, 20 and 190, 20 and 180, 20 and 170, 20 and 160, 20 and 150, 20 and 125, 20 and 120, 20 and 115, 20 and 110, 20 and 100, 20 and 95, 20 and 90, 20 and 85, 20 and 80, 20 and 75, 20 and 70, 20 and 65, 20 and 60, 20 and 55, 20 and 50, 20 and 45, 20 and 40, 20 and 35, 20 and 30, and 20 and 25 nucleotides. In some embodiments, the size of excised portion is between 50 and 250, 50 and 225, 50 and 200, 50 and 190, 50 and 180, 50 and 170, 50 and 160, 50 and 150, 50 and 125, 50 and 120, 50 and 115, 50 and 110, and 50 and 100 nucleotides. In some embodiments, the size of excised portion of the exon is between 8 and 167 nucleotides.

[0072] In particular embodiments, if the target is exon 45, 51 or 53 of the dystrophin gene, then the precise deletion facilitates a "3n+1" edit of the dystrophin gene, wherein "n" is any negative whole number (e.g., any negative whole number between -10 and -75). In some embodiments, "n" is -10, -11, -12, -13, -14, -15, -16, -17, -18, -19, -20, -21, -22, -23, -24, -25, -26, -27, -28, -29, -30, -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, -61, -62, -63, -64, -65, -66, -67, -68, -69, -70, -71, -72, -73, -74, -75, -76, -77, -78, -79, or -80. For example, if "n" is -10, a 3n+1 edit would be -30 nucleotides +1 nucleotide, i.e., -29 nucleotides, meaning that the actual excision product would be 29 nucleotides in length. With this in mind, in some embodiments, the actual excision product may be any of the following lengths: 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62, 65, 68, 71, 74, 77, 80, 83, 86, 89, 92, 95, 98, 101, 104, 107, 110, 113, 116, 119, 122, 125, 128, 131, 134, 137, 140, 143, 146, 149, 152, 155, 158, 161, 164, 167, 170, 173, 176, 179, 182, 185, 188, 191, 194, 197, 200, 203, 206, 209, 212, 215, or 218 nucleotides in length. In particular embodiments, the excised portion is 92 nucleotides in length. In other embodiments, the excised portion is 188 nucleotides in length. In particular embodiments, the excised portion is 71 nucleotides in length. In other embodiments, the excised portion is 92 nucleotides in length. In other embodiments, the excised portion is 188 nucleotides in length. In other embodiments, the excised portion is 119 nucleotides in length.

[0073] In particular embodiments, if the target is exon 44 or 50 of the dystrophin gene, then the precise deletion facilitates a "3n+2" edit of the dystrophin gene, wherein "n" is any negative whole number (e.g., any negative whole number between -10 and -75). In some embodiments, "n" is -10, -11, -12, -13, -14, -15, -16, -17, -18, -19, -20, -21, -22, -23, -24, -25, -26, -27, -28, -29, -30, -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, -61, -62, -63, -64, -65, -66, -67, -68, -69, -70, -71, -72, -73, -74, -75, -76, -77, -78, -79, or -80. For example, if "n" is -10, a 3n+2 edit would be -30 nucleotides +2 nucleotide, i.e., -28 nucleotides, meaning that the actual excision product would be 28 nucleotides in length. With this in mind, in some embodiments, the actual excision product may be any of the following lengths: 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61, 64, 67, 70, 73, 76, 79, 82, 85, 88, 91, 94, 97, 100, 103, 106, 109, 112, 115, 118, 121, 124, 127, 130, 133, 136, 139, 142, 145, 148, 151, 154, 157, 160, 163, 166, 169, 172, 175, 178, 181, 184, 187, 190, 193, 196, 199, 202, 205, 208, 211, 214, or 217 nucleotides in length.

[0074] In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in the presence of an appropriate endonuclease (e.g., SaCas9 or SluCas9), the endonuclease excises a portion of the exon, wherein the size of the excised portion of the exon is between 5, 6, 7, 8, 9, 10, 15, or 20 and 250 nucleotides in length. In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in the presence of an appropriate endonuclease (e.g., SaCas9 or SluCas9), the endonuclease excises a portion of the exon, wherein the size of excised portion of the exon is between 150 and 250, 100 and 250, 5 and 250, 5 and 200, 5 and 150, 5 and 100, 5 and 75, 5 and 50, 5 and 25, 5 and 10, 20 and 250, 20 and 200, 20 and 150, 20 and 100, 20 and 75, 20 and 50, 20 and 25, 50 and 250, 50 and 200, 50 and 150, 50 and 100, and 50 and 75 nucleotides.

[0075] In some embodiments, the disclosure provides for a composition comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in the presence of an appropriate endonuclease (e.g., SaCas9 or SluCas9), the endonuclease excises a portion of the exon, wherein the size of excised portion of the exon is between 8 and 167 nucleotides.

[0076] In some embodiments, a guide RNA and a Cas9 are encoded on a single nucleic acid molecule. In some embodiments, the single nucleic acid molecule comprises a nucleic acid encoding a guide RNA and a nucleic acid encoding a SaCas9 or SluCas9. In some embodiments, two guide RNAs and a Cas9 are encoded on a single nucleic acid molecule. In some embodiments, the single nucleic acid molecule comprises a nucleic acid encoding a first guide RNA, a nucleic acid encoding a second guide RNA, and a nucleic acid encoding a SaCas9 or SluCas9. In some embodiments, the spacer sequences of the first and second guide RNAs are identical. In some embodiments, the spacer sequences of the first and second guide RNAs are not identical.

[0077] In some embodiments, a single nucleic acid molecule comprises a nucleic acid encoding a Cas9 and a nucleic acid encoding two guide RNAs, wherein the nucleic acid molecule encodes no more than two guide RNAs

[0078] In some embodiments, the single nucleic acid molecule is a single vector or comprised in a single vector. In some embodiments, the single vector expresses the two guide RNAs and Cas9. In some embodiments, a pair of guide RNAs and a Cas9 are provided on a single vector. In some embodiments, the single vector comprises a nucleic acid encoding a pair of guide RNAs and a nucleic acid encoding a SaCas9 or SluCas9. In some embodiments, two guide RNAs and a Cas9 are encoded on a single vector. In some embodiments, the single vector comprises a nucleic acid encoding a first guide RNA, a nucleic acid encoding a second guide RNA, and a nucleic acid encoding a SaCas9 or SluCas9. In some embodiments, the spacer sequences of the first and second guide RNAs are identical. In some embodiments, the spacer sequences of the first and second guide RNAs are not identical.

[0079] In some embodiments, the first nucleic acid molecule encodes for a Cas9 molecule and also encodes for one or more copies of a first guide RNA and one or more copies of a second guide RNA. In some embodiments, the first nucleic acid molecule encodes for a Cas9 molecule, but does not encode for any guide RNAs. In some embodiments, the second nucleic acid molecule encodes for one or more copies of a first guide RNA and one or more copies of a second guide RNA, wherein the second nucleic acid molecule does not encode for a Cas9 molecule.

[0080] In some embodiments, the disclosure provides for a composition comprising one or more guide sequences, or comprises any of the nucleic acid molecules disclosed herein encoding for one or more guide sequences. In some embodiments, the guide sequence is SEQ ID NO: 1; In some embodiments, the guide sequence is SEQ ID NO: 2; In some embodiments, the guide sequence is SEQ ID NO: 3; In some embodiments, the guide sequence is SEQ ID NO: 4; In some embodiments, the guide sequence is SEQ ID NO: 5; In some embodiments, the guide sequence is SEQ ID NO: 6; In some embodiments, the guide sequence is SEQ ID NO: 7; In some embodiments, the guide sequence is SEQ ID NO: 8; In some embodiments, the guide sequence is SEQ ID NO: 9; In some embodiments, the guide sequence is SEQ ID NO: 10; In some embodiments, the guide sequence is SEQ ID NO: 11; In some embodiments, the guide sequence is SEQ ID NO: 12; In some embodiments, the guide sequence is SEQ ID NO: 13; In some embodiments, the guide sequence is SEQ ID NO: 14; In some embodiments, the guide sequence is SEQ ID NO: 15; In some embodiments, the guide sequence is SEQ ID NO: 16; In some embodiments, the guide sequence is SEQ ID NO: 17; In some embodiments, the guide sequence is SEQ ID NO: 18; In some embodiments, the guide sequence is SEQ ID NO: 19; In some embodiments, the guide sequence is SEQ ID NO: 20; In some embodiments, the guide sequence is SEQ ID NO: 21; In some embodiments, the guide sequence is SEQ ID NO: 22; In some embodiments, the guide sequence is SEQ ID NO: 23; In some embodiments, the guide sequence is SEQ ID NO: 24; In some embodiments, the guide sequence is SEQ ID NO: 25; In some embodiments, the guide sequence is SEQ ID NO: 26; In some embodiments, the guide sequence is SEQ ID NO: 27; In some embodiments, the guide sequence is SEQ ID NO: 28; In some embodiments, the guide sequence is SEQ ID NO: 29; In some embodiments, the guide sequence is SEQ ID NO: 30; In some embodiments, the guide sequence is SEQ ID NO: 31; In some embodiments, the guide sequence is SEQ ID NO: 32; In some embodiments, the guide sequence is SEQ ID NO: 33; In some embodiments, the guide sequence is SEQ ID NO: 34; In some embodiments, the guide sequence is SEQ ID NO: 35; In some embodiments, the guide sequence is SEQ ID NO: 36; In some embodiments, the guide sequence is SEQ ID NO: 37; In some embodiments, the guide sequence is SEQ ID NO: 38; In some embodiments, the guide sequence is SEQ ID NO: 39; In some embodiments, the guide sequence is SEQ ID NO: 40; In some embodiments, the guide sequence is SEQ ID NO: 41; In some embodiments, the guide sequence is SEQ ID NO: 42; In some embodiments, the guide sequence is SEQ ID NO: 43; In some embodiments, the guide sequence is SEQ ID NO: 44; In some embodiments, the guide sequence is SEQ ID NO: 45; In some embodiments, the guide sequence is SEQ ID NO: 46; In some embodiments, the guide sequence is SEQ ID NO: 47; In some embodiments, the guide sequence is SEQ ID NO: 48; In some embodiments, the guide sequence is SEQ ID NO: 49; In some embodiments, the guide sequence is SEQ ID NO: 50; In some embodiments, the guide sequence is SEQ ID NO: 51; In some embodiments, the guide sequence is SEQ ID NO: 52; In some embodiments, the guide sequence is SEQ ID NO: 53; In some embodiments, the guide sequence is SEQ ID NO: 54; In some embodiments, the guide sequence is SEQ ID NO: 55; In some embodiments, the guide sequence is SEQ ID NO: 56; In some embodiments, the guide sequence is SEQ ID NO: 57; In some embodiments, the guide sequence is SEQ ID NO: 58; In some embodiments, the guide sequence is SEQ ID NO: 59; In some embodiments, the guide sequence is SEQ ID NO: 60; In some embodiments, the guide sequence is

SEQ ID NO: 61; In some embodiments, the guide sequence is SEQ ID NO: 62; In some embodiments, the guide sequence is SEQ ID NO: 63; In some embodiments, the guide sequence is SEQ ID NO: 64; In some embodiments, the guide sequence is SEQ ID NO: 65; In some embodiments, the guide sequence is SEQ ID NO: 66; In some embodiments, the guide sequence is SEQ ID NO: 67; In some embodiments, the guide sequence is SEQ ID NO: 68; In some embodiments, the guide sequence is SEQ ID NO: 69; In some embodiments, the guide sequence is SEQ ID NO: 70; In some embodiments, the guide sequence is SEQ ID NO: 71; In some embodiments, the guide sequence is SEQ ID NO: 72; In some embodiments, the guide sequence is SEQ ID NO: 73; In some embodiments, the guide sequence is SEQ ID NO: 74; In some embodiments, the guide sequence is SEQ ID NO: 75; In some embodiments, the guide sequence is SEQ ID NO: 76; In some embodiments, the guide sequence is SEQ ID NO: 77; In some embodiments, the guide sequence is SEQ ID NO: 78; In some embodiments, the guide sequence is SEQ ID NO: 79; In some embodiments, the guide sequence is SEQ ID NO: 80; In some embodiments, the guide sequence is SEQ ID NO: 81; In some embodiments, the guide sequence is SEQ ID NO: 82; In some embodiments, the guide sequence is SEQ ID NO: 83; In some embodiments, the guide sequence is SEQ ID NO: 84; In some embodiments, the guide sequence is SEQ ID NO: 85; In some embodiments, the guide sequence is SEQ ID NO: 86; In some embodiments, the guide sequence is SEQ ID NO: 87; In some embodiments, the guide sequence is SEQ ID NO: 88; In some embodiments, the guide sequence is SEQ ID NO: 89; In some embodiments, the guide sequence is SEQ ID NO: 90; In some embodiments, the guide sequence is SEQ ID NO: 91; In some embodiments, the guide sequence is SEQ ID NO: 92; In some embodiments, the guide sequence is SEQ ID NO: 93; In some embodiments, the guide sequence is SEQ ID NO: 94; In some embodiments, the guide sequence is SEQ ID NO: 95; In some embodiments, the guide sequence is SEQ ID NO: 96; In some embodiments, the guide sequence is SEQ ID NO: 97; In some embodiments, the guide sequence is SEQ ID NO: 98; In some embodiments, the guide sequence is SEQ ID NO: 99; In some embodiments, the guide sequence is SEQ ID NO: 100; In some embodiments, the guide sequence is SEQ ID NO: 101; In some embodiments, the guide sequence is SEQ ID NO: 102; In some embodiments, the guide sequence is SEQ ID NO: 103. In some embodiments, the guide sequence is SEQ ID NO: 104; In some embodiments, the guide sequence is SEQ ID NO: 105; In some embodiments, the guide sequence is SEQ ID NO: 106; In some embodiments, the guide sequence is SEQ ID NO: 107; In some embodiments, the guide sequence is SEQ ID NO: 108; In some embodiments, the guide sequence is SEQ ID NO: 109; In some embodiments, the guide sequence is SEQ ID NO: 110; In some embodiments, the guide sequence is SEQ ID NO: 111; In some embodiments, the guide sequence is SEQ ID NO: 112; In some embodiments, the guide sequence is SEQ ID NO: 113; In some embodiments, the guide sequence is SEQ ID NO: 114; In some embodiments, the guide sequence is SEQ ID NO: 115; In some embodiments, the guide sequence is SEQ ID NO: 116; In some embodiments, the guide sequence is SEQ ID NO: 117; In some embodiments, the guide sequence is SEQ ID NO: 118; In some embodiments, the guide sequence is SEQ ID NO: 119; In some embodiments, the guide sequence is SEQ ID NO: 120; In some embodiments, the guide sequence is SEQ ID NO: 121; In some embodiments, the guide sequence is SEQ ID NO: 122; In some embodiments, the guide sequence is SEQ ID NO: 123; In some embodiments, the guide sequence is SEQ ID NO: 124; In some embodiments, the guide sequence is SEQ ID NO: 125; In some embodiments, the guide sequence is SEQ ID NO: 126; In some embodiments, the guide sequence is SEQ ID NO: 127; In some embodiments, the guide sequence is SEQ ID NO: 128; In some embodiments, the guide sequence is SEQ ID NO: 129; In some embodiments, the guide sequence is SEQ ID NO: 130; In some embodiments, the guide sequence is SEQ ID NO: 131; In some embodiments, the guide sequence is SEQ ID NO: 132; In some embodiments, the guide sequence is SEQ ID NO: 133; In some embodiments, the guide sequence is SEQ ID NO: 134; In some embodiments, the guide sequence is SEQ ID NO: 135; In some embodiments, the guide sequence is SEQ ID NO: 136; In some embodiments, the guide sequence is SEQ ID NO: 137; In some embodiments, the guide sequence is SEQ ID NO: 138; In some embodiments, the guide sequence is SEQ ID NO: 139; In some embodiments, the guide sequence is SEQ ID NO: 140; In some embodiments, the guide sequence is SEQ ID NO: 141; In some embodiments, the guide sequence is SEQ ID NO: 142; In some embodiments, the guide sequence is SEQ ID NO: 143; In some embodiments, the guide sequence is SEQ ID NO: 144; In some embodiments, the guide sequence is SEQ ID NO: 145; In some embodiments, the guide sequence is SEQ ID NO: 146; In some embodiments, the guide sequence is SEQ ID NO: 147; In some embodiments, the guide sequence is SEQ ID NO: 148; In some embodiments, the guide sequence is SEQ ID NO: 149; In some embodiments, the guide sequence is SEQ ID NO: 150; In some embodiments, the guide sequence is SEQ ID NO: 151; In some embodiments, the guide sequence is SEQ ID NO: 152; In some embodiments, the guide sequence is SEQ ID NO: 153; In some embodiments, the guide sequence is SEQ ID NO: 154; In some embodiments, the guide sequence is SEQ ID NO: 155; In some embodiments, the guide sequence is SEQ ID NO: 156; In some embodiments, the guide sequence is SEQ ID NO: 157; In some embodiments, the guide sequence is SEQ ID NO: 158; In some embodiments, the guide sequence is SEQ ID NO: 159; In some embodiments, the guide sequence is SEQ ID NO: 201; In some embodiments, the guide sequence is SEQ ID NO: 202; In some embodiments, the guide sequence is SEQ ID NO: 203; In some embodiments, the guide sequence is SEQ ID NO: 204; In some embodiments, the guide sequence is SEQ ID NO: 205; In some embodiments, the guide sequence is SEQ ID NO: 206; In some embodiments, the guide sequence is SEQ ID NO: 207; In some embodiments, the guide sequence is SEQ ID NO: 208; In some embodiments, the guide sequence is SEQ ID NO: 209; In some embodiments, the guide sequence is SEQ ID NO: 210; In some embodiments, the guide sequence is SEQ ID NO: 211; In some embodiments, the guide sequence is SEQ ID NO: 212; In some embodiments, the guide sequence is

SEQ ID NO: 213; In some embodiments, the guide sequence is SEQ ID NO: 214; In some embodiments, the guide sequence is SEQ ID NO: 215; In some embodiments, the guide sequence is SEQ ID NO: 216; In some embodiments, the guide sequence is SEQ ID NO: 217; In some embodiments, the guide sequence is SEQ ID NO: 218; In some embodiments, the guide sequence is SEQ ID NO: 219; In some embodiments, the guide sequence is SEQ ID NO: 220; In some embodiments, the guide sequence is SEQ ID NO: 221; In some embodiments, the guide sequence is SEQ ID NO: 222; In some embodiments, the guide sequence is SEQ ID NO: 223; In some embodiments, the guide sequence is SEQ ID NO: 224; In some embodiments, the guide sequence is SEQ ID NO: 225; In some embodiments, the guide sequence is SEQ ID NO: 226; In some embodiments, the guide sequence is SEQ ID NO: 227; In some embodiments, the guide sequence is SEQ ID NO: 228; In some embodiments, the guide sequence is SEQ ID NO: 229; In some embodiments, the guide sequence is SEQ ID NO: 230; In some embodiments, the guide sequence is SEQ ID NO: 231; In some embodiments, the guide sequence is SEQ ID NO: 232; In some embodiments, the guide sequence is SEQ ID NO: 233; In some embodiments, the guide sequence is SEQ ID NO: 234; In some embodiments, the guide sequence is SEQ ID NO: 235; In some embodiments, the guide sequence is SEQ ID NO: 236; In some embodiments, the guide sequence is SEQ ID NO: 237; In some embodiments, the guide sequence is SEQ ID NO: 238; In some embodiments, the guide sequence is SEQ ID NO: 239; In some embodiments, the guide sequence is SEQ ID NO: 240; In some embodiments, the guide sequence is SEQ ID NO: 241; In some embodiments, the guide sequence is SEQ ID NO: 242; In some embodiments, the guide sequence is SEQ ID NO: 243; In some embodiments, the guide sequence is SEQ ID NO: 244; In some embodiments, the guide sequence is SEQ ID NO: 245; In some embodiments, the guide sequence is SEQ ID NO: 246; In some embodiments, the guide sequence is SEQ ID NO: 247; In some embodiments, the guide sequence is SEQ ID NO: 248; In some embodiments, the guide sequence is SEQ ID NO: 249; In some embodiments, the guide sequence is SEQ ID NO: 250; In some embodiments, the guide sequence is SEQ ID NO: 251; In some embodiments, the guide sequence is SEQ ID NO: 252; In some embodiments, the guide sequence is SEQ ID NO: 253; In some embodiments, the guide sequence is SEQ ID NO: 254; In some embodiments, the guide sequence is SEQ ID NO: 255; In some embodiments, the guide sequence is SEQ ID NO: 256; In some embodiments, the guide sequence is SEQ ID NO: 257; In some embodiments, the guide sequence is SEQ ID NO: 258; In some embodiments, the guide sequence is SEQ ID NO: 259; In some embodiments, the guide sequence is SEQ ID NO: 260; In some embodiments, the guide sequence is SEQ ID NO: 261; In some embodiments, the guide sequence is SEQ ID NO: 262; In some embodiments, the guide sequence is SEQ ID NO: 263; In some embodiments, the guide sequence is SEQ ID NO: 264; In some embodiments, the guide sequence is SEQ ID NO: 265; In some embodiments, the guide sequence is SEQ ID NO: 266; In some embodiments, the guide sequence is SEQ ID NO: 267; In some embodiments, the guide sequence is SEQ ID NO: 268; In some embodiments, the guide sequence is SEQ ID NO: 269; In some embodiments, the guide sequence is SEQ ID NO: 270; In some embodiments, the guide sequence is SEQ ID NO: 271; In some embodiments, the guide sequence is SEQ ID NO: 272; In some embodiments, the guide sequence is SEQ ID NO: 273; In some embodiments, the guide sequence is SEQ ID NO: 274; In some embodiments, the guide sequence is SEQ ID NO: 275; In some embodiments, the guide sequence is SEQ ID NO: 276; In some embodiments, the guide sequence is SEQ ID NO: 277; In some embodiments, the guide sequence is SEQ ID NO: 278; In some embodiments, the guide sequence is SEQ ID NO: 279; In some embodiments, the guide sequence is SEQ ID NO: 280; In some embodiments, the guide sequence is SEQ ID NO: 281; In some embodiments, the guide sequence is SEQ ID NO: 282; In some embodiments, the guide sequence is SEQ ID NO: 283; In some embodiments, the guide sequence is SEQ ID NO: 284; In some embodiments, the guide sequence is SEQ ID NO: 285; In some embodiments, the guide sequence is SEQ ID NO: 286; In some embodiments, the guide sequence is SEQ ID NO: 287; In some embodiments, the guide sequence is SEQ ID NO: 288; In some embodiments, the guide sequence is SEQ ID NO: 289; In some embodiments, the guide sequence is SEQ ID NO: 290; In some embodiments, the guide sequence is SEQ ID NO: 291; In some embodiments, the guide sequence is SEQ ID NO: 292; In some embodiments, the guide sequence is SEQ ID NO: 924; In some embodiments, the guide sequence is SEQ ID NO: 925; In some embodiments, the guide sequence is SEQ ID NO: 926; In some embodiments, the guide sequence is SEQ ID NO: 927; In some embodiments, the guide sequence is SEQ ID NO: 928; In some embodiments, the guide sequence is SEQ ID NO: 929; In some embodiments, the guide sequence is SEQ ID NO: 930; In some embodiments, the guide sequence is SEQ ID NO: 931; In some embodiments, the guide sequence is SEQ ID NO: 932; In some embodiments, the guide sequence is SEQ ID NO: 933; In some embodiments, the guide sequence is SEQ ID NO: 934; In some embodiments, the guide sequence is SEQ ID NO: 935; In some embodiments, the guide sequence is SEQ ID NO: 936; In some embodiments, the guide sequence is SEQ ID NO: 937; In some embodiments, the guide sequence is SEQ ID NO: 938.

[0081] In some embodiments, a composition is provided comprising: a) one or more nucleic acid molecules encoding a SaCas9 or SluCas9 and b) a pair of guide sequences comprising a first guide sequence and a second guide sequence, wherein the pair is selected from any of the following pairs: SEQ ID NO: 1 and SEQ ID NO: 3; SEQ ID NO: 3 and SEQ ID NO: 4; SEQ ID NO: 3 and SEQ ID NO: 5; SEQ ID NO: 3 and SEQ ID NO: 6; SEQ ID NO: 3 and SEQ ID NO: 7; SEQ ID NO: 3 and SEQ ID NO: 8; SEQ ID NO: 3 and SEQ ID NO: 9; SEQ ID NO: 4 and SEQ ID NO: 5; SEQ ID NO: 4 and SEQ ID NO: 6; SEQ ID NO: 4 and SEQ ID NO: 7; SEQ ID NO: 4 and SEQ ID NO: 8; SEQ ID NO: 4 and SEQ ID NO: 9; SEQ ID NO: 5 and SEQ ID NO: 6; SEQ ID NO: 5 and SEQ ID NO: 7; SEQ ID NO: 5 and SEQ ID NO: 8; SEQ ID NO: 5 and SEQ ID NO: 9; SEQ ID NO: 6 and SEQ ID NO: 7; SEQ ID NO: 6 and SEQ ID NO: 8; SEQ ID NO: 6 and SEQ ID NO: 9; SEQ ID NO: 7 and

SEQ ID NO: 8; SEQ ID NO: 7 and SEQ ID NO: 9; SEQ ID NO: 8 and SEQ ID NO: 9; SEQ ID NO: 11 and SEQ ID NO: 12; SEQ ID NO: 11 and SEQ ID NO: 13; SEQ ID NO: 11 and SEQ ID NO: 14; SEQ ID NO: 11 and SEQ ID NO: 15; SEQ ID NO: 12 and SEQ ID NO: 13; SEQ ID NO: 12 and SEQ ID NO: 14; SEQ ID NO: 12 and SEQ ID NO: 15; SEQ ID NO: 13 and SEQ ID NO: 14; SEQ ID NO: 13 and SEQ ID NO: 15; SEQ ID NO: 14 and SEQ ID NO: 15; SEQ ID NO: 16 and SEQ ID NO: 17; SEQ ID NO: 16 and SEQ ID NO: 18; SEQ ID NO: 16 and SEQ ID NO: 19; SEQ ID NO: 16 and SEQ ID NO: 20; SEQ ID NO: 16 and SEQ ID NO: 21; SEQ ID NO: 16 and SEQ ID NO: 22; SEQ ID NO: 16 and SEQ ID NO: 23; SEQ ID NO: 16 and SEQ ID NO: 24; SEQ ID NO: 16 and SEQ ID NO: 25; SEQ ID NO: 16 and SEQ ID NO: 26; SEQ ID NO: 17 and SEQ ID NO: 18; SEQ ID NO: 17 and SEQ ID NO: 19; SEQ ID NO: 17 and SEQ ID NO: 20; SEQ ID NO: 17 and SEQ ID NO: 21; SEQ ID NO: 17 and SEQ ID NO: 22; SEQ ID NO: 17 and SEQ ID NO: 23; SEQ ID NO: 17 and SEQ ID NO: 24; SEQ ID NO: 17 and SEQ ID NO: 25; SEQ ID NO: 17 and SEQ ID NO: 26; SEQ ID NO: 18 and SEQ ID NO: 19; SEQ ID NO: 18 and SEQ ID NO: 20; SEQ ID NO: 18 and SEQ ID NO: 21; SEQ ID NO: 18 and SEQ ID NO: 22; SEQ ID NO: 18 and SEQ ID NO: 23; SEQ ID NO: 18 and SEQ ID NO: 24; SEQ ID NO: 18 and SEQ ID NO: 25; SEQ ID NO: 18 and SEQ ID NO: 26; SEQ ID NO: 19 and SEQ ID NO: 20; SEQ ID NO: 19 and SEQ ID NO: 21; SEQ ID NO: 19 and SEQ ID NO: 22; SEQ ID NO: 19 and SEQ ID NO: 23; SEQ ID NO: 19 and SEQ ID NO: 24; SEQ ID NO: 19 and SEQ ID NO: 25; SEQ ID NO: 19 and SEQ ID NO: 26; SEQ ID NO: 20 and SEQ ID NO: 21; SEQ ID NO: 20 and SEQ ID NO: 22; SEQ ID NO: 20 and SEQ ID NO: 23; SEQ ID NO: 20 and SEQ ID NO: 24; SEQ ID NO: 20 and SEQ ID NO: 25; SEQ ID NO: 20 and SEQ ID NO: 26; SEQ ID NO: 21 and SEQ ID NO: 22; SEQ ID NO: 21 and SEQ ID NO: 23; SEQ ID NO: 21 and SEQ ID NO: 24; SEQ ID NO: 21 and SEQ ID NO: 25; SEQ ID NO: 21 and SEQ ID NO: 26; SEQ ID NO: 22 and SEQ ID NO: 23; SEQ ID NO: 22 and SEQ ID NO: 24; SEQ ID NO: 22 and SEQ ID NO: 25; SEQ ID NO: 22 and SEQ ID NO: 26; SEQ ID NO: 23 and SEQ ID NO: 24; SEQ ID NO: 23 and SEQ ID NO: 25; SEQ ID NO: 23 and SEQ ID NO: 26; SEQ ID NO: 24 and SEQ ID NO: 25; SEQ ID NO: 24 and SEQ ID NO: 26; SEQ ID NO: 25 and SEQ ID NO: 26; SEQ ID NO: 110 and SEQ ID NO: 120; SEQ ID NO: 110 and SEQ ID NO: 121; SEQ ID NO: 110 and SEQ ID NO: 122; SEQ ID NO: 110 and SEQ ID NO: 123; SEQ ID NO: 110 and SEQ ID NO: 124; SEQ ID NO: 110 and SEQ ID NO: 125; SEQ ID NO: 111 and SEQ ID NO: 112; SEQ ID NO: 111 and SEQ ID NO: 113; SEQ ID NO: 111 and SEQ ID NO: 114; SEQ ID NO: 111 and SEQ ID NO: 115; SEQ ID NO: 111 and SEQ ID NO: 116; SEQ ID NO: 111 and SEQ ID NO: 117; SEQ ID NO: 111 and SEQ ID NO: 118; SEQ ID NO: 111 and SEQ ID NO: 119; SEQ ID NO: 111 and SEQ ID NO: 120; SEQ ID NO: 111 and SEQ ID NO: 121; SEQ ID NO: 111 and SEQ ID NO: 122; SEQ ID NO: 111 and SEQ ID NO: 123; SEQ ID NO: 111 and SEQ ID NO: 124; SEQ ID NO: 111 and SEQ ID NO: 125; SEQ ID NO: 112 and SEQ ID NO: 113; SEQ ID NO: 112 and SEQ ID NO: 114; SEQ ID NO: 112 and SEQ ID NO: 115; SEQ ID NO: 112 and SEQ ID NO: 116; SEQ ID NO: 112 and SEQ ID NO: 117; SEQ ID NO: 112 and SEQ ID NO: 118; SEQ ID NO: 112 and SEQ ID NO: 119; SEQ ID NO: 112 and SEQ ID NO: 120; SEQ ID NO: 112 and SEQ ID

NO: 121; SEQ ID NO: 112 and SEQ ID NO: 122; SEQ ID NO: 112 and SEQ ID NO: 123; SEQ ID NO: 112 and SEQ ID NO: 124; SEQ ID NO: 112 and SEQ ID NO: 125; SEQ ID NO: 113 and SEQ ID NO: 114; SEQ ID NO: 113 and SEQ ID NO: 115; SEQ ID NO: 113 and SEQ ID NO: 116; SEQ ID NO: 113 and SEQ ID NO: 117; SEQ ID NO: 113 and SEQ ID NO: 118; SEQ ID NO: 113 and SEQ ID NO: 119; SEQ ID NO: 113 and SEQ ID NO: 120; SEQ ID NO: 113 and SEQ ID NO: 121; SEQ ID NO: 113 and SEQ ID NO: 122; SEQ ID NO: 113 and SEQ ID NO: 123; SEQ ID NO: 113 and SEQ ID NO: 124; SEQ ID NO: 113 and SEQ ID NO: 125; SEQ ID NO: 114 and SEQ ID NO: 115; SEQ ID NO: 114 and SEQ ID NO: 116; SEQ ID NO: 114 and SEQ ID NO: 117; SEQ ID NO: 114 and SEQ ID NO: 118; SEQ ID NO: 114 and SEQ ID NO: 119; SEQ ID NO: 114 and SEQ ID NO: 120; SEQ ID NO: 114 and SEQ ID NO: 121; SEQ ID NO: 114 and SEQ ID NO: 122; SEQ ID NO: 114 and SEQ ID NO: 123; SEQ ID NO: 114 and SEQ ID NO: 124; SEQ ID NO: 114 and SEQ ID NO: 125; SEQ ID NO: 115 and SEQ ID NO: 116; SEQ ID NO: 115 and SEQ ID NO: 117; SEQ ID NO: 115 and SEQ ID NO: 118; SEQ ID NO: 115 and SEQ ID NO: 119; SEQ ID NO: 115 and SEQ ID NO: 120; SEQ ID NO: 115 and SEQ ID NO: 121; SEQ ID NO: 115 and SEQ ID NO: 122; SEQ ID NO: 115 and SEQ ID NO: 123; SEQ ID NO: 115 and SEQ ID NO: 124; SEQ ID NO: 115 and SEQ ID NO: 125; SEQ ID NO: 116 and SEQ ID NO: 117; SEQ ID NO: 116 and SEQ ID NO: 118; SEQ ID NO: 116 and SEQ ID NO: 119; SEQ ID NO: 116 and SEQ ID NO: 120; SEQ ID NO: 116 and SEQ ID NO: 121; SEQ ID NO: 116 and SEQ ID NO: 122; SEQ ID NO: 116 and SEQ ID NO: 123; SEQ ID NO: 116 and SEQ ID NO: 124; SEQ ID NO: 116 and SEQ ID NO: 125; SEQ ID NO: 117 and SEQ ID NO: 118; SEQ ID NO: 117 and SEQ ID NO: 119; SEQ ID NO: 117 and SEQ ID NO: 120; SEQ ID NO: 117 and SEQ ID NO: 121; SEQ ID NO: 117 and SEQ ID NO: 122; SEQ ID NO: 117 and SEQ ID NO: 123; SEQ ID NO: 117 and SEQ ID NO: 124; SEQ ID NO: 117 and SEQ ID NO: 125; SEQ ID NO: 118 and SEQ ID NO: 119; SEQ ID NO: 118 and SEQ ID NO: 120; SEQ ID NO: 118 and SEQ ID NO: 121; SEQ ID NO: 118 and SEQ ID NO: 122; SEQ ID NO: 118 and SEQ ID NO: 123; SEQ ID NO: 118 and SEQ ID NO: 124; SEQ ID NO: 118 and SEQ ID NO: 125; SEQ ID NO: 119 and SEQ ID NO: 120; SEQ ID NO: 119 and SEQ ID NO: 121; SEQ ID NO: 119 and SEQ ID NO: 122; SEQ ID NO: 119 and SEQ ID NO: 123; SEQ ID NO: 119 and SEQ ID NO: 124; SEQ ID NO: 119 and SEQ ID NO: 125; SEQ ID NO: 120 and SEQ ID NO: 121; SEQ ID NO: 120 and SEQ ID NO: 122; SEQ ID NO: 120 and SEQ ID NO: 123; SEQ ID NO: 120 and SEQ ID NO: 124; SEQ ID NO: 120 and SEQ ID NO: 125; SEQ ID NO: 121 and SEQ ID NO: 122; SEQ ID NO: 121 and SEQ ID NO: 123; SEQ ID NO: 121 and SEQ ID NO: 124; SEQ ID NO: 121 and SEQ ID NO: 125; SEQ ID NO: 122 and SEQ ID NO: 123; SEQ ID NO: 122 and SEQ ID NO: 124; SEQ ID NO: 122 and SEQ ID NO: 125; SEQ ID NO: 123 and SEQ ID NO: 124; SEQ ID NO: 123 and SEQ ID NO: 125; SEQ ID NO: 124 and SEQ ID NO: 125; SEQ ID NO: 126 and SEQ ID NO: 127; SEQ ID NO: 126 and SEQ ID NO: 128; SEQ ID NO: 126 and SEQ ID NO: 129; SEQ ID NO: 126 and SEQ ID NO: 130; SEQ ID NO: 126 and SEQ ID NO: 131; SEQ ID NO: 126 and SEQ ID NO: 132; SEQ ID NO: 126 and SEQ ID NO: 133; SEQ ID NO: 126 and SEQ ID NO: 134; SEQ ID

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NO: 292; SEQ ID NO: 277 and SEQ ID NO: 278; SEQ ID NO: 277 and SEQ ID NO: 279; SEQ ID NO: 277 and SEQ ID NO: 280; SEQ ID NO: 277 and SEQ ID NO: 281; SEQ ID NO: 277 and SEQ ID NO: 282; SEQ ID NO: 277 and SEQ ID NO: 283; SEQ ID NO: 277 and SEQ ID NO: 284; SEQ ID NO: 277 and SEQ ID NO: 285; SEQ ID NO: 277 and SEQ ID NO: 286; SEQ ID NO: 277 and SEQ ID NO: 287; SEQ ID NO: 277 and SEQ ID NO: 288; SEQ ID NO: 277 and SEQ ID NO: 289; SEQ ID NO: 277 and SEQ ID NO: 290; SEQ ID NO: 277 and SEQ ID NO: 291; SEQ ID NO: 277 and SEQ ID NO: 292; SEQ ID NO: 278 and SEQ ID NO: 279; SEQ ID NO: 278 and SEQ ID NO: 280; SEQ ID NO: 278 and SEQ ID NO: 281; SEQ ID NO: 278 and SEQ ID NO: 282; SEQ ID NO: 278 and SEQ ID NO: 283; SEQ ID NO: 278 and SEQ ID NO: 284; SEQ ID NO: 278 and SEQ ID NO: 285; SEQ ID NO: 278 and SEQ ID NO: 286; SEQ ID NO: 278 and SEQ ID NO: 287; SEQ ID NO: 278 and SEQ ID NO: 288; SEQ ID NO: 278 and SEQ ID NO: 289; SEQ ID NO: 278 and SEQ ID NO: 290; SEQ ID NO: 278 and SEQ ID NO: 291; SEQ ID NO: 278 and SEQ ID NO: 292; SEQ ID NO: 279 and SEQ ID NO: 280; SEQ ID NO: 279 and SEQ ID NO: 281; SEQ ID NO: 279 and SEQ ID NO: 282; SEQ ID NO: 279 and SEQ ID NO: 283; SEQ ID NO: 279 and SEQ ID NO: 284; SEQ ID NO: 279 and SEQ ID NO: 285; SEQ ID NO: 279 and SEQ ID NO: 286; SEQ ID NO: 279 and SEQ ID NO: 287; SEQ ID NO: 279 and SEQ ID NO: 288; SEQ ID NO: 279 and SEQ ID NO: 289; SEQ ID NO: 279 and SEQ ID NO: 290; SEQ ID NO: 279 and SEQ ID NO: 291; SEQ ID NO: 279 and SEQ ID NO: 292; SEQ ID NO: 280 and SEQ ID NO: 281; SEQ ID NO: 280 and SEQ ID NO: 282; SEQ ID NO: 280 and SEQ ID NO: 283; SEQ ID NO: 280 and SEQ ID NO: 284; SEQ ID NO: 280 and SEQ ID NO: 285; SEQ ID NO: 280 and SEQ ID NO: 286; SEQ ID NO: 280 and SEQ ID NO: 287; SEQ ID NO: 280 and SEQ ID NO: 288; SEQ ID NO: 280 and SEQ ID NO: 289; SEQ ID NO: 280 and SEQ ID NO: 290; SEQ ID NO: 280 and SEQ ID NO: 291; SEQ ID NO: 280 and SEQ ID NO: 292; SEQ ID NO: 281 and SEQ ID NO: 282; SEQ ID NO: 281 and SEQ ID NO: 283; SEQ ID NO: 281 and SEQ ID NO: 284; SEQ ID NO: 281 and SEQ ID NO: 285; SEQ ID NO: 281 and SEQ ID NO: 286; SEQ ID NO: 281 and SEQ ID NO: 287; SEQ ID NO: 281 and SEQ ID NO: 288; SEQ ID NO: 281 and SEQ ID NO: 289; SEQ ID NO: 281 and SEQ ID NO: 290; SEQ ID NO: 281 and SEQ ID NO: 291; SEQ ID NO: 281 and SEQ ID NO: 292; SEQ ID NO: 282 and SEQ ID NO: 283; SEQ ID NO: 282 and SEQ ID NO: 284; SEQ ID NO: 282 and SEQ ID NO: 285; SEQ ID NO: 282 and SEQ ID NO: 286; SEQ ID NO: 282 and SEQ ID NO: 287; SEQ ID NO: 282 and SEQ ID NO: 288; SEQ ID NO: 282 and SEQ ID NO: 289; SEQ ID NO: 282 and SEQ ID NO: 290; SEQ ID NO: 282 and SEQ ID NO: 291; SEQ ID NO: 282 and SEQ ID NO: 292; SEQ ID NO: 283 and SEQ ID NO: 284; SEQ ID NO: 283 and SEQ ID NO: 285; SEQ ID NO: 283 and SEQ ID NO: 286; SEQ ID NO: 283 and SEQ ID NO: 287; SEQ ID NO: 283 and SEQ ID NO: 288; SEQ ID NO: 283 and SEQ ID NO: 289; SEQ ID NO: 283 and SEQ ID NO: 290; SEQ ID NO: 283 and SEQ ID NO: 291; SEQ ID NO: 283 and SEQ ID NO: 292; SEQ ID NO: 284 and SEQ ID NO: 285; SEQ ID NO: 284 and SEQ ID NO: 286; SEQ ID NO: 284 and SEQ ID NO: 287; SEQ ID NO: 284 and SEQ ID NO: 288; SEQ ID NO: 284 and SEQ ID NO: 289; SEQ ID NO: 284 and SEQ ID NO: 290; SEQ ID

NO: 284 and SEQ ID NO: 291; SEQ ID NO: 284 and SEQ ID NO: 292; SEQ ID NO: 285 and SEQ ID NO: 286; SEQ ID NO: 285 and SEQ ID NO: 287; SEQ ID NO: 285 and SEQ ID NO: 288; SEQ ID NO: 285 and SEQ ID NO: 289; SEQ ID NO: 285 and SEQ ID NO: 290; SEQ ID NO: 285 and SEQ ID NO: 291; SEQ ID NO: 285 and SEQ ID NO: 292; SEQ ID NO: 286 and SEQ ID NO: 287; SEQ ID NO: 286 and SEQ ID NO: 288; SEQ ID NO: 286 and SEQ ID NO: 289; SEQ ID NO: 286 and SEQ ID NO: 290; SEQ ID NO: 286 and SEQ ID NO: 291; SEQ ID NO: 286 and SEQ ID NO: 292; SEQ ID NO: 287 and SEQ ID NO: 288; SEQ ID NO: 287 and SEQ ID NO: 289; SEQ ID NO: 287 and SEQ ID NO: 290; SEQ ID NO: 287 and SEQ ID NO: 291; SEQ ID NO: 287 and SEQ ID NO: 292; SEQ ID NO: 288 and SEQ ID NO: 289; SEQ ID NO: 288 and SEQ ID NO: 290; SEQ ID NO: 288 and SEQ ID NO: 291; SEQ ID NO: 288 and SEQ ID NO: 292; SEQ ID NO: 289 and SEQ ID NO: 290; SEQ ID NO: 289 and SEQ ID NO: 291; SEQ ID NO: 289 and SEQ ID NO: 292; SEQ ID NO: 290 and SEQ ID NO: 291; SEQ ID NO: 290 and SEQ ID NO: 292; SEQ ID NO: 291 and SEQ ID NO: 292.

[0082] In one aspect, a composition is provided comprising a single nucleic acid molecule encoding, or two nucleic acid molecules where one molecule encodes, 1) one or more guide RNA that comprises a guide sequence selected from any one of SEQ ID NOs: 1-159; and 2) a SaCas9. In one aspect, a composition is provided comprising a single nucleic acid molecule encoding, or two nucleic acid molecules where one molecule encodes, 1) one or more guide RNA that comprises a guide sequence selected from any one of SEQ ID NOs: 200-292, 924-938, or 950-955; and 2) a SluCas9.

[0083] In one aspect, a composition is provided comprising a single nucleic acid molecule encoding, or two nucleic acid molecules where one molecule encodes, a) one or more guide RNA that comprises a guide sequence that is at least 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, or 90% identical to any one of SEQ ID NOs: 1-159 and a SaCas9; or b) one or more guide RNA that comprises a guide sequence that is at least 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, or 90% identical to any one of SEQ ID NOs: 200-292, 924-938, or 950-955; and a SluCas9. In one aspect, a composition is provided comprising a single nucleic acid molecule encoding a) one or more guide RNA that comprises a guide sequence that is at least 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, or 90% identical to any one of 1) SEQ ID NOs: 200-292, 924-938, or 950-955, and a SluCas9; or b) one or more guide RNA that comprises a guide sequence that is at least 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, or 90% identical to any one of SEQ ID NOs: 1-159, and a SaCas9.

[0084] In another aspect, a composition is provided comprising a single nucleic acid molecule encoding, or two nucleic acid molecules where one molecule encodes, a) one or more guide RNA that comprises a guide sequence comprising at least 16, 17, 18, 19, or 20 contiguous nucleotides of a spacer sequence selected from any one of SEQ ID NOs: 1-159 and a SaCas9; or b) one or more guide RNA that comprises a guide sequence comprising at least 16, 17, 18, 19, or 20 contiguous nucleotides of a spacer sequence selected from any one of SEQ ID NOs: 200-292, 924-938, or 950-955 and a

SluCas9. In another aspect, a composition is provided comprising a single nucleic acid molecule encoding, or two nucleic acid molecules where one molecule encodes, a) one or more guide RNA that comprises a guide sequence comprising at least 16, 17, 18, 19, or 20 contiguous nucleotides of a spacer sequence selected from any one of SEQ ID NOs: 1-159 and a SaCas9; or b) one or more guide RNA that comprises a guide sequence comprising at least 16, 17, 18, 19, or 20 contiguous nucleotides of a spacer sequence selected from any one of SEQ ID NOs: 200-292, 924-938, or 950-955 and a SluCas9.

[0085] In some embodiments, any of the guides disclosed herein may be used as a research tool, e.g., to study trafficking, expression, and processing by cells.

Scaffold Sequences

[0086] Each of the guide sequences shown in **Table 6** may further comprise additional nucleotides to form or encode a crRNA, e.g., using any known sequence appropriate for the Cas9 being used. In some embodiments, the crRNA comprises (5' to 3') at least a spacer sequence and a first complementarity domain. The first complementary domain is sufficiently complementary to a second complementarity domain, which may be part of the same molecule in the case of an sgRNA or in a tracrRNA in the case of a dual or modular gRNA, to form a duplex. See, e.g., US 2017/0007679 for detailed discussion of crRNA and gRNA domains, including first and second complementarity domains.

[0087] A single-molecule guide RNA (sgRNA) can comprise, in the 5' to 3' direction, an optional spacer extension sequence, a spacer sequence, a minimum CRISPR repeat sequence, a single-molecule guide linker, a minimum tracrRNA sequence, a 3' tracrRNA sequence and/or an optional tracrRNA extension sequence. The optional tracrRNA extension can comprise elements that contribute additional functionality (*e.g.*, stability) to the guide RNA. The single-molecule guide linker can link the minimum CRISPR repeat and the minimum tracrRNA sequence to form a hairpin structure. The optional tracrRNA extension can comprise one or more hairpins. In particular embodiments, the disclosure provides for an sgRNA comprising a spacer sequence and a tracrRNA sequence.

[0088] The guide RNA can be considered to comprise a scaffold sequence necessary for endonuclease binding and a spacer sequence required to bind to the genomic target sequence. In some embodiments, the guide RNA comprises any of the scaffold sequences disclosed herein and any of the spacer sequences disclosed herein. In some embodiments, the guide RNA comprises any of the scaffold sequences disclosed herein and any of the spacer sequences disclosed herein, without any nucleotides between the scaffold sequence and the spacer sequence.

An exemplary scaffold sequence suitable for use with SaCas9 to follow the guide sequence at its 3' end is:

GTTTAAGTACTCTGTGCTGGAAACAGCACAGAATCTACTTAAACAAGGCAAAATGCCGT GTTTATCTCGTCAACTTGTTGGCGAGA (SEQ ID NO: 500) in 5' to 3' orientation. In some embodiments, an exemplary scaffold sequence for use with SaCas9 to follow the 3' end of the guide sequence is a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 500, or a sequence that differs from SEQ ID NO: 500 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0089] In some embodiments, a variant of an SaCas9 scaffold sequence may be used. In some embodiments, the SaCas9 scaffold to follow the guide sequence at its 3' end is referred to as "SaScaffoldV1" and is: GTTTTAGTACTCTGGAAACAGAATCTACTAAAACAAGGCAAAATGCCGTGTTTATCTCGT CAACTTGTTGGCGAGAT (SEQ ID NO: 501) in 5' to 3' orientation. In some embodiments, an exemplary scaffold sequence for use with SaCas9 to follow the 3' end of the guide sequence is a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 501, or a sequence that differs from SEQ ID NO: 501 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0090] In some embodiments, a variant of an SaCas9 scaffold sequence may be used. In some embodiments, the SaCas9 scaffold to follow the guide sequence at its 3' end is referred to as "SaScaffoldV2" and is: GTTTAAGTACTCTGTGCTGGAAACAGCACAGAATCTACTTAAACAAGGCAAAATGCCGT GTTTATCTCGTCAACTTGTTGGCGAGAT (SEQ ID NO: 502) in 5' to 3' orientation. In some embodiments, an exemplary scaffold sequence for use with SaCas9 to follow the 3' end of the guide sequence is a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 502, or a sequence that differs from SEQ ID NO: 502 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0091] In some embodiments, a variant of an SaCas9 scaffold sequence may be used. In some embodiments, the SaCas9 scaffold to follow the guide sequence at its 3' end is referred to as "SaScaffoldV3" and is: GTTTAAGTACTCTGGAAACAGAATCTACTTAAACAAGGCAAAATGCCGTGTTTATCTCGT CAACTTGTTGGCGAGAT (SEQ ID NO: 503) in 5' to 3' orientation. In some embodiments, an exemplary scaffold sequence for use with SaCas9 to follow the 3' end of the guide sequence is a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 503, or a sequence that differs from SEQ ID NO: 503 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0092] In some embodiments, a variant of an SaCas9 scaffold sequence may be used. In some embodiments, the SaCas9 scaffold to follow the guide sequence at its 3' end is referred to as "SaScaffoldV5" and is: GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGGCAAAATGCCGTGTTTATCTCGT

CAACTTGTTGGCGAGAT (SEQ ID NO: 504) in 5' to 3' orientation. In some embodiments, an exemplary scaffold sequence for use with SaCas9 to follow the 3' end of the guide sequence is a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 504, or a sequence that differs from SEQ ID NO: 504 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0093] Two exemplary scaffold sequences suitable for use with SluCas9 to follow the guide sequence at its 3' end are: GTTTTAGTACTCTGGAAACAGAATCTACTGAAACAAGACAATATGTCGTGTTTATCCCATCAATTTATTGGTGGGA (SEQ ID NO: 600), or GTTTAAGTACTCTGTGCTGGAAACAGCACAGAATCTACTGAAACAAGACAATATGTCGTGTTTATCCCATCAATTTATTGGTGGGA (SEQ ID NO: 601) in 5' to 3' orientation. In some embodiments, an exemplary sequence for use with SluCas9 to follow the 3' end of the guide sequence is a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 600 or SEQ ID NO: 601, or a sequence that differs from SEQ ID NO: 600 or SEQ ID NO: 601 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0094] Exemplary scaffold sequences suitable for use with SluCas9 to follow the guide sequence at its 3' end are also shown below in the 5' to 3' orientation.

[0095] **Table 7**:

Scaffold ID	**SEQ ID NO**	**Scaffold Sequence (5' to 3')**	**Homology to Slu v5**	**Streak of Homology to Slu v5 (# nucleotides)**
Wildtype	900	GTTTTAGTACTCTGGAAACAGAATCTACTGAAACAAGACAATATGTCGTGTTTATCCCATCAATTTATTGGTGGGAT	N/A	N/A
Slu-VCGT-4.5	601	GTTTAAGTACTCTGTGCTGGAAACAGCACAGAATCTACTGAAACAAGACAATATGTCGTGTTTATCCCATCAATTTATTGGTGGGA	N/A	N/A
Slu_v5	901	GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGACAATATGTCGTGTTTATCCCATCAATTTATTGGTGGGAT	100.00%	77
Slu_v5-1	902	GTTTggTaACcTaGGAAACTagATCTTaccAAACAAGACAATATGTCGTGTTTATCCCATCAATTTATTGGTGGGAT	87.50%	47
Slu_v5-2	903	GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGgCAAaATGcCGTGTTTATCCCATCAATTTATTGGTGGGAT	96.10%	37
Slu_v5-3	904	GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGACAATATGTCGcgcccaTCCCATCAATTTATTGGTGGGAT	94.81%	48
Slu_v5-4	905	GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGACAATATGTCGTGTTTATgggTTgAATTTATTcGacccAT	91.55%	55
Slu_v5-5	906	GTTTggTaACcTaGGAAACTagATCTTaccAAACAAGgCAAaATGcCGTGTTTATCCCATCAATTTATTGGTGGGAT	83.75%	31

Slu_v5-6	907	GTTTggTaACcTaGGAAACTagATCTTaccAAACAAGACAATATGTCGcgcccaTCCCATCAATTTATTGGTGGGAT	82.50%	23
Slu_v5-7	908	GTTTggTaACcTaGGAAACTagATCTTaccAAACAAGACAATATGTCGTGTTTATgggTTgAATTTATTcGacccAT	78.38%	25
Slu_v5-8	909	GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGgCAAaATGcCGcgcccaTCCCATCAATTTATTGGTGGGAT	90.91%	37
Slu_v5-9	910	GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGgCAAaATGcCGTGTTTATgggTTgAATTTATTcGacccAT	87.32%	37
Slu_v5-10	911	GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGACAATATGTCGcgcccaTgggTTgAATTTATTcGacccAT	82.89%	48
Slu_v5-11	912	GTTTggTaACcTaGGAAACTagATCTTaccAAACAAGgCAAaATGcCGcgcccaTCCCATCAATTTATTGGTGGGAT	78.75%	23
Slu_v5-12	913	GTTTggTaACcTaGGAAACTagATCTTaccAAACAAGgCAAaATGcCGTGTTTATgggTTgAATTTATTcGacccAT	74.32%	9
Slu_v5-13	914	GTTTggTaACcTaGGAAACTagATCTTaccAAACAAGACAATATGTCGcgcccaTgggTTgAATTTATTcGacccAT	70.89%	18
Slu_v5-14	915	GTTTCAGTACTCTGGAAACAGAATCTACTGAAACAAGgCAAaATGcCGcgcccaTgggTTgAATTTATTcGacccAT	78.95%	37
Slu_v5-15	916	GTTTggTaACcTaGGAAACTagATCTTaccAAACAAGgCAAaATGcCGcgcccaTgggTTgAATTTATTcGacccAT	67.09%	8
Slu v4	917	GTTTCAGTACTCTGTGCTGGAAACAGCACAGAATCTACTGAAACAAGACAATATGTCGTGTTTATCCCATCAATTTATTGGTGGGAT	N/A	N/A

[0096] In some embodiments, the scaffold sequence suitable for use with SaCas9 to follow the guide sequence at its 3’ end is selected from any one of SEQ ID NOs: 500-504 in 5’ to 3 orientation. In some embodiments, an exemplary sequence for use with SaCas9 to follow the 3’ end of the guide sequence is a sequence that is at least 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to any one off SEQ ID NOs: 500-504, or a sequence that differs from any one of SEQ ID NOs: 500-504 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0097] In some embodiments, the scaffold sequence suitable for use with SluCas9 to follow the guide sequence at its 3’ end is selected from any one of SEQ ID NOs: 900 or 601, or 901-917 in 5’ to 3 orientation. In some embodiments, an exemplary sequence for use with SluCas9 to follow the 3’ end of the guide sequence is a sequence that is at least 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to any one off SEQ ID NOs: 900 or 601, or 901-917, or a sequence that differs from any one of SEQ ID NOs: 900 or 601, or 901-917 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0098] In some embodiments, any scaffold sequence (e.g., any of the scaffold sequences disclosed herein) is suitable for use with any sRGN disclosed herein, such as any one of sRGN1, sRGN2, sRGN3, sRGN3.1, sRGN3.2, sRGN3.3, sRGN4, or a nucleic acid molecule encoding the same. In some embodiments, a scaffold sequence suitable for use with a sRGN, such as at the 3' end of a guide RNA sequence within an expression vector comprising the sRGN (e.g., an expression vector as shown in FIGS. 5A-5B) is selected from any one of SEQ ID NOs: 500-504, 601, or 900-917. In some embodiments, a scaffold sequence suitable for use with a sRGN, such as at the 3' end of a guide RNA sequence within an expression vector comprising the sRGN (e.g., an expression vector as shown in FIGS. 5A-5B) is a sequence that is at least 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to any one of SEQ ID NOs: 500-504, 601, or 900-917, or a sequence that differs from any one of SEQ ID NOs: 500-504, 601, or 900-917 by no more than 1, 2, 3, 4, 5, 10, 15, 20, or 25 nucleotides.

[0099] In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 500. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 501. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 502. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 503. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 504. In some embodiments, comprising a pair of gRNAs, one of the gRNAs comprises a sequence selected from any one of SEQ ID NOs: 500-504. In some embodiments, comprising a pair of gRNAs, both of the gRNAs comprise a sequence selected from any one of SEQ ID NOs: 500-504. In some embodiments, comprising a pair of gRNAs, the nucleotides 3' of the guide sequence of the gRNAs are the same sequence. In some embodiments, comprising a pair of gRNAs, the nucleotides 3' of the guide sequence of the gRNAs are different sequences.

[00100] In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 900. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 601. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 900. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 901. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 902. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 903. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 904. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 905. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 906. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 907. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 908. In some embodiments, the nucleic acid encoding

the gRNA comprises a sequence comprising SEQ ID NO: 909. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 910. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 911. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 912. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 913. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 914. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 915. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 916. In some embodiments, the nucleic acid encoding the gRNA comprises a sequence comprising SEQ ID NO: 917. In some embodiments, comprising a pair of gRNAs, one of the gRNAs comprises a sequence selected from any one of SEQ ID NOs: 900 or 601, or 901-917. In some embodiments, comprising a pair of gRNAs, both of the gRNAs comprise a sequence selected from any one of SEQ ID NOs: 900 or 601, or 901-917. In some embodiments, comprising a pair of gRNAs, the nucleotides 3' of the guide sequence of the gRNAs are the same sequence. In some embodiments, comprising a pair of gRNAs, the nucleotides 3' of the guide sequence of the gRNAs are different sequences.

[00101] In some embodiments, the scaffold sequence comprises one or more alterations in the stem loop 1 as compared to the stem loop 1 of a wildtype SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 900) or a reference SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 901). In some embodiments, the scaffold sequence comprises one or more alterations in the stem loop 2 as compared to the stem loop 2 of a wildtype SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 900) or a reference SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 901). In some embodiments, the scaffold sequence comprises one or more alterations in the tetraloop as compared to the tetraloop of a wildtype SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 900) or a reference SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 901). In some embodiments, the scaffold sequence comprises one or more alterations in the repeat region as compared to the repeat region of a wildtype SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 900) or a reference SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 901). In some embodiments, the scaffold sequence comprises one or more alterations in the anti-repeat region as compared to the anti-repeat region of a wildtype SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 900) or a reference SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 901). In some embodiments, the scaffold sequence comprises one or more alterations in the linker region as compared to the linker region of a wildtype SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 900) or a

reference SluCas9 scaffold sequence (e.g., a scaffold comprising the sequence of SEQ ID NO: 901). See, e.g., Nishimasu et al., 2015, Cell, 162:1113-1126 for description of regions of a scaffold.

[00102] Where a tracrRNA is used, in some embodiments, it comprises (5' to 3') a second complementary domain and a proximal domain. In the case of a sgRNA, guide sequences together with additional nucleotides (e.g., SEQ ID Nos: 500-504 (for SaCas9), and 900 or 601, or 901-917 (for SluCas9)) form or encode a sgRNA. In some embodiments, an sgRNA comprises (5' to 3') at least a spacer sequence, a first complementary domain, a linking domain, a second complementary domain, and a proximal domain. A sgRNA or tracrRNA may further comprise a tail domain. The linking domain may be hairpin-forming. See, e.g., US 2017/0007679 for detailed discussion and examples of crRNA and gRNA domains, including second complementarity domains, linking domains, proximal domains, and tail domains.

[00103] In some embodiments, the disclosure provides for specific nucleic acid sequences encoding one or more guide RNA components (e.g., any of the spacer and or scaffold sequences disclosed herein). The disclosure contemplates RNA equivalents of any of the DNA sequences provided herein (i.e., in which "T"s are replaced with "U"s), or DNA equivalents of any of the RNA sequences provided herein (i.e., in which "U"s are replaced with "T"s), as well as complements (including reverse complements) of any of the sequences disclosed herein.

[00104] In some embodiments, a composition is provided comprising a guide RNA, or nucleic acid encoding a guide RNA, wherein the guide RNA further comprises a trRNA. In each composition and method embodiment described herein, the crRNA (comprising the spacer sequence) and trRNA may be associated as a single RNA (sgRNA) or may be on separate RNAs (dgRNA). In the context of sgRNAs, the crRNA and trRNA components may be covalently linked, e.g., via a phosphodiester bond or other covalent bond.

Vectors

[00105] In any embodiment comprising a nucleic acid molecule encoding a guide RNA and/or a Cas9, the nucleic acid molecule may be a vector. In some embodiments, a composition is provided comprising a single nucleic acid molecule encoding at least one guide RNA and Cas9, wherein the nucleic acid molecule is a vector. In some embodiments, a composition is provided comprising more than one nucleic acid molecule encoding a guide RNA and Cas9, wherein the nucleic acid molecule is a vector. In some embodiments, a composition is provided comprising more than one nucleic acid molecule wherein one molecule encodes one or more guide RNA, and the other molecule encodes Cas9 plus or minus at least one guide RNA, wherein the nucleic acid molecule is a vector.

[00106] Any type of vector, such as any of those described herein, may be used. In some embodiments, the vector is a lipid nanoparticle. In some embodiments, the vector is a viral vector. In some embodiments, the viral vector is a non-integrating viral vector (i.e., that does not insert sequence from the vector into a host chromosome). In some embodiments, the viral vector is an adeno-

associated virus vector (AAV), a lentiviral vector, an integrase-deficient lentiviral vector, an adenoviral vector, a vaccinia viral vector, an alphaviral vector, or a herpes simplex viral vector. In some embodiments, the vector comprises a muscle-specific promoter. Exemplary muscle-specific promoters include a muscle creatine kinase promoter, a desmin promoter, an MHCK7 promoter, or an SPc5-12 promoter. *See* US 2004/0175727 A1; Wang et al., *Expert Opin Drug Deliv.* (2014) 11, 345–364; Wang et al., *Gene Therapy* (2008) 15, 1489–1499. In some embodiments, the muscle-specific promoter is a CK8 promoter. In some embodiments, the muscle-specific promoter is a CK8e promoter. In any of the foregoing embodiments, the vector may be an adeno-associated virus vector (AAV).

[00107] In some embodiments, the vector is a lipid nanoparticle comprising an endonuclease (e.g., any of the endonucleases disclosed herein) and one or more of any of the guide RNAs disclosed herein. In some embodiments, the vector is a lipid nanoparticle comprising a nucleic acid encoding an endonuclease (e.g., any of the endonucleases disclosed herein) and one or more of any of the guide RNAs disclosed herein. In some embodiments, the vector is a lipid nanoparticle comprising a nucleic acid encoding an endonuclease (e.g., any of the endonucleases disclosed herein) and a nucleic acid encoding one or more of any of the guide RNAs disclosed herein.

[00108] Where a vector is used, it may be a viral vector, such as a non-integrating viral vector. In some embodiments, the viral vector is an adeno-associated virus vector, a lentiviral vector, an integrase-deficient lentiviral vector, an adenoviral vector, a vaccinia viral vector, an alphaviral vector, or a herpes simplex viral vector. In some embodiments, the viral vector is an adeno-associated virus (AAV) vector. In some embodiments, the AAV vector is an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAVrh10 (*see, e.g.*, SEQ ID NO: 81 of US 9,790,472, which is incorporated by reference herein in its entirety), AAVrh74 (*see, e.g.*, SEQ ID NO: 1 of US 2015/0111955, which is incorporated by reference herein in its entirety), or AAV9 vector, wherein the number following AAV indicates the AAV serotype. In some embodiments, the AAV vector is a single-stranded AAV (ssAAV). In some embodiments, the AAV vector is a double-stranded AAV (dsAAV). Any variant of an AAV vector or serotype thereof, such as a self-complementary AAV (scAAV) vector, is encompassed within the general terms AAV vector, AAV1 vector, etc. See, e.g., McCarty et al., *Gene Ther.* 2001;8:1248–54, Naso et al., *BioDrugs* 2017; 31:317-334, and references cited therein for detailed discussion of various AAV vectors. In some embodiments, the AAV vector size is measured in length of nucleotides from ITR to ITR, inclusive of both ITRs. In some embodiments, the AAV vector is less than 5 kb in size from ITR to ITR, inclusive of both ITRs. In particular embodiments, the AAV vector is less than 4.9 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV vector is less than 4.85 kb in size from ITR to ITR, inclusive of both ITRs. In further embodiments, the AAV vector is less than 4.8 kb in size from ITR to ITR, inclusive of both ITRs. In further embodiments, the AAV vector is less than 4.75 kb in size from ITR to ITR, inclusive of both ITRs. In further embodiments, the AAV vector is less than 4.7 kb in size from ITR to ITR,

inclusive of both ITRs. In some embodiments, the vector is between 3.9-5 kb, 4-5 kb, 4.2-5 kb, 4.4-5 kb, 4.6-5 kb, 4.7-5 kb, 3.9-4.9 kb, 4.2-4.9 kb, 4.4-4.9 kb, 4.7-4.9 kb, 3.9-4.85 kb, 4.2-4.85 kb, 4.4-4.85 kb, 4.6-4.85 kb, 4.7-4.85 kb, 4.7-4.9 kb, 3.9-4.8 kb, 4.2-4.8 kb, 4.4-4.8 kb or 4.6-4.8 kb from ITR to ITR in size, inclusive of both ITRs. In some embodiments, the vector is between 4.4-4.85 kb in size from ITR to ITR, inclusive of both ITRs. In some embodiments, the vector is an AAV9 vector.

[00109] In some embodiments, the vector (e.g., viral vector, such as an adeno-associated viral vector) comprises a tissue-specific (e.g., muscle-specific) promoter, e.g., which is operatively linked to a sequence encoding the guide RNA and/or the Cas protein. In some embodiments, the muscle-specific promoter is a muscle creatine kinase promoter, a desmin promoter, an MHCK7 promoter, or an SPc5-12 promoter. In some embodiments, the muscle-specific promoter is a CK8 promoter. In some embodiments, the muscle-specific promoter is a CK8e promoter. Muscle-specific promoters are described in detail, e.g., in US2004/0175727 A1; Wang et al., *Expert Opin Drug Deliv.* (2014) 11, 345–364; Wang et al., *Gene Therapy* (2008) 15, 1489–1499. In some embodiments, the tissue-specific promoter is a neuron-specific promoter, such as an enolase promoter. See, e.g., Naso et al., *BioDrugs* 2017; 31:317-334; Dashkoff et al., *Mol Ther Methods Clin Dev.* 2016;3:16081, and references cited therein for detailed discussion of tissue-specific promoters including neuron-specific promoters.

[00110] In some embodiments, in addition to guide RNA and Cas9 sequences, the vectors further comprise nucleic acids that do not encode guide RNAs. Nucleic acids that do not encode guide RNA and Cas9 include, but are not limited to, promoters, enhancers, and regulatory sequences. In some embodiments, the vector comprises one or more nucleotide sequence(s) encoding a crRNA, a trRNA, or a crRNA and trRNA. In some embodiments, the muscle specific promoter is the CK8 promoter. The CK8 promoter has the following sequence (SEQ ID NO. 700):

```
1      CTAGACTAGC ATGCTGCCCA TGTAAGGAGG CAAGGCCTGG GGACACCCGA GATGCCTGGT
61     TATAATTAAC CCAGACATGT GGCTGCCCCC CCCCCCCCAA CACCTGCTGC CTCTAAAAAT
121    AACCCTGCAT GCCATGTTCC CGGCGAAGGG CCAGCTGTCC CCCGCCAGCT AGACTCAGCA
181    CTTAGTTTAG GAACCAGTGA GCAAGTCAGC CCTTGGGGCA GCCCATACAA GGCCATGGGG
241    CTGGGCAAGC TGCACGCCTG GGTCCGGGGT GGGCACGGTG CCCGGGCAAC GAGCTGAAAG
301    CTCATCTGCT CTCAGGGGCC CCTCCCTGGG GACAGCCCCT CCTGGCTAGT CACACCCTGT
361    AGGCTCCTCT ATATAACCCA GGGGCACAGG GGCTGCCCTC ATTCTACCAC CACCTCCACA
421    GCACAGACAG ACACTCAGGA GCCAGCCAGC
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[00111] In some embodiments, the muscle-cell cell specific promoter is a variant of the CK8 promoter, called CK8e. In some embodiments, the size of the CK8e promoter is 436 bp. The CK8e promoter has the following sequence (SEQ ID NO. 701):

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  1    TGCCCATGTA AGGAGGCAAG GCCTGGGGAC ACCCGAGATG CCTGGTTATA ATTAACCCAG
 61    ACATGTGGCT GCCCCCCCCC CCCCAACACC TGCTGCCTCT AAAAATAACC CTGCATGCCA
121    TGTTCCCGGC GAAGGGCCAG CTGTCCCCCG CCAGCTAGAC TCAGCACTTA GTTTAGGAAC
181    CAGTGAGCAA GTCAGCCCTT GGGGCAGCCC ATACAAGGCC ATGGGGCTGG GCAAGCTGCA
241    CGCCTGGGTC CGGGGTGGGC ACGGTGCCCG GGCAACGAGC TGAAAGCTCA TCTGCTCTCA
301    GGGGCCCCTC CCTGGGGACA GCCCCTCCTG GCTAGTCACA CCCTGTAGGC TCCTCTATAT
361    AACCCAGGGG CACAGGGGCT GCCCTCATTC TACCACCACC TCCACAGCAC AGACAGACAC
421    TCAGGAGCCA GCCAGC
```

[00112] In some embodiments, the Ck8e promoter comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 701.

[00113] In some embodiments, the vector comprises one or more of a U6, H1, or 7SK promoter. In some embodiments, the U6 promoter is the human U6 promoter (*e.g.*, the U6L promoter or U6S promoter). In some embodiments, the promoter is the murine U6 promoter. In some embodiments, the 7SK promoter is a human 7SK promoter. In some embodiments, the 7SK promoter is the 7SK1 promoter. In some embodiments, the 7SK promoter is the 7SK2 promoter. In some embodiments, the H1 promoter is a human H1 promoter (*e.g.*, the H1L promoter or the H1S promoter). In some embodiments, the vector comprises multiple guide sequences, wherein each guide sequence is under the control of a separate promoter. In some embodiments, each of the multiple guide sequences comprises a different sequence. In some embodiments, each of the multiple guide sequences comprise the same sequence (e.g., each of the multiple guide sequences comprise the same spacer sequence). In some embodiments, each of the multiple guide sequences comprises the same spacer sequence and the same scaffold sequence. In some embodiments, each of the multiple guide sequences comprises different spacer sequences and different scaffold sequences. In some embodiments, each of the multiple guide sequences comprises the same spacer sequence, but comprises a different scaffold sequence. In some embodiments, each of the multiple guide sequences comprises different spacer sequences and different scaffold sequences. In some embodiments, each of the separate promoters comprises the same nucleotide sequence (*e.g.*, the U6 promoter sequence). In some embodiments, each of the separate promoters comprises a different nucleotide sequence (*e.g.*, the U6, H1, and/or 7SK promoter sequence).

[00114] In some embodiments, the U6 promoter comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 702:

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cgagtccaac acccgtggga atcccatggg caccatggcc cctcgctcca aaaatgcttt        60
cgcgtcgcgc agacactgct cggtagtttc ggggatcagc gtttgagtaa gagcccgcgt       120
ctgaaccctc cgcgccgccc cggccccagt ggaaagacgc gcaggcaaaa cgcaccacgt       180
gacggagcgt gaccgcgcgc cgagcgcgcg ccaaggtcgg gcaggaagag ggcctatttc       240
ccatgattcc ttcatatttg catatacgat acaaggctgt tagagagata attagaatta       300
atttgactgt aaacacaaag atattagtac aaaatacgtg acgtagaaag taataatttc       360
ttgggtagtt tgcagtttta aaattatgtt ttaaaatgga ctatcatatg cttaccgtaa       420
cttgaaagta tttcgatttc ttggctttat atatcttgtg gaaaggacga aa               472
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[00115] In some embodiments, the H1 promoter comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 703:

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gctcggcgcg cccatatttg catgtcgcta tgtgttctgg gaaatcacca taaacgtgaa        60
atgtctttgg atttgggaat cttataagtt ctgtatgaga ccacggta                   108
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[00116] In some embodiments, the 7SK promoter comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 704:

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tgacggcgcg ccctgcagta tttagcatgc cccacccatc tgcaaggcat tctggatagt      60
gtcaaaacag ccggaaatca agtccgttta tctcaaactt tagcattttg ggaataaatg     120
atatttgcta tgctggttaa attagatttt agttaaattt cctgctgaag ctctagtacg     180
ataagtaact tgacctaagt gtaaagttga gatttccttc aggtttatat agcttgtgcg     240
ccgcctgggt a
                                                             251
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[00117] In some embodiments, the U6 promoter is a hU6c promoter and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 705:

GAGGGCCTATTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTTAGAGAG
ATAATTGGAATTAATTTGACTGTAAACACAAAGATATTAGTACAAAATACGTGACGTAG
AAAGTAATAATTTCTTGGGTAGTTTGCAGTTTTAAAATTATGTTTTAAAATGGACTATCAT
ATGCTTACCGTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGGAAAGGAC
GAAACACC.

[00118] In some embodiments, the U6 promoter is a variant of the hU6c promoter. In some embodiments, the variant of the hU6c promoter comprises alternative nucleotides as compared to the sequence of SEQ ID NO: 705. In some embodiments, the variant of the hU6c promoter comprises fewer nucleotides as compared to the 249 nucleotides of SEQ ID NO: 705. In some embodiments, the variant of the hU6c promoter has fewer nucleotides in the nucleosome binding sequence of the hU6c promoter of SEQ ID NO: 705. In some embodiments, the variant of the hU6c promoter lacks all of or at least a portion of (e.g., at least 5, 10, 15, 20, 25, or 30 nucleotides) the nucleotides corresponding to nucleotides 96-125 of SEQ ID NO: 705. In some embodiments, the variant of the hU6c promoter lacks all of or at least a portion of (e.g., at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, or 60 nucleotides) the nucleotides corresponding to nucleotides 81-140 of SEQ ID NO: 705. In some embodiments, the variant of the hU6c promoter lacks all of or at least a portion of (e.g., at least 10, 20, 30, 40, 50, 60, 65, 70, 75, 80, or 85 nucleotides) the nucleotides corresponding to nucleotides 66-150 of SEQ ID NO: 705. In some embodiments, the variant of the hU6c promoter lacks all of or at least a portion of (e.g., at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 120 nucleotides) the nucleotides corresponding to nucleotides 51-170 of SEQ ID NO: 705. In some embodiments, the variant of the hU6c promoter lacks the nucleotides corresponding to nucleotides 96-125 of SEQ ID NO: 705. In some embodiments, the variant of the hU6c promoter comprises 129-219 nucleotides. In some embodiments, the variant of the hU6c promoter comprises 219 nucleotides. In some embodiments, the variant of the hU6c promoter comprises 189 nucleotides. In some embodiments, the variant of the hU6c promoter comprises 159 nucleotides. In some embodiments, the variant of the hU6c promoter comprises 129 nucleotides.

[00119] In some embodiments, the U6 promoter is hU6d30 and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 9001:
GAGGGCCTATTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTTAGAGAGATAATTGGAATTAATTTGACTGTAAACACAAAGATATAATTTCTTGGGTAGTTTGCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACCGTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGGAAAGGACGAAACACC.

[00120] In some embodiments, the U6 promoter is hU6d60 and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 9002:
GAGGGCCTATTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTTAGAGAGATAATTGGAATTAATTTGACGTTTGCAGTTTTAAAATTATGTTTTAAAATGGACTATCATATGCTTACCGTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGGAAAGGACGAAACACC.

[00121] In some embodiments, the U6 promoter is hU6d90 and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 9003:
GAGGGCCTATTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCTGTTAGAGAGATAATATTATGTTTTAAAATGGACTATCATATGCTTACCGTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGGAAAGGACGAAACACC.

[00122] In some embodiments, the U6 promoter is hU6d120 and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 9004:
GAGGGCCTATTTCCCATGATTCCTTCATATTTGCATATACGATACAAGGCGGACTATCATATGCTTACCGTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGGAAAGGACGAAACACC.

[00123] In some embodiments, the 7SK promoter is a 7SK2 promoter and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 706:
CTGCAGTATTTAGCATGCCCCACCCATCTGCAAGGCATTCTGGATAGTGTCAAAACAGCCGGAAATCAAGTCCGTTTATCTCAAACTTTAGCATTTTGGGAATAAATGATATTTGCTATGCTGGTTAAATTAGATTTTAGTTAAATTTCCTGCTGAAGCTCTAGTACGATAAGCAACTTGACCTAAGTGTAAAGTTGAGACTTCCTTCAGGTTTATATAGCTTGTGCGCCGCTTGGGTACCTC.

[00124] In some embodiments, the 7SK promoter is a variant of the 7SK2 promoter. In some embodiments, the variant of the 7SK2 promoter comprises alternative nucleotides as compared to the sequence of SEQ ID NO: 706. In some embodiments, the variant of the 7SK2 promoter e.g.,

comprises fewer nucleotides as compared to the 243 nucleotides of SEQ ID NO: 706. In some embodiments, the variant of the 7SK2 promoter has fewer nucleotides in the nucleosome binding sequence of the 7SK2 promoter of SEQ ID NO: 706. In some embodiments, the variant of the 7SK2 promoter lacks all of or at least a portion of (e.g., at least 5, 10, 15, 20, 25, or 30 nucleotides) the nucleotides corresponding to nucleotides 95-124 of SEQ ID NO: 706. In some embodiments, the variant of the 7SK2 promoter lacks all of or at least a portion of (e.g., at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, or 60 nucleotides) the nucleotides corresponding to nucleotides 81-140 of SEQ ID NO: 706. In some embodiments, the variant of the 7SK2 promoter lacks all of or at least a portion of (e.g., at least 10, 20, 30, 40, 50, 60, 65, 70, 75, 80, 85 or 90 nucleotides) the nucleotides corresponding to nucleotides 67-156 of SEQ ID NO: 706. In some embodiments, the variant of the 7SK2 promoter lacks all of or at least a portion of (e.g., at least 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, or 120 nucleotides) the nucleotides corresponding to nucleotides 52-171 of SEQ ID NO: 706. In some embodiments, the variant of the 7SK2 promoter comprises 123-213 nucleotides. In some embodiments, the variant of the 7SK2 promoter comprises 213 nucleotides. In some embodiments, the variant of the 7SK2 promoter comprises 183 nucleotides. In some embodiments, the variant of the 7SK2 promoter comprises 153 nucleotides. In some embodiments, the variant of the 7SK2 promoter comprises 123 nucleotides.

[00125] In some embodiments, the 7SK promoter is 7SKd30 and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 9006:
CTGCAGTATTTAGCATGCCCCACCCATCTGCAAGGCATTCTGGATAGTGTCAAAACAGCC
GGAAATCAAGTCCGTTTATCTCAAACTTTAGCATTTAAATTAGATTTTAGTTAAATTTCCT
GCTGAAGCTCTAGTACGATAAGCAACTTGACCTAAGTGTAAAGTTGAGACTTCCTTCAGG
TTTATATAGCTTGTGCGCCGCTTGGGTACCTC.

[00126] In some embodiments, the 7SK promoter is 7SKd60 and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 9007:
CTGCAGTATTTAGCATGCCCCACCCATCTGCAAGGCATTCTGGATAGTGTCAAAACAGCC
GGAAATCAAGTCCGTTTATCTTAAATTTCCTGCTGAAGCTCTAGTACGATAAGCAACTTG
ACCTAAGTGTAAAGTTGAGACTTCCTTCAGGTTTATATAGCTTGTGCGCCGCTTGGGTAC
CTC.

[00127] In some embodiments, the 7SK promoter is 7SKd90 and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 9008:
CTGCAGTATTTAGCATGCCCCACCCATCTGCAAGGCATTCTGGATAGTGTCAAAACAGCC
GGAAATAGCTCTAGTACGATAAGCAACTTGACCTAAGTGTAAAGTTGAGACTTCCTTCAG
GTTTATATAGCTTGTGCGCCGCTTGGGTACCTC.

[00128] In some embodiments, the 7SK promoter is 7SKd120 and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 9009:

[00129] CTGCAGTATTTAGCATGCCCCACCCATCTGCAAGGCATTCTGGATAGTGTCAGCAACTTGACCTAAGTGTAAAGTTGAGACTTCCTTCAGGTTTATATAGCTTGTGCGCCGCTTGGGTACCTC.In some embodiments, the H1 promoter is a H1m or mH1 promoter and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 707: AATATTTGCATGTCGCTATGTGTTCTGGGAAATCACCATAAACGTGAAATGTCTTTGGATTTGGGAATCTTATAAGTTCTGTATGAGACCACTCTTTCCC.

[00130] In some embodiments, the promoter is an M11 promoter and comprises a nucleotide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 708: ATATTTAGCATGTCGCTATGTGTTCTGGGAAACTTGACCTAAGTGTAAAGTTGAGATTTCCTTCAGGTTTATATAGTTCTGTATGAGACCACTCTTTCCC.

[00131] In some embodiments, the vector comprises multiple inverted terminal repeats (ITRs). These ITRs may be of an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, or AAV9 serotype. In some embodiments, the ITRs are of an AAV2 serotype. In some embodiments, the 5' ITR comprises a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of SEQ ID NO: 709: GGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCT.

[00132] In some embodiments, the 5' ITR comprises a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of SEQ ID NO: 939: CGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCT.

[00133] In some embodiments, the 3'ITR comprises a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of SEQ ID NO: 710: AGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGAGAGGGA.

[00134] In some embodiments, the 3' ITR comprises a sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of SEQ ID NO: 940:
AGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGG
CCGGGCGACCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAG
CGAGCGCGCAGAGAGGGAA.

[00135] In some embodiments, a vector comprising a single nucleic acid molecule encoding 1) two or more guide RNA comprising any one or more of the spacer sequences of **Table 6**; and 2) a SaCas9 (for any one or more of SEQ ID Nos: 1-159) or SluCas9 (for any one or more of SEQ ID NO: 200-292, 924-938, or 950-955) is provided. In some embodiments, the vector is an AAV vector. In some embodiments, the AAV vector is administered to a subject to treat DMD. In some embodiments, only one vector is needed due to the use of a particular guide sequence that is useful in the context of SaCas9 or SluCas9.

[00136] In some embodiments, the vector comprises a nucleic acid encoding a Cas9 protein (e.g., an SaCas9 or SluCas9 protein) and further comprises a nucleic acid encoding one or more single guide RNA(s). In some embodiments, the nucleic acid encoding the Cas9 protein is under the control of a CK8e promoter. In some embodiments, the nucleic acid encoding the guide RNA sequence is under the control of a hU6c promoter. In some embodiments, the vector is AAV9.

[00137] In some embodiments, the vector comprises multiple nucleic acids encoding more than one guide RNA. In some embodiments, the vector comprises two nucleic acids encoding two different guide RNA sequences.

[00138] In some embodiments, the vector comprises a nucleic acid encoding a Cas9 protein (e.g., an SaCas9 protein or SluCas9 protein), a nucleic acid encoding a first guide RNA, and a nucleic acid encoding a second guide RNA. In some embodiments, the vector does not comprise a nucleic acid encoding more than two guide RNAs. In some embodiments, the nucleic acid encoding the first guide RNA is the same as the nucleic acid encoding the second guide RNA. In some embodiments, the nucleic acid encoding the first guide RNA is different from the nucleic acid encoding the second guide RNA. In some embodiments, the vector comprises a single nucleic acid molecule, wherein the single nucleic acid molecule comprises a nucleic acid encoding a Cas9 protein, a nucleic acid encoding a first guide RNA, and a nucleic acid that is the reverse complement to the coding sequence for the second guide RNA. In some embodiments, the vector comprises a single nucleic acid molecule, wherein the single nucleic acid molecule comprises a nucleic acid encoding a Cas9 protein, a nucleic acid that is the reverse complement to the coding sequence for the first guide RNA, and a nucleic acid that is the reverse complement to the coding sequence for the second guide RNA. In some embodiments, the nucleic acid encoding a Cas9 protein (e.g., an SaCas9 or SluCas9 protein) is under the control of the CK8e promoter. In some embodiments, the first guide is under the control of the hU6c promoter and the second guide is under the control of the hU6c promoter. In some

embodiments, the first guide is under the control of the 7SK2 promoter, and the second guide is under the control of the H1m promoter. In some embodiments, the first guide is under the control of the H1m promoter, and the second guide is under the control of the 7SK2 promoter. In some embodiments, the first guide is under the control of the hU6c promoter, and the second guide is under the control of the H1m promoter. In some embodiments, the first guide is under the control of the H1m promoter, and the second guide is under the control of the hU6c promoter. In some embodiments, the nucleic acid encoding the Cas9 protein is: a) between the nucleic acids encoding the guide RNAs, b) between the nucleic acids that are the reverse complement to the coding sequences for the guide RNAs, c) between the nucleic acid encoding the first guide RNA and the nucleic acid that is the reverse complement to the coding sequence for the second guide RNA, d) between the nucleic acid encoding the second guide RNA and the nucleic acid that is the reverse complement to the coding sequence for the first guide RNA, e) 5' to the nucleic acids encoding the guide RNAs, f) 5' to the nucleic acids that are the reverse complements to the coding sequences for the guide RNAs, g) 5' to a nucleic acid encoding one of the guide RNAs and 5' to a nucleic acid that is the reverse complement to the coding sequence for the other guide RNA, h) 3' to the nucleic acids encoding the guide RNAs, i) 3' to the nucleic acids that are the reverse complements to the coding sequences for the guide RNAs, or j) 3' to a nucleic acid encoding one of the guide RNAs and 3' to a nucleic acid that is the reverse complement to the coding sequence for the other guide RNA. In some embodiments, any of the vectors disclosed herein is AAV9. In preferred embodiments, the AAV9 vector is less than 5 kb from ITR to ITR in size, inclusive of both ITRs. In particular embodiments, the AAV9 vector is less than 4.9 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV9 vector is less than 4.85 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV9 vector is less than 4.8 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV9 vector is less than 4.75 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV9 vector is less than 4.7 kb from ITR to ITR in size, inclusive of both ITRs. In some embodiments, the vector is between 3.9-5 kb, 4-5 kb, 4.2-5 kb, 4.4-5 kb, 4.6-5 kb, 4.7-5 kb, 3.9-4.9 kb, 4.2-4.9 kb, 4.4-4.9 kb, 4.7-4.9 kb, 3.9-4.85 kb, 4.2-4.85 kb, 4.4-4.85 kb, 4.6-4.85 kb, 4.7-4.85 kb, 4.7-4.9 kb, 3.9-4.8 kb, 4.2-4.8 kb, 4.4-4.8 kb or 4.6-4.8 kb from ITR to ITR in size, inclusive of both ITRs. In some embodiments, the vector is between 4.4-4.85 kb from ITR to ITR in size, inclusive of both ITRs. In some embodiments, the vector is an AAV9 vector.

[00139] In some embodiments, any of the vectors disclosed herein comprises a nucleic acid encoding at least a first guide RNA and a second guide RNA. In some embodiments, the nucleic acid comprises a spacer-encoding sequence for the first guide RNA, a scaffold-encoding sequence for the first guide RNA, a spacer-encoding sequence for the second guide RNA, and a scaffold-encoding sequence of the second guide RNA. In some embodiments, the spacer-encoding sequence (e.g., encoding any of the spacer sequences disclosed herein) for the first guide RNA is identical to the

spacer-encoding sequence for the second guide RNA. In some embodiments, the spacer-encoding sequence (e.g., encoding any of the spacer sequences disclosed herein) for the first guide RNA is different from the spacer-encoding sequence for the second guide RNA. In some embodiments, the scaffold-encoding sequence for the first guide RNA is identical to the scaffold-encoding sequence for the second guide RNA. In some embodiments, the scaffold-encoding sequence for the first guide RNA is different from the scaffold-encoding sequence for the nucleic acid encoding the second guide RNA. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises a sequence selected from the group consisting of SEQ ID Nos: 500-504 (for SaCas9) and 601 or 900-917 (for SluCas9), and the scaffold-encoding sequence for the second guide RNA comprises a different sequence selected from the group consisting of SEQ ID Nos: 500-504 (for SaCas9) and 601 or 900-917 (for SluCas9). In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 500, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 501. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 500, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 502. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 500, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 503. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 500, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 504. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 501, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 502. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 501, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 503. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 501, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 504. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 502, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 503. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 502, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 504. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 503, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 504. In particular embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 504, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 504. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 900. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 901. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 902. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 903. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 904. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 905. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 906. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 907. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 908. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 909. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 910. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 911. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 912. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 913. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 914. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 915. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 916. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 600, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 917. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 902. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 903. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 904. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 905. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 906. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 907. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 908. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 909. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 910. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 911. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 912. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 913. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 914. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 915. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 916. In some embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 917. In particular embodiments, the scaffold-encoding sequence for the first guide RNA comprises the sequence of SEQ ID NO: 901, and the scaffold-encoding sequence for the second guide RNA comprises the sequence of SEQ ID NO: 901. In some embodiments, the spacer encoding sequence for the first guide RNA is the same as the spacer-encoding sequence in the second guide RNA, and the scaffold-encoding sequence for the first guide RNA is different from the scaffold-encoding sequence in the nucleic acid encoding the second guide RNA.

[00140] In some embodiments, the AAV vector is in a particular configuration. Some examples of these AAV vector configurations are provided herein, and the order of elements in these exemplary vectors are referenced in a 5' to 3' manner with respect to the plus strand. For these configurations, it should be understood that the recited elements may not be directly contiguous, and that one or more nucleotides or one or more additional elements may be present between the recited elements. However, in some embodiments, it is possible that no nucleotides or no additional elements are present between the recited elements. Also, unless otherwise stated, "a promoter for expression of element X" means that the promoter is oriented in a manner to facilitate expression of the recited element X. In addition, unless otherwise stated, references to an "sgRNA scaffold sequence" or "a guide RNA scaffold sequence" are synonymous with "a nucleotide sequence/nucleic acid encoding an sgRNA scaffold sequence" or "a nucleotide sequence/nucleic acid encoding a guide RNA scaffold sequence." In some embodiments, the disclosure provides for a nucleic acid encoding an SaCas9 (e.g., an SaCas9-KKH) or SluCas9. In some embodiments, the nucleic acid encodes for one or more nuclear localization signals (e.g., the SV40 NLS and/or the c-Myc NLS) on the C-terminus of the encoded SaCas9 or SluCas9. In some embodiments, the nucleic acid encodes for one or more NLSs (e.g., the SV40 NLS and/or the c-Myc NLS) on the C-terminus of the encoded SaCas9 or SluCas9, and the nucleic acid does not encode for an NLS on the N-terminus of the encoded SaCas9 or SluCas9. In some embodiments, the nucleic acid encodes for one or more nuclear localization signals (e.g., the SV40 NLS and/or the c-Myc NLS) on the N-terminus of the encoded SaCas9 or SluCas9. In some embodiments, the nucleic acid encodes for one or more NLSs (e.g., the SV40 NLS and/or the c-Myc NLS) on the N-terminus of the encoded SaCas9 or SluCas9, and the nucleic acid does not encode for an NLS on the C-terminus of the encoded SaCas9 or SluCas9. In some embodiments, the nucleic acid encodes for one or more nuclear localization signals (e.g., the SV40 NLS and/or the c-Myc NLS) on the C-terminus of the encoded SaCas9 or SluCas9 and also encodes for one or more NLSs on the N-terminus of the encoded SaCas9 or SluCas9 (e.g., the SV40 NLS and/or the c-Myc NLS). In some embodiments, the nucleic acid encodes one NLS. In some embodiments, the nucleic

acid encodes two NLSs. In some embodiments, the nucleic acid encodes three NLSs. The one, two, or three NLS may all be C-terminal, N-terminal, or any combination of C- and N-terminal. The NLS may be fused/attached directly to the C- or N-terminus or to another NLS, or may be fused/attached indirectly attached through a linker. In some embodiments, an additional domain may be: a) fused to the N- or C-terminus of the Cas protein (e.g., a Cas9 protein), b) fused to the N-terminus of an NLS fused to the N-terminus of a Cas protein, or c) fused to the C-terminus of an NLS fused to the C-terminus of a Cas protein, with or without a linker. In some embodiments, an NLS is fused to the N- and/or C-terminus of the Cas protein by means of a linker. In some embodiments, an NLS is fused to the N-terminus of an N-terminally-fused NLS on a Cas protein by means of a linker, and/or an NLS is fused to the C-terminus of a C-terminally fused NLS on a Cas protein by means of a linker. In some embodiments, the linker is GSVD (SEQ ID NO: 550) or GSGS (SEQ ID NO: 551). In some embodiments, the Cas protein comprises a c-Myc NLS fused to the N-terminus of the Cas protein (or to an N-terminally-fused NLS on the Cas protein), optionally by means of a linker. In some embodiments, the Cas protein comprises an SV40 NLS fused to the C-terminus of the Cas protein (or to a C-terminally-fused NLS on the Cas protein), optionally by means of a linker. In some embodiments, the Cas protein comprises a nucleoplasmin NLS fused to the C-terminus of the Cas protein (or to a C-terminally-fused NLS on the Cas protein), optionally by means of a linker. In some embodiments, the Cas protein comprises: a) a c-Myc NLS fused to the N-terminus of the Cas protein, optionally by means of a linker, b) an SV40 NLS fused to the C-terminus of the Cas protein, optionally by means of a linker, and c) a nucleoplasmin NLS fused to the C-terminus of the SV40 NLS, optionally by means of a linker. In some embodiments, the Cas protein comprises: a) a c-Myc NLS fused to the N-terminus of the Cas protein, optionally by means of a linker, b) a nucleoplasmin NLS fused to the C-terminus of the Cas protein, optionally by means of a linker, and c) an SV40 NLS fused to the C-terminus of the nucleoplasmin NLS, optionally by means of a linker. In some embodiments, a c-myc NLS is fused to the N-terminus of the Cas and an SV40 NLS and/or nucleoplasmin NLS is fused to the C-terminus of the Cas. In some embodiments, a c-myc NLS is fused to the N-terminus of the Cas (e.g., by means of a linker such as GSVD), an SV40 NLS is fused to the C-terminus of the Cas (e.g., by means of a linker such as GSGS), and a nucleoplasmin NLS is fused to the C-terminus of the SV-40 NLS (e.g., by means of a linker such as GSGS).

[00141] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first sgRNA scaffold sequence, the reverse complement of a nucleic acid encoding a first sgRNA guide sequence, the reverse complement of a promoter for expression of the nucleic acid encoding the first sgRNA, a promoter for expression of a nucleic acid encoding SaCas9 (e.g., CK8e), a nucleic acid encoding SaCas9, a polyadenylation sequence, a promoter for expression of a second sgRNA, a second sgRNA guide sequence, and a second sgRNA scaffold sequence. In some embodiments, the first sgRNA is associated with weaker expression than

the second sgRNA when compared individually in a sgRNA expression assay, e.g., in an assay in which each guide is separately assessed (i.e., not in the same construct) using the same promoter, same concentration of genetic material/vector/RNP in substantially the same conditions (e.g., time, pH, temperature, buffer conditions). In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA is any of the hU6c promoters disclosed herein. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 705. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 9001. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 9002. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 9003. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 9004. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA is any of the 7SK2 promoters disclosed herein. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 705. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 9006. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 9007. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 9008. In some embodiments the promoter for expression of the nucleic acid encoding the first sgRNA comprises SEQ ID NO: 9009. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA is any of the hU6c promoters disclosed herein. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 705. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 9001. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 9002. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 9003. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 9004. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA is any of the 7SK2 promoters disclosed herein. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 705. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 9006. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 9007. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO: 9008. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA comprises SEQ ID NO:

9009. In some embodiments the promoter for expression of the nucleic acid encoding the second sgRNA is any of the H1m promoters disclosed herein. In some embodiments, the promoter for SaCas9 is the CK8e promoter. In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to a nucleic acid sequence encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to two nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to three nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the one or more NLSs is an SV40 NLS. In some embodiments, the one or more NLSs is a c-Myc NLS. In some embodiments, the one or more NLSs is a nucleoplasmin NLS. In some embodiments, the NLS is fused to the SaCas9 with a linker.

[00142] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first sgRNA scaffold sequence, the reverse complement of a nucleic acid encoding a first sgRNA guide sequence, the reverse complement of an hU6c promoter for expression of the nucleic acid encoding the first sgRNA, a promoter for expression of a nucleic acid encoding SaCas9 (e.g., CK8e), a nucleic acid encoding SaCas9, a polyadenylation sequence, an hU6c promoter for expression of a second sgRNA, a second sgRNA guide sequence, and a second sgRNA scaffold sequence. In some embodiments, the first sgRNA and the second sgRNA are selected from **Table 6**. In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to a nucleic acid sequence encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to two nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to three nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the one or more NLSs is an SV40 NLS. In some embodiments, the one or more NLSs is a c-Myc NLS. In some embodiments, the NLS is fused to the SaCas9 with a linker.

[00143] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first sgRNA scaffold sequence, the reverse complement of a nucleic acid encoding a first sgRNA guide sequence, the reverse complement of an hU6c promoter for expression of the nucleic acid encoding the first sgRNA, a promoter for expression of a nucleic acid encoding SaCas9 (e.g., CK8e), a nucleic acid encoding SaCas9, a polyadenylation sequence, an 7SK promoter for expression of a second sgRNA, a second sgRNA guide sequence, and a second sgRNA scaffold sequence. In some embodiments, the first sgRNA and the second sgRNA are selected from **Table 6**. In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to a nucleic acid sequence encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to two nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding SaCas9 is fused to three nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some

embodiments, the one or more NLSs is an SV40 NLS. In some embodiments, the one or more NLSs is a c-Myc NLS. In some embodiments, the NLS is fused to the SaCas9 with a linker.

[00144] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first sgRNA scaffold sequence, the reverse complement of a nucleic acid encoding a first sgRNA guide sequence, the reverse complement of an hU6c promoter for expression of the nucleic acid encoding the first sgRNA, a promoter for expression of a nucleic acid encoding Cas9 (e.g., CK8e), a nucleic acid encoding Cas9, a polyadenylation sequence, an H1m promoter for expression of a second sgRNA, a second sgRNA guide sequence, and a second sgRNA scaffold sequence. In some embodiments, the first sgRNA and the second sgRNA are selected from **Table 6**. In some embodiments, the nucleic acid sequence encoding Cas9 is fused to a nucleic acid sequence encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding Cas9 is fused to two nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding Cas9 is fused to three nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the one or more NLSs is an SV40 NLS. In some embodiments, the one or more NLSs is a c-Myc NLS. In some embodiments, the NLS is fused to the Cas9 with a linker.

[00145] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first sgRNA scaffold sequence, the reverse complement of a nucleic acid encoding a first sgRNA guide sequence, the reverse complement of an 7SK promoter for expression of the nucleic acid encoding the first sgRNA, a promoter for expression of a nucleic acid encoding Cas9 (e.g., CK8e), a nucleic acid encoding Cas9, a polyadenylation sequence, an H1m promoter for expression of a second sgRNA, a second sgRNA guide sequence, and a second sgRNA scaffold sequence. In some embodiments, the first sgRNA and the second sgRNA are selected from **Table 6**. In some embodiments, the nucleic acid sequence encoding Cas9 is fused to a nucleic acid sequence encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding Cas9 is fused to two nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the nucleic acid sequence encoding Cas9 is fused to three nucleic acid sequences each encoding a nuclear localization sequence (NLS). In some embodiments, the one or more NLSs is an SV40 NLS. In some embodiments, the one or more NLSs is a c-Myc NLS. In some embodiments, the NLS is fused to the Cas9 with a linker.

[00146] In some embodiments, the disclosure provides for a composition comprising at least two nucleic acids. In some embodiments, the composition comprises at least two nucleic acid molecules, wherein the first nucleic acid molecule comprises a sequence encoding any of the endonucleases disclosed herein (e.g., a SaCas9, SluCas9, or a sRGN), wherein the second nucleic acid molecule encodes a first guide RNA and a second guide RNA, wherein the first guide RNA and the second guide RNA are not the same sequence, and wherein the second nucleic acid molecule does not encode an endonuclease. In some embodiments, the first nucleic acid molecule also encodes a copy of the

first guide RNA and a copy of the second guide RNA. In some embodiments, the first nucleic acid molecule does not encode any guide RNAs. In some embodiments, the second nucleic acid molecule encodes two copies of the first guide RNA and two copies of the second guide RNA. In some embodiments, the second nucleic molecule encodes two copies of the first guide RNA, and one copy of the second guide RNA. In some embodiments, the second nucleic acid molecule encodes one copy of the first guide RNA, and two copies of the second guide RNA. In some embodiments, the second nucleic acid molecule comprises two copies of the first guide RNA, and three copies of the second guide RNA. In some embodiments, the second nucleic acid molecule comprises three copies of the first guide RNA, and two copies of the second guide RNA. In some embodiments, the second nucleic acid does not encode a Cas protein. In some embodiments, the second nucleic acid molecule encodes three copies of the first guide RNA and three copies of the second guide RNA. In some embodiments, the first nucleic acid molecule comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first guide RNA scaffold sequence, the reverse complement of a nucleotide sequence encoding the first guide RNA sequence, the reverse complement of a promoter for expression of the nucleotide sequence encoding the first guide RNA sequence, a promoter for expression of a nucleotide sequence encoding the endonuclease, a nucleotide sequence encoding an endonuclease, a polyadenylation sequence, a promoter for expression of the second guide RNA in the same direction as the promoter for the endonuclease, the second guide RNA sequence, and a second guide RNA scaffold sequence. In some embodiments, the promoter for expression of the nucleotide sequence encoding the first guide RNA sequence in the first nucleic acid molecule is a U6 promoter and the promoter for expression of the nucleotide sequence encoding the second guide RNA in the first nucleic acid molecule is a U6 promoter.

[00147] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: a promoter for expression of a nucleic acid encoding a first sgRNA, a nucleic acid encoding the first sgRNA guide sequence, the first sgRNA scaffold sequence, a promoter for expression of Cas9 (e.g., CK8e), a nucleic acid encoding Cas9, a polyadenylation sequence, a promoter for expression of a second sgRNA, the second sgRNA guide sequence, and a second sgRNA scaffold sequence. See **Fig. 5A** at "Design 1".

[00148] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first sgRNA scaffold sequence, the reverse complement of a nucleic acid encoding a first sgRNA guide sequence, the reverse complement of a promoter for expression of the nucleic acid encoding the first sgRNA, a promoter for expression of a nucleic acid encoding Cas9 (e.g., CK8e), a nucleic acid encoding Cas9, a polyadenylation sequence, a promoter for expression of a second sgRNA, a second sgRNA guide sequence, and a second sgRNA scaffold sequence. See **Fig. 5A** at "Design 2".

[00149] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: a promoter for expression of a nucleic acid encoding a first sgRNA, a nucleic acid encoding

the first sgRNA guide sequence, a first sgRNA scaffold sequence, a promoter for expression of a second sgRNA, a second sgRNA guide sequence, and a second sgRNA scaffold sequence, a promoter for Cas9 (e.g., CK8e), a nucleic acid encoding Cas9, and a polyadenylation sequence. See **Fig. 5A** at "Design 3".

[00150] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: a promoter for expression of a nucleic acid encoding Cas9 (e.g., CK8e), a nucleic acid encoding Cas9, a polyadenylation sequence, a promoter for expression of the nucleic acid encoding a first guide RNA, a nucleic acid encoding the first sgRNA guide sequence, a first sgRNA scaffold sequence, a promoter for expression of the second sgRNA, a second sgRNA guide sequence, and a second sgRNA scaffold sequence. See **Fig. 5A** at "Design 4".

[00151] In some embodiments, the AAV vector comprises from 5' to 3' with respect to the plus strand: a first sgRNA scaffold sequence (e.g., V5), a nucleic acid encoding a first sgRNA guide sequence (e.g., Slu3 or Slu7), a promoter (e.g., U6) for expression of the nucleic acid encoding the first sgRNA guide sequence, a promoter (e.g., CK8e) for expression (in the opposite direction of expression of the nucleic acid encoding the first sgRNA guide sequence) of a nucleic acid encoding a SluCas9, a nucleic acid encoding a first NLS, a nucleic acid encoding a SluCas9, a nucleic acid encoding a second NLS, a nucleic acid encoding a third NLS, a promoter (e.g., U6) for expression (in the same direction as expression of the nucleic acid encoding the SluCas9) of a second sgRNA guide sequence (e.g., Slu 7 or Slu 3), a nucleic acid encoding the second sgRNA guide sequence, and a second sgRNA scaffold sequence (e.g., V5). See **Fig. 5B** at "Design 5" and "Design 6". Designs 5 and 6 are specific versions of Design 2, as described herein.

[00152] In a particular embodiment, the AAV vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first V5 scaffold sequence, the reverse complement of a nucleic acid encoding a Slu3 guide RNA sequence selected from SEQ ID NOs: 217 or 950-955, the reverse complement of a U6 promoter for expression of the nucleic acid encoding the Slu3 guide RNA sequence, a CK8e promoter for expression (in the opposite direction of expression of the nucleic acid encoding the Slu3 sgRNA guide sequence) of a nucleic acid encoding a SluCas9, a nucleic acid encoding a c-Myc NLS, a nucleic acid encoding a SluCas9, a nucleic acid encoding a SV40 NLS, a nucleic acid encoding a NP NLS, a U6 promoter for expression (in the same direction as expression of the nucleic acid encoding the SluCas9) of a Slu7 guide RNA sequence of SEQ ID NO: 275, a nucleic acid encoding the Slu7 guide RNA sequence, and a second V5 scaffold sequence. See **Fig. 5B** at "Design 5" and "Design 6". Designs 5 and 6 are specific versions of Design 2, as described herein.

[00153] In another particular embodiment, the AAV vector comprises from 5' to 3' with respect to the plus strand: the reverse complment of a first V5 scaffold sequence, the reverse complement of a nucleic acid encoding a Slu7 guide RNA sequence of SEQ ID NO: 275, the reverse complement of a U6 promoter for expression of the nucleic acid encoding the Slu7 guide RNA sequence, a CK8e promoter for expression (in the opposite direction of expression of the nucleic acid encoding the Slu7

sgRNA guide sequence) of a nucleic acid encoding a SluCas9, a nucleic acid encoding a c-Myc NLS, a nucleic acid encoding a SluCas9, a nucleic acid encoding a SV40 NLS, a nucleic acid encoding a NP NLS, a U6 promoter for expression (in the same direction as expression of the nucleic acid encoding the SluCas9) of a Slu3 guide RNA sequence selected from SEQ ID NOs: 217 or 950-955, a nucleic acid encoding the Slu3 guide RNA sequence, and a second V5 scaffold sequence. See **Fig. 5B** at "Design 5" and "Design 6". Designs 5 and 6 are specific versions of Design 2, as described herein.

[00154] In some embodiments, the first nucleic acid molecule is in a first vector (e.g., AAV9), and the second nucleic acid is in a separate second vector. In some embodiments, the first vector is AAV9. In some embodiments, the second vector is AAV9. In preferred embodiments, the AAV9 vector is less than 5 kb from ITR to ITR in size, inclusive of both ITRs. In particular embodiments, the AAV9 vector is less than 4.9 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV9 vector is less than 4.85 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV9 vector is less than 4.8 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV9 vector is less than 4.75 kb from ITR to ITR in size, inclusive of both ITRs. In further embodiments, the AAV9 vector is less than 4.7 kb from ITR to ITR in size, inclusive of both ITRs. In some embodiments, the second vector comprises from 5' to 3' with respect to the plus strand: a promoter for expression of a first copy of a first guide RNA (e.g., a U6 promoter), a first copy of a nucleotide sequence encoding a first guide RNA, a first copy of a nucleotide sequence encoding a first guide RNA scaffold, a promoter for expression of a second copy of the first guide RNA (e.g., a H1 promoter), a second copy of the nucleotide sequence encoding the first guide RNA, a second copy of the nucleotide sequence encoding the first guide RNA scaffold, a promoter for expression of a second guide RNA (e.g., a 7SK promoter), a nucleotide sequence encoding a second guide RNA, and a nucleotide sequence encoding a second guide RNA scaffold. In some embodiments, the second vector comprises from 5' to 3' with respect to the plus strand: a promoter for expression of a first guide RNA (e.g., a U6 promoter), a nucleotide sequence encoding a first guide RNA, a nucleotide sequence encoding a first guide RNA scaffold, a promoter for expression of a second guide RNA (e.g., a 7SK promoter), a nucleotide sequence encoding a second guide RNA, and a nucleotide sequence encoding a second guide RNA scaffold. In some embodiments, the second vector comprises a stuffer sequence (e.g., a 3'UTR desmin sequence) between the nucleotide sequence encoding the first guide scaffold sequence and the promoter for expression of the second guide sequence. In some embodiments, the second vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a nucleotide sequence encoding a scaffold for a first guide RNA, the reverse complement of a nucleotide sequence encoding a first guide RNA, the reverse complement of a promoter for expression of the first guide RNA (e.g., a U6c promoter), a promoter for expression of a second guide RNA (e.g., a U6c promoter), a nucleotide sequence encoding a second guide RNA, and a nucleotide sequence encoding a second guide RNA scaffold. In some embodiments, the second vector comprises a stuffer sequence (e.g., a 3'UTR

desmin sequence) between the reverse complement of the promoter for expression of the first guide RNA and the promoter for expression of the second guide RNA. In some embodiments, the second vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a nucleotide sequence encoding a first copy of a first guide RNA scaffold, the reverse complement of a nucleotide sequence encoding a first copy of the first guide RNA, the reverse complement of a promoter for expression of the first copy of the first guide RNA (e.g., a 7SK2 promoter), the reverse complement of a second copy of the nucleotide sequence encoding the first guide RNA scaffold, the reverse complement of a second copy of the nucleotide sequence encoding the first guide RNA, the reverse complement of a promoter for expression of the second copy of the nucleotide sequence encoding the first guide RNA (e.g., a hU6c promoter), a promoter for expression of a first copy of a second guide RNA (e.g., a hU6c promoter), a first copy of a nucleotide sequence encoding a second guide RNA, a first copy of a nucleotide sequence encoding a second guide RNA scaffold, a promoter for expression of a second copy of the second guide RNA (e.g., a 7Sk2 promoter), a second copy of the nucleotide sequence encoding the second guide RNA, and a second copy of the nucleotide sequence encoding the second guide RNA scaffold. In some embodiments, the second vector comprises a stuffer sequence (e.g., a 3'UTR desmin sequence) between the reverse complement of the promoter for expression of the second copy of the first guide RNA and the promoter for expression of the first copy of the second guide RNA. In some embodiments, the second vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a nucleotide sequence encoding a first copy of a first guide RNA scaffold, the reverse complement of a first copy of a nucleotide sequence encoding the first guide RNA, the reverse complement of a promoter for expression of the first copy of the first guide RNA (e.g., a 7SK2 promoter), the reverse complement of a first copy of a nucleotide sequence encoding a second guide RNA scaffold, the reverse complement of a nucleotide sequence encoding the first copy of the second guide RNA, the reverse complement of a promoter for expression of the first copy of the second guide RNA (e.g., a hU6c promoter), a promoter for expression of a second copy of the second guide RNA (e.g., a hU6c promoter), a second copy of the nucleotide sequence encoding the second guide RNA, a second copy of the nucleotide sequence encoding the second guide RNA scaffold, a promoter for expression of a second copy of the first guide RNA (e.g., a 7SK2 promoter), a second copy of the nucleotide sequence encoding the first guide RNA, and a second copy of the nucleotide sequence encoding the first guide RNA scaffold. In some embodiments, the second vector comprises a stuffer sequence (e.g., a 3'UTR desmin sequence) between the reverse complement of the promoter for expression of the first copy of the second guide RNA and the promoter for expression of the second copy of the first guide RNA. In some embodiments, the second vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a nucleotide sequence encoding a first guide RNA scaffold, the reverse complement of a nucleotide sequence encoding a first guide RNA, the reverse complement of a promoter for expression of a first guide RNA (e.g., a hU6c promoter), a promoter for expression of a second guide RNA (e.g., a hU6c promoter), a nucleotide sequence encoding a second guide RNA, and a nucleotide sequence encoding a second guide RNA scaffold. In some embodiments, the second vector comprises a stuffer sequence (e.g., a 3'UTR desmin sequence) between the reverse complement of the promoter for expression of the first guide RNA and the promoter for expression of the second guide RNA. In particular embodiments, the first guide RNA is different from the second guide RNA. In some embodiments, the first guide RNA comprises a sequence of **Table 6** and the second guide RNA comprises a different sequence from **Table 6**.

[00155] In some embodiments, if the composition comprises one or more nucleic acids encoding an RNA-targeted endonuclease and one or more guide RNAs, the one or more nucleic acids are designed such that they express the one or more guide RNAs at an equivalent or higher level (e.g., a greater number of expressed transgene copies) as compared to the expression level of the RNA-targeted endonuclease. In some embodiments, the one or more nucleic acids are designed such that they express (e.g., on average in 100 cells) the one or more guide RNAs at least a 1.1, 1.2, 1.3, 1.4, or 1.5 times higher level (e.g., a greater number of expressed transgene copies) as compared to the expression level of the RNA-targeted endonuclease. In some embodiments, the one or more nucleic acids are designed such that they express the one or more guide RNAs at 1.01-1.5, 1.01-1.4, 1.01-1.3, 1.01-1.2, 1.01-1.1, 1.1-2.0, 1.1-1.8, 1.1-1.6, 1.1-1.4, 1.1-1.3, 1.2-2.0, 1.2-1.8, 1.2-1.6, 1.2-1.4, 1.4-2.0, 1.4-1.8, 1.4-1.6, 1.6-2.0, 1.6-1.8, or 1.8-2.0 times higher level (e.g., a greater number of expressed transgene copies) as compared to the expression level of the RNA-targeted endonuclease. In some embodiments, the one or more guide RNAs are designed to express a higher level than the RNA-targeted endonuclease by: a) utilizing one or more regulatory elements (e.g., promoters or enhancers) that express the one or more guide RNAs at a higher level as compared to the regulatory elements (e.g., promoters or enhancers) for expression of the RNA-targeted endonuclease; and/or b) expressing more copies of one or more of the guide RNAs as compared to the number of copies of the RNA-targeted endonuclease (e.g., 2x or 3x as many copies of the nucleotide sequences encoding the one or more guide RNAs as compared to the number of copies of the nucleotide sequences encoding the RNA-targeted endonuclease). For example, in some embodiments, the composition comprises multiple nucleic acid molecules (e.g., in multiple vectors), wherein for every nucleotide sequence encoding an RNA-targeted endonuclease in the nucleic acid molecules in the composition, there are two or three copies of the nucleotide sequence encoding the guide RNA in the nucleic acid molecules in the composition. In some embodiments, the composition comprises a first guide RNA and a second guide RNA, wherein the first guide RNA and the second guide RNA are not the same (e.g., any of the guide RNA pairs disclosed herein), and for every nucleotide sequence encoding an RNA-targeted endonuclease in the nucleic acid molecules in the composition, there are two or three copies of the nucleotide sequence encoding the first guide RNA and/or the second guide RNA.

Endonucleases

[00156] In some embodiments, any of the nucleic acids disclosed herein encodes an RNA-targeted endonuclease. In some embodiments, the RNA-targeted endonuclease has cleavase activity, which can also be referred to as double-strand endonuclease activity. In some embodiments, the RNA-targeted endonuclease comprises a Cas nuclease. Examples of Cas9 nucleases include those of the type II CRISPR systems.

[00157] In some embodiments, the Cas protein comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 941 (designated herein as SpCas9):
MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEAT
RLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDE
VAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQL
VQTYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNF
KSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKA
PLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKP
ILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEK
ILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNE
KVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKE
DYFKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDRE
MIEERLKTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRN
FMQLIHDDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRH
KPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQ
NGRDMYVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKK
MKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRM
NTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKY
PKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIET
NGETGEIVWDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDW
DPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKE
VKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPED
NEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTL
TNLGAPAAFKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD.

[00158] In some embodiments, the nucleic acid encoding SaCas9 encodes an SaCas9 comprising an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 711:
KRNYILGLDIGITSVGYGIIDYETRDVIDAGVRLFKEANVENNEGRRSKRGARRLKRRRRHRI
QRVKKLLFDYNLLTDHSELSGINPYEARVKGLSQKLSEEEFSAALLHLAKRRGVHNVNEVEE

DTGNELSTKEQISRNSKALEEKYVAELQLERLKKDGEVRGSINRFKTSDYVKEAKQLLKVQK
AYHQLDQSFIDTYIDLLETRRTYYEGPGEGSPFGWKDIKEWYEMLMGHCTYFPEELRSVKYA
YNADLYNALNDLNNLVITRDENEKLEYYEKFQIIENVFKQKKKPTLKQIAKEILVNEEDIKGY
RVTSTGKPEFTNLKVYHDIKDITARKEIIENAELLDQIAKILTIYQSSEDIQEELTNLNSELTQEE
IEQISNLKGYTGTHNLSLKAINLILDELWHTNDNQIAIFNRLKLVPKKVDLSQQKEIPTTLVDD
FILSPVVKRSFIQSIKVINAIIKKYGLPNDIIIELAREKNSKDAQKMINEMQKRNRQTNERIEEIIR
TTGKENAKYLIEKIKLHDMQEGKCLYSLEAIPLEDLLNNPFNYEVDHIIPRSVSFDNSFNNKVL
VKQEENSKKGNRTPFQYLSSSDSKISYETFKKHILNLAKGKGRISKTKKEYLLEERDINRFSVQ
KDFINRNLVDTRYATRGLMNLLRSYFRVNNLDVKVKSINGGFTSFLRRKWKFKKERNKGYK
HHAEDALIIANADFIFKEWKKLDKAKKVMENQMFEEKQAESMPEIETEQEYKEIFITPHQIKHI
KDFKDYKYSHRVDKKPNRELINDTLYSTRKDDKGNTLIVNNLNGLYDKDNDKLKKLINKSP
EKLLMYHHDPQTYQKLKLIMEQYGDEKNPLYKYYEETGNYLTKYSKKDNGPVIKKIKYYGN
KLNAHLDITDDYPNSRNKVVKLSLKPYRFDVYLDNGVYKFVTVKNLDVIKKENYYEVNSKC
YEEAKKLKKISNQAEFIASFYNNDLIKINGELYRVIGVNNDLLNRIEVNMIDITYREYLENMN
DKRPPRIIKTIASKTQSIKKYSTDILGNLYEVKSKKHPQIIKKG.

[00159] In some embodiments, the nucleic acid encoding SaCas9 comprises the nucleic acid of SEQ ID NO: 9014:

[00160] AAGCGCAATTACATCCTGGGCCTGGATATCGGCATCACCTCCGTGGGCTACG
GCATCATCGACTATGAGACACGGGATGTGATCGACGCCGGCGTGAGACTGTTCAAGGAG
GCCAACGTGGAGAACAATGAGGGCCGGCGGAGCAAGAGGGGAGCAAGGCGCCTGAAGC
GGAGAAGGCGCCACAGAATCCAGAGAGTGAAGAAGCTGCTGTTCGATTACAACCTGCTG
ACCGACCACTCCGAGCTGTCTGGCATCAATCCTTATGAGGCCCGGGTGAAGGGCCTGTCC
CAGAAGCTGTCTGAGGAGGAGTTTTCTGCCGCCCTGCTGCACCTGGCAAAGAGGAGAGG
CGTGCACAACGTGAATGAGGTGGAGGAGGACACCGGCAACGAGCTGAGCACAAAGGAG
CAGATCAGCCGCAATTCCAAGGCCCTGGAGGAGAAGTATGTGGCCGAGCTGCAGCTGGA
GCGGCTGAAGAAGGATGGCGAGGTGAGGGGCTCCATCAATCGCTTCAAGACCTCTGACT
ACGTGAAGGAGGCCAAGCAGCTGCTGAAGGTGCAGAAGGCCTACCACCAGCTGGATCAG
AGCTTTATCGATACATATATCGACCTGCTGGAGACCAGGCGCACATACTATGAGGGACC
AGGAGAGGGCTCCCCCTTCGGCTGGAAGGACATCAAGGAGTGGTACGAGATGCTGATGG
GCCACTGCACCTATTTTCCAGAGGAGCTGAGATCCGTGAAGTACGCCTATAACGCCGATC
TGTACAACGCCCTGAATGACCTGAACAACCTGGTCATCACCAGGGATGAGAACGAGAAG
CTGGAGTACTATGAGAAGTTCCAGATCATCGAGAACGTGTTCAAGCAGAAGAAGAAGCC
TACACTGAAGCAGATCGCCAAGGAGATCCTGGTGAACGAGGAGGACATCAAGGGCTACC
GCGTGACCAGCACAGGCAAGCCAGAGTTCACCAATCTGAAGGTGTATCACGATATCAAG
GACATCACAGCCCGGAAGGAGATCATCGAGAACGCCGAGCTGCTGGATCAGATCGCCAA
GATCCTGACCATCTATCAGAGCTCCGAGGACATCCAGGAGGAGCTGACCAACCTGAATA
GCGAGCTGACACAGGAGGAGATCGAGCAGATCAGCAATCTGAAGGGCTACACCGGCAC

ACACAACCTGTCCCTGAAGGCCATCAATCTGATCCTGGATGAGCTGTGGCACACAAACGACAATCAGATCGCCATCTTTAACAGGCTGAAGCTGGTGCCAAAGAAGGTGGACCTGAGCCAGCAGAAGGAGATCCCAACCACACTGGTGGACGATTTCATCCTGTCCCCCGTGGTGAAGCGGAGCTTCATCCAGAGCATCAAAGTGATCAACGCCATCATCAAGAAGTACGGCCTGCCCAATGATATCATCATCGAGCTGGCCAGGGAGAAGAACTCTAAGGACGCCCAGAAGATGATCAATGAGATGCAGAAGAGGAACCGCCAGACCAATGAGCGGATCGAGGAGATCATCAGAACCACAGGCAAGGAGAACGCCAAGTACCTGATCGAGAAGATCAAGCTGCACGATATGCAGGAGGGCAAGTGTCTGTATAGCCTGGAGGCCATCCCTCTGGAGGACCTGCTGAACAATCCATTCAACTACGAGGTGGATCACATCATCCCCCGGAGCGTGAGCTTCGACAATTCCTTTAACAATAAGGTGCTGGTGAAGCAGGAGGAGAACTCTAAGAAGGGCAATAGGACCCCTTTCCAGTACCTGTCTAGCTCCGATTCTAAGATCAGCTACGAGACCTTCAAGAAGCACATCCTGAATCTGGCCAAGGGCAAGGGCCGCATCTCTAAGACCAAGAAGGAGTACCTGCTGGAGGAGCGGGACATCAACAGATTCAGCGTGCAGAAGGACTTCATCAACCGGAATCTGGTGGACACCAGATACGCCACACGCGGCCTGATGAATCTGCTGCGGTCCTATTTCAGAGTGAACAATCTGGATGTGAAGGTGAAGAGCATCAACGGCGGCTTCACCTCCTTTCTGCGGAGAAAGTGGAAGTTTAAGAAGGAGAGAAACAAGGGCTATAAGCACCACGCCGAGGATGCCCTGATCATCGCCAATGCCGACTTCATCTTTAAGGAGTGGAAGAAGCTGGACAAGGCCAAGAAAGTGATGGAGAACCAGATGTTCGAGGAGAAGCAGGCCGAGAGCATGCCCGAGATCGAGACCGAGCAGGAGTACAAGGAGATTTTCATCACACCTCACCAGATCAAGCACATCAAGGACTTCAAGGACTACAAGTATTCCCACAGGGTGGATAAGAAGCCCAACCGCGAGCTGATCAATGACACCCTGTATTCTACAAGGAAGGACGATAAGGGCAATACCCTGATCGTGAACAATCTGAACGGCCTGTACGACAAGGATAATGACAAGCTGAAGAAGCTGATCAACAAGAGCCCCGAGAAGCTGCTGATGTACCACCACGATCCTCAGACATATCAGAAGCTGAAGCTGATCATGGAGCAGTACGGCGACGAGAAGAACCCACTGTATAAGTACTATGAGGAGACCGGCAACTACCTGACAAAGTATTCCAAGAAGGATAATGGCCCCGTGATCAAGAAGATCAAGTACTATGGCAACAAGCTGAATGCCCACCTGGACATCACCGACGATTACCCCAACAGCCGGAATAAGGTGGTGAAGCTGAGCCTGAAGCCATACAGGTTCGACGTGTACCTGGACAACGGCGTGTATAAGTTTGTGACAGTGAAGAATCTGGATGTGATCAAGAAGGAGAACTACTATGAAGTGAATAGCAAGTGCTACGAGGAGGCCAAGAAGCTGAAGAAGATCAGCAACCAGGCCGAGTTCATCGCCTCTTTTTACAACAATGACCTGATCAAGATCAATGGCGAGCTGTATAGAGTGATCGGCGTGAACAATGATCTGCTGAACCGCATCGAAGTGAATATGATCGACATCACCTACCGGGAGTATCTGGAGAACATGAATGATAAGAGGCCCCCTCGCATCATCAAGACCATCGCCTCTAAGACACAGAGCATCAAGAAGTACTCTACAGACATCCTGGGCAACCTGTATGAGGTGAAGAGCAAGAAGCACCCTCAGATCATCAAGAAGGGC.In some embodiments comprising a nucleic acid encoding SaCas9, the SaCas9 comprises an amino acid sequence of SEQ ID NO: 711.

[00161] In some embodiments, the SaCas9 is a variant of the amino acid sequence of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an amino acid other than an E at the position

corresponding to position 781 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an amino acid other than an N at the position corresponding to position 967 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an amino acid other than an R at the position corresponding to position 1014 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises a K at the position corresponding to position 781 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises a K at the position corresponding to position 967 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an H at the position corresponding to position 1014 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an amino acid other than an E at the position corresponding to position 781 of SEQ ID NO: 711; an amino acid other than an N at the position corresponding to position 967 of SEQ ID NO: 711; and an amino acid other than an R at the position corresponding to position 1014 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises a K at the position corresponding to position 781 of SEQ ID NO: 711; a K at the position corresponding to position 967 of SEQ ID NO: 711; and an H at the position corresponding to position 1014 of SEQ ID NO: 711.

[00162] In some embodiments, the SaCas9 comprises an amino acid other than an R at the position corresponding to position 244 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an amino acid other than an N at the position corresponding to position 412 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an amino acid other than an N at the position corresponding to position 418 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an amino acid other than an R at the position corresponding to position 653 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an amino acid other than an R at the position corresponding to position 244 of SEQ ID NO: 711; an amino acid other than an N at the position corresponding to position 412 of SEQ ID NO: 711; an amino acid other than an N at the position corresponding to position 418 of SEQ ID NO: 711; and an amino acid other than an R at the position corresponding to position 653 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an A at the position corresponding to position 244 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an A at the position corresponding to position 412 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an A at the position corresponding to position 418 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an A at the position corresponding to position 653 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an A at the position corresponding to position 244 of SEQ ID NO: 711; an A at the position corresponding to position 412 of SEQ ID NO: 711; an A at the position corresponding to position 418 of SEQ ID NO: 711; and an A at the position corresponding to position 653 of SEQ ID NO: 711.

[00163] In some embodiments, the SaCas9 comprises an amino acid other than an R at the position corresponding to position 244 of SEQ ID NO: 711; an amino acid other than an N at the position corresponding to position 412 of SEQ ID NO: 711; an amino acid other than an N at the position corresponding to position 418 of SEQ ID NO: 711; an amino acid other than an R at the

position corresponding to position 653 of SEQ ID NO: 711; an amino acid other than an E at the position corresponding to position 781 of SEQ ID NO: 711; an amino acid other than an N at the position corresponding to position 967 of SEQ ID NO: 711; and an amino acid other than an R at the position corresponding to position 1014 of SEQ ID NO: 711. In some embodiments, the SaCas9 comprises an A at the position corresponding to position 244 of SEQ ID NO: 711; an A at the position corresponding to position 412 of SEQ ID NO: 711; an A at the position corresponding to position 418 of SEQ ID NO: 711; an A at the position corresponding to position 653 of SEQ ID NO: 711; a K at the position corresponding to position 781 of SEQ ID NO: 711; a K at the position corresponding to position 967 of SEQ ID NO: 711; and an H at the position corresponding to position 1014 of SEQ ID NO: 711.

[00164] In some embodiments, the SaCas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 715 (designated herein as SaCas9-KKH or SACAS9KKH):

KRNYILGLDIGITSVGYGIIDYETRDVIDAGVRLFKEANVENNEGRRSKRGARRLKRRRRHRI
QRVKKLLFDYNLLTDHSELSGINPYEARVKGLSQKLSEEEFSAALLHLAKRRGVHNVNEVEE
DTGNELSTKEQISRNSKALEEKYVAELQLERLKKDGEVRGSINRFKTSDYVKEAKQLLKVQK
AYHQLDQSFIDTYIDLLETRRTYYEGPGEGSPFGWKDIKEWYEMLMGHCTYFPEELRSVKYA
YNADLYNALNDLNNLVITRDENEKLEYYEKFQIIENVFKQKKKPTLKQIAKEILVNEEDIKGY
RVTSTGKPEFTNLKVYHDIKDITARKEIIENAELLDQIAKILTIYQSSEDIQEELTNLNSELTQEE
IEQISNLKGYTGTHNLSLKAINLILDELWHTNDNQIAIFNRLKLVPKKVDLSQQKEIPTTLVDD
FILSPVVKRSFIQSIKVINAIIKKYGLPNDIIIELAREKNSKDAQKMINEMQKRNRQTNERIEEIIR
TTGKENAKYLIEKIKLHDMQEGKCLYSLEAIPLEDLLNNPFNYEVDHIIPRSVSFDNSFNNKVL
VKQEENSKKGNRTPFQYLSSSDSKISYETFKKHILNLAKGKGRISKTKKEYLLEERDINRFSVQ
KDFINRNLVDTRYATRGLMNLLRSYFRVNNLDVKVKSINGGFTSFLRRKWKFKKERNKGYK
HHAEDALIIANADFIFKEWKKLDKAKKVMENQMFEEKQAESMPEIETEQEYKEIFITPHQIKHI
KDFKDYKYSHRVDKKPNRKLINDTLYSTRKDDKGNTLIVNNLNGLYDKDNDKLKKLINKSP
EKLLMYHHDPQTYQKLKLIMEQYGDEKNPLYKYYEETGNYLTKYSKKDNGPVIKKIKYYGN
KLNAHLDITDDYPNSRNKVVKLSLKPYRFDVYLDNGVYKFVTVKNLDVIKKENYYEVNSKC
YEEAKKLKKISNQAEFIASFYKNDLIKINGELYRVIGVNNDLLNRIEVNMIDITYREYLENMN
DKRPPHIIKTIASKTQSIKKYSTDILGNLYEVKSKKHPQIIKKG.

[00165] In some embodiments, the SaCas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 716 (designated herein as SaCas9-HF):

KRNYILGLDIGITSVGYGIIDYETRDVIDAGVRLFKEANVENNEGRRSKRGARRLKRRRRHRI
QRVKKLLFDYNLLTDHSELSGINPYEARVKGLSQKLSEEEFSAALLHLAKRRGVHNVNEVEE
DTGNELSTKEQISRNSKALEEKYVAELQLERLKKDGEVRGSINRFKTSDYVKEAKQLLKVQK
AYHQLDQSFIDTYIDLLETRRTYYEGPGEGSPFGWKDIKEWYEMLMGHCTYFPEELASVKYA

YNADLYNALNDLNNLVITRDENEKLEYYEKFQIIENVFKQKKKPTLKQIAKEILVNEEDIKGY
RVTSTGKPEFTNLKVYHDIKDITARKEIIENAELLDQIAKILTIYQSSEDIQEELTNLNSELTQEE
IEQISNLKGYTGTHNLSLKAINLILDELWHTNDAQIAIFARLKLVPKKVDLSQQKEIPTTLVDD
FILSPVVKRSFIQSIKVINAIIKKYGLPNDIIIELAREKNSKDAQKMINEMQKRNRQTNERIEEIIR
TTGKENAKYLIEKIKLHDMQEGKCLYSLEAIPLEDLLNNPFNYEVDHIIPRSVSFDNSFNNKVL
VKQEENSKKGNRTPFQYLSSSDSKISYETFKKHILNLAKGKGRISKTKKEYLLEERDINRFSVQ
KDFINRNLVDTRYATAGLMNLLRSYFRVNNLDVKVKSINGGFTSFLRRKWKFKKERNKGYK
HHAEDALIIANADFIFKEWKKLDKAKKVMENQMFEEKQAESMPEIETEQEYKEIFITPHQIKHI
KDFKDYKYSHRVDKKPNRELINDTLYSTRKDDKGNTLIVNNLNGLYDKDNDKLKKLINKSP
EKLLMYHHDPQTYQKLKLIMEQYGDEKNPLYKYYEETGNYLTKYSKKDNGPVIKKIKYYGN
KLNAHLDITDDYPNSRNKVVKLSLKPYRFDVYLDNGVYKFVTVKNLDVIKKENYYEVNSKC
YEEAKKLKKISNQAEFIASFYNNDLIKINGELYRVIGVNNDLLNRIEVNMIDITYREYLENMN
DKRPPRIIKTIASKTQSIKKYSTDILGNLYEVKSKKHPQIIKKG.

[00166] In some embodiments, the SaCas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 717 (designated herein as SaCas9-KKH-HF):

KRNYILGLDIGITSVGYGIIDYETRDVIDAGVRLFKEANVENNEGRRSKRGARRLKRRRRHRI
QRVKKLLFDYNLLTDHSELSGINPYEARVKGLSQKLSEEEFSAALLHLAKRRGVHNVNEVEE
DTGNELSTKEQISRNSKALEEKYVAELQLERLKKDGEVRGSINRFKTSDYVKEAKQLLKVQK
AYHQLDQSFIDTYIDLLETRRTYYEGPGEGSPFGWKDIKEWYEMLMGHCTYFPEELASVKYA
YNADLYNALNDLNNLVITRDENEKLEYYEKFQIIENVFKQKKKPTLKQIAKEILVNEEDIKGY
RVTSTGKPEFTNLKVYHDIKDITARKEIIENAELLDQIAKILTIYQSSEDIQEELTNLNSELTQEE
IEQISNLKGYTGTHNLSLKAINLILDELWHTNDAQIAIFARLKLVPKKVDLSQQKEIPTTLVDD
FILSPVVKRSFIQSIKVINAIIKKYGLPNDIIIELAREKNSKDAQKMINEMQKRNRQTNERIEEIIR
TTGKENAKYLIEKIKLHDMQEGKCLYSLEAIPLEDLLNNPFNYEVDHIIPRSVSFDNSFNNKVL
VKQEENSKKGNRTPFQYLSSSDSKISYETFKKHILNLAKGKGRISKTKKEYLLEERDINRFSVQ
KDFINRNLVDTRYATAGLMNLLRSYFRVNNLDVKVKSINGGFTSFLRRKWKFKKERNKGYK
HHAEDALIIANADFIFKEWKKLDKAKKVMENQMFEEKQAESMPEIETEQEYKEIFITPHQIKHI
KDFKDYKYSHRVDKKPNRKLINDTLYSTRKDDKGNTLIVNNLNGLYDKDNDKLKKLINKSP
EKLLMYHHDPQTYQKLKLIMEQYGDEKNPLYKYYEETGNYLTKYSKKDNGPVIKKIKYYGN
KLNAHLDITDDYPNSRNKVVKLSLKPYRFDVYLDNGVYKFVTVKNLDVIKKENYYEVNSKC
YEEAKKLKKISNQAEFIASFYKNDLIKINGELYRVIGVNNDLLNRIEVNMIDITYREYLENMN
DKRPPHIIKTIASKTQSIKKYSTDILGNLYEVKSKKHPQIIKKG.

[00167] In some embodiments, the nucleic acid encoding SluCas9 encodes a SluCas9 comprising an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 712:

NQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLERVKKLLEDYNLLDQSQIPQSTNPYAIRVKGLSEALSKDELVIALLHIAKRRGIHKIDVIDSNDDVGNELSTKEQLNKNSKLLKDKFVCQIQLERMNEGQVRGEKNRFKTADIIKEIIQLLNVQKNFHQLDENFINKYIELVEMRREYFEGPGKGSPYGWEGDPKAWYETLMGHCTYFPDELRSVKYAYSADLFNALNDLNNLVIQRDGLSKLEYHEKYHIIENVFKQKKKPTLKQIANEINVNPEDIKGYRITKSGKPQFTEFKLYHDLKSVLFDQSILENEDVLDQIAEILTIYQDKDSIKSKLTELDILLNEEDKENIAQLTGYTGTHRLSLKCIRLVLEEQWYSSRNQMEIFTHLNIKPKKINLTAANKIPKAMIDEFILSPVVKRTFGQAINLINKIIEKYGVPEDIIIELARENNSKDKQKFINEMQKKNENTRKRINEIIGKYGNQNAKRLVEKIRLHDEQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNKVLVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKFEVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQVQDIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPEKFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNKLGSHLDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDKLKLGKAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEPRIKKTIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN.

[00168] In some embodiments, the SluCas9 is a variant of the amino acid sequence of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an amino acid other than an Q at the position corresponding to position 781 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an amino acid other than an R at the position corresponding to position 1013 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises a K at the position corresponding to position 781 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises a K at the position corresponding to position 966 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an H at the position corresponding to position 1013 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an amino acid other than an Q at the position corresponding to position 781 of SEQ ID NO: 712; and an amino acid other than an R at the position corresponding to position 1013 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises a K at the position corresponding to position 781 of SEQ ID NO: 712; a K at the position corresponding to position 966 of SEQ ID NO: 712; and an H at the position corresponding to position 1013 of SEQ ID NO: 712.

[00169] In some embodiments, the SluCas9 comprises an amino acid other than an R at the position corresponding to position 246 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an amino acid other than an N at the position corresponding to position 414 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an amino acid other than a T at the position corresponding to position 420 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an amino acid other than an R at the position corresponding to position 655 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an amino acid other than an R at the position

corresponding to position 246 of SEQ ID NO: 712; an amino acid other than an N at the position corresponding to position 414 of SEQ ID NO: 712; an amino acid other than a T at the position corresponding to position 420 of SEQ ID NO: 712; and an amino acid other than an R at the position corresponding to position 655 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an A at the position corresponding to position 246 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an A at the position corresponding to position 414 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an A at the position corresponding to position 420 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an A at the position corresponding to position 655 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an A at the position corresponding to position 246 of SEQ ID NO: 712; an A at the position corresponding to position 414 of SEQ ID NO: 712; an A at the position corresponding to position 420 of SEQ ID NO: 712; and an A at the position corresponding to position 655 of SEQ ID NO: 712.

[00170] In some embodiments, the SluCas9 comprises an amino acid other than an R at the position corresponding to position 246 of SEQ ID NO: 712; an amino acid other than an N at the position corresponding to position 414 of SEQ ID NO: 712; an amino acid other than a T at the position corresponding to position 420 of SEQ ID NO: 712; an amino acid other than an R at the position corresponding to position 655 of SEQ ID NO: 712; an amino acid other than an Q at the position corresponding to position 781 of SEQ ID NO: 712; a K at the position corresponding to position 966 of SEQ ID NO: 712; and an amino acid other than an R at the position corresponding to position 1013 of SEQ ID NO: 712. In some embodiments, the SluCas9 comprises an A at the position corresponding to position 246 of SEQ ID NO: 712; an A at the position corresponding to position 414 of SEQ ID NO: 712; an A at the position corresponding to position 420 of SEQ ID NO: 712; an A at the position corresponding to position 655 of SEQ ID NO: 712; a K at the position corresponding to position 781 of SEQ ID NO: 712; a K at the position corresponding to position 966 of SEQ ID NO: 712; and an H at the position corresponding to position 1013 of SEQ ID NO: 712.

[00171] In some embodiments, the SluCas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 718 (designated herein as SluCas9-KH or SLUCAS9KH):

NQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLE
RVKKLLEDYNLLDQSQIPQSTNPYAIRVKGLSEALSKDELVIALLHIAKRRGIHKIDVIDSNDD
VGNELSTKEQLNKNSKLLKDKFVCQIQLERMNEGQVRGEKNRFKTADIIKEIIQLLNVQKNFH
QLDENFINKYIELVEMRREYFEGPGKGSPYGWEGDPKAWYETLMGHCTYFPDELRSVKYAY
SADLFNALNDLNNLVIQRDGLSKLEYHEKYHIIENVFKQKKKPTLKQIANEINVNPEDIKGYRI
TKSGKPQFTEFKLYHDLKSVLFDQSILENEDVLDQIAEILTIYQDKDSIKSKLTELDILLNEEDK
ENIAQLTGYTGTHRLSLKCIRLVLEEQWYSSRNQMEIFTHLNIKPKKINLTAANKIPKAMIDEF
ILSPVVKRTFGQAINLINKIIEKYGVPEDIIIELARENNSKDKQKFINEMQKKNENTRKRINEIIG
KYGNQNAKRLVEKIRLHDEQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNKV

LVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKFE
VQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNH
GYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQVQ
DIKDFRNFKYSHRVDKKPNRKLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPE
KFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNK
LGSHLDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDK
LKLGKAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEP
HIKKTIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN.

[00172] In some embodiments, the SluCas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 719 (designated herein as SluCas9-HF):

NQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLE
RVKKLLEDYNLLDQSQIPQSTNPYAIRVKGLSEALSKDELVIALLHIAKRRGIHKIDVIDSNDD
VGNELSTKEQLNKNSKLLKDKFVCQIQLERMNEGQVRGEKNRFKTADIIKEIIQLLNVQKNFH
QLDENFINKYIELVEMRREYFEGPGKGSPYGWEGDPKAWYETLMGHCTYFPDELASVKYAY
SADLFNALNDLNNLVIQRDGLSKLEYHEKYHIIENVFKQKKKPTLKQIANEINVNPEDIKGYRI
TKSGKPQFTEFKLYHDLKSVLFDQSILENEDVLDQIAEILTIYQDKDSIKSKLTELDILLNEEDK
ENIAQLTGYTGTHRLSLKCIRLVLEEQWYSSRAQMEIFAHLNIKPKKINLTAANKIPKAMIDEF
ILSPVVKRTFGQAINLINKIIEKYGVPEDIIIELARENNSKDKQKFINEMQKKNENTRKRINEIIG
KYGNQNAKRLVEKIRLHDEQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNKV
LVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKFE
VQKEFINRNLVDTRYATAELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNH
GYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQVQ
DIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPE
KFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNK
LGSHLDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDK
LKLGKAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEP
RIKKTIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN.

[00173] In some embodiments, the SluCas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 720 (designated herein as SluCas9-HF-KH):

NQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLE
RVKKLLEDYNLLDQSQIPQSTNPYAIRVKGLSEALSKDELVIALLHIAKRRGIHKIDVIDSNDD
VGNELSTKEQLNKNSKLLKDKFVCQIQLERMNEGQVRGEKNRFKTADIIKEIIQLLNVQKNFH
QLDENFINKYIELVEMRREYFEGPGKGSPYGWEGDPKAWYETLMGHCTYFPDELASVKYAY
SADLFNALNDLNNLVIQRDGLSKLEYHEKYHIIENVFKQKKKPTLKQIANEINVNPEDIKGYRI
TKSGKPQFTEFKLYHDLKSVLFDQSILENEDVLDQIAEILTIYQDKDSIKSKLTELDILLNEEDK

ENIAQLTGYTGTHRLSLKCIRLVLEEQWYSSRAQMEIFAHLNIKPKKINLTAANKIPKAMIDEF
ILSPVVKRTFGQAINLINKIIEKYGVPEDIIIELARENNSKDKQKFINEMQKKNENTRKRINEIIG
KYGNQNAKRLVEKIRLHDEQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNKV
LVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKFE
VQKEFINRNLVDTRYATAELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNH
GYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQVQ
DIKDFRNFKYSHRVDKKPNRKLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPE
KFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNK
LGSHLDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDK
LKLGKAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEP
HIKKTIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN.

[00174] In some embodiments, the Cas protein is any of the engineered Cas proteins disclosed in Schmidt et al., 2021, Nature Communications, "Improved CRISPR genome editing using small highly active and specific engineered RNA-guided nucleases."

[00175] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7021 (designated herein as sRGN1):
MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL
DRVKHLLAEYDLLDLTNIPKSTNPYQTRVKGLNEKLSKDELVIALLHIAKRRGIHNVDVAAD
KEETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDT
QMQYYPEIDETFKEKYISLVETRREYFEGPGKGSPFGWEGNIKKWFEQMMGHCTYFPEELRS
VKYSYSAELFNALNDLNNLVITRDEDAKLNYGEKFQIIENVFKQKKTPNLKQIAIEIGVHETEI
KGYRVNKSGTPEFTEFKLYHDLKSIVFDKSILENEAILDQIAEILTIYQDEQSIKEELNKLPEILN
EQDKAEIAKLIGYNGTHRLSLKCIHLINEELWQTSRNQMEIFNYLNIKPNKVDLSEQNKIPKD
MVNDFILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRI
NEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLKDIPLEDLLRNPNNYDIDHIIPRSVSFDDSM
HNKVLVRREQNAKKNNQTPYQYLTSGYADIKYSVFKQHVLNLAENKDRMTKKKREYLLEE
RDINKFEVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKF
KKERNHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFI
IPKQVQDIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQ
FDKSPEKFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLK
YIGNKLGSHLDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPE
QKYDKLKLGKAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELN
NIKGEPRIKKTIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN.

[00176] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7022 (designated herein as sRGN2):

MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLERVKSLLSEYKIISGLAPTNNQPYNIRVKGLTEQLTKDELAVALLHIAKRRGIHKIDVIDSNDDVGNELSTKEQLNKNSKLLKDKFVCQIQLERMNEGQVRGEKNRFKTADIIKEIIQLLNVQKNFHQLDENFINKYIELVEMRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVKYAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKGYRITKSGTPEFTEFKLYHDLKSVLFDQSILENEDVLDQIAEILTIYQDKDSIKSKLTELDILLNEEDKENIAQLTGYNGTHRLSLKCIRLVLEEQWYSSRNQMEIFTHLNIKPKKINLTAANKIPKAMIDEFILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRINEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIALMDLLNNPQNYEVDHIIPRSVAFDNSIHNKVLVKQIENSKKGNRTPYQYLNSSDAKLSYNQFKQHILNLSKSKDRISKKKKDYLLEERDINKFEVQKEFINRNLVDTRYATRELTSYLKAYFSANNMDVKVKTINGSFTNHLRKVWRFDKYRNHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQVQDIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPEKFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNKLGSHLDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDKLKLGKAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEPRIKKTIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN.

[00177] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7023 (designated herein as sRGN3):

MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKEETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQMQYYPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVKYAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKGYRITKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLMSEADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIPTDMIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRINEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNKVLVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKFEVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQVQDIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPEKFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNKLGSHLDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDKLKLGKAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEPRIKKTIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN.

[00178] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7024 (designated herein as sRGN3.1):

MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL
ERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKE
ETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQM
QYYPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSV
KYAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIK
GYRITKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLM
SEADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIP
TDMIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRK
RINEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNS
YHNKVLVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEER
DINKFEVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFK
KERNHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFII
PKQVQDIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQF
DKSPEKFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLK
YIGNKLGSHLDVTHQFKSSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYIP
KDKYQELKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYCEI
NNIKGEPRIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL.

[00179] In some embodiments, the Cas9 comprises an amino acid sequence that is encoded by a nucleic acid molecule at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 918 (an exemplary nucleic acid molecule encoding sRGN3.1):

ATGAATCAGAAATTCATCCTGGGACTGGACATCGGCATTACCTCTGTGGGCTACGGCTTG
ATTGACTACGAGACCAAGAACATCATCGACGCCGGCGTTAGACTGTTTCCTGAGGCCAAT
GTGGAAAACAACGAGGGCAGACGGTCTAAGCGGGGCTCTAGACGACTGAAAAGAAGAA
GAATCCACAGACTGGAAAGAGTGAAGCTGCTGCTGACCGAGTACGACCTGATCAATAAG
GAACAGATCCCTACAAGCAACAACCCCTACCAGATTAGAGTGAAGGGCCTGAGCGAGAT
CCTGAGCAAAGACGAGCTGGCCATCGCCCTGCTGCACCTGGCCAAGCGGAGGGGCATCC
ACAACGTGGATGTGGCCGCCGACAAGGAGGAAACCGCCAGCGACTCCCTGAGCACCAAA
GATCAGATCAACAAGAATGCCAAGTTCCTGGAGAGCAGATACGTGTGCGAGCTGCAGAA
GGAGAGATTGGAGAACGAGGGCCACGTGCGGGGCGTGGAGAATAGATTCCTGACAAAA
GATATCGTGCGGGAAGCCAAGAAGATCATCGACACCCAGATGCAGTACTATCCTGAAAT
CGACGAAACCTTCAAGGAGAAGTACATCAGCCTGGTCGAAACCAGACGCGAGTATTTCG
AGGGCCCCGGACAGGGCTCTCCTTTCGGCTGGAACGGCGATCTGAAGAAGTGGTACGAG
ATGCTGATGGGACACTGCACCTACTTCCCTCAAGAGCTGAGATCTGTGAAGTACGCCTAC

AGCGCCGATCTGTTCAACGCCCTGAACGATCTGAACAACCTTATCATCCAGCGGGACAAT
TCTGAGAAGCTGGAATACCACGAGAAATATCATATCATCGAGAACGTCTTTAAACAAAA
GAAAAAGCCTACCCTGAAGCAGATCGCCAAGGAGATCGGAGTGAATCCTGAGGATATCA
AAGGCTACAGAATCACAAAGTCCGGCACCCCTGAGTTCACCAGCTTTAAGCTGTTCCACG
ACCTGAAGAAGGTCGTGAAAGACCACGCCATCCTCGATGACATCGATCTGCTGAACCAG
ATCGCTGAGATCCTGACAATCTACCAGGACAAAGATTCTATCGTGGCTGAACTGGGACA
GCTGGAATACCTTATGAGCGAGGCCGACAAGCAAAGCATCTCCGAACTGACCGGCTACA
CGGGCACCCATAGCCTGAGCCTGAAGTGTATGAACATGATCATCGATGAGCTGTGGCAC
TCTAGCATGAACCAGATGGAAGTTTTCACCTACCTGAACATGCGGCCTAAGAAGTACGA
GCTGAAGGGCTACCAGAGAATCCCCACCGATATGATCGACGACGCCATCCTGAGCCCCG
TGGTGAAAAGAACATTCATCCAGAGCATCAACGTGATCAACAAGGTGATCGAGAAGTAC
GGCATTCCAGAGGACATCATCATCGAGCTGGCCAGAGAAAACAACAGCGACGATAGAA
AGAAGTTTATCAACAACCTGCAGAAAAAAAACGAGGCCACCCGGAAGAGAATTAATGA
GATCATCGGCCAGACAGGCAACCAGAACGCCAAAAGGATCGTGGAAAAAATCAGACTG
CACGACCAGCAGGAGGGCAAGTGCCTGTACTCTCTGGAAAGCATCCCCCTGGAGGACCT
GCTGAACAATCCAAATCACTACGAGGTGGACCACATCATCCCTAGAAGCGTCAGCTTCG
ACAACAGCTACCACAACAAGGTGCTGGTGAAGCAGAGCGAAAACAGTAAGAAATCCAA
CCTGACACCTTACCAGTACTTTAACAGCGGCAAGAGCAAGCTGAGCTACAACCAGTTCA
AGCAGCACATCCTGAACCTGTCCAAATCTCAGGATAGAATCTCCAAGAAAAAGAAGGAA
TACCTGCTGGAGGAGAGAGATATCAACAAGTTCGAAGTCCAAAAGGAGTTCATCAACAG
GAACCTGGTGGACACCCGGTACGCCACAAGAGAGCTGACAAACTACCTGAAAGCCTACT
TCAGCGCTAACAACATGAACGTGAAGGTGAAAACCATCAATGGAAGTTTCACAGACTAC
CTTCGGAAGGTGTGGAAGTTCAAGAAGGAACGGAATCACGGCTACAAGCACCACGCAGA
GGACGCCCTGATTATAGCTAATGCCGATTTCCTGTTCAAAGAAAACAAGAAGCTGAAAG
CCGTGAACAGCGTTCTGGAAAAGCCTGAAATTGAGACCAAGCAACTGGATATACAGGTG
GACAGCGAGGACAACTACTCCGAGATGTTCATCATCCCTAAACAGGTGCAGGACATCAA
AGACTTCAGAAATTTCAAGTACAGCCACAGAGTGGACAAGAAACCCAACCGGCAGCTGA
TCAATGACACCCTGTATAGCACCCGCAAGAAGGATAACAGCACCTACATCGTCCAGACC
ATCAAGGACATCTACGCTAAGGACAACACCACCCTGAAAAAGCAATTTGATAAGTCCCC
CGAAAAGTTTCTGATGTACCAACACGATCCTAGAACCTTCGAAAAGTTGGAGGTGATCAT
GAAGCAATATGCCAACGAGAAGAACCCACTGGCCAAGTACCATGAGGAGACAGGAGAA
TACCTGACCAAGTATTCTAAGAAGAATAACGGCCCCATCGTGAAGTCCCTGAAGTACATT
GGGAACAAACTCGGAAGCCACCTGGACGTGACGCACCAGTTCAAGAGCAGCACCAAGA
AGCTAGTGAAACTGAGCATCAAGAACTACAGATTCGACGTGTACCTGACAGAAAAGGGC
TACAAATTTGTGACCATCGCTTACCTGAATGTGTTCAAAAAGGACAATTATTACTACATC
CCAAAGGACAAGTACCAGGAGCTTAAAGAGAAAAAAAGATCAAGGATACCGACCAGT
TTATCGCTAGCTTCTACAAGAACGACCTGATTAAGCTGAACGGCGACCTGTACAAGATCA

TCGGCGTGAACTCTGACGACCGGAACATAATAGAGCTGGATTATTATGACATCAAGTAC
AAGGACTACTGCGAGATCAACAACATCAAGGGCGAGCCTAGAATCAAAAAGACCATCG
GGAAGAAAACCGAGTCTATCGAAAAGTTTACAACAGACGTGCTGGGCAACCTGTACCTG
CACAGCACGGAAAAGGCCCCTCAGCTCATCTTCAAGAGAGGCCTG

[00180] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7025 (designated herein as sRGN3.2):
MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL
ERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKE
ETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQM
QYYPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSV
KYAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIK
GYRITKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLM
SEADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIP
TDMIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRK
RINEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNS
YHNKVLVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEER
DINKFEVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFK
KERNHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFII
PKQVQDIKDFRNFKFSHRVDKKPNRQLINDTLYSTRMKDEHDYIVQTITDIYGKDNTNLKKQ
FNKNPEKFLMYQNDPKTFEKLSIIMKQYSDEKNPLAKYYEETGEYLTKYSKKNNGPIVKKIK
LLGNKVGNHLDVTNKYENSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYI
PKDKYQELKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYC
EINNIKGEPRIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL.

[00181] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7026 (designated herein as sRGN3.3):
MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL
ERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKE
ETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQM
QYYPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSV
KYAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIK
GYRITKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLM
SEADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIP
TDMIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRK
RINEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNS
YHNKVLVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEER

DINKFEVQKEFINRNLVDTRYATRELTSYLKAYFSANNMDVKVKTINGSFTNHLRKVWRFD
KYRNHGYKHHAEDALIIANADFLFKENKKLQNTNKILEKPTIENNTKKVTVEKEEDYNNVFE
TPKLVEDIKQYRDYKFSHRVDKKPNRQLINDTLYSTRMKDEHDYIVQTITDIYGKDNTNLKK
QFNKNPEKFLMYQNDPKTFEKLSIIMKQYSDEKNPLAKYYEETGEYLTKYSKKNNGPIVKKI
KLLGNKVGNHLDVTNKYENSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYY
IPKDKYQELKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYC
EINNIKGEPRIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL.

[00182] In some embodiments, the Cas9 comprises an amino acid sequence that is encoded by a nucleic acid molecule at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 919 (an exemplary nucleic acid molecule encoding sRGN3.3):

AACCAGAAGTTTATCCTGGGCCTGGATATCGGCATCACATCCGTGGGCTACGGCCTGATT
GATTACGAAACCAAGAACATCATTGATGCCGGCGTCCGGCTTTTCCCTGAAGCTAACGTG
GAAAACAATGAGGGCAGACGGAGCAAGAGAGGCAGCAGACGGCTGAAGCGGAGAAGA
ATCCATAGACTCGAACGGGTGAAGCTGCTGCTGACCGAGTACGACCTGATCAACAAGGA
GCAGATCCCCACCAGCAACAACCCATACCAGATCAGAGTGAAAGGCCTTTCTGAGATTC
TGAGCAAGGATGAGCTGGCTATCGCTCTGCTCCACCTGGCCAAGAGAAGGGGAATCCAC
AACGTTGACGTGGCCGCCGATAAGGAAGAGACCGCCAGCGATAGCCTGAGCACCAAGG
ACCAGATCAACAAGAACGCCAAGTTCCTGGAAAGCAGATACGTGTGCGAGCTGCAAAAA
GAGAGACTGGAAAATGAGGGCCATGTGCGGGGCGTTGAGAACAGATTCCTGACCAAAG
ACATCGTCAGAGAGGCCAAGAAAATTATTGACACCCAGATGCAGTACTATCCTGAGATA
GACGAGACCTTTAAGGAAAAGTACATCAGCCTGGTGGAAACAAGAAGAGAATACTTCGA
AGGACCTGGCCAGGGCTCCCCTTTCGGCTGGAACGGCGACCTGAAGAAGTGGTACGAGA
TGCTGATGGGCCACTGCACCTACTTCCCCCAGGAGCTGCGGAGCGTGAAGTACGCTTACA
GCGCCGACCTGTTCAATGCCCTGAACGACCTGAACAATCTTATCATCCAAAGAGATAACA
GCGAGAAATTAGAATACCACGAGAAGTACCACATCATCGAGAATGTGTTCAAGCAAAAG
AAGAAGCCTACCCTGAAGCAGATCGCCAAAGAGATCGGCGTGAACCCTGAGGACATCAA
GGGCTATCGGATCACCAAGTCCGGCACCCCTGAATTCACCAGCTTCAAGCTGTTTCACGA
CCTCAAAAAGGTCGTGAAGGACCACGCCATCCTGGACGACATCGATCTGCTGAATCAGA
TCGCCGAGATCCTGACCATCTACCAGGACAAGGACTCTATCGTGGCCGAGCTTGGACAG
CTGGAGTACCTGATGAGCGAGGCTGACAAGCAGAGCATCAGCGAGCTGACCGGCTACAC
CGGAACCCACAGCCTGTCCCTGAAGTGCATGAACATGATCATCGACGAGCTGTGGCACT
CTAGCATGAACCAGATGGAAGTGTTCACCTACCTGAACATGAGACCTAAGAAGTACGAA
CTGAAGGGTTACCAGAGAATCCCAACCGACATGATCGACGACGCCATCCTGAGCCCCGT
GGTGAAGCGGACCTTTATCCAGAGCATCAATGTGATCAACAAGGTGATCGAGAAATACG
GCATCCCCGAGGACATCATCATCGAACTGGCCAGAGAGAATAACTCTGATGACCGGAAG
AAGTTCATCAACAACCTGCAGAAGAAGAACGAAGCCACCAGAAAGCGCATCAACGAGA

TCATCGGCCAAACAGGGAATCAGAACGCCAAGAGGATCGTGGAAAAGATTCGGCTGCAC
GACCAGCAGGAGGGAAAATGCCTGTACAGCCTGGAAAGCATCCCCCTGGAAGATCTACT
GAACAACCCCAACCACTACGAGGTGGATCACATCATCCCTAGAAGCGTGTCCTTTGACA
ACAGTTACCACAACAAGGTGCTGGTGAAGCAATCCGAGAACTCGAAGAAGAGCAACCTG
ACACCTTACCAGTACTTTAACAGCGGCAAGTCCAAGCTGTCTTATAACCAGTTCAAGCAG
CACATCCTCAACCTGTCAAAGTCTCAGGACAGAATCTCTAAGAAGAAGAAGGAGTATCT
GCTGGAAGAGCGGGACATCAACAAGTTCGAGGTGCAGAAAGAGTTCATTAACAGAAACC
TGGTCGACACCCGGTACGCCACACGCGAACTGACAAGCTACCTGAAGGCCTACTTCTCCG
CCAACAATATGGACGTGAAGGTCAAGACCATCAATGGCAGCTTCACAAATCACCTGAGA
AAGGTCTGGCGGTTCGACAAGTACAGAAACCACGGCTACAAGCACCACGCCGAGGATGC
TCTGATTATCGCCAACGCCGACTTCCTGTTCAAGGAAAACAAAAAACTGCAGAACACCA
ACAAGATCCTGGAAAAACCTACAATCGAGAACAACACAAAGAAAGTGACAGTGGAAAA
AGAGGAAGATTACAACAACGTGTTTGAGACACCTAAGCTGGTTGAGGATATCAAGCAGT
ACCGGGACTATAAGTTTAGCCACAGAGTGGACAAGAAACCTAACAGGCAGCTGATCAAC
GACACTCTGTACAGCACAAGAATGAAAGATGAGCACGATTACATCGTGCAGACCATTAC
CGACATCTACGGCAAGGACAACACCAATCTGAAGAAGCAGTTCAACAAAAATCCCGAGA
AGTTCCTGATGTACCAAAATGACCCTAAGACATTCGAGAAGCTGAGCATCATCATGAAA
CAGTACTCTGATGAGAAGAACCCACTGGCCAAGTACTACGAGGAAACAGGCGAATACCT
GACCAAGTACTCTAAGAAGAACAACGGCCCTATCGTGAAGAAGATCAAACTGCTGGGCA
ACAAAGTGGGAAATCATCTGGATGTGACCAATAAATACGAGAACTCTACAAAGAAACTG
GTGAAGCTGAGCATTAAGAACTACAGATTCGACGTCTACCTGACAGAAAAGGGATACAA
GTTCGTGACCATCGCCTACCTGAACGTGTTCAAGAAAGACAACTACTACTACATCCCAAA
AGACAAGTACCAAGAGTTAAAAGAGAAGAAGAAGATAAAGGATACCGACCAGTTTATC
GCTTCTTTCTACAAGAACGACCTGATCAAGCTGAACGGTGATCTGTACAAAATCATCGGA
GTGAATAGCGATGACAGAAATATCATCGAACTGGATTACTATGACATCAAGTACAAAGA
TTATTGTGAAATCAACAACATCAAGGGAGAGCCCAGAATTAAGAAAACCATCGGCAAGA
AAACAGAGAGCATCGAGAAATTCACCACAGATGTGCTGGGCAACCTGTACCTGCACAGC
ACAGAGAAAGCCCCTCAGCTCATCTTCAAGAGAGGCCTG

[00183] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7027 (designated herein as sRGN4):

MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL
ERVKKLLEDYNLLDQSQIPQSTNPYAIRVKGLSEALSKDELVIALLHIAKRRGIHNINVSSEDE
DASNELSTKEQINRNNKLLKDKYVCEVQLQRLKEGQIRGEKNRFKTTDILKEIDQLLKVQKD
YHNLDIDFINQYKEIVETRREYFEGPGKGSPYGWEGDPKAWYETLMGHCTYFPDELRSVKY
AYSADLFNALNDLNNLVIQRDGLSKLEYHEKYHIIENVFKQKKKPTLKQIANEINVNPEDIKG
YRITKSGKPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLMS

EADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIPT
DMIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKR
INEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSY
HNKVLVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDI
NKFEVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKE
RNHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPK
QVQDIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFD
KSPEKFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYI
GNKLGSHLDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQK
YDKLKLGKAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNI
KGEPRIKKTIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN.

[00184] In some embodiments, the Cas9 comprises an amino acid sequence that is encoded by a nucleic acid molecule at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 920 (an exemplary nucleic acid molecule encoding sRGN4):

ATGAATCAAAAGTTTATCCTGGGTCTGGACATCGGCATCACATCTGTGGGCTACGGCCTT
ATCGATTACGAGACCAAGAATATCATTGATGCTGGCGTACGGCTGTTCCCTGAGGCTAAC
GTGGAAAACAACGAGGGTAGACGGAGCAAGAGAGGCAGCAGACGGCTGAAACGGCGTA
GAATCCACCGGCTGGAGAGAGTGAAGAAGTTGCTGGAAGATTACAACTTGCTGGATCAA
TCCCAGATCCCCCAGAGCACTAATCCTTATGCTATCCGGGTGAAGGGCCTGTCTGAAGCC
CTGAGCAAAGACGAGCTGGTGATTGCCCTGCTGCACATCGCGAAGAGAAGAGGCATCCA
CAATATCAATGTGTCCTCTGAGGATGAGGATGCCAGCAACGAGCTGAGCACTAAGGAAC
AGATCAATCGGAACAACAAGCTGCTGAAGGACAAGTACGTGTGTGAAGTGCAGCTGCAG
AGACTGAAGGAAGGCCAGATAAGAGGCGAAAAGAACAGATTCAAGACAACAGACATCC
TGAAAGAAATCGACCAGCTGCTGAAGGTCCAGAAGGACTACCACAACCTCGACATCGAT
TTCATTAACCAGTACAAGGAAATCGTGGAAACCAGGAGAGAGTACTTCGAGGGCCCTGG
CAAGGGCTCCCCATACGGCTGGGAGGGCGACCCCAAGGCCTGGTACGAAACCCTGATGG
GCCACTGCACCTACTTCCCCGACGAACTGAGAAGCGTCAAGTACGCCTACAGCGCCGAT
CTGTTCAACGCCCTGAACGACCTGAACAACCTGGTGATCCAGCGGGACGGCCTGAGCAA
ACTGGAGTACCATGAAAAGTATCATATCATCGAGAACGTGTTCAAGCAGAAGAAAAAC
CTACCCTGAAGCAGATCGCCAACGAGATCAACGTGAACCCTGAGGACATTAAAGGCTAC
AGAATCACCAAAAGCGGCAAGCCAGAGTTCACCAGCTTCAAGCTGTTTCACGACCTGAA
GAAGGTCGTGAAAGACCACGCCATCCTGGACGACATCGATCTGCTTAACCAGATCGCTG
AAATCCTCACAATCTACCAGGACAAGGACTCTATCGTGGCCGAGCTGGGACAGCTGGAA
TACCTGATGAGCGAGGCCGATAAGCAGAGCATCAGCGAGCTGACCGGCTACACCGGAAC
CCACAGCCTGAGCCTGAAGTGTATGAACATGATCATCGACGAGCTGTGGCACAGCTCTAT
GAACCAGATGGAAGTATTCACCTACCTGAACATGAGACCTAAGAAGTACGAACTGAAGG

GCTATCAGAGAATCCCTACAGACATGATCGACGATGCCATCCTGTCTCCTGTGGTGAAGA
GAACCTTCATCCAGTCTATCAACGTGATCAACAAGGTGATCGAAAAGTACGGAATCCCT
GAAGATATCATCATCGAACTGGCCAGAGAGAACAACTCCGACGACAGAAAGAAATTCAT
CAACAACCTGCAGAAGAAGAATGAGGCCACACGGAAGCGGATTAATGAGATCATCGGC
CAAACCGGCAACCAGAACGCCAAAAGAATCGTGGAAAAGATCCGGCTGCACGATCAGC
AGGAGGGCAAATGCCTGTACAGCCTGGAGAGCATCCCCCTGGAGGACCTGCTCAACAAC
CCCAACCACTACGAGGTGGATCACATCATCCCAAGATCTGTTAGCTTCGACAACAGCTAC
CACAACAAGGTGCTGGTGAAGCAAAGCGAAAACTCTAAGAAATCTAACCTGACACCTTA
CCAGTACTTTAACAGCGGCAAGTCCAAGCTGTCTTATAACCAGTTTAAGCAGCACATCCT
GAACCTGAGCAAGTCCCAGGATAGAATCAGCAAAAAAAAGAAGGAATACCTGCTGGAG
GAACGCGACATCAATAAATTTGAGGTGCAAAAGGAGTTCATCAACCGGAACCTGGTGGA
CACCCGGTACGCCACCAGAGAACTGACCAACTACCTGAAAGCCTACTTCAGCGCCAACA
ACATGAACGTGAAGGTGAAAACCATCAACGGAAGCTTCACCGACTACCTGCGGAAGGTG
TGGAAGTTCAAGAAAGAGCGGAATCACGGCTATAAGCACCACGCTGAGGACGCTCTGAT
CATCGCCAATGCCGATTTCCTGTTCAAGGAAAACAAGAAGTTAAAGGCCGTGAACTCTGT
CCTGGAGAAGCCCGAGATCGAGACAAAGCAGCTGGACATCCAAGTGGACTCAGAGGAC
AATTACTCTGAGATGTTCATCATCCCCAAGCAGGTGCAGGACATCAAGGATTTTAGAAAT
TTCAAGTACAGCCATAGAGTGGACAAGAAGCCCAATAGACAGCTGATCAACGATACACT
GTACAGCACCAGAAAGAAGGACAACAGCACATATATCGTCCAGACCATCAAGGACATTT
ACGCAAAGGATAACACCACACTGAAGAAGCAGTTCGACAAAAGCCCTGAGAAGTTCCTG
ATGTACCAACACGACCCTCGGACCTTCGAGAAGTTAGAGGTTATCATGAAACAGTACGC
CAACGAGAAAAACCCTCTGGCCAAGTACCACGAGGAAACCGGAGAATACCTGACAAAA
TATAGCAAGAAGAACAACGGCCCCATCGTGAAAAGCCTGAAGTACATCGGCAACAAGCT
GGGCAGCCACCTGGACGTGACCCACCAGTTCAAGAGCAGCACCAAGAAGCTGGTCAAGC
TGAGCATCAAGCCTTATAGGTTCGACGTGTACCTGACAGATAAGGGATACAAGTTCATCA
CCATCAGCTACCTGGATGTTCTGAAAAAGGACAATTACTACTACATCCCTGAGCAGAAGT
ACGACAAACTCAAGCTGGGCAAGGCCATCGATAAGAATGCCAAGTTCATCGCATCTTTTT
ACAAGAACGACCTGATCAAACTGGACGGCGAGATCTACAAGATCATAGGAGTGAACAGC
GACACCAGGAATATGATCGAGCTCGATCTGCCTGACATCAGATACAAGGAATACTGCGA
GCTGAACAACATCAAGGGAGAGCCTAGAATCAAGAAAACCATCGGCAAGAAGGTGAAC
AGCATCGAGAAACTTACAACAGATGTGCTCGGCAACGTGTTCACCAACACCCAGTACAC
CAAGCCACAGCTGCTGTTTAAGCGGGGGAAC

[00185] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7028 (designated herein as *Staphylococcus hyicus* Cas9 or ShyCas9):

MNNYILGLDIGITSVGYGIVDSDTREIKDAGVRLFPEANVDNNEGRRSKRGARRLKR
RRIHRLDRVKHLLAEYDLLDLTNIPKSTNPYQTRVKGLNEKLSKDELVIALLHIAKRRGIHNV

NVMMDDNDSGNELSTKDQLKKNAKALSDKYVCELQLERFEQDYKVRGEKNRFKTEDFVRE
ARKLLETQSKFFEIDQTFIMRYIELIETRREYFEGPGKGSPFGWEGNIKKWFEQMMGHCTYFP
EELRSVKYSYSAELFNALNDLNNLVITRDEDAKLNYGEKFQIIENVFKQKKTPNLKQIAIEIGV
HETEIKGYRVNKSGKPEFTQFKLYHDLKNIFKDPKYLNDIQLMDNIAEIITIYQDAESIIKELNQ
LPELLSEREKEKISALSGYSGTHRLSLKCINLLLDDLWESSLNQMELFTKLNLKPKKIDLSQQH
KIPSKLVDDFILSPVVKRAFIQSIQVVNAIIDKYGLPEDIIIELARENNSDDRRKFLNQLQKQNE
ETRKQVEKVLREYGNDNAKRIVQKIKLHNMQEGKCLYSLKDIPLEDLLRNPHHYEVDHIIPRS
VAFDNSMHNKVLVRADENSKKGNRTPYQYLNSSESSLSYNEFKQHILNLSKTKDRITKKKRE
YLLEERDINKFDVQKEFINRNLVDTRYATRELTSLLKAYFSANNLDVKVKTINGSFTNYLRKV
WKFDKDRNKGYKHHAEDALIIANADFLFKHNKKLRNINKVLDAPSKEVDKKRVTVQSEDEY
NQIFEDTQKAQAIKKFEIRKFSHRVDKKPNRQLINDTLYSTRNIDGIEYVVESIKDIYSVNNDK
VKTKFKKDPHRLLMYRNDPQTFEKFEKVFKQYESEKNPFAKYYEETGEKIRKFSKTGQGPYI
NKIKYLRERLGRHCDVTNKYINSRNKIVQLKIYSYRFDIYQYGNNYKMITISYIDLEQKSNYY
YISREKYEQKKKDKQIDDSYKFIGSFYKNDIINYNGEMYRVIGVNDSEKNKIQLDMIDISIKDY
MELNNIKKTGVIYKTIGKSTTHIEKYTTDILGNLYKAAPPKKPQLIFK.

[00186] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7029 (designated herein as *Staphylococcus microti* Cas9 or Smi Cas9):

MEKDYILGLDIGIGSVGYGLIDYDTKSIIDAGVRLFPEANADNNLGRRAKRGARRLKRRRIHR
LERVKSLLSEYKIISGLAPTNNQPYNIRVKGLTEQLTKDELAVALLHIAKRRGIHNVDVAADK
EETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQ
MQYYPEIDETFKEKYISLVETRREYYEGPGKGSPYGWDADVKKWYQLMMGHCTYFPVEFRS
VKYAYTADLYNALNDLNNLTIARDDNPKLEYHEKYHIIENVFKQKRNPTLKQIAKEIGVNDI
NISGYRVTKSGKPQFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLE
YLMSEADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGY
QRIPTDMIDDAILSPVVKRSFKQAIGVVNAIIKKYGLPKDIIIELARESNSAEKSRYLRAIQKKN
EKTRERIEAIIKEYGNENAKGLVQKIKLHDAQEGKCLYSLKDIPLEDLLRNPNNYDIDHIIPRS
VSFDDSMHNKVLVRREQNAKKNNQTPYQYLTSGYADIKYSVFKQHVLNLAENKDRMTKKK
REYLLEERNINKYDVQKEFINRNLVDTRYTTRELTTLLKTYFTINNLDVKVKTINGSFTDFLR
KRWGFKKNRDEGYKHHAEDALIIANADYLFKEHKLLKEIKDVSDLAGDERNSNVKDEDQYE
EVFGGYFKIEDIKKYKIKKFSHRVDKKPNRQLINDTIYSTRVKDDKRYLINTLKNLYDKSNGD
LKERMQKDPESLLMYHHDPQTFEKLKIVMSQYENEKNPLAKYFEETGQYLTKYAKHDNGPA
IHKIKYYGNKLVEHLDITKNYHNPQNKVVQLSQKSFRFDVYQTDKGYKFISIAYLTLKNEKN
YYAISQEKYDQLKSEKKISNNAVFIGSFYTSDIIEINNEKFRVIGVNSDKNNLIEVDRIDIRQKEF
IELEEEKKNNRIKVTIGRKTTNIEKFHTDILGNMYKSKRPKAPQLVFKKG.

[00187] In some embodiments, the Cas9 comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7030 (designated herein as *Staphylococcus pasteuri* Cas9 or Spa Cas9):

MKEKYILGLDLGITSVGYGIINFETKKIIDAGVRLFPEANVDNNEGRRSKRGSRRLKRRRIHRL
ERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNINVSSEDED
ASNELSTKEQINRNNKLLKDKYVCEVQLQRLKEGQIRGEKNRFKTTDILKEIDQLLKVQKDY
HNLDIDFINQYKEIVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVKYA
YSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKGYR
ITKSGTPQFTEFKLYHDLKSIVFDKSILENEAILDQIAEILTIYQDEQSIKEELNKLPEILNEQDK
AEIAKLIGYNGTHRLSLKCIHLINEELWQTSRNQMEIFNYLNIKPNKVDLSEQNKIPKDMVND
FILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRINEIIG
QTGNQNAKRIVEKIRLHDQQEGKCLYSLESIALMDLLNNPQNYEVDHIIPRSVAFDNSIHNKV
LVKQIENSKKGNRTPYQYLNSSDAKLSYNQFKQHILNLSKSKDRISKKKKDYLLEERDINKFE
VQKEFINRNLVDTRYATRELTSYLKAYFSANNMDVKVKTINGSFTNHLRKVWRFDKYRNHG
YKHHAEDALIIANADFLFKENKKLQNTNKILEKPTIENNTKKVTVEKEEDYNNVFETPKLVED
IKQYRDYKFSHRVDKKPNRQLINDTLYSTRMKDEHDYIVQTITDIYGKDNTNLKKQFNKNPE
KFLMYQNDPKTFEKLSIIMKQYSDEKNPLAKYYEETGEYLTKYSKKNNGPIVKKIKLLGNKV
GNHLDVTNKYENSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYIPKDKYQ
ELKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYCEINNIKG
EPRIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL.

[00188] In some embodiments, the Cas protein comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7031 (designated herein as Cas12i1):

MSNKEKNASETRKAYTTKMIPRSHDRMKLLGNFMDYLMDGTPIFFELWNQFGGGIDRDIISG
TANKDKISDDLLLAVNWFKVMPINSKPQGVSPSNLANLFQQYSGSEPDIQAQEYFASNFDTE
KHQWKDMRVEYERLLAELQLSRSDMHHDLKLMYKEKCIGLSLSTAHYITSVMFGTGAKNN
RQTKHQFYSKVIQLLEESTQINSVEQLASIILKAGDCDSYRKLRIRCSRKGATPSILKIVQDYEL
GTNHDDEVNVPSLIANLKEKLGRFEYECEWKCMEKIKAFLASKVGPYYLGSYSAMLENALS
PIKGMTTKNCKFVLKQIDAKNDIKYENEPFGKIVEGFFDSPYFESDTNVKWVLHPHHIGESNI
KTLWEDLNAIHSKYEEDIASLSEDKKEKRIKVYQGDVCQTINTYCEEVGKEAKTPLVQLLRY
LYSRKDDIAVDKIIDGITFLSKKHKVEKQKINPVIQKYPSFNFGNNSKLLGKIISPKDKLKHNL
KCNRNQVDNYIWIEIKVLNTKTMRWEKHHYALSSTRFLEEVYYPATSENPPDALAARFRTKT
NGYEGKPALSAEQIEQIRSAPVGLRKVKKRQMRLEAARQQNLLPRYTWGKDFNINICKRGN
NFEVTLATKVKKKKEKNYKVVLGYDANIVRKNTYAAIEAHANGDGVIDYNDLPVKPIESGF
VTVESQVRDKSYDQLSYNGVKLLYCKPHVESRRSFLEKYRNGTMKDNRGNNIQIDFMKDFE
AIADDETSLYYFNMKYCKLLQSSIRNHSSQAKEYREEIFELLRDGKLSVLKLSSLSNLSFVMF
KVAKSLIGTYFGHLLKKPKNSKSDVKAPPITDEDKQKADPEMFALRLALEEKRLNKVKSKKE

VIANKIVAKALELRDKYGPVLIKGENISDTTKKGKKSSTNSFLMDWLARGVANKVKEMVMMHQGLEFVEVNPNFTSHQDPFVHKNPENTFRARYSRCTPSELTEKNRKEILSFLSDKPSKRPTNAYYNEGAMAFLATYGLKKNDVLGVSLEKFKQIMANILHQRSEDQLLFPSRGGMFYLATYKLDADATSVNWNGKQFWVCNADLVAAYNVGLVDIQKDFKKK.

[00189] In some embodiments, the Cas protein comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of SEQ ID NO: 7032 (designated herein as Cas12i2): MSSAIKSYKSVLRPNERKNQLLKSTIQCLEDGSAFFFKMLQGLFGGITPEIVRFSTEQEKQQQDIALWCAVNWFRPVSQDSLTHTIASDNLVEKFEEYYGGTASDAIKQYFSASIGESYYWNDCRQQYYDLCRELGVEVSDLTHDLEILCREKCLAVATESNQNNSIISVLFGTGEKEDRSVKLRITKKILEAISNLKEIPKNVAPIQEIILNVAKATKETFRQVYAGNLGAPSTLEKFIAKDGQKEFDLKKLQTDLKKVIRGKSKERDWCCQEELRSYVEQNTIQYDLWAWGEMFNKAHTALKIKSTRNYNFAKQRLEQFKEIQSLNNLLVVKKLNDFFDSEFFSGEETYTICVHHLGGKDLSKLYKAWEDDPADPENAIVVLCDDLKNNFKKEPIRNILRYIFTIRQECSAQDILAAAKYNQQLDRYKSQKANPSVLGNQGFTWTNAVILPEKAQRNDRPNSLDLRIWLYLKLRHPDGRWKKHHIPFYDTRFFQEIYAAGNSPVDTCQFRTPRFGYHLPKLTDQTAIRVNKKHVKAAKTEARIRLAIQQGTLPVSNLKITEISATINSKGQVRIPVKFDVGRQKGTLQIGDRFCGYDQNQTASHAYSLWEVVKEGQYHKELGCFVRFISSGDIVSITENRGNQFDQLSYEGLAYPQYADWRKKASKFVSLWQITKKNKKKEIVTVEAKEKFDAICKYQPRLYKFNKEYAYLLRDIVRGKSLVELQQIRQEIFRFIEQDCGVTRLGSLSLSTLETVKAVKGIIYSYFSTALNASKNNPISDEQRKEFDPELFALLEKLELIRTRKKKQKVERIANSLIQTCLENNIKFIRGEGDLSTTNNATKKKANSRSMDWLARGVFNKIRQLAPMHNITLFGCGSLYTSHQDPLVHRNPDKAMKCRWAAIPVKDIGDWVLRKLSQNLRAKNIGTGEYYHQGVKEFLSHYELQDLEEELLKWRSDRKSNIPCWVLQNRLAEKLGNKEAVVYIPVRGGRIYFATHKVATGAVSIVFDQKQVWVCNADHVAAANIALTVKGIGEQSSDEENPDGSRIKLQLTS.

Modified guide RNAs

[00190] In some embodiments, the guide RNA is chemically modified. A guide RNA comprising one or more modified nucleosides or nucleotides is called a "modified" guide RNA or "chemically modified" guide RNA, to describe the presence of one or more non-naturally and/or naturally occurring components or configurations that are used instead of or in addition to the canonical A, G, C, and U residues. In some embodiments, a modified guide RNA is synthesized with a non-canonical nucleoside or nucleotide, is here called "modified." Modified nucleosides and nucleotides can include one or more of: (i) alteration, e.g., replacement, of one or both of the non-linking phosphate oxygens and/or of one or more of the linking phosphate oxygens in the phosphodiester backbone linkage (an exemplary backbone modification); (ii) alteration, e.g., replacement, of a constituent of the ribose sugar, e.g., of the 2' hydroxyl on the ribose sugar (an exemplary sugar modification); (iii) wholesale replacement of the phosphate moiety with "dephospho" linkers (an exemplary backbone

modification); (iv) modification or replacement of a naturally occurring nucleobase, including with a non-canonical nucleobase (an exemplary base modification); (v) replacement or modification of the ribose-phosphate backbone (an exemplary backbone modification); (vi) modification of the 3' end or 5' end of the oligonucleotide, e.g., removal, modification or replacement of a terminal phosphate group or conjugation of a moiety, cap or linker (such 3' or 5' cap modifications may comprise a sugar and/or backbone modification); and (vii) modification or replacement of the sugar (an exemplary sugar modification).

[00191] Chemical modifications such as those listed above can be combined to provide modified guide RNAs comprising nucleosides and nucleotides (collectively "residues") that can have two, three, four, or more modifications. For example, a modified residue can have a modified sugar and a modified nucleobase, or a modified sugar and a modified phosphodiester. In some embodiments, every base of a guide RNA is modified, *e.g.*, all bases have a modified phosphate group, such as a phosphorothioate group. In certain embodiments, all, or substantially all, of the phosphate groups of a guide RNA molecule are replaced with phosphorothioate groups. In some embodiments, modified guide RNAs comprise at least one modified residue at or near the 5' end of the RNA. In some embodiments, modified guide RNAs comprise at least one modified residue at or near the 3' end of the RNA.

[00192] In some embodiments, the guide RNA comprises one, two, three or more modified residues. In some embodiments, at least 5% (*e.g.*, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100%) of the positions in a modified guide RNA are modified nucleosides or nucleotides.

[00193] Unmodified nucleic acids can be prone to degradation by, *e.g.*, intracellular nucleases or those found in serum. For example, nucleases can hydrolyze nucleic acid phosphodiester bonds. Accordingly, in one aspect the guide RNAs described herein can contain one or more modified nucleosides or nucleotides, *e.g.*, to introduce stability toward intracellular or serum-based nucleases. In some embodiments, the modified guide RNA molecules described herein can exhibit a reduced innate immune response when introduced into a population of cells, both *in vivo* and *ex vivo*. The term "innate immune response" includes a cellular response to exogenous nucleic acids, including single stranded nucleic acids, which involves the induction of cytokine expression and release, particularly the interferons, and cell death.

[00194] In some embodiments of a backbone modification, the phosphate group of a modified residue can be modified by replacing one or more of the oxygens with a different substituent. Further, the modified residue, *e.g.*, modified residue present in a modified nucleic acid, can include the wholesale replacement of an unmodified phosphate moiety with a modified phosphate group as described herein. In some embodiments, the backbone modification of the phosphate backbone can

include alterations that result in either an uncharged linker or a charged linker with unsymmetrical charge distribution.

[00195] Examples of modified phosphate groups include, phosphorothioate, phosphoroselenates, borano phosphates, borano phosphate esters, hydrogen phosphonates, phosphoroamidates, alkyl or aryl phosphonates and phosphotriesters. The phosphorous atom in an unmodified phosphate group is achiral. However, replacement of one of the non-bridging oxygens with one of the above atoms or groups of atoms can render the phosphorous atom chiral. The stereogenic phosphorous atom can possess either the "R" configuration (herein Rp) or the "S" configuration (herein Sp). The backbone can also be modified by replacement of a bridging oxygen, (*i.e.*, the oxygen that links the phosphate to the nucleoside), with nitrogen (bridged phosphoroamidates), sulfur (bridged phosphorothioates) and carbon (bridged methylenephosphonates). The replacement can occur at either linking oxygen or at both of the linking oxygens.

[00196] The phosphate group can be replaced by non-phosphorus containing connectors in certain backbone modifications. In some embodiments, the charged phosphate group can be replaced by a neutral moiety. Examples of moieties which can replace the phosphate group can include, without limitation, *e.g.*, methyl phosphonate, hydroxylamino, siloxane, carbonate, carboxymethyl, carbamate, amide, thioether, ethylene oxide linker, sulfonate, sulfonamide, thioformacetal, formacetal, oxime, methyleneimino, methylenemethylimino, methylenehydrazo, methylenedimethylhydrazo and methyleneoxymethylimino.

[00197] Scaffolds that can mimic nucleic acids can also be constructed wherein the phosphate linker and ribose sugar are replaced by nuclease resistant nucleoside or nucleotide surrogates. Such modifications may comprise backbone and sugar modifications. In some embodiments, the nucleobases can be tethered by a surrogate backbone. Examples can include, without limitation, the morpholino, cyclobutyl, pyrrolidine and peptide nucleic acid (PNA) nucleoside surrogates.

[00198] The modified nucleosides and modified nucleotides can include one or more modifications to the sugar group, *i.e.* at sugar modification. For example, the 2' hydroxyl group (OH) can be modified, *e.g.* replaced with a number of different "oxy" or "deoxy" substituents. In some embodiments, modifications to the 2' hydroxyl group can enhance the stability of the nucleic acid since the hydroxyl can no longer be deprotonated to form a 2'-alkoxide ion.

[00199] Examples of 2' hydroxyl group modifications can include alkoxy or aryloxy (OR, wherein "R" can be, *e.g.*, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or a sugar); polyethyleneglycols (PEG), $O(CH_2CH_2O)_nCH_2CH_2OR$ wherein R can be, *e.g.*, H or optionally substituted alkyl, and n can be an integer from 0 to 20 (*e.g.*, from 0 to 4, from 0 to 8, from 0 to 10, from 0 to 16, from 1 to 4, from 1 to 8, from 1 to 10, from 1 to 16, from 1 to 20, from 2 to 4, from 2 to 8, from 2 to 10, from 2 to 16, from 2 to 20, from 4 to 8, from 4 to 10, from 4 to 16, and from 4 to 20). In some embodiments, the 2'

hydroxyl group modification can be 2'-O-Me. In some embodiments, the 2' hydroxyl group modification can be a 2'-fluoro modification, which replaces the 2' hydroxyl group with a fluoride. In some embodiments, the 2' hydroxyl group modification can include "locked" nucleic acids (LNA) in which the 2' hydroxyl can be connected, *e.g.*, by a C_{1-6} alkylene or C_{1-6} heteroalkylene bridge, to the 4' carbon of the same ribose sugar, where exemplary bridges can include methylene, propylene, ether, or amino bridges; O-amino (wherein amino can be, *e.g.*, NH_2; alkylamino, dialkylamino, heterocyclyl, arylamino, diarylamino, heteroarylamino, or diheteroarylamino, ethylenediamine, or polyamino) and aminoalkoxy, $O(CH_2)_n$-amino, (wherein amino can be, *e.g.*, NH_2; alkylamino, dialkylamino, heterocyclyl, arylamino, diarylamino, heteroarylamino, or diheteroarylamino, ethylenediamine, or polyamino). In some embodiments, the 2' hydroxyl group modification can include "unlocked" nucleic acids (UNA) in which the ribose ring lacks the C2'-C3' bond. In some embodiments, the 2' hydroxyl group modification can include the methoxyethyl group (MOE), ($OCH_2CH_2OCH_3$, *e.g.*, a PEG derivative).

[00200] "Deoxy" 2' modifications can include hydrogen (*i.e.* deoxyribose sugars, *e.g.*, at the overhang portions of partially dsRNA); halo (*e.g.*, bromo, chloro, fluoro, or iodo); amino (wherein amino can be, *e.g.*, NH_2; alkylamino, dialkylamino, heterocyclyl, arylamino, diarylamino, heteroarylamino, diheteroarylamino, or amino acid); $NH(CH_2CH_2NH)_nCH2CH_2$- amino (wherein amino can be, *e.g.*, as described herein), -NHC(O)R (wherein R can be, *e.g.*, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or sugar), cyano; mercapto; alkyl-thio-alkyl; thioalkoxy; and alkyl, cycloalkyl, aryl, alkenyl and alkynyl, which may be optionally substituted with *e.g.*, an amino as described herein.

[00201] The sugar modification can comprise a sugar group which may also contain one or more carbons that possess the opposite stereochemical configuration than that of the corresponding carbon in ribose. Thus, a modified nucleic acid can include nucleotides containing *e.g.*, arabinose, as the sugar. The modified nucleic acids can also include abasic sugars. These abasic sugars can also be further modified at one or more of the constituent sugar atoms. The modified nucleic acids can also include one or more sugars that are in the L form, *e.g.* L- nucleosides.

[00202] The modified nucleosides and modified nucleotides described herein, which can be incorporated into a modified nucleic acid, can include a modified base, also called a nucleobase. Examples of nucleobases include, but are not limited to, adenine (A), guanine (G), cytosine (C), and uracil (U). These nucleobases can be modified or wholly replaced to provide modified residues that can be incorporated into modified nucleic acids. The nucleobase of the nucleotide can be independently selected from a purine, a pyrimidine, a purine analog, or pyrimidine analog. In some embodiments, the nucleobase can include, for example, naturally-occurring and synthetic derivatives of a base.

[00203] In embodiments employing a dual guide RNA, each of the crRNA and the tracr RNA can contain modifications. Such modifications may be at one or both ends of the crRNA and/or tracr RNA. In embodiments comprising sgRNA, one or more residues at one or both ends of the sgRNA may be chemically modified, and/or internal nucleosides may be modified, and/or the entire sgRNA may be chemically modified. Certain embodiments comprise a 5' end modification. Certain embodiments comprise a 3' end modification.

[00204] Modifications of 2'-O-methyl are encompassed.

[00205] 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. Modifications of 2'-fluoro (2'-F) are encompassed.

[00206] 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 in the bonds between nucleotides bases. When phosphorothioates are used to generate oligonucleotides, the modified oligonucleotides may also be referred to as S-oligos.

[00207] Abasic nucleotides refer to those which lack nitrogenous bases.

[00208] 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).

[00209] 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.

[00210] In some embodiments, one or more of the first three, four, or five nucleotides at the 5' terminus, and one or more of the last three, four, or five nucleotides at the 3' terminus are modified. In some embodiments, the modification is a 2'-O-Me, 2'-F, inverted abasic nucleotide, PS bond, or other nucleotide modification well known in the art to increase stability and/or performance.

[00211] In some embodiments, the first four nucleotides at the 5' terminus, and the last four nucleotides at the 3' terminus are linked with phosphorothioate (PS) bonds.

[00212] In some embodiments, the first three nucleotides at the 5' terminus, and the last three nucleotides at the 3' terminus comprise a 2'-O-methyl (2'-O-Me) modified nucleotide. In some embodiments, the first three nucleotides at the 5' terminus, and the last three nucleotides at the 3' terminus comprise a 2'-fluoro (2'-F) modified nucleotide.

Ribonucleoprotein complex

[00213] In some embodiments, a composition is encompassed comprising: a) one or more guide RNAs comprising one or more guide sequences from **Table 6** and b) SaCas9 (when combined with a

gRNA comprising any one of or combination of SEQ ID Nos: 1-159) or SluCas9 (when combined with a gRNA comprising any one of or combination of SEQ ID Nos: 200-292, 924-938, or 950-955), or any of the mutant Cas9 proteins disclosed herein. In some embodiments, the guide RNA together with a Cas9 is called a ribonucleoprotein complex (RNP).

[00214] In some embodiments, the disclosure provides for an RNP complex, wherein the guide RNA (*e.g.*, any of the guide RNAs disclosed herein) binds to or is capable of binding to a target sequence in the dystrophin gene.

[00215] In some embodiments, chimeric Cas9 (SaCas9 or SluCas9) nucleases are used, where one domain or region of the protein is replaced by a portion of a different protein. In some embodiments, a Cas9 nuclease domain may be replaced with a domain from a different nuclease such as Fok1. In some embodiments, a Cas9 nuclease may be a modified nuclease.

[00216] In some embodiments, the Cas9 is modified to contain only one functional nuclease domain. For example, the agent protein may be modified such that one of the nuclease domains is mutated or fully or partially deleted to reduce its nucleic acid cleavage activity.

[00217] In some embodiments, a conserved amino acid within a Cas9 protein nuclease domain is substituted to reduce or alter nuclease activity. In some embodiments, a Cas9 nuclease 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). *See*, *e.g.*, Zetsche et al. (2015) *Cell* Oct 22:163(3): 759-771. In some embodiments, the Cas9 nuclease 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 S. *pyogenes* Cas9 protein). *See*, *e.g.*, Zetsche et al. (2015). Further exemplary amino acid substitutions include D917A, E1006A, and D1255A (based on the *Francisella novicida* U112 Cpf1 (FnCpf1) sequence (UniProtKB - A0Q7Q2 (CPF1_FRATN)). Further exemplary amino acid substitutions include D10A and N580A (based on the *S. aureus* Cas9 protein). *See, e.g.*, Friedland et al., 2015, Genome Biol., 16:257.

[00218] In some embodiments, the Cas9 lacks cleavase activity. In some embodiments, the Cas9 comprises a dCas DNA-binding polypeptide. A dCas polypeptide has DNA-binding activity while essentially lacking catalytic (cleavase/nickase) activity. In some embodiments, the dCas polypeptide is a dCas9 polypeptide. In some embodiments, the Cas9 lacking cleavase activity or the dCas DNA-binding polypeptide is a version of a Cas nuclease (e.g., a Cas9 nuclease discussed above) in which its endonucleolytic active sites are inactivated, e.g., by one or more alterations (e.g., point mutations) in its catalytic domains. See, e.g., US 2014/0186958 A1; US 2015/0166980 A1.

[00219] In some embodiments, the Cas9 comprises one or more heterologous functional domains (e.g., is or comprises a fusion polypeptide).

[00220] In some embodiments, the heterologous functional domain may facilitate transport of the Cas9 into the nucleus of a cell. For example, the heterologous functional domain may be a nuclear

localization signal (NLS). In some embodiments, the Cas9 may be fused with 1-10 NLS(s). In some embodiments, the Cas9 may be fused with 1-5 NLS(s). In some embodiments, the Cas9 may be fused with 1-3 NLS(s). In some embodiments, the Cas9 may be fused with one NLS. Where one NLS is used, the NLS may be attached at the N-terminus or the C-terminus of the Cas9 sequence, and may be directly fused/attached. In some embodiments, where more than one NLS is used, one or more NLS may be attached at the N-terminus and/or one or more NLS may be attached at the C-terminus. In some embodiments, one or more NLSs are directly attached to the Cas9. In some embodiments, one or more NLSs are attached to the Cas9 by means of a linker. In some embodiments, the linker is between 3-25 amino acids in length. In some embodiments, the linker is between 3-6 amino acids in length. In some embodiments, the linker comprises glycine and serine. In some embodiments, the linker comprises the sequence of GSVD (SEQ ID NO: 550) or GSGS (SEQ ID NO: 551). It may also be inserted within the Cas9 sequence. In other embodiments, the Cas9 may be fused with more than one NLS. In some embodiments, the Cas9 may be fused with 2, 3, 4, or 5 NLSs. In some embodiments, the Cas9 may be fused with two NLSs. In certain circumstances, the two NLSs may be the same (*e.g.*, two SV40 NLSs) or different. In some embodiments, the Cas9 protein is fused with one or more SV40 NLSs. In some embodiments, the SV40 NLS comprises the amino acid sequence of SEQ ID NO: 713 (PKKKRKV). In some embodiments, the Cas9 protein (e.g., the SaCas9 or SluCas9 protein) is fused to one or more nucleoplasmin NLSs. In some embodiments, the Cas protein is fused to one or more c-myc NLSs. In some embodiments, the Cas protein is fused to one or more E1A NLSs. In some embodiments, the Cas protein is fused to one or more BP (bipartite) NLSs. In some embodiments, the nucleoplasmin NLS comprises the amino acid sequence of SEQ ID NO: 714 (KRPAATKKAGQAKKKK). In some embodiments, the Cas9 protein is fused with a c-Myc NLS. In some embodiments, the c-Myc NLS comprises the amino acid sequence of SEQ ID NO: 942 (PAAKKKKLD) and/or is encoded by the nucleic acid sequence of SEQ ID NO: 722 (CCGGCAGCTAAGAAAAAGAAACTGGAT). In some embodiments, the Cas9 is fused to two SV40 NLS sequences linked at the carboxy terminus. In some embodiments, the Cas9 may be fused with two NLSs, one linked at the N-terminus and one at the C-terminus. In some embodiments, the Cas9 may be fused with 3 NLSs. In some embodiments, the Cas9 may be fused with 3 NLSs, two linked at the N-terminus and one linked at the C-terminus. In some embodiments, the Cas9 may be fused with 3 NLSs, one linked at the N-terminus and two linked at the C-terminus. In some embodiments, the Cas9 may be fused with no NLS. In some embodiments, the Cas9 may be fused with one NLS. In some embodiments, the Cas9 may be fused with an NLS on the C-terminus and does not comprise an NLS fused on the N-terminus. In some embodiments, the Cas9 may be fused with an NLS on the N-terminus and does not comprise an NLS fused on the C-terminus. In some embodiments, the Cas9 protein is fused to an SV40 NLS and to a nucleoplasmin NLS. In some embodiments, the Cas9 protein is fused to an SV40 NLS and to a c-Myc NLS. In some embodiments, the SV40 NLS is fused to the C-terminus of the Cas9, while the nucleoplasmin NLS is fused to the N-terminus of the Cas9 protein. In some embodiments, the SV40 NLS is fused to the C-terminus of the Cas9, while the c-Myc NLS is fused to the N-terminus of the Cas9 protein. In some embodiments, the SV40 NLS is fused to the N-terminus of the Cas9, while the nucleoplasmin NLS is fused to the C-terminus of the Cas9 protein. In some embodiments, the SV40 NLS is fused to the N-terminus of the Cas9, while the c-Myc NLS is fused to the C-terminus of the Cas9 protein. In some embodiments, the SV40 NLS is fused to the Cas9 protein by means of a linker. In some embodiments, the SV40 NLS and linker is encoded by the nucleic acid sequence of SEQ ID NO: 723 (ATGATGGCCCCAAAGAAGAAGCGGAAGGTCGGTATCCACGGAGTCCCAGCAGCC). In some embodiments, the nucleoplasmin NLS is fused to the Cas9 protein by means of a linker. In some embodiments, the c-Myc NLS is fused to the Cas9 protein by means of a linker. In some embodiments, an additional domain may be: a) fused to the N- or C-terminus of the Cas protein (e.g., a Cas9 protein), b) fused to the N-terminus of an NLS fused to the N-terminus of a Cas protein, or c) fused to the C-terminus of an NLS fused to the C-terminus of a Cas protein. In some embodiments, an NLS is fused to the N- and/or C-terminus of the Cas protein by means of a linker. In some embodiments, an NLS is fused to the N-terminus of an N-terminally-fused NLS on a Cas protein by means of a linker, and/or an NLS is fused to the C-terminus of a C-terminally fused NLS on a Cas protein by means of a linker. In some embodiments, the linker is GSVD (SEQ ID NO: 550) or GSGS (SEQ ID NO: 551). In some embodiments, the Cas protein comprises a c-Myc NLS fused to the N-terminus of the Cas protein (or to an N-terminally-fused NLS on the Cas protein), optionally by means of a linker. In some embodiments, the Cas protein comprises an SV40 NLS fused to the C-terminus of the Cas protein (or to a C-terminally-fused NLS on the Cas protein), optionally by means of a linker. In some embodiments, the Cas protein comprises a nucleoplasmin NLS fused to the C-terminus of the Cas protein (or to a C-terminally-fused NLS on the Cas protein), optionally by means of a linker. In some embodiments, the Cas protein comprises: a) a c-Myc NLS fused to the N-terminus of the Cas protein, optionally by means of a linker, b) an SV40 NLS fused to the C-terminus of the Cas protein, optionally by means of a linker, and c) a nucleoplasmin NLS fused to the C-terminus of the SV40 NLS, optionally by means of a linker. In some embodiments, the Cas protein comprises: a) a c-Myc NLS fused to the N-terminus of the Cas protein, optionally by means of a linker, b) a nucleoplasmin NLS fused to the C-terminus of the Cas protein, optionally by means of a linker, and c) an SV40 NLS fused to the C-terminus of the nucleoplasmin NLS, optionally by means of a linker. In some embodiments, a c-myc NLS is fused to the N-terminus of the Cas9 and an SV40 NLS and/or nucleoplasmin NLS is fused to the C-terminus of the Cas9. In some embodiments, a c-myc NLS is fused to the N-terminus of the Cas9 (e.g., by means of a linker such as GSVD), an SV40 NLS is fused to the C-terminus of the Cas9 (e.g., by means of a linker such as GSGS), and a nucleoplasmin NLS is fused to the C-terminus of the SV-40 NLS (e.g., by means of a linker such as GSGS).

[00221] In some embodiments, the heterologous functional domain may be capable of modifying the intracellular half-life of the Cas9. In some embodiments, the half-life of the Cas9 may be increased. In some embodiments, the half-life of the Cas9 may be reduced. In some embodiments, the heterologous functional domain may be capable of increasing the stability of the Cas9. In some embodiments, the heterologous functional domain may be capable of reducing the stability of the Cas9. In some embodiments, the heterologous functional domain may act as a signal peptide for protein degradation. In some embodiments, the protein degradation may be mediated by proteolytic enzymes, such as, for example, proteasomes, lysosomal proteases, or calpain proteases. In some embodiments, the heterologous functional domain may comprise a PEST sequence. In some embodiments, the Cas9 may be modified by addition of ubiquitin or a polyubiquitin chain. In some embodiments, the ubiquitin may be a ubiquitin-like protein (UBL). Non-limiting examples of ubiquitin-like proteins include small ubiquitin-like modifier (SUMO), ubiquitin cross-reactive protein (UCRP, also known as interferon-stimulated gene-15 (ISG15)), ubiquitin-related modifier-1 (URM1), neuronal-precursor-cell-expressed developmentally downregulated protein-8 (NEDD8, also called Rub1 in *S. cerevisiae*), human leukocyte antigen F-associated (FAT10), autophagy-8 (ATG8) and -12 (ATG12), Fau ubiquitin-like protein (FUB1), membrane-anchored UBL (MUB), ubiquitin fold-modifier-1 (UFM1), and ubiquitin-like protein-5 (UBL5).

[00222] In some embodiments, the heterologous functional domain may be a marker domain. Non-limiting examples of marker domains include fluorescent proteins, purification tags, epitope tags, and reporter gene sequences. In some embodiments, the marker domain may be a fluorescent protein. Non-limiting examples of suitable fluorescent proteins include green fluorescent proteins (*e.g.*, GFP, GFP-2, tagGFP, turboGFP, sfGFP, EGFP, Emerald, Azami Green, Monomeric Azami Green, CopGFP, AceGFP, ZsGreen1), yellow fluorescent proteins (*e.g.*, YFP, EYFP, Citrine, Venus, YPet, PhiYFP, ZsYellow1), blue fluorescent proteins (*e.g.*, EBFP, EBFP2, Azurite, mKalamal, GFPuv, Sapphire, T-sapphire,), cyan fluorescent proteins (*e.g.*, ECFP, Cerulean, CyPet, AmCyan1, Midoriishi-Cyan), red fluorescent proteins (*e.g.*, mKate, mKate2, mPlum, DsRed monomer, mCherry, mRFP1, DsRed-Express, DsRed2, DsRed-Monomer, HcRed-Tandem, HcRed1, AsRed2, eqFP611, mRasberry, mStrawberry, Jred), and orange fluorescent proteins (mOrange, mKO, Kusabira-Orange, Monomeric Kusabira-Orange, mTangerine, tdTomato) or any other suitable fluorescent protein. In other embodiments, the marker domain may be a purification tag and/or an epitope tag. Non-limiting exemplary tags include glutathione-S-transferase (GST), chitin binding protein (CBP), maltose binding protein (MBP), thioredoxin (TRX), poly(NANP), tandem affinity purification (TAP) tag, myc, AcV5, AU1, AU5, E, ECS, E2, FLAG, HA, nus, Softag 1, Softag 3, Strep, SBP, Glu-Glu, HSV, KT3, S, S1, T7, V5, VSV-G, 6xHis, 8xHis, biotin carboxyl carrier protein (BCCP), poly-His, and calmodulin. Non-limiting exemplary reporter genes include glutathione-S-transferase (GST), horseradish peroxidase (HRP), chloramphenicol acetyltransferase (CAT), beta-galactosidase, beta-glucuronidase, luciferase, or fluorescent proteins.

[00223] In additional embodiments, the heterologous functional domain may target the Cas9 to a specific organelle, cell type, tissue, or organ. In some embodiments, the heterologous functional domain may target the Cas9 to muscle.

[00224] In further embodiments, the heterologous functional domain may be an effector domain. When the Cas9 is directed to its target sequence, *e.g.*, when a Cas9 is directed to a target sequence by a guide RNA, the effector domain may modify or affect the target sequence. In some embodiments, the effector domain may be chosen from a nucleic acid binding domain or a nuclease domain (e.g., a non-Cas nuclease domain). In some embodiments, the heterologous functional domain is a nuclease, such as a FokI nuclease. See, e.g., US Pat. No. 9,023,649.

[00225] In some embodiments, any of the compositions disclosed herein comprising any of the guides and/or endonucleases disclosed herein is sterile and/or substantially pyrogen-free. In particular embodiments, any of the compositions disclosed herein comprise a pharmaceutically acceptable carrier. The phrase "pharmaceutically or pharmacologically acceptable" refers to molecular entities and compositions that do not produce an adverse, allergic, or other untoward reaction when administered to an animal or human. As used herein “pharmaceutically acceptable carrier” includes any and all solvents (e.g., water), dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible, including pharmaceutically acceptable cell culture media. Pharmaceutically acceptable carriers include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. In some embodiments, the composition comprises a preservative to prevent the growth of microorganisms.

Determination of efficacy of guide RNAs

[00226] In some embodiments, the efficacy of a guide RNA is determined when delivered or expressed together with other components forming an RNP. In some embodiments, the guide RNA is expressed together with a SaCas9 or SluCas9. In some embodiments, the guide RNA is delivered to or expressed in a cell line that already stably expresses an SaCas9 or SluCas9. In some embodiments the guide RNA is delivered to a cell as part of an RNP. In some embodiments, the guide RNA is delivered to a cell along with a nucleic acid (e.g., mRNA) encoding SaCas9 or SluCas9.

[00227] In some embodiments, the efficacy of particular guide RNAs is determined based on *in vitro* models. In some embodiments, the *in vitro* model is a cell line.

[00228] In some embodiments, the efficacy of particular guide RNAs is determined across multiple *in vitro* cell models for a guide RNA selection process. In some embodiments, a cell line comparison of data with selected guide RNAs is performed. In some embodiments, cross screening in multiple cell models is performed.

[00229] In some embodiments, the efficacy of particular guide RNAs is determined based on *in vivo* models. In some embodiments, the *in vivo* model is a rodent model. In some embodiments, the

rodent model is a mouse which expresses a mutated dystrophin gene. In some embodiments, the *in vivo* model is a non-human primate, for example cynomolgus monkey.

III. Methods of Gene Editing and Treating DMD

[00230] This disclosure provides methods for gene editing and treating Duchenne Muscular Dystrophy (DMD). In some embodiments, any of the compositions described herein may be administered to a subject in need thereof for use in making a double or single strand break, or excising a portion (e.g., less than about 250 nucleotides) in any one or more of exons 44, 45, 50, 51, or 53 of the dystrophin (DMD) gene and to treat DMD. In some embodiments, pairs of guide RNAs described herein, in any of the vector configurations described herein, may be administered to a subject in need thereof to make a single or double-strand break, excise a portion of a DMD, and treat DMD. In some embodiments, any of the compositions described herein may be administered to a subject in need thereof for use in treating DMD exon. In some embodiments, a nucleic acid molecule comprising a first nucleic acid encoding one or more guide RNAs of **Table 6** and a second nucleic acid encoding either SaCas9 or SluCas9 (depending on the guide) is administered to a subject to treat DMD. In some embodiments, a single nucleic acid molecule (which may be a vector, including an AAV vector) comprising a first nucleic acid encoding one or more guide RNAs of **Table 6** and a second nucleic acid encoding either SaCas9 or SluCas9 (depending on the guide) is administered to a subject to treat DMD. In some embodiments, more than one nucleic acid molecules (which may be a vectors, including an AAV vectors) are administered to a subject to treat DMD, wherein a first nucleic acid encoding one or more guide RNAs of **Table 6** and a second nucleic acid encoding either SaCas9 or SluCas9 (depending on the guide) are together on one nucleic acid molecule or separated on different nucleic acid molecules.

[00231] In some embodiments, any of the compositions described herein is administered to a subject in need thereof to treat Duchenne Muscular Dystrophy (DMD).

[00232] In some embodiments, any of the compositions described herein is administered to a subject in need thereof to induce a double or single strand break in any one or more of exons 44, 45, 50, 51, or 53 of the dystrophin gene.

[00233] In some embodiments, any of the compositions described herein is administered to a subject in need thereof to delete a portion (e.g., excise a portion) any one of exons 44, 45, 50, 51, or 53 of the dystrophin gene.

[00234] In some embodiments, a method of treating Duchenne Muscular Dystrophy (DMD) is provided, the method comprising delivering to a cell any one of the compositions described herein, wherein the cell comprises a mutation in the dystrophin gene that is known to be associated with DMD.

[00235] In some embodiments, methods are provided for treating Duchenne Muscular Dystrophy (DMD), the method comprising delivering to a cell at least one nucleic acid molecule comprising a

pair of guide RNAs comprising a first and second spacer sequence, wherein the pair of first and spacer sequences are selected from any one of the following pairs: SEQ ID NO: 1 and SEQ ID NO: 3; SEQ ID NO: 3 and SEQ ID NO: 4; SEQ ID NO: 3 and SEQ ID NO: 5; SEQ ID NO: 3 and SEQ ID NO: 6; SEQ ID NO: 3 and SEQ ID NO: 7; SEQ ID NO: 3 and SEQ ID NO: 8; SEQ ID NO: 3 and SEQ ID NO: 9; SEQ ID NO: 4 and SEQ ID NO: 5; SEQ ID NO: 4 and SEQ ID NO: 6; SEQ ID NO: 4 and SEQ ID NO: 7; SEQ ID NO: 4 and SEQ ID NO: 8; SEQ ID NO: 4 and SEQ ID NO: 9; SEQ ID NO: 5 and SEQ ID NO: 6; SEQ ID NO: 5 and SEQ ID NO: 7; SEQ ID NO: 5 and SEQ ID NO: 8; SEQ ID NO: 5 and SEQ ID NO: 9; SEQ ID NO: 6 and SEQ ID NO: 7; SEQ ID NO: 6 and SEQ ID NO: 8; SEQ ID NO: 6 and SEQ ID NO: 9; SEQ ID NO: 7 and SEQ ID NO: 8; SEQ ID NO: 7 and SEQ ID NO: 9; SEQ ID NO: 8 and SEQ ID NO: 9; SEQ ID NO: 11 and SEQ ID NO: 12; SEQ ID NO: 11 and SEQ ID NO: 13; SEQ ID NO: 11 and SEQ ID NO: 14; SEQ ID NO: 11 and SEQ ID NO: 15; SEQ ID NO: 12 and SEQ ID NO: 13; SEQ ID NO: 12 and SEQ ID NO: 14; SEQ ID NO: 12 and SEQ ID NO: 15; SEQ ID NO: 13 and SEQ ID NO: 14; SEQ ID NO: 13 and SEQ ID NO: 15; SEQ ID NO: 14 and SEQ ID NO: 15; SEQ ID NO: 16 and SEQ ID NO: 17; SEQ ID NO: 16 and SEQ ID NO: 18; SEQ ID NO: 16 and SEQ ID NO: 19; SEQ ID NO: 16 and SEQ ID NO: 20; SEQ ID NO: 16 and SEQ ID NO: 21; SEQ ID NO: 16 and SEQ ID NO: 22; SEQ ID NO: 16 and SEQ ID NO: 23; SEQ ID NO: 16 and SEQ ID NO: 24; SEQ ID NO: 16 and SEQ ID NO: 25; SEQ ID NO: 16 and SEQ ID NO: 26; SEQ ID NO: 17 and SEQ ID NO: 18; SEQ ID NO: 17 and SEQ ID NO: 19; SEQ ID NO: 17 and SEQ ID NO: 20; SEQ ID NO: 17 and SEQ ID NO: 21; SEQ ID NO: 17 and SEQ ID NO: 22; SEQ ID NO: 17 and SEQ ID NO: 23; SEQ ID NO: 17 and SEQ ID NO: 24; SEQ ID NO: 17 and SEQ ID NO: 25; SEQ ID NO: 17 and SEQ ID NO: 26; SEQ ID NO: 18 and SEQ ID NO: 19; SEQ ID NO: 18 and SEQ ID NO: 20; SEQ ID NO: 18 and SEQ ID NO: 21; SEQ ID NO: 18 and SEQ ID NO: 22; SEQ ID NO: 18 and SEQ ID NO: 23; SEQ ID NO: 18 and SEQ ID NO: 24; SEQ ID NO: 18 and SEQ ID NO: 25; SEQ ID NO: 18 and SEQ ID NO: 26; SEQ ID NO: 19 and SEQ ID NO: 20; SEQ ID NO: 19 and SEQ ID NO: 21; SEQ ID NO: 19 and SEQ ID NO: 22; SEQ ID NO: 19 and SEQ ID NO: 23; SEQ ID NO: 19 and SEQ ID NO: 24; SEQ ID NO: 19 and SEQ ID NO: 25; SEQ ID NO: 19 and SEQ ID NO: 26; SEQ ID NO: 20 and SEQ ID NO: 21; SEQ ID NO: 20 and SEQ ID NO: 22; SEQ ID NO: 20 and SEQ ID NO: 23; SEQ ID NO: 20 and SEQ ID NO: 24; SEQ ID NO: 20 and SEQ ID NO: 25; SEQ ID NO: 20 and SEQ ID NO: 26; SEQ ID NO: 21 and SEQ ID NO: 22; SEQ ID NO: 21 and SEQ ID NO: 23; SEQ ID NO: 21 and SEQ ID NO: 24; SEQ ID NO: 21 and SEQ ID NO: 25; SEQ ID NO: 21 and SEQ ID NO: 26; SEQ ID NO: 22 and SEQ ID NO: 23; SEQ ID NO: 22 and SEQ ID NO: 24; SEQ ID NO: 22 and SEQ ID NO: 25; SEQ ID NO: 22 and SEQ ID NO: 26; SEQ ID NO: 23 and SEQ ID NO: 24; SEQ ID NO: 23 and SEQ ID NO: 25; SEQ ID NO: 23 and SEQ ID NO: 26; SEQ ID NO: 24 and SEQ ID NO: 25; SEQ ID NO: 24 and SEQ ID NO: 26; SEQ ID NO: 25 and SEQ ID NO: 26; SEQ ID NO: 110 and SEQ ID NO: 120; SEQ ID NO: 110 and SEQ ID NO: 121; SEQ ID NO: 110 and SEQ ID NO: 122; SEQ ID NO: 110 and SEQ ID NO: 123; SEQ ID NO: 110 and SEQ ID NO: 124; SEQ ID NO: 110 and SEQ ID NO: 125; SEQ ID NO: 111 and SEQ ID NO: 112; SEQ ID NO: 111 and

SEQ ID NO: 113; SEQ ID NO: 111 and SEQ ID NO: 114; SEQ ID NO: 111 and SEQ ID NO: 115; SEQ ID NO: 111 and SEQ ID NO: 116; SEQ ID NO: 111 and SEQ ID NO: 117; SEQ ID NO: 111 and SEQ ID NO: 118; SEQ ID NO: 111 and SEQ ID NO: 119; SEQ ID NO: 111 and SEQ ID NO: 120; SEQ ID NO: 111 and SEQ ID NO: 121; SEQ ID NO: 111 and SEQ ID NO: 122; SEQ ID NO: 111 and SEQ ID NO: 123; SEQ ID NO: 111 and SEQ ID NO: 124; SEQ ID NO: 111 and SEQ ID NO: 125; SEQ ID NO: 112 and SEQ ID NO: 113; SEQ ID NO: 112 and SEQ ID NO: 114; SEQ ID NO: 112 and SEQ ID NO: 115; SEQ ID NO: 112 and SEQ ID NO: 116; SEQ ID NO: 112 and SEQ ID NO: 117; SEQ ID NO: 112 and SEQ ID NO: 118; SEQ ID NO: 112 and SEQ ID NO: 119; SEQ ID NO: 112 and SEQ ID NO: 120; SEQ ID NO: 112 and SEQ ID NO: 121; SEQ ID NO: 112 and SEQ ID NO: 122; SEQ ID NO: 112 and SEQ ID NO: 123; SEQ ID NO: 112 and SEQ ID NO: 124; SEQ ID NO: 112 and SEQ ID NO: 125; SEQ ID NO: 113 and SEQ ID NO: 114; SEQ ID NO: 113 and SEQ ID NO: 115; SEQ ID NO: 113 and SEQ ID NO: 116; SEQ ID NO: 113 and SEQ ID NO: 117; SEQ ID NO: 113 and SEQ ID NO: 118; SEQ ID NO: 113 and SEQ ID NO: 119; SEQ ID NO: 113 and SEQ ID NO: 120; SEQ ID NO: 113 and SEQ ID NO: 121; SEQ ID NO: 113 and SEQ ID NO: 122; SEQ ID NO: 113 and SEQ ID NO: 123; SEQ ID NO: 113 and SEQ ID NO: 124; SEQ ID NO: 113 and SEQ ID NO: 125; SEQ ID NO: 114 and SEQ ID NO: 115; SEQ ID NO: 114 and SEQ ID NO: 116; SEQ ID NO: 114 and SEQ ID NO: 117; SEQ ID NO: 114 and SEQ ID NO: 118; SEQ ID NO: 114 and SEQ ID NO: 119; SEQ ID NO: 114 and SEQ ID NO: 120; SEQ ID NO: 114 and SEQ ID NO: 121; SEQ ID NO: 114 and SEQ ID NO: 122; SEQ ID NO: 114 and SEQ ID NO: 123; SEQ ID NO: 114 and SEQ ID NO: 124; SEQ ID NO: 114 and SEQ ID NO: 125; SEQ ID NO: 115 and SEQ ID NO: 116; SEQ ID NO: 115 and SEQ ID NO: 117; SEQ ID NO: 115 and SEQ ID NO: 118; SEQ ID NO: 115 and SEQ ID NO: 119; SEQ ID NO: 115 and SEQ ID NO: 120; SEQ ID NO: 115 and SEQ ID NO: 121; SEQ ID NO: 115 and SEQ ID NO: 122; SEQ ID NO: 115 and SEQ ID NO: 123; SEQ ID NO: 115 and SEQ ID NO: 124; SEQ ID NO: 115 and SEQ ID NO: 125; SEQ ID NO: 116 and SEQ ID NO: 117; SEQ ID NO: 116 and SEQ ID NO: 118; SEQ ID NO: 116 and SEQ ID NO: 119; SEQ ID NO: 116 and SEQ ID NO: 120; SEQ ID NO: 116 and SEQ ID NO: 121; SEQ ID NO: 116 and SEQ ID NO: 122; SEQ ID NO: 116 and SEQ ID NO: 123; SEQ ID NO: 116 and SEQ ID NO: 124; SEQ ID NO: 116 and SEQ ID NO: 125; SEQ ID NO: 117 and SEQ ID NO: 118; SEQ ID NO: 117 and SEQ ID NO: 119; SEQ ID NO: 117 and SEQ ID NO: 120; SEQ ID NO: 117 and SEQ ID NO: 121; SEQ ID NO: 117 and SEQ ID NO: 122; SEQ ID NO: 117 and SEQ ID NO: 123; SEQ ID NO: 117 and SEQ ID NO: 124; SEQ ID NO: 117 and SEQ ID NO: 125; SEQ ID NO: 118 and SEQ ID NO: 119; SEQ ID NO: 118 and SEQ ID NO: 120; SEQ ID NO: 118 and SEQ ID NO: 121; SEQ ID NO: 118 and SEQ ID NO: 122; SEQ ID NO: 118 and SEQ ID NO: 123; SEQ ID NO: 118 and SEQ ID NO: 124; SEQ ID NO: 118 and SEQ ID NO: 125; SEQ ID NO: 119 and SEQ ID NO: 120; SEQ ID NO: 119 and SEQ ID NO: 121; SEQ ID NO: 119 and SEQ ID NO: 122; SEQ ID NO: 119 and SEQ ID NO: 123; SEQ ID NO: 119 and SEQ ID NO: 124; SEQ ID NO: 119 and SEQ ID NO: 125; SEQ ID NO: 120 and SEQ ID NO: 121; SEQ ID NO: 120 and SEQ ID NO: 122;

SEQ ID NO: 120 and SEQ ID NO: 123; SEQ ID NO: 120 and SEQ ID NO: 124; SEQ ID NO: 120 and SEQ ID NO: 125; SEQ ID NO: 121 and SEQ ID NO: 122; SEQ ID NO: 121 and SEQ ID NO: 123; SEQ ID NO: 121 and SEQ ID NO: 124; SEQ ID NO: 121 and SEQ ID NO: 125; SEQ ID NO: 122 and SEQ ID NO: 123; SEQ ID NO: 122 and SEQ ID NO: 124; SEQ ID NO: 122 and SEQ ID NO: 125; SEQ ID NO: 123 and SEQ ID NO: 124; SEQ ID NO: 123 and SEQ ID NO: 125; SEQ ID NO: 124 and SEQ ID NO: 125; SEQ ID NO: 126 and SEQ ID NO: 127; SEQ ID NO: 126 and SEQ ID NO: 128; SEQ ID NO: 126 and SEQ ID NO: 129; SEQ ID NO: 126 and SEQ ID NO: 130; SEQ ID NO: 126 and SEQ ID NO: 131; SEQ ID NO: 126 and SEQ ID NO: 132; SEQ ID NO: 126 and SEQ ID NO: 133; SEQ ID NO: 126 and SEQ ID NO: 134; SEQ ID NO: 126 and SEQ ID NO: 135; SEQ ID NO: 126 and SEQ ID NO: 136; SEQ ID NO: 126 and SEQ ID NO: 137; SEQ ID NO: 126 and SEQ ID NO: 138; SEQ ID NO: 126 and SEQ ID NO: 139; SEQ ID NO: 126 and SEQ ID NO: 140; SEQ ID NO: 126 and SEQ ID NO: 141; SEQ ID NO: 126 and SEQ ID NO: 142; SEQ ID NO: 126 and SEQ ID NO: 143; SEQ ID NO: 126 and SEQ ID NO: 144; SEQ ID NO: 126 and SEQ ID NO: 145; SEQ ID NO: 126 and SEQ ID NO: 146; SEQ ID NO: 126 and SEQ ID NO: 147; SEQ ID NO: 127 and SEQ ID NO: 128; SEQ ID NO: 127 and SEQ ID NO: 129; SEQ ID NO: 127 and SEQ ID NO: 130; SEQ ID NO: 127 and SEQ ID NO: 131; SEQ ID NO: 127 and SEQ ID NO: 132; SEQ ID NO: 127 and SEQ ID NO: 133; SEQ ID NO: 127 and SEQ ID NO: 134; SEQ ID NO: 127 and SEQ ID NO: 135; SEQ ID NO: 127 and SEQ ID NO: 136; SEQ ID NO: 127 and SEQ ID NO: 137; SEQ ID NO: 127 and SEQ ID NO: 138; SEQ ID NO: 127 and SEQ ID NO: 139; SEQ ID NO: 127 and SEQ ID NO: 140; SEQ ID NO: 127 and SEQ ID NO: 141; SEQ ID NO: 127 and SEQ ID NO: 142; SEQ ID NO: 127 and SEQ ID NO: 143; SEQ ID NO: 127 and SEQ ID NO: 144; SEQ ID NO: 127 and SEQ ID NO: 145; SEQ ID NO: 127 and SEQ ID NO: 146; SEQ ID NO: 127 and SEQ ID NO: 147; SEQ ID NO: 128 and SEQ ID NO: 129; SEQ ID NO: 128 and SEQ ID NO: 130; SEQ ID NO: 128 and SEQ ID NO: 131; SEQ ID NO: 128 and SEQ ID NO: 132; SEQ ID NO: 128 and SEQ ID NO: 133; SEQ ID NO: 128 and SEQ ID NO: 134; SEQ ID NO: 128 and SEQ ID NO: 135; SEQ ID NO: 128 and SEQ ID NO: 136; SEQ ID NO: 128 and SEQ ID NO: 137; SEQ ID NO: 128 and SEQ ID NO: 138; SEQ ID NO: 128 and SEQ ID NO: 139; SEQ ID NO: 128 and SEQ ID NO: 140; SEQ ID NO: 128 and SEQ ID NO: 141; SEQ ID NO: 128 and SEQ ID NO: 142; SEQ ID NO: 128 and SEQ ID NO: 143; SEQ ID NO: 128 and SEQ ID NO: 144; SEQ ID NO: 128 and SEQ ID NO: 145; SEQ ID NO: 128 and SEQ ID NO: 146; SEQ ID NO: 128 and SEQ ID NO: 147; SEQ ID NO: 129 and SEQ ID NO: 130; SEQ ID NO: 129 and SEQ ID NO: 131; SEQ ID NO: 129 and SEQ ID NO: 132; SEQ ID NO: 129 and SEQ ID NO: 133; SEQ ID NO: 129 and SEQ ID NO: 134; SEQ ID NO: 129 and SEQ ID NO: 135; SEQ ID NO: 129 and SEQ ID NO: 136; SEQ ID NO: 129 and SEQ ID NO: 137; SEQ ID NO: 129 and SEQ ID NO: 138; SEQ ID NO: 129 and SEQ ID NO: 139; SEQ ID NO: 129 and SEQ ID NO: 140; SEQ ID NO: 129 and SEQ ID NO: 141; SEQ ID NO: 129 and SEQ ID NO: 142; SEQ ID NO: 129 and SEQ ID NO: 143; SEQ ID NO: 129 and SEQ ID NO: 144; SEQ ID NO: 129 and SEQ ID NO: 145; SEQ ID NO: 129 and SEQ ID NO: 146; SEQ ID NO: 129

and SEQ ID NO: 147; SEQ ID NO: 130 and SEQ ID NO: 131; SEQ ID NO: 130 and SEQ ID NO: 132; SEQ ID NO: 130 and SEQ ID NO: 133; SEQ ID NO: 130 and SEQ ID NO: 134; SEQ ID NO: 130 and SEQ ID NO: 135; SEQ ID NO: 130 and SEQ ID NO: 136; SEQ ID NO: 130 and SEQ ID NO: 137; SEQ ID NO: 130 and SEQ ID NO: 138; SEQ ID NO: 130 and SEQ ID NO: 139; SEQ ID NO: 130 and SEQ ID NO: 140; SEQ ID NO: 130 and SEQ ID NO: 141; SEQ ID NO: 130 and SEQ ID NO: 142; SEQ ID NO: 130 and SEQ ID NO: 143; SEQ ID NO: 130 and SEQ ID NO: 144; SEQ ID NO: 130 and SEQ ID NO: 145; SEQ ID NO: 130 and SEQ ID NO: 146; SEQ ID NO: 130 and SEQ ID NO: 147; SEQ ID NO: 131 and SEQ ID NO: 132; SEQ ID NO: 131 and SEQ ID NO: 133; SEQ ID NO: 131 and SEQ ID NO: 134; SEQ ID NO: 131 and SEQ ID NO: 135; SEQ ID NO: 131 and SEQ ID NO: 136; SEQ ID NO: 131 and SEQ ID NO: 137; SEQ ID NO: 131 and SEQ ID NO: 138; SEQ ID NO: 131 and SEQ ID NO: 139; SEQ ID NO: 131 and SEQ ID NO: 140; SEQ ID NO: 131 and SEQ ID NO: 141; SEQ ID NO: 131 and SEQ ID NO: 142; SEQ ID NO: 131 and SEQ ID NO: 143; SEQ ID NO: 131 and SEQ ID NO: 144; SEQ ID NO: 131 and SEQ ID NO: 145; SEQ ID NO: 131 and SEQ ID NO: 146; SEQ ID NO: 131 and SEQ ID NO: 147; SEQ ID NO: 132 and SEQ ID NO: 133; SEQ ID NO: 132 and SEQ ID NO: 134; SEQ ID NO: 132 and SEQ ID NO: 135; SEQ ID NO: 132 and SEQ ID NO: 136; SEQ ID NO: 132 and SEQ ID NO: 137; SEQ ID NO: 132 and SEQ ID NO: 138; SEQ ID NO: 132 and SEQ ID NO: 139; SEQ ID NO: 132 and SEQ ID NO: 140; SEQ ID NO: 132 and SEQ ID NO: 141; SEQ ID NO: 132 and SEQ ID NO: 142; SEQ ID NO: 132 and SEQ ID NO: 143; SEQ ID NO: 132 and SEQ ID NO: 144; SEQ ID NO: 132 and SEQ ID NO: 145; SEQ ID NO: 132 and SEQ ID NO: 146; SEQ ID NO: 132 and SEQ ID NO: 147; SEQ ID NO: 133 and SEQ ID NO: 134; SEQ ID NO: 133 and SEQ ID NO: 135; SEQ ID NO: 133 and SEQ ID NO: 136; SEQ ID NO: 133 and SEQ ID NO: 137; SEQ ID NO: 133 and SEQ ID NO: 138; SEQ ID NO: 133 and SEQ ID NO: 139; SEQ ID NO: 133 and SEQ ID NO: 140; SEQ ID NO: 133 and SEQ ID NO: 141; SEQ ID NO: 133 and SEQ ID NO: 142; SEQ ID NO: 133 and SEQ ID NO: 143; SEQ ID NO: 133 and SEQ ID NO: 144; SEQ ID NO: 133 and SEQ ID NO: 145; SEQ ID NO: 133 and SEQ ID NO: 146; SEQ ID NO: 133 and SEQ ID NO: 147; SEQ ID NO: 134 and SEQ ID NO: 135; SEQ ID NO: 134 and SEQ ID NO: 136; SEQ ID NO: 134 and SEQ ID NO: 137; SEQ ID NO: 134 and SEQ ID NO: 138; SEQ ID NO: 134 and SEQ ID NO: 139; SEQ ID NO: 134 and SEQ ID NO: 140; SEQ ID NO: 134 and SEQ ID NO: 141; SEQ ID NO: 134 and SEQ ID NO: 142; SEQ ID NO: 134 and SEQ ID NO: 143; SEQ ID NO: 134 and SEQ ID NO: 144; SEQ ID NO: 134 and SEQ ID NO: 145; SEQ ID NO: 134 and SEQ ID NO: 146; SEQ ID NO: 134 and SEQ ID NO: 147; SEQ ID NO: 135 and SEQ ID NO: 136; SEQ ID NO: 135 and SEQ ID NO: 137; SEQ ID NO: 135 and SEQ ID NO: 138; SEQ ID NO: 135 and SEQ ID NO: 139; SEQ ID NO: 135 and SEQ ID NO: 140; SEQ ID NO: 135 and SEQ ID NO: 141; SEQ ID NO: 135 and SEQ ID NO: 142; SEQ ID NO: 135 and SEQ ID NO: 143; SEQ ID NO: 135 and SEQ ID NO: 144; SEQ ID NO: 135 and SEQ ID NO: 145; SEQ ID NO: 135 and SEQ ID NO: 146; SEQ ID NO: 135 and SEQ ID NO: 147; SEQ ID NO: 136 and SEQ ID NO: 137; SEQ ID NO: 136 and SEQ ID NO: 138; SEQ ID NO: 136 and SEQ ID NO:

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[00236] In some embodiments, methods are provided for treating Duchenne Muscular Dystrophy (DMD), the method comprising delivering to a cell at least one nucleic acid molecule comprising a pair of guide RNAs comprising a first and second spacer sequence, wherein the pair of first and spacer sequences are selected from any one of the following pairs: SEQ ID NO: 200 and SEQ ID NO: 201; SEQ ID NO: 200 and SEQ ID NO: 202; SEQ ID NO: 200 and SEQ ID NO: 203; SEQ ID NO: 200 and SEQ ID NO: 204; SEQ ID NO: 200 and SEQ ID NO: 205; SEQ ID NO: 200 and SEQ ID NO: 206; SEQ ID NO: 200 and SEQ ID NO: 207; SEQ ID NO: 200 and SEQ ID NO: 208; SEQ ID NO: 201 and SEQ ID NO: 202; SEQ ID NO: 201 and SEQ ID NO: 203; SEQ ID NO: 201 and SEQ ID NO: 204; SEQ ID NO: 201 and SEQ ID NO: 205; SEQ ID NO: 201 and SEQ ID NO: 206; SEQ ID NO: 201 and SEQ ID NO: 207; SEQ ID NO: 201 and SEQ ID NO: 208; SEQ ID NO: 202 and SEQ ID NO: 203; SEQ ID NO: 202 and SEQ ID NO: 204; SEQ ID NO: 202 and SEQ ID NO: 205; SEQ ID NO: 202 and SEQ ID NO: 206; SEQ ID NO: 202 and SEQ ID NO: 207; SEQ ID NO: 202 and SEQ ID NO: 208; SEQ ID NO: 203 and SEQ ID NO: 204; SEQ ID NO: 203 and SEQ ID NO: 205; SEQ ID NO: 203 and SEQ ID NO: 206; SEQ ID NO: 203 and SEQ ID NO: 207; SEQ ID NO: 203 and SEQ ID NO: 208; SEQ ID NO: 204 and SEQ ID NO: 205; SEQ ID NO: 204 and SEQ ID

NO: 206; SEQ ID NO: 204 and SEQ ID NO: 207; SEQ ID NO: 204 and SEQ ID NO: 208; SEQ ID NO: 205 and SEQ ID NO: 206; SEQ ID NO: 205 and SEQ ID NO: 207; SEQ ID NO: 205 and SEQ ID NO: 208; SEQ ID NO: 206 and SEQ ID NO: 207; SEQ ID NO: 206 and SEQ ID NO: 208; SEQ ID NO: 207 and SEQ ID NO: 208; SEQ ID NO: 209 and SEQ ID NO: 210; SEQ ID NO: 209 and SEQ ID NO: 211; SEQ ID NO: 209 and SEQ ID NO: 212; SEQ ID NO: 209 and SEQ ID NO: 213; SEQ ID NO: 209 and SEQ ID NO: 214; SEQ ID NO: 209 and SEQ ID NO: 215; SEQ ID NO: 209 and SEQ ID NO: 216; SEQ ID NO: 209 and SEQ ID NO: 217; SEQ ID NO: 209 and SEQ ID NO: 218; SEQ ID NO: 209 and SEQ ID NO: 219; SEQ ID NO: 209 and SEQ ID NO: 220; SEQ ID NO: 209 and SEQ ID NO: 221; SEQ ID NO: 209 and SEQ ID NO: 222; SEQ ID NO: 209 and SEQ ID NO: 223; SEQ ID NO: 209 and SEQ ID NO: 224; SEQ ID NO: 209 and SEQ ID NO: 225; SEQ ID NO: 209 and SEQ ID NO: 226; SEQ ID NO: 209 and SEQ ID NO: 227; SEQ ID NO: 209 and SEQ ID NO: 228; SEQ ID NO: 209 and SEQ ID NO: 229; SEQ ID NO: 209 and SEQ ID NO: 230; SEQ ID NO: 210 and SEQ ID NO: 211; SEQ ID NO: 210 and SEQ ID NO: 212; SEQ ID NO: 210 and SEQ ID NO: 213; SEQ ID NO: 210 and SEQ ID NO: 214; SEQ ID NO: 210 and SEQ ID NO: 215; SEQ ID NO: 210 and SEQ ID NO: 216; SEQ ID NO: 210 and SEQ ID NO: 217; SEQ ID NO: 210 and SEQ ID NO: 218; SEQ ID NO: 210 and SEQ ID NO: 219; SEQ ID NO: 210 and SEQ ID NO: 220; SEQ ID NO: 210 and SEQ ID NO: 221; SEQ ID NO: 210 and SEQ ID NO: 222; SEQ ID NO: 210 and SEQ ID NO: 223; SEQ ID NO: 210 and SEQ ID NO: 224; SEQ ID NO: 210 and SEQ ID NO: 225; SEQ ID NO: 210 and SEQ ID NO: 226; SEQ ID NO: 210 and SEQ ID NO: 227; SEQ ID NO: 210 and SEQ ID NO: 228; SEQ ID NO: 210 and SEQ ID NO: 229; SEQ ID NO: 210 and SEQ ID NO: 230; SEQ ID NO: 211 and SEQ ID NO: 212; SEQ ID NO: 211 and SEQ ID NO: 213; SEQ ID NO: 211 and SEQ ID NO: 214; SEQ ID NO: 211 and SEQ ID NO: 215; SEQ ID NO: 211 and SEQ ID NO: 216; SEQ ID NO: 211 and SEQ ID NO: 217; SEQ ID NO: 211 and SEQ ID NO: 218; SEQ ID NO: 211 and SEQ ID NO: 219; SEQ ID NO: 211 and SEQ ID NO: 220; SEQ ID NO: 211 and SEQ ID NO: 221; SEQ ID NO: 211 and SEQ ID NO: 222; SEQ ID NO: 211 and SEQ ID NO: 223; SEQ ID NO: 211 and SEQ ID NO: 224; SEQ ID NO: 211 and SEQ ID NO: 225; SEQ ID NO: 211 and SEQ ID NO: 226; SEQ ID NO: 211 and SEQ ID NO: 227; SEQ ID NO: 211 and SEQ ID NO: 228; SEQ ID NO: 211 and SEQ ID NO: 229; SEQ ID NO: 211 and SEQ ID NO: 230; SEQ ID NO: 212 and SEQ ID NO: 213; SEQ ID NO: 212 and SEQ ID NO: 214; SEQ ID NO: 212 and SEQ ID NO: 215; SEQ ID NO: 212 and SEQ ID NO: 216; SEQ ID NO: 212 and SEQ ID NO: 217; SEQ ID NO: 212 and SEQ ID NO: 218; SEQ ID NO: 212 and SEQ ID NO: 219; SEQ ID NO: 212 and SEQ ID NO: 220; SEQ ID NO: 212 and SEQ ID NO: 221; SEQ ID NO: 212 and SEQ ID NO: 222; SEQ ID NO: 212 and SEQ ID NO: 223; SEQ ID NO: 212 and SEQ ID NO: 224; SEQ ID NO: 212 and SEQ ID NO: 225; SEQ ID NO: 212 and SEQ ID NO: 226; SEQ ID NO: 212 and SEQ ID NO: 227; SEQ ID NO: 212 and SEQ ID NO: 228; SEQ ID NO: 212 and SEQ ID NO: 229; SEQ ID NO: 212 and SEQ ID NO: 230; SEQ ID NO: 213 and SEQ ID NO: 214; SEQ ID NO: 213 and SEQ ID NO: 215; SEQ ID NO: 213 and SEQ ID NO: 216; SEQ ID NO: 213 and SEQ ID NO: 217; SEQ ID

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SEQ ID NO: 935; SEQ ID NO: 288 and SEQ ID NO: 936; SEQ ID NO: 288 and SEQ ID NO: 937; SEQ ID NO: 288 and SEQ ID NO: 938; SEQ ID NO: 289 and SEQ ID NO: 924; SEQ ID NO: 289 and SEQ ID NO: 925; SEQ ID NO: 289 and SEQ ID NO: 926; SEQ ID NO: 289 and SEQ ID NO: 927; SEQ ID NO: 289 and SEQ ID NO: 928; SEQ ID NO: 289 and SEQ ID NO: 929; SEQ ID NO: 289 and SEQ ID NO: 930; SEQ ID NO: 289 and SEQ ID NO: 931; SEQ ID NO: 289 and SEQ ID NO: 932; SEQ ID NO: 289 and SEQ ID NO: 933; SEQ ID NO: 289 and SEQ ID NO: 934; SEQ ID NO: 289 and SEQ ID NO: 935; SEQ ID NO: 289 and SEQ ID NO: 936; SEQ ID NO: 289 and SEQ ID NO: 937; SEQ ID NO: 289 and SEQ ID NO: 938; SEQ ID NO: 290 and SEQ ID NO: 924; SEQ ID NO: 290 and SEQ ID NO: 925; SEQ ID NO: 290 and SEQ ID NO: 926; SEQ ID NO: 290 and SEQ ID NO: 927; SEQ ID NO: 290 and SEQ ID NO: 928; SEQ ID NO: 290 and SEQ ID NO: 929; SEQ ID NO: 290 and SEQ ID NO: 930; SEQ ID NO: 290 and SEQ ID NO: 931; SEQ ID NO: 290 and SEQ ID NO: 932; SEQ ID NO: 290 and SEQ ID NO: 933; SEQ ID NO: 290 and SEQ ID NO: 934; SEQ ID NO: 290 and SEQ ID NO: 935; SEQ ID NO: 290 and SEQ ID NO: 936; SEQ ID NO: 290 and SEQ ID NO: 937; SEQ ID NO: 290 and SEQ ID NO: 938; SEQ ID NO: 291 and SEQ ID NO: 924; SEQ ID NO: 291 and SEQ ID NO: 925; SEQ ID NO: 291 and SEQ ID NO: 926; SEQ ID NO: 291 and SEQ ID NO: 927; SEQ ID NO: 291 and SEQ ID NO: 928; SEQ ID NO: 291 and SEQ ID NO: 929; SEQ ID NO: 291 and SEQ ID NO: 930; SEQ ID NO: 291 and SEQ ID NO: 931; SEQ ID NO: 291 and SEQ ID NO: 932; SEQ ID NO: 291 and SEQ ID NO: 933; SEQ ID NO: 291 and SEQ ID NO: 934; SEQ ID NO: 291 and SEQ ID NO: 935; SEQ ID NO: 291 and SEQ ID NO: 936; SEQ ID NO: 291 and SEQ ID NO: 937; SEQ ID NO: 291 and SEQ ID NO: 938; SEQ ID NO: 292 and SEQ ID NO: 924; SEQ ID NO: 292 and SEQ ID NO: 925; SEQ ID NO: 292 and SEQ ID NO: 926; SEQ ID NO: 292 and SEQ ID NO: 927; SEQ ID NO: 292 and SEQ ID NO: 928; SEQ ID NO: 292 and SEQ ID NO: 929; SEQ ID NO: 292 and SEQ ID NO: 930; SEQ ID NO: 292 and SEQ ID NO: 931; SEQ ID NO: 292 and SEQ ID NO: 932; SEQ ID NO: 292 and SEQ ID NO: 933; SEQ ID NO: 292 and SEQ ID NO: 934; SEQ ID NO: 292 and SEQ ID NO: 935; SEQ ID NO: 292 and SEQ ID NO: 936; SEQ ID NO: 292 and SEQ ID NO: 937; SEQ ID NO: 292 and SEQ ID NO: 938; SEQ ID NO: 950 and SEQ ID NO: 275; SEQ ID NO: 951 and SEQ ID NO: 275; SEQ ID NO: 952 and SEQ ID NO: 275; SEQ ID NO: 953 and SEQ ID NO: 275; SEQ ID NO: 954 and SEQ ID NO: 275; or SEQ ID NO: 955 and SEQ ID NO: 275; and a nucleic acid encoding a *Staphylococcus lugdunensis* (SluCas9), wherein the nucleic acid encoding the SluCas9 may be on the same or different nucleic acid molecule as the pair of guide RNAs.

[00237] In some embodiments, a method for treating DMD is provided comprising administering a composition comprising one or more guide RNAs wherein each guide RNA comprises a guide sequence of **Table 6**, or comprises a guide sequence comprising at least 16, 17, 18, 19, or 20 contiguous nucleotides of a guide sequence of **Table 6**, or is at least 90% identical to guide sequence selected from **Table 6**. In each instance, the composition may comprise a nucleic acid encoding the guide RNA(s). In some embodiments, a method for treating DMD is provided comprising

administering a composition comprising one or more nucleic acid molecules encoding one or more guide RNAs, wherein each guide RNA comprises a guide sequence of **Table 6**, or at least 16, 17, 18, 19, or 20 contiguous nucleotides of a guide sequence of **Table 6**, or is at least 90% identical to guide sequence selected from **Table 6**.

[00238] In some embodiments, a method for treating DMD is provided comprising administering a composition comprising a guide RNA wherein the guide RNA comprises a guide sequence of **Table 6**, or at least 16, 17, 18, 19, or 20 contiguous nucleotides of a guide sequence of **Table 6,** or is at least 90% identical to guide sequence of **Table 6**. In each instance, the composition may comprise a nucleic acid encoding the guide RNA.

[00239] In some embodiments, a method for treating DMD is provided comprising administering a composition comprising a guide RNA comprising no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 contiguous nucleotides of a guide sequence of **Table 6**, or is at least 90% identical to no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 contiguous nucleotides of a guide sequence of **Table 6**. In each instance, the composition may comprise a nucleic acid encoding the guide RNA.

[00240] In some embodiments, a method for treating DMD is provided comprising administering a composition comprising two or more guide RNAs wherein each guide RNA comprises a guide sequence of **Table 6**, or at least 16, 17, 18, 19, or 20 contiguous nucleotides of a guide sequence of **Table 6,** or is at least 90% identical to guide sequence selected from **Table 6**. In each instance, the composition may comprise a nucleic acid encoding the guide RNA.

[00241] In some embodiments, a method for treating DMD is provided comprising administering a composition comprising two or more guide RNAs wherein at least one of the two or more guide RNAs, optionally each guide RNA, comprises no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 contiguous nucleotides of a guide sequence of **Table 6**, is at least 90% identical to no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 contiguous nucleotides of a guide sequence selected from **Table 6**. In each instance, the composition may comprise a nucleic acid encoding the guide RNA.

[00242] In some embodiments, a method for treating DMD is provided comprising administering a composition comprising a SaCas9 or SluCas9 or one or more nucleic acid molecules encoding a SaCas9 or SluCas9 and a pair of guide RNAs comprising a first guide sequence and a second guide sequence, wherein the first and second guide sequence are selected from the guide sequence pairs of:

a. For exon 44 (with e.g., SaCas9), SEQ ID NOs: 1 and 3; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111

and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; 124 and 125;

b. For exon 44 (with, e.g., SluCas9), SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and 203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208;

c. For exon 45 (with, e.g., SaCas9), SEQ ID NOs: 3 and 4; 3 and 5; 3 and 6; 3 and 7; 3 and 8; 3 and 9; 4 and 5; 4 and 6; 4 and 7; 4 and 8; 4 and 9; 5 and 6; 5 and 7; 5 and 8; 5 and 9; 6 and 7; 6 and 8; 6 and 9; 7 and 8; 7 and 9; 8 and 9; 126 and 127; 126 and 128; 126 and 129; 126 and 130; 126 and 131; 126 and 132; 126 and 133; 126 and 134; 126 and 135; 126 and 136; 126 and 137; 126 and 138; 126 and 139; 126 and 140; 126 and 141; 126 and 142; 126 and 143; 126 and 144; 126 and 145; 126 and 146; 126 and 147; 127 and 128; 127 and 129; 127 and 130; 127 and 131; 127 and 132; 127 and 133; 127 and 134; 127 and 135; 127 and 136; 127 and 137; 127 and 138; 127 and 139; 127 and 140; 127 and 141;

127 and 142; 127 and 143; 127 and 144; 127 and 145; 127 and 146; 127 and 147; 128 and 129; 128 and 130; 128 and 131; 128 and 132; 128 and 133; 128 and 134; 128 and 135; 128 and 136; 128 and 137; 128 and 138; 128 and 139; 128 and 140; 128 and 141; 128 and 142; 128 and 143; 128 and 144; 128 and 145; 128 and 146; 128 and 147; 129 and 130; 129 and 131; 129 and 132; 129 and 133; 129 and 134; 129 and 135; 129 and 136; 129 and 137; 129 and 138; 129 and 139; 129 and 140; 129 and 141; 129 and 142; 129 and 143; 129 and 144; 129 and 145; 129 and 146; 129 and 147; 130 and 131; 130 and 132; 130 and 133; 130 and 134; 130 and 135; 130 and 136; 130 and 137; 130 and 138; 130 and 139; 130 and 140; 130 and 141; 130 and 142; 130 and 143; 130 and 144; 130 and 145; 130 and 146; 130 and 147; 131 and 132; 131 and 133; 131 and 134; 131 and 135; 131 and 136; 131 and 137; 131 and 138; 131 and 139; 131 and 140; 131 and 141; 131 and 142; 131 and 143; 131 and 144; 131 and 145; 131 and 146; 131 and 147; 132 and 133; 132 and 134; 132 and 135; 132 and 136; 132 and 137; 132 and 138; 132 and 139; 132 and 140; 132 and 141; 132 and 142; 132 and 143; 132 and 144; 132 and 145; 132 and 146; 132 and 147; 133 and 134; 133 and 135; 133 and 136; 133 and 137; 133 and 138; 133 and 139; 133 and 140; 133 and 141; 133 and 142; 133 and 143; 133 and 144; 133 and 145; 133 and 146; 133 and 147; 134 and 135; 134 and 136; 134 and 137; 134 and 138; 134 and 139; 134 and 140; 134 and 141; 134 and 142; 134 and 143; 134 and 144; 134 and 145; 134 and 146; 134 and 147; 135 and 136; 135 and 137; 135 and 138; 135 and 139; 135 and 140; 135 and 141; 135 and 142; 135 and 143; 135 and 144; 135 and 145; 135 and 146; 135 and 147; 136 and 137; 136 and 138; 136 and 139; 136 and 140; 136 and 141; 136 and 142; 136 and 143; 136 and 144; 136 and 145; 136 and 146; 136 and 147; 137 and 138; 137 and 139; 137 and 140; 137 and 141; 137 and 142; 137 and 143; 137 and 144; 137 and 145; 137 and 146; 137 and 147; 138 and 139; 138 and 140; 138 and 141; 138 and 142; 138 and 143; 138 and 144; 138 and 145; 138 and 146; 138 and 147; 139 and 140; 139 and 141; 139 and 142; 139 and 143; 139 and 144; 139 and 145; 139 and 146; 139 and 147; 140 and 141; 140 and 142; 140 and 143; 140 and 144; 140 and 145; 140 and 146; 140 and 147; 141 and 142; 141 and 143; 141 and 144; 141 and 145; 141 and 146; 141 and 147; 142 and 143; 142 and 144; 142 and 145; 142 and 146;

142 and 147; 143 and 144; 143 and 145; 143 and 146; 143 and 147; 144 and 145; 144 and 146; 144 and 147; 145 and 146; 145 and 147; 146 and 147;

d. For exon 45 (with, e.g., SluCas9), SEQ ID NOs: 209 and 210; 209 and 211; 209 and 212; 209 and 213; 209 and 214; 209 and 215; 209 and 216; 209 and 217; 209 and 218; 209 and 219; 209 and 220; 209 and 221; 209 and 222; 209 and 223; 209 and 224; 209 and 225; 209 and 226; 209 and 227; 209 and 228; 209 and 229; 209 and 230; 210 and 211; 210 and 212; 210 and 213; 210 and 214; 210 and 215; 210 and 216; 210 and 217; 210 and 218; 210 and 219; 210 and 220; 210 and 221; 210 and 222; 210 and 223; 210 and 224; 210 and 225; 210 and 226; 210 and 227; 210 and 228; 210 and 229; 210 and 230; 211 and 212; 211 and 213; 211 and 214; 211 and 215; 211 and 216; 211 and 217; 211 and 218; 211 and 219; 211 and 220; 211 and 221; 211 and 222; 211 and 223; 211 and 224; 211 and 225; 211 and 226; 211 and 227; 211 and 228; 211 and 229; 211 and 230; 212 and 213; 212 and 214; 212 and 215; 212 and 216; 212 and 217; 212 and 218; 212 and 219; 212 and 220; 212 and 221; 212 and 222; 212 and 223; 212 and 224; 212 and 225; 212 and 226; 212 and 227; 212 and 228; 212 and 229; 212 and 230; 213 and 214; 213 and 215; 213 and 216; 213 and 217; 213 and 218; 213 and 219; 213 and 220; 213 and 221; 213 and 222; 213 and 223; 213 and 224; 213 and 225; 213 and 226; 213 and 227; 213 and 228; 213 and 229; 213 and 230; 214 and 215; 214 and 216; 214 and 217; 214 and 218; 214 and 219; 214 and 220; 214 and 221; 214 and 222; 214 and 223; 214 and 224; 214 and 225; 214 and 226; 214 and 227; 214 and 228; 214 and 229; 214 and 230; 215 and 216; 215 and 217; 215 and 218; 215 and 219; 215 and 220; 215 and 221; 215 and 222; 215 and 223; 215 and 224; 215 and 225; 215 and 226; 215 and 227; 215 and 228; 215 and 229; 215 and 230; 216 and 217; 216 and 218; 216 and 219; 216 and 220; 216 and 221; 216 and 222; 216 and 223; 216 and 224; 216 and 225; 216 and 226; 216 and 227; 216 and 228; 216 and 229; 216 and 230; 217 and 218; 217 and 219; 217 and 220; 217 and 221; 217 and 222; 217 and 223; 217 and 224; 217 and 225; 217 and 226; 217 and 227; 217 and 228; 217 and 229; 217 and 230; 218 and 219; 218 and 220; 218 and 221; 218 and 222; 218 and 223; 218 and 224; 218 and 225; 218 and 226; 218 and 227; 218 and 228; 218 and 229; 218 and 230; 219 and 220; 219 and 221; 219 and 222; 219 and 223; 219 and 224; 219 and 225; 219 and 226; 219 and 227; 219 and 228; 219 and 229; 219 and 230; 220 and 221; 220 and 222; 220 and 223; 220 and 224; 220 and 225; 220 and 226; 220 and 227; 220 and 228; 220 and 229; 220 and 230; 221 and 222; 221 and 223; 221 and 224;

221 and 225; 221 and 226; 221 and 227; 221 and 228; 221 and 229; 221 and 230; 222 and 223; 222 and 224; 222 and 225; 222 and 226; 222 and 227; 222 and 228; 222 and 229; 222 and 230; 223 and 224; 223 and 225; 223 and 226; 223 and 227; 223 and 228; 223 and 229; 223 and 230; 224 and 225; 224 and 226; 224 and 227; 224 and 228; 224 and 229; 224 and 230; 225 and 226; 225 and 227; 225 and 228; 225 and 229; 225 and 230; 226 and 227; 226 and 228; 226 and 229; 226 and 230; 227 and 228; 227 and 229; 227 and 230; 228 and 229; 228 and 230; 229 and 230;

e. For exon 50 (with, e.g., SaCas9), SEQ ID NOs: 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; 158 and 159;

f. For exon 50 (with, e.g., SluCas9), SEQ ID NOs: 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232 and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and 239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; 241 and 242;

g. For exon 51 (with, e.g., SaCas9), SEQ ID NOs: 11 and 12; 11 and 13; 11 and 14; 11 and 15; 12 and 13; 12 and 14; 12 and 15; 13 and 14; 13 and 15; 14 and

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j. For exon 53 (with, e.g., SluCas9), SEQ ID NOs: 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and 277; 270 and 278; 270 and 279; 270 and 280; 270 and 281; 270 and 282; 270 and 283; 270 and 284; 270 and 285; 270 and 286; 270 and 287; 270 and 288; 270 and 289; 270 and 290; 270 and 291; 270 and 292; 271 and 272; 271 and 273; 271 and 274; 271 and 275; 271 and 276; 271 and 277; 271 and 278; 271 and 279; 271 and 280; 271 and 281; 271 and 282; 271 and 283; 271 and 284; 271 and 285; 271 and 286; 271 and 287; 271 and 288; 271 and 289; 271 and 290; 271 and 291; 271 and 292; 272 and 273; 272 and 274; 272 and 275; 272 and 276; 272 and 277; 272 and 278; 272 and 279; 272 and 280; 272 and 281; 272 and 282; 272 and 283; 272 and 284; 272 and 285; 272 and 286; 272 and 287; 272 and 288; 272 and 289; 272 and 290; 272 and 291; 272 and 292; 273 and 274; 273 and 275; 273 and 276; 273 and 277; 273 and 278; 273 and 279; 273 and 280; 273 and 281; 273 and 282; 273 and 283; 273 and 284; 273 and 285; 273 and 286; 273 and 287; 273 and 288; 273 and 289; 273 and 290; 273 and 291; 273 and 292; 274 and 275; 274 and 276; 274 and 277; 274 and 278; 274 and 279; 274 and 280; 274 and 281; 274 and 282; 274 and 283; 274 and 284; 274 and 285; 274 and 286; 274 and 287; 274 and 288; 274 and 289; 274 and 290; 274 and 291; 274 and 292; 275 and 276; 275 and 277; 275 and 278; 275 and 279; 275 and 280; 275 and 281; 275 and 282; 275 and 283; 275 and 284; 275 and 285; 275 and 286; 275 and 287; 275 and 288; 275 and 289; 275 and 290; 275 and 291; 275 and 292; 276 and 277; 276 and 278; 276 and 279; 276 and 280; 276 and 281; 276 and 282; 276 and 283; 276 and 284; 276 and 285; 276 and 286; 276 and 287; 276 and 288; 276 and 289; 276 and 290; 276 and 291; 276 and 292; 277 and 278; 277 and 279; 277 and 280; 277 and 281; 277 and 282; 277 and 283; 277 and 284; 277 and 285; 277 and 286; 277 and 287; 277 and 288; 277 and 289; 277 and 290; 277 and 291; 277 and 292; 278 and 279; 278 and 280; 278 and 281; 278 and 282; 278 and 283; 278 and 284; 278 and 285; 278 and 286; 278 and 287; 278 and 288; 278 and 289; 278 and 290; 278 and

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and 278; 929 and 279; 929 and 280; 929 and 281; 929 and 282; 929 and 283; 929 and 284; 929 and 285; 929 and 286; 929 and 287; 929 and 288; 929 and 289; 929 and 290; 929 and 291; 929 and 292; 930 and 270; 930 and 272; 930 and 273; 930 and 274; 930 and 275; 930 and 276; 930 and 277; 930 and 278; 930 and 279; 930 and 280; 930 and 281; 930 and 282; 930 and 283; 930 and 284; 930 and 285; 930 and 286; 930 and 287; 930 and 288; 930 and 289; 930 and 290; 930 and 291; 930 and 292; 931 and 270; 931 and 272; 931 and 273; 931 and 274; 931 and 275; 931 and 276; 931 and 277; 931 and 278; 931 and 279; 931 and 280; 931 and 281; 931 and 282; 931 and 283; 931 and 284; 931 and 285; 931 and 286; 931 and 287; 931 and 288; 931 and 289; 931 and 290; 931 and 291; 931 and 292; 932 and 270; 932 and 272; 932 and 273; 932 and 274; 932 and 275; 932 and 276; 932 and 277; 932 and 278; 932 and 279; 932 and 280; 932 and 281; 932 and 282; 932 and 283; 932 and 284; 932 and 285; 932 and 286; 932 and 287; 932 and 288; 932 and 289; 932 and 290; 932 and 291; 932 and 292; 933 and 270; 933 and 272; 933 and 273; 933 and 274; 933 and 275; 933 and 276; 933 and 277; 933 and 278; 933 and 279; 933 and 280; 933 and 281; 933 and 282; 933 and 283; 933 and 284; 933 and 285; 933 and 286; 933 and 287; 933 and 288; 933 and 289; 933 and 290; 933 and 291; 933 and 292; 934 and 270; 934 and 272; 934 and 273; 934 and 274; 934 and 275; 934 and 276; 934 and 277; 934 and 278; 934 and 279; 934 and 280; 934 and 281; 934 and 282; 934 and 283; 934 and 284; 934 and 285; 934 and 286; 934 and 287; 934 and 288; 934 and 289; 934 and 290; 934 and 291; 934 and 292; 935 and 270; 935 and 272; 935 and 273; 935 and 274; 935 and 275; 935 and 276; 935 and 277; 935 and 278; 935 and 279; 935 and 280; 935 and 281; 935 and 282; 935 and 283; 935 and 284; 935 and 285; 935 and 286; 935 and 287; 935 and 288; 935 and 289; 935 and 290; 935 and 291; 935 and 292; 936 and 270; 936 and 272; 936 and 273; 936 and 274; 936 and 275; 936 and 276; 936 and 277; 936 and 278; 936 and 279; 936 and 280; 936 and 281; 936 and 282; 936 and 283; 936 and 284; 936 and 285; 936 and 286; 936 and 287; 936 and 288; 936 and 289; 936 and 290; 936 and 291; 936 and 292; 937 and 270; 937 and 272; 937 and 273; 937 and 274; 937 and 275; 937 and 276; 937 and 277; 937 and 278; 937 and 279; 937 and 280; 937 and 281; 937 and 282; 937 and 283; 937 and 284; 937 and 285; 937 and 286; 937 and 287; 937 and 288; 937 and 289; 937 and 290; 937 and 291; 937 and 292; 938 and 270; 938 and 272; 938 and 273; 938 and 274; 938 and 275; 938 and 276; 938 and 277; 938 and 278; 938 and 279; 938 and 280; 938 and 281; 938 and 282; 938 and 283; 938 and 284; 938 and 285; 938 and 286; 938 and 287; 938 and 288; 938 and 289;

938 and 290; 938 and 291; 938 and 292; 950 and 275; 951 and 275; 952 and 275; 953 and 275; 954 and 275; or 955 and 275;

k. For exon 44 with SluCas9: SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;
l. For exon 45 with SluCas9, SEQ ID NOs: 223 and 230; or 224 and 212.
m. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;
n. For exon 51 with SaCas9, SEQ ID NOs: 28 and 57; 31 and 57; 31 and 46; 32 and 69; 33 and 57; 33 and 69; 34 and 57; 36 and 69; 37 and 69; 37 and 46; 39 and 46; 40 and 46; 46 and 35; 46 and 62; 46 and 65; 46 and 67; 47 and 57; 48 and 57; 49 and 57; 51 and 57; 53 and 46; 54 and 46; 55 and 46; 58 and 46; 59 and 46; 60 and 46; 61 and 69; or 69 and 30;
o. For exon 51 with SluCas9, SEQ ID NOs: 243 and 252; 245 and 252; 252 and 253; 252 and 254; 252 and 256; 252 and 257; 252 and 258; 252 and 262; 252 and 264; 252 and 265; or 252 and 266;
p. For exon 53 with SaCas9, SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and
q. For exon 53 with SluCas9, SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

[00243] In some embodiments, a method for treating DMD is provided comprising administering a composition comprising a Cas protein or a nucleic acid encoding a Cas protein and a pair of guide RNAs, wherein the pair of guide RNAs comprise or consist of any one of the pairs of guide sequences of any one of **Tables 1B** or **1D** for exon 44, **Tables 2B** or **2D** for exon 45, **Tables 3B** or **3D** for exon 50, **Tables 4B** or **4D** for exon 51, and **Tables 5B** or **5D** for exon 53.

[00244] In some embodiments, a method for treating DMD is provided comprising administering a Cas protein or a nucleic acid encoding a Cas protein and a composition comprising one or more nucleic acid molecules encoding a pair of guide RNAs, wherein the pair of guide RNAs comprise or consist of one or more nucleic acid molecules encoding any one of the pairs of guide sequences of any one of **Tables 1B** or **1D** for exon 44, **Tables 2B** or **2D** for exon 45, **Tables 3B** or **3D** for exon 50, **Tables 4B** or **4D** for exon 51, and **Tables 5B** or **5D** for exon 53.

[00245] In some embodiments, a method for treating DMD is provided comprising administering a Cas protein or a nucleic acid encoding a Cas protein and a composition comprising a

pair of guide RNAs comprising or consisting of any one of the pairs of guide sequences of any one of the following:

a. For exon 44 with SluCas9, SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;
b. For exon 45 with SluCas9, SEQ ID NOs: 223 and 230; or 224 and 212;
c. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;
d. For exon 51 with SaCas9, SEQ ID NOs: 28 and 57; 31 and 57; 31 and 46; 32 and 69; 33 and 57; 33 and 69; 34 and 57; 36 and 69; 37 and 69; 37 and 46; 39 and 46; 40 and 46; 46 and 35; 46 and 62; 46 and 65; 46 and 67; 47 and 57; 48 and 57; 49 and 57; 51 and 57; 53 and 46; 54 and 46; 55 and 46; 58 and 46; 59 and 46; 60 and 46; 61 and 69; or 69 and 30;
e. For exon 51 with SluCas9, SEQ ID NOs: 243 and 252; 245 and 252; 252 and 253; 252 and 254; 252 and 256; 252 and 257; 252 and 258; 252 and 262; 252 and 264; 252 and 265; or 252 and 266;
f. For exon 53 with SaCas9, SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and
g. For exon 53 with SluCas9, SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

[00246] In some embodiments, a method for treating DMD is provided comprising administering a Cas protein or a nucleic acid encoding a Cas protein and a composition comprising one or more nucleic acid molecules encoding a pair of guide RNAs, wherein the pair of guide RNAs comprise or consist of one or more nucleic acid molecules encoding any one of the pairs of guide sequences of any one of the following:

a. For exon 44 with SluCas9, SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;
b. For exon 45 with SluCas9, SEQ ID NOs: 223 and 230; or 224 and 212.
c. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;

d. For exon 51 with SaCas9, SEQ ID NOs: 28 and 57; 31 and 57; 31 and 46; 32 and 69; 33 and 57; 33 and 69; 34 and 57; 36 and 69; 37 and 69; 37 and 46; 39 and 46; 40 and 46; 46 and 35; 46 and 62; 46 and 65; 46 and 67; 47 and 57; 48 and 57; 49 and 57; 51 and 57; 53 and 46; 54 and 46; 55 and 46; 58 and 46; 59 and 46; 60 and 46; 61 and 69; or 69 and 30;
e. For exon 51 with SluCas9, SEQ ID NOs: 243 and 252; 245 and 252; 252 and 253; 252 and 254; 252 and 256; 252 and 257; 252 and 258; 252 and 262; 252 and 264; 252 and 265; or 252 and 266;
f. For exon 53 with SaCas9, SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and
g. For exon 53 with SluCas9, SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

[00247] In some embodiments, a method for treating DMD further comprises administering a nucleic acid encoding an endonuclease. The appropriate endonuclease for use with each of the guide RNAs is provided herein, for example, in **Table 6**, column "enzyme."

[00248] In some embodiments, the subject is a mammal. In some embodiments, the subject is human.

[00249] For treatment of a subject (e.g., a human), any of the compositions disclosed herein may be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective. The compositions may be readily administered in a variety of dosage forms, such as injectable solutions. For parenteral administration in an aqueous solution, for example, the solution will generally be suitably buffered and the liquid diluent first rendered isotonic with, for example, sufficient saline or glucose. Such aqueous solutions may be used, for example, for intravenous, intramuscular, subcutaneous, and/or intraperitoneal administration.

Combination Therapy

[00250] In some embodiments, the invention comprises combination therapies comprising any of the methods or uses described herein together with an additional therapy suitable for ameliorating DMD.

Delivery of Guide RNA Compositions

[00251] The methods and uses disclosed herein may use any suitable approach for delivering the guide RNAs and compositions described herein. Exemplary delivery approaches include vectors, such as viral vectors; lipid nanoparticles; transfection; and electroporation. In some embodiments, vectors

or LNPs associated with the single-vector guide RNAs/Cas9's disclosed herein are for use in preparing a medicament for treating DMD.

[00252] Lipid nanoparticles (LNPs) are a known means for delivery of nucleotide and protein cargo, and may be used for delivery of the guide RNAs, compositions, or pharmaceutical formulations disclosed herein. In some embodiments, the LNPs deliver nucleic acid, protein, or nucleic acid together with protein.

[00253] Electroporation is a well-known means for delivery of cargo, and any electroporation methodology may be used for delivering the single vectors disclosed herein.

[00254] In some embodiments, the invention comprises a method for delivering any one of the single vectors disclosed herein to an ex vivo cell, wherein the guide RNA is encoded by a vector, associated with an LNP, or in aqueous solution. In some embodiments, the guide RNA/LNP or guide RNA is also associated with a Cas9 or sequence encoding Cas9 (e.g., in the same vector, LNP, or solution).

[00255] In some embodiments, the disclosure provides for methods of using any of the guides, endonucleases, cells, or compositions disclosed herein in research methods. For example, any of the guides or endonucleases disclosed herein may be used alone or in combination in experiments under various parameters (e.g., temperatures, pH, types of cells) or combined with other reagents to evaluate the activity of the guides and/or endonucleases.

EXAMPLES

[00256] 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: Exemplary DMD sgRNAs

[00257] Guide RNA comprising the guide sequences shown in **Table 6** were prepared according to standard methods in a single guide (sgRNA) format. A single AAV vector, or two AAV vectors, were prepared that expresses one or more of the guide RNAs and a SaCas9 (for guide sequences having SEQ ID NOs: 1-159) or SluCas9 (for guide sequences having SEQ ID NOs: 200-292, 924-938, or 950-955). The AAV vector was administered to cells *in vitro* to assess the ability of the AAV to express the guide RNA and Cas9, edit the targeted exon (see **Table 6**), and thereby treat DMD.

Example 2: Evaluation of sgRNA Pairs

A. Materials and Methods

1. sgRNA selection

[00258] A subset of SaCas9-KKH or SluCas9 sgRNAs found within the *DMD* gene was selected for indel frequency and profile evaluation. The selected sgRNAs for pair evaluation are shown in

Table 6 and were prepared according to standard methods. The criteria used to select these sgRNAs included their potential to induce exon reframing and or skipping as a pair, in addition to the existence of a mouse, dog and NHP homologue counterpart. This selection included 4 sgRNAs located within exon 45, 43 sgRNAs located within exon 51 and 29 sgRNAs located within exon 53. The number of predicted off target sites was determined for each sgRNA.

2. Human primary skeletal muscle myoblasts (HsMMs) culture

[00259] On day one, frozen vials of HsMMs (lot 20TL070666 for Figures 2, 6, and 7A; lot 18TL269121 for Figure 7B) were thawed and grown in complete growth media in a 37°C, 5% CO_2, humidified incubator in T75 flasks. On day two, the growth media was renewed. On day three, the cells were passaged into T150 flasks. On day five, the media in each flask were changed. On day 6, the cells were harvested and electroporated with RNP (nucleofection).

3. Nucleofection of HsMM cells

[00260] The selected sgRNAs for pair evaluation are shown in **Tables 1A-1D and 2** and were chemically synthesized (Sythego). The Cas9 nuclease is recombinant purified SluCas9 (Aldevron). HsMM cells were nucleofected with RNP using the Lonza 4D nucleofector. For each sample, formulated RNP and $0.3x10^6$ cells were mixed in P5 solution. For dual-cut samples that contain two gRNAs, two separate RNPs were formulated with either gRNA of the pair. To formulate RNPs, the gRNA and protein were incubated for about 20 minutes at room temperature. For the experiment shown in Figure 2, the RNPs were prepared in a 3:1 gRNA:Cas9 ratio at 18.75 pmols of sgRNA and of 6.25 pmols of Cas9; total of 37.5 pmols of RNA component and 12.5 pmols of Cas9 component. For the experiment shown in Figure 6, the RNPs were prepared in a 6:1 gRNA:Cas9 ratio at 18.75 pmols of sgRNA and of 3.125 pmols of Cas9; total of 37.5 pmols of RNA component and 6.25 pmols of Cas9 component. For the experiment shown in Figure 7, the RNPs were prepared in a 6:1 gRNA:Cas9 ratio at three different total RNP doses: i) high dose (H) at 75 pmol of sgRNA with 12.5 pmols of Cas9, ii) medium dose (M) at 37.5 pmol of sgRNA with 6.25pmol of Cas9, and iii) low dose (L) 18.75 pmols of sgRNA and of 3.125 pmols of Cas9. For dual RNP nucleofections (Figure 7), the total RNP dose reflects the sum of each RNP, e.g., high dose includes 37.5 pmols of sgRNA-1, 6.25 pmol Cas9 as RNP1, 37.5 pmols of sgRNA-2, and 6.25 pmol Cas9 as RNP2. After electroporation, 80 µL of complete growth media was added to each sample and samples were incubated in a 37°C, 5% CO^2, humidified incubator for 10 minutes. After this recovery, the samples were transferred to 12-well plates containing 2 mL of complete growth media that had been previously equilibrated in a 37°C, 5% CO^2, humidified incubator.

4. Cell harvesting and gDNA extraction

[00261] To determine cell viability 48 hours after nucleofection, the cells were stained with Hoechst and Propidium Iodide (Life Technologies). Cell viability was then assessed using ImageXpress Micro (Molecular Devices). In general, samples with an overall cell viability above 80% were harvested and analyzed for indel analysis. To isolate genomic DNA from HsMMs, the cells were washed with saline buffer, trypsinized and centrifuged. The cell pellets were treated with lysis buffer from the Maxwell RSC Blood DNA Kit (Promega #AS1400), and genomic DNAs were extracted using a Maxwell® RSC48 instrument (Promega #AS8500) according to the manufacturer's instruction. The concentrations of genomic DNAs were determined using Qubit™ 1x dsDNA HS Assay Kit (Thermo Fisher Scientific Q33231) according to the manufacturer's instruction.

5. Sequencing Analysis

[00262] For the data in Figures 6-8 and 10, the editing outcomes from the sequencing data were characterized computationally. Indel frequencies at the cut site were tabulated using the reference amplicon sequence, protospacer sequence, cleavage offset, and the size of the quantification window centered around the cut site.

[00263] A stringent set of QC criteria was applied to filter poor quality samples. These criteria included:

- Average base quality in the sample
- Minimum fraction of reads that are of high sequencing quality
- Minimum fraction of reads with a minimum read length post-trimming
- Minimum fraction of reads remaining after decontamination (i.e., removing phiX reads)
- Minimum fraction of reads that successfully merged
- Minimum fraction of reads that successfully aligned
- Minimum number of aligned reads

[00264] For samples passing all QC criteria, indels identified were classified into three expected types of indels:

- Precise dual-cut: Edits that properly reframe the transcript resulting from the expected cuts from both gRNAs.
- Reframing edits: Indels other than precise dual-cut that properly reframe the transcript.
- Other edits: Indels that do not properly reframe the transcript.

6. For each sample, total % editing and % editing for each type of expected indels (precise dual-cut, reframing edits, other edits) were reported. Transfection of HEK293FT cells

To evaluate indel frequency and profile, human HEK293FT cell line was used. HEK293FT cells were transfected in 12-well plates with 750 ng plasmid + 2.5 µL of Lipofectamine 2000. Three days after transfection, cells were trypsinized and sorted for green fluorescent protein (GFP). GFP-positive cells were sorted directly into lysis buffer, and DNA extraction was performed for exon 51 using the Maxwell RSC Blood DNA Kit (Promega #AS1400) and using a Maxwell® RSC48 instrument (Promega #AS8500) according to the manufacturer's instruction. PCR was then performed on the genomic DNA using DMD exon 53-specific primers that targeted the relevant cut site.

7. Amplicon deep sequencing library preparation and data analysis

[00265] For the data in Figures 1-3, Exon 53 or 51 was amplified by PCR and the products were used to prepare sequencing libraries using MiSeq reagent kit V3. Indel analysis was performed using CRISPResso2 ±10-nt quantification window. (*See*, e.g., Clement et al., Nat Biotechnol. 2019 Mar; 37(3):224-226). Indel profiling consisted of six mutually exclusive indel categories, described below:

NE: non-edited;

Precise deletion (i.e. CleanCut);

RF.+1 (i.e. +1bp): 1-nucleotide (nt) insertion leading to reframe;

RF.Other (i.e. Reframe): indels other than 1-nt insertion leading to reframe:

Deletion: not extending outside of the reframing window

Insertion: < 17-nt (i.e., < 6 amino acids);

Exon skipping: indels that disrupt the ± 6-nt window of the exon/intron boundaries leading to potential exon skipping (outcome requiring validation):

The indel has >= 9-nt overlap with the splicing window (to disrupt the GT/AG splicing sites)

OE: Other indels.

[00266] The following sequences of selected primers were used for amplification of the specific human locus containing the sgRNA targeting sites (**Tables 8A-8B**)

[00267] **Table 8A. Primers for Amplification (Human)**

Targeting exon	Primer ID	Sequence
53	hEX53_F1	AAATGTGAGATAACGTTTGGAAG (SEQ ID NO: 804)
	hEX53_R1	TTTCAGCTTTAACGTGATTTTCTG (SEQ ID NO: 805)

[00268] **Table 8B. Primer + MiSeq Adapter Sequence (Human)**

Exon	ID	Sequence
53	MiSeq_hEX53_F1	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGAAATGTGAGATAACGTTTGGAAG

		(SEQ ID NO: 810)
	MiSeq_hEX53_R1	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGTTTCAGCTTTAACGTGATTTTCTG (SEQ ID NO: 811)

8. AAV configurations for the dual cut single vector candidates

[00269] A combination of promoter orientations, promoter configurations, NLSs and scaffolds were selected for generating AAV plasmids and evaluation on sgRNA transgene expression, AAV manufacturability, and editing efficiency *in vitro* and *in vivo*. AAV plasmid configurations are listed in **Table 9**.

[00270] **Table 9:**

Pol III Promoter	Orientation	Configuration	NLS1	Endonuclease	NLS2	NLS3	Scaffold
hU6c:hU6c	← ⇨ →	hU6c-Cas9-hU6c	c-Myc-GSVD	SluCas9	SV-40-GSGS	Nucleoplasmin-GSGS	V5
	← ⇨ →	hU6c-Cas9-hU6c	c-Myc-GSVD	SaCas9-KKH	SV-40-GSGS	Nucleoplasmin-GSGS	V2
	← ⇨ →	hU6c-Cas9-hU6c	c-Myc-GSVD	SluCas9	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V5
	← ⇨ →	hU6c-Cas9-hU6c	c-Myc-GSVD	SaCas9-KKH	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V2
hU6:7SK2	← ⇨ →	hU6c-Cas9-7SK2	c-Myc-GSVD	SluCas9	SV-40-GSGS	Nucleoplasmin-GSGS	V5
	← ⇨ →	hU6c-Cas9-7SK2	c-Myc-GSVD	SaCas9-KKH	SV-40-GSGS	Nucleoplasmin-GSGS	V2
	← ⇨ →	hU6c-Cas9-7SK2	c-Myc-GSVD	SluCas9	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V5
	← ⇨ →	hU6c-Cas9-7SK2	c-Myc-GSVD	SaCas9-KKH	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V2
hU6c:H1m	← ⇨ →	hU6c-Cas9-H1m	c-Myc-GSVD	SluCas9	SV-40-GSGS	Nucleoplasmin-GSGS	V5
	← ⇨ →	hU6c-Cas9-H1m	c-Myc-GSVD	SaCas9-KKH	SV-40-GSGS	Nucleoplasmin-GSGS	V2
7SK2:H1m	← ⇨ →	7SK2-Cas9-H1m	SV-40-GS	SluCas9	Nucleoplasmin	N/A	V5
	← ⇨ →	7SK2-Cas9-H1m	SV-40-GS	SaCas9-KKH	Nucleoplasmin	N/A	V2
	← ⇨ →	7SK2-Cas9-H1m	SV-40 (+)	SluCas9	Nucleoplasmin	N/A	V5
	← ⇨ →	7SK2-Cas9-H1m	SV-40 (+)	SaCas9-KKH	Nucleoplasmin	N/A	V2
	← ⇨ →	7SK2-Cas9-H1m	c-Myc-GSVD	SluCas9	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V5
	← ⇨ →	7SK2-Cas9-H1m	c-Myc-GSVD	SaCas9-KKH	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V2
	← ⇨ →	7SK2-Cas9-H1m	c-Myc-GSVD	SluCas9	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V2
H1m:M11	← ⇨ →	H1m-Cas9-M11	c-Myc-GSVD	SluCas9	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V5
	← ⇨ →	H1m-Cas9-M11	c-Myc-GSVD	SaCas9-KKH	SV-40-MCS-GSGS	Nucleoplasmin-GSGS	V5

[00271] Sequences of selected primers used for amplification of the specific human locus containing the sgRNA sites are shown in **Table 10**.

Table 10:

Name	Sequence
MiSeq_hE45_F	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGGTCTTTCTGTCTTGTATCCTTTGG (SEQ ID NO: 724)
MiSeq_hE45_R	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGAATGTTAGTGCCTTTCACCC (SEQ ID NO: 725)
TIDE_hE45_F*	GTCTTTCTGTCTTGTATCCTTTGG (SEQ ID NO: 726)

*TIDE_hE45_F is used for Sanger sequencing.

9. Results

[00272] A set of sgRNAs found within the DMD gene was selected for evaluation of indel frequency and profile. Among this selection, 4 sgRNAs were located within exon 45, 43 sgRNAs were located within exon 51 and 29 sgRNAs were located within exon 53.

[00273] To evaluate indel frequency and editing profiles, plasmid transfection was performed in HEK293FT (**Figures 1, 3**), and Human Skeletal Muscle Myoblasts (HsMM) (**Figure 2A-B**).

[00274] The editing frequency and indel profile of selected SaCas9, SaCas9-KKH and SluCas9 sgRNA pairs targeting Exon 51 of *DMD* gene was determined, as shown in **Figure 1**. Each stack bar represents a sgRNA pair and the bar height depicts the average frequency of the total edit. Different indel profiles for each pair of sgRNAs are represented by using distinct patterns. Error bars denote the standard deviation for each indel group.

[00275] The average indel frequency of sgRNAs targeting exon 51 of the DMD gene was determined in HEK294FT cells (**Figure 1**), including precise deletions. The deletion size is shown at bottom.

[00276] The average indel frequency of sgRNAs targeting Exon 45 or Exon 51 of the DMD gene was determined in HsMM cells (**Figure 2A-B**) as calculated by Inference of CRISPR Edit (ICE) via Sanger sequencing signal decomposition (**Figure 2A**) and next generation sequencing (NGS) (**Figure 2B**).

[00277] The average indel frequency of sgRNAs targeting exon 45 (left) and exon 53 (right) of the DMD gene was determined in HEK294FT cells (**Figure 3**), including precise deletions. The deletion size is shown at bottom.

[00278] Using a different formulation (see Materials and Methods: Nucleofection of HsMM cells, above), the average indel frequency of sgRNAs targeting Exon 51 of the *DMD* gene was again determined in HsMM cells (**Figures 6A-B**) as calculated by next generation sequencing (NGS).

Based on these results, the following guide pairs were selected for additional characterization: Slu31-Slu5 (SEQ ID NOs: 269 and 247), Slu31-Slu7 (SEQ ID NOs: 269 and 249), Slu10-24 (SEQ ID NOs: 252 and 262), Slu10-26 (SEQ ID NOs: 252 and 264), and Slu10-16 (SEQ ID NOs: 252 and 254).

[00279] Nuclease activity of the selected guide pairs was evaluated as a function of dose (**Figures 7A-B**). The results show that Slu31-Slu5 (SEQ ID NOs: 269 and 247) (**Figure 7A**) generated the highest precise deletion levels of the selected guide pairs, followed by Slu10-Slu16 (SEQ ID NOs: 252 and 254) (**Figure 7B**).

[00280] The robustness of the precise deletion regime was evaluated in response to perturbations in RNP stoichiometry (**Figures 8A-B**). The dual cut system appeared more robust for the E51Slu10 (SEQ ID NO: 252) dilution than the E51Slu16 (SEQ ID NO: 254) dilution, suggesting that an AAV configuration with Slu16-Slu10 may be more efficacious at lower doses than several of the other pairs tested. (**Figure 8A**). The dual cut system displayed equal robustness for the dilution of either E51Slu10 or E51Slu26 (SEQ ID NO: 264) (**Figure 8B**).

Example 3: Pair Selection for Exon 44 and Exon 50

A. Materials and Methods

[00281] To obtain exemplary guide pairs for exon 44 and exon 50, the reframing window was detected. The reframing window for exon 44 and 50 was defined as the region in which a change in frame would not induce a premature stop codon. The reframing window was calculated by searching premature stop codons in the mutant exon sequence, which was generated by omitting the first base of the exon sequence. Since exon 44 was not in the neutral frame, the searching was conducted from the beginning of exon 43. The window between last premature stop codon and the end of the exon was then determined as the reframing window. Pairs of guide RNAs were then located where the cut-site of at least one guide RNA was within the reframing window. The candidate clean-cut pairs that reframed the exon to a desired frame were a subset of guides for which the cut-distance between the two guides can be represented by the expression "3n+2". An exemplary reframe is shown in **Figure 4A and B.**

Example 4: Exon 53 HEK239FT sRGN On-Target Screening

A. Materials and Methods

1. Transfection of HEK293FT cells

[00282] To evaluate indel frequency and profile, human HEK293FT cell lines were used. About 200k HEK293FT cells were seeded and transfected in each well of 12-well plates, with 750 ng plasmid + 2.5 µL of Lipofectamine 2000 per well. Each plasmid expressed the appropriate nuclease and two sgRNAs for dual-cut editing. The Slu_v5 scaffold (SEQ ID NO: 901) was used for all samples, except for one triplicate of a E45Slu18/4 sample. Three days after transfection, cells were

trypsinized and sorted for green fluorescent protein (GFP). About 100k GFP-positive cells were sorted directly into lysis buffer, and DNA extraction was performed using the Maxwell RSC Blood genomic DNA purification kit.

2. Amplicon Deep Sequencing, Library Preparation, And Data Analysis

[00283] To determine the gene editing efficiency, the genomic DNAs were amplified using primers flanking the *DMD* exon 53 genomic region. The following primer sequences were used: hEX53_F1 AAATGTGAGATAACGTTTGGAAG (SEQ ID NO: 804) and hEX53_R1 TTTCAGCTTTAACGTGATTTTCTG (SEQ ID NO: 805). The size of the amplicons was verified by analyzing a small amount of the PCR products on 2% E-gels. The PCR product was purified by AMPure XP beads. The purified PCR product was amplified again with primers that contain barcodes and Illumina adaptors: i5_UDP0003 AATGATACGGCGACCACCGAGATCTACACTATAGTAGCTTCGTCGGCAGCGTC (SEQ ID NO: 921), and variable i7 indexing primers CAAGCAGAAGACGGCATACGAGAT[variable_10nt_i7_barcode]GTCTCGTGGGCTCGG (CAAGCAGAAGACGGCATACGAGATNNNNNNNNNNGTCTCGTGGGCTCGG, SEQ ID NO: 922). Multiple barcoded samples were pooled, combined with PhiX library, and loaded onto the Illumina Mi-Seq platform. MiSeq Reagent Kit v3 was used to produce a 600-cycle run.

[00284] Indel analysis was performed using CRISPResso2 ±10-nt quantification window. (See, e.g., Clement et al., Nat Biotechnol. 2019 Mar; 37(3):224-226). Indel profiling was assessed using the mutually exclusive indel categories below:

a) Precise Deletion: precision deletion of the DNA sequence between the predicted cut sites of the sgRNA pairs, which leads to reframe;

b) RF.Other: indels other than precise deletion leading to reframe:

c) OE: Other indels.

3. Results

[00285] Results of the Exon 53 HEK293FT sRGN on-target screening are shown in Figures 9-11. As shown in Figure 10, the three sRGNs tested (3.1, 3.3, and 4) had higher % precise deletions than SluCas9 for Slu14+7 (SEQ ID NOs: 281 and 275, respectively), Slu 16+23 (SEQ ID NOS: 283 and 290, respectively) and Slu3+7 (SEQ ID NOs: 271 and 275, respectively). Additionally, sRGN3.3 E53SL3+7 showed the highest % precise deletions (67.8%). For each guide pair, sRGN3.3 had the highest % precise deletions.

Example 5: Exon 53 HsMM sRGN On-Target Screening

A. Materials and Methods

1. Transfection of HsMM cells

[00286] To evaluate indel frequency and profile, primary human skeletal muscle myoblast (HsMM donor number 20TL356515, Lonza) cells were used. Nucleases were delivered as capped mRNA with N1-methylpseudouridine substitutions, produced through *in vitro* transcription by GenScript. sgRNAs were delivered as modified ssRNA synthesized by Synthego. About 50,000 HsMM cells were seeded and transfected in each well of 12-well plates. In each well, 3000 ng plasmid + 0.5 µL of 12.5 µM of each sgRNA were added along with Lipofectamine messengerMAX transfection reagent. The Slu_v5 scaffold (SEQ ID NO: 901) was used for all sgRNAs. Two days after transfection, cells were trypsinized, and genomic DNA extraction was performed using the Maxwell RSC Blood genomic DNA purification kit.

2. Amplicon Deep Sequencing, Library Preparation, and Data Analysis

[00287] To determine the gene editing efficiency, the genomic DNAs were amplified using primers flanking the *DMD* exon 53 genomic region. The following primer sequences were used: hEX53_F1 AAATGTGAGATAACGTTTGGAAG (SEQ ID NO: 804) and hEX53_R1 TTTCAGCTTTAACGTGATTTTCTG (SEQ ID NO: 805). The size of the amplicons was verified by analyzing a small amount of the PCR products on 2% E-gels. The PCR product was purified using AMPure XP beads. The purified PCR product was amplified again with primers that contain barcodes and Illumina adaptors: i5_UDP0003 AATGATACGGCGACCACCGAGATCTACACTATAGTAGCTTCGTCGGCAGCGTC (SEQ ID NO: 921), and variable i7 indexing primers CAAGCAGAAGACGGCATACGAGAT[variable_10nt_i7_barcode]GTCTCGTGGGCTCGG (CAAGCAGAAGACGGCATACGAGATNNNNNNNNNNGTCTCGTGGGCTCGG, SEQ ID NO: 922). Multiple barcoded samples were pooled, combined with PhiX library, and loaded onto the Illumina Mi-Seq platform. MiSeq Reagent Kit v3 was used to produce a 600-cycle run.

[00288] Indel analysis was performed using CRISPResso2 ± 10-nt quantification window (See Clement et al., Nat Biotechnol. 2019 Mar; 37(3):224-226). Indel profiling was assessed using the mutually exclusive indel categories below:

a) Precise Deletion: precision deletion of the DNA sequence between the predicted cut sites of the sgRNA pairs, which leads to reframe;

b) RF.Other: indels other than precise deletion leading to reframe:

c) OE: Other indels.

3. Results

[00289] Results of the Exon 53 HsMM sRGN on-target screening are shown in Figure 12. The three sRGNs tested (3.1, 3.3, and 4) exhibited higher % precise deletions than SluCas9 for both Slu16+23 (SEQ ID NOs: 283 and 290, respectively) and Slu3+7 (SEQ ID NOs: 271 and 275, respectively), with increases in % precise deletions greatest for the three sRGNs with Slu16+23 as compared to SluCas9 with Slu16+23.

[00290] 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. 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.

[00291] 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.

What is claimed is:

1. A composition comprising one or more guide RNAs or a nucleic acid encoding one or more guide RNAs, wherein the one or more guide RNAs comprise i) a guide sequence of **Table 6**; ii) at least 16, 17, 18, 19, or 20 contiguous nucleotides of a guide sequence of **Table 6**; iii) a guide sequence that is at least 90% identical to a guide sequence of **Table 6**; or iv) any one of the guide sequence pairs shown in **Tables 1B**, **1D**, **3B**, **3D**, **5B**, and **5D**, optionally further comprising a SaCas9 or a nucleic acid encoding a SaCas9 (for SEQ ID NOs: 1-159) or a SluCas9 or a nucleic acid encoding a SluCas9 (for SEQ ID NOs: 200-292, 924-938, or 950-955).
2. A composition comprising a pair of guide RNAs or a nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprise or consist of a first and a second guide sequence, wherein the first and the second guide sequences are selected from any of the following pairs of guide sequences:
   a. For exon 44 with SaCas9, SEQ ID NOs: 1 and 3; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; or 124 and 125;
   b. For exon 44 with SluCas9, SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and

203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208;

c. For exon 50 with SaCas9, SEQ ID NOs: 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; or 158 and 159;

d. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232 and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and 239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; or 241 and 242;

e. For exon 53 with SaCas9, SEQ ID NOs: 16 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20; 17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 71 and 72; 71 and 73; 71 and 74; 71 and 75; 71 and 76; 71 and 77; 71 and 78; 71 and 84; 71 and 85; 71 and 86; 71

and 87; 71 and 88; 71 and 89; 71 and 90; 71 and 91; 71 and 92; 71 and 93; 71 and 94; 71 and 95; 71 and 96; 71 and 97; 71 and 98; 71 and 99; 71 and 100; 71 and 101; 71 and 102; 72 and 73; 72 and 74; 72 and 75; 72 and 76; 72 and 77; 72 and 78; 72 and 84; 72 and 85; 72 and 86; 72 and 87; 72 and 88; 72 and 89; 72 and 90; 72 and 91; 72 and 92; 72 and 93; 72 and 94; 72 and 95; 72 and 96; 72 and 97; 72 and 98; 72 and 99; 72 and 100; 72 and 101; 72 and 102; 73 and 74; 73 and 75; 73 and 76; 73 and 77; 73 and 78; 73 and 84; 73 and 85; 73 and 86; 73 and 87; 73 and 88; 73 and 89; 73 and 90; 73 and 91; 73 and 92; 73 and 93; 73 and 94; 73 and 95; 73 and 96; 73 and 97; 73 and 98; 73 and 99; 73 and 100; 73 and 101; 73 and 102; 74 and 75; 74 and 76; 74 and 77; 74 and 78; 74 and 84; 74 and 85; 74 and 86; 74 and 87; 74 and 88; 74 and 89; 74 and 90; 74 and 91; 74 and 92; 74 and 93; 74 and 94; 74 and 95; 74 and 96; 74 and 97; 74 and 98; 74 and 99; 74 and 100; 74 and 101; 74 and 102; 75 and 76; 75 and 77; 75 and 78; 75 and 84; 75 and 85; 75 and 86; 75 and 87; 75 and 88; 75 and 89; 75 and 90; 75 and 91; 75 and 92; 75 and 93; 75 and 94; 75 and 95; 75 and 96; 75 and 97; 75 and 98; 75 and 99; 75 and 100; 75 and 101; 75 and 102; 76 and 77; 76 and 78; 76 and 84; 76 and 85; 76 and 86; 76 and 87; 76 and 88; 76 and 89; 76 and 90; 76 and 91; 76 and 92; 76 and 93; 76 and 94; 76 and 95; 76 and 96; 76 and 97; 76 and 98; 76 and 99; 76 and 100; 76 and 101; 76 and 102; 77 and 78; 77 and 84; 77 and 85; 77 and 86; 77 and 87; 77 and 88; 77 and 89; 77 and 90; 77 and 91; 77 and 92; 77 and 93; 77 and 94; 77 and 95; 77 and 96; 77 and 97; 77 and 98; 77 and 99; 77 and 100; 77 and 101; 77 and 102; 78 and 84; 78 and 85; 78 and 86; 78 and 87; 78 and 88; 78 and 89; 78 and 90; 78 and 91; 78 and 92; 78 and 93; 78 and 94; 78 and 95; 78 and 96; 78 and 97; 78 and 98; 78 and 99; 78 and 100; 78 and 101; 78 and 102; 84 and 85; 84 and 86; 84 and 87; 84 and 88; 84 and 89; 84 and 90; 84 and 91; 84 and 92; 84 and 93; 84 and 94; 84 and 95; 84 and 96; 84 and 97; 84 and 98; 84 and 99; 84 and 100; 84 and 101; 84 and 102; 85 and 86; 85 and 87; 85 and 88; 85 and 89; 85 and 90; 85 and 91; 85 and 92; 85 and 93; 85 and 94; 85 and 95; 85 and 96; 85 and 97; 85 and 98; 85 and 99; 85 and 100; 85 and 101; 85 and 102; 86 and 87; 86 and 88; 86 and 89; 86 and 90; 86 and 91; 86 and 92; 86 and 93; 86 and 94; 86 and 95; 86 and 96; 86 and 97; 86 and 98; 86 and 99; 86 and 100; 86 and 101; 86 and 102; 87 and 88; 87 and 89; 87 and 90; 87 and 91; 87 and 92; 87 and 93; 87 and 94; 87 and 95; 87 and 96; 87 and 97; 87 and 98; 87 and 99; 87 and 100; 87 and 101; 87 and 102; 88 and 89; 88 and 90; 88 and 91; 88 and 92; 88 and 93; 88 and 94; 88 and 95; 88 and 96; 88 and 97; 88 and 98; 88 and 99; 88 and 100; 88 and 101; 88 and 102; 89 and 90; 89 and 91; 89 and 92; 89 and 93; 89 and 94; 89 and 95; 89 and 96; 89 and 97; 89 and 98; 89 and 99; 89 and 100; 89 and 101; 89 and 102; 90 and 91; 90 and 92; 90 and 93; 90 and 94; 90 and 95; 90 and 96; 90 and 97; 90 and 98; 90 and 99; 90 and 100; 90 and 101; 90 and 102; 91 and 92; 91 and 93; 91 and 94;

91 and 95; 91 and 96; 91 and 97; 91 and 98; 91 and 99; 91 and 100; 91 and 101; 91 and 102; 92 and 93; 92 and 94; 92 and 95; 92 and 96; 92 and 97; 92 and 98; 92 and 99; 92 and 100; 92 and 101; 92 and 102; 93 and 94; 93 and 95; 93 and 96; 93 and 97; 93 and 98; 93 and 99; 93 and 100; 93 and 101; 93 and 102; 94 and 95; 94 and 96; 94 and 97; 94 and 98; 94 and 99; 94 and 100; 94 and 101; 94 and 102; 95 and 96; 95 and 97; 95 and 98; 95 and 99; 95 and 100; 95 and 101; 95 and 102; 96 and 97; 96 and 98; 96 and 99; 96 and 100; 96 and 101; 96 and 102; 97 and 98; 97 and 99; 97 and 100; 97 and 101; 97 and 102; 98 and 99; 98 and 100; 98 and 101; 98 and 102; 99 and 100; 99 and 101; 99 and 102; 100 and 101; 100 and 102; or 101 and 102;

f. For exon 53 with SluCas9, SEQ ID NOs: 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and 277; 270 and 278; 270 and 279; 270 and 280; 270 and 281; 270 and 282; 270 and 283; 270 and 284; 270 and 285; 270 and 286; 270 and 287; 270 and 288; 270 and 289; 270 and 290; 270 and 291; 270 and 292; 271 and 272; 271 and 273; 271 and 274; 271 and 275; 271 and 276; 271 and 277; 271 and 278; 271 and 279; 271 and 280; 271 and 281; 271 and 282; 271 and 283; 271 and 284; 271 and 285; 271 and 286; 271 and 287; 271 and 288; 271 and 289; 271 and 290; 271 and 291; 271 and 292; 272 and 273; 272 and 274; 272 and 275; 272 and 276; 272 and 277; 272 and 278; 272 and 279; 272 and 280; 272 and 281; 272 and 282; 272 and 283; 272 and 284; 272 and 285; 272 and 286; 272 and 287; 272 and 288; 272 and 289; 272 and 290; 272 and 291; 272 and 292; 273 and 274; 273 and 275; 273 and 276; 273 and 277; 273 and 278; 273 and 279; 273 and 280; 273 and 281; 273 and 282; 273 and 283; 273 and 284; 273 and 285; 273 and 286; 273 and 287; 273 and 288; 273 and 289; 273 and 290; 273 and 291; 273 and 292; 274 and 275; 274 and 276; 274 and 277; 274 and 278; 274 and 279; 274 and 280; 274 and 281; 274 and 282; 274 and 283; 274 and 284; 274 and 285; 274 and 286; 274 and 287; 274 and 288; 274 and 289; 274 and 290; 274 and 291; 274 and 292; 275 and 276; 275 and 277; 275 and 278; 275 and 279; 275 and 280; 275 and 281; 275 and 282; 275 and 283; 275 and 284; 275 and 285; 275 and 286; 275 and 287; 275 and 288; 275 and 289; 275 and 290; 275 and 291; 275 and 292; 276 and 277; 276 and 278; 276 and 279; 276 and 280; 276 and 281; 276 and 282; 276 and 283; 276 and 284; 276 and 285; 276 and 286; 276 and 287; 276 and 288; 276 and 289; 276 and 290; 276 and 291; 276 and 292; 277 and 278; 277 and 279; 277 and 280; 277 and 281; 277 and 282; 277 and 283; 277 and 284; 277 and 285; 277 and 286; 277 and 287; 277 and 288; 277 and 289; 277 and 290; 277 and 291; 277 and 292; 278 and 279; 278 and 280; 278 and 281; 278 and 282; 278 and 283; 278 and 284; 278 and 285; 278 and 286; 278 and 287; 278 and 288; 278 and 289; 278 and 290; 278 and 291; 278 and 292; 279 and 280; 279 and 281; 279 and 282; 279 and

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g. For exon 44 with SluCas9, SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;

   h. For exon 50 with SluCas9, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;
   i. For exon 53 with SaCas9, SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and
   j. For exon 53 with SluCas9, SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

3. A composition comprising: one or more nucleic acid molecules encoding
   a. a SaCas9 or SluCas9; and
   b. a first guide sequence and a second guide sequence, wherein the first and the second guide sequences are selected from any of the following pairs of guide sequences: SEQ ID NO: 1 and SEQ ID NO: 3; SEQ ID NO: 16 and SEQ ID NO: 17; SEQ ID NO: 16 and SEQ ID NO: 18; SEQ ID NO: 16 and SEQ ID NO: 19; SEQ ID NO: 16 and SEQ ID NO: 20; SEQ ID NO: 16 and SEQ ID NO: 21; SEQ ID NO: 16 and SEQ ID NO: 22; SEQ ID NO: 16 and SEQ ID NO: 23; SEQ ID NO: 16 and SEQ ID NO: 24; SEQ ID NO: 16 and SEQ ID NO: 25; SEQ ID NO: 16 and SEQ ID NO: 26; SEQ ID NO: 17 and SEQ ID NO: 18; SEQ ID NO: 17 and SEQ ID NO: 19; SEQ ID NO: 17 and SEQ ID NO: 20; SEQ ID NO: 17 and SEQ ID NO: 21; SEQ ID NO: 17 and SEQ ID NO: 22; SEQ ID NO: 17 and SEQ ID NO: 23; SEQ ID NO: 17 and SEQ ID NO: 24; SEQ ID NO: 17 and SEQ ID NO: 25; SEQ ID NO: 17 and SEQ ID NO: 26; SEQ ID NO: 18 and SEQ ID NO: 19; SEQ ID NO: 18 and SEQ ID NO: 20; SEQ ID NO: 18 and SEQ ID NO: 21; SEQ ID NO: 18 and SEQ ID NO: 22; SEQ ID NO: 18 and SEQ ID NO: 23; SEQ ID NO: 18 and SEQ ID NO: 24; SEQ ID NO: 18 and SEQ ID NO: 25; SEQ ID NO: 18 and SEQ ID NO: 26; SEQ ID NO: 19 and SEQ ID NO: 20; SEQ ID NO: 19 and SEQ ID NO: 21; SEQ ID NO: 19 and SEQ ID NO: 22; SEQ ID NO: 19 and SEQ ID NO: 23; SEQ ID NO: 19 and SEQ ID NO: 24; SEQ ID NO: 19 and SEQ ID NO: 25; SEQ ID NO: 19 and SEQ ID NO: 26; SEQ ID NO: 20 and SEQ ID NO: 21; SEQ ID NO: 20 and SEQ ID NO: 22; SEQ ID NO: 20 and SEQ ID NO: 23; SEQ ID NO: 20 and SEQ ID NO: 24; SEQ ID NO: 20 and SEQ ID NO: 25; SEQ ID NO: 20 and SEQ ID NO: 26; SEQ ID NO: 21 and SEQ ID NO: 22; SEQ ID NO: 21 and SEQ ID NO: 23; SEQ ID NO: 21 and SEQ ID NO: 24; SEQ ID NO: 21 and SEQ ID NO: 25; SEQ ID NO: 21 and SEQ ID NO: 26; SEQ ID NO: 22 and SEQ ID NO: 23; SEQ ID NO: 22 and SEQ ID NO: 24; SEQ ID NO: 22 and SEQ ID NO: 25; SEQ ID NO: 22 and SEQ ID NO: 26; SEQ ID NO: 23 and SEQ ID NO: 24; SEQ ID NO: 23 and SEQ ID NO: 25; SEQ ID NO: 23 and SEQ ID NO: 26; SEQ ID NO:

24 and SEQ ID NO: 25; SEQ ID NO: 24 and SEQ ID NO: 26; SEQ ID NO: 25 and SEQ ID NO: 26; SEQ ID NO: 110 and SEQ ID NO: 120; SEQ ID NO: 110 and SEQ ID NO: 121; SEQ ID NO: 110 and SEQ ID NO: 122; SEQ ID NO: 110 and SEQ ID NO: 123; SEQ ID NO: 110 and SEQ ID NO: 124; SEQ ID NO: 110 and SEQ ID NO: 125; SEQ ID NO: 111 and SEQ ID NO: 112; SEQ ID NO: 111 and SEQ ID NO: 113; SEQ ID NO: 111 and SEQ ID NO: 114; SEQ ID NO: 111 and SEQ ID NO: 115; SEQ ID NO: 111 and SEQ ID NO: 116; SEQ ID NO: 111 and SEQ ID NO: 117; SEQ ID NO: 111 and SEQ ID NO: 118; SEQ ID NO: 111 and SEQ ID NO: 119; SEQ ID NO: 111 and SEQ ID NO: 120; SEQ ID NO: 111 and SEQ ID NO: 121; SEQ ID NO: 111 and SEQ ID NO: 122; SEQ ID NO: 111 and SEQ ID NO: 123; SEQ ID NO: 111 and SEQ ID NO: 124; SEQ ID NO: 111 and SEQ ID NO: 125; SEQ ID NO: 112 and SEQ ID NO: 113; SEQ ID NO: 112 and SEQ ID NO: 114; SEQ ID NO: 112 and SEQ ID NO: 115; SEQ ID NO: 112 and SEQ ID NO: 116; SEQ ID NO: 112 and SEQ ID NO: 117; SEQ ID NO: 112 and SEQ ID NO: 118; SEQ ID NO: 112 and SEQ ID NO: 119; SEQ ID NO: 112 and SEQ ID NO: 120; SEQ ID NO: 112 and SEQ ID NO: 121; SEQ ID NO: 112 and SEQ ID NO: 122; SEQ ID NO: 112 and SEQ ID NO: 123; SEQ ID NO: 112 and SEQ ID NO: 124; SEQ ID NO: 112 and SEQ ID NO: 125; SEQ ID NO: 113 and SEQ ID NO: 114; SEQ ID NO: 113 and SEQ ID NO: 115; SEQ ID NO: 113 and SEQ ID NO: 116; SEQ ID NO: 113 and SEQ ID NO: 117; SEQ ID NO: 113 and SEQ ID NO: 118; SEQ ID NO: 113 and SEQ ID NO: 119; SEQ ID NO: 113 and SEQ ID NO: 120; SEQ ID NO: 113 and SEQ ID NO: 121; SEQ ID NO: 113 and SEQ ID NO: 122; SEQ ID NO: 113 and SEQ ID NO: 123; SEQ ID NO: 113 and SEQ ID NO: 124; SEQ ID NO: 113 and SEQ ID NO: 125; SEQ ID NO: 114 and SEQ ID NO: 115; SEQ ID NO: 114 and SEQ ID NO: 116; SEQ ID NO: 114 and SEQ ID NO: 117; SEQ ID NO: 114 and SEQ ID NO: 118; SEQ ID NO: 114 and SEQ ID NO: 119; SEQ ID NO: 114 and SEQ ID NO: 120; SEQ ID NO: 114 and SEQ ID NO: 121; SEQ ID NO: 114 and SEQ ID NO: 122; SEQ ID NO: 114 and SEQ ID NO: 123; SEQ ID NO: 114 and SEQ ID NO: 124; SEQ ID NO: 114 and SEQ ID NO: 125; SEQ ID NO: 115 and SEQ ID NO: 116; SEQ ID NO: 115 and SEQ ID NO: 117; SEQ ID NO: 115 and SEQ ID NO: 118; SEQ ID NO: 115 and SEQ ID NO: 119; SEQ ID NO: 115 and SEQ ID NO: 120; SEQ ID NO: 115 and SEQ ID NO: 121; SEQ ID NO: 115 and SEQ ID NO: 122; SEQ ID NO: 115 and SEQ ID NO: 123; SEQ ID NO: 115 and SEQ ID NO: 124; SEQ ID NO: 115 and SEQ ID NO: 125; SEQ ID NO: 116 and SEQ ID NO: 117; SEQ ID NO: 116 and SEQ ID NO: 118; SEQ ID NO: 116 and SEQ ID NO: 119; SEQ ID NO: 116 and SEQ ID NO: 120; SEQ ID NO: 116 and SEQ ID NO: 121; SEQ ID NO: 116 and SEQ ID NO: 122;

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SEQ ID NO: 952 and SEQ ID NO: 275; SEQ ID NO: 953 and SEQ ID NO: 275; SEQ ID NO: 954 and SEQ ID NO: 275; or SEQ ID NO: 955 and SEQ ID NO: 275.

4. A composition comprising:

  a. a single nucleic acid molecule comprising:

    i. a nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and at least one, at least two, or at least three guide RNAs; or

    ii. a nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or

    iii. a nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and 1, 2, or 3 guide RNAs;

  wherein each guide RNA is selected from **Table 6**, optionally wherein the composition comprises at least one pair of guide RNAs, wherein the at least one pair is selected from the pairs shown in **Tables 1B, 1D, 3B, 3D, 5B,** or **5D**; or

  b. two nucleic acid molecules comprising:

    i. a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9); and

    a second nucleic acid that does not encode a SaCas9 or SluCas9 and encodes any one of the following:

      1. at least one, at least two, at least three, at least four, at least five, or at least six guide RNAs; or
      2. from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or
      3. from one to six guide RNAs; or

    ii. a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and

      1. at least one, at least two, or at least three guide RNAs; or

2. from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or
3. 1, 2, or 3 guide RNAs; and

a second nucleic acid that does not encode a SaCas9 or SluCas9, optionally wherein the second nucleic acid comprises any one of the following:

1. at least one, at least two, at least three, at least four, at least five, or at least six guide RNAs; or
2. from one to n guide RNAs, wherein n is no more than the maximum number of guide RNAs that can be expressed from said nucleic acid; or
3. from one to six guide RNAs; or

iii. a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and at least one, at least two, or at least three guide RNAs; and

a second nucleic acid that does not encode a SaCas9 or SluCas9 and encodes from one to six guide RNAs; or

iv. a first nucleic acid encoding *Staphylococcus aureus* Cas9 (SaCas9) or *Staphylococcus lugdunensis* (SluCas9) and at least two guide RNAs, wherein a first guide RNA of the at least two guide RNAs binds upstream of a target sequence and a second guide RNA of the at least two guide RNAs binds downstream of the target sequence; and

a second nucleic acid that does not encode a SaCas9 or SluCas9 and encodes at least one additional copy of each of the guide RNAs encoded in the first nucleic acid;

wherein each guide RNA is selected from **Table 6**, optionally wherein the composition comprises at least one pair of guide RNAs, wherein the at least one pair is selected from the pairs shown in **Tables 1B, 1D, 3B, 3D, 5B,** or **5D**.

5. The composition of any one of claims 1-4, comprising a pair of guide RNAs, wherein the pair of guide RNAs is capable of excising a DNA fragment from the DMD gene; wherein the DNA fragment is between 5-250 nucleotides in length.

6. The composition of claim 5, wherein the excised DNA fragment does not comprise an entire exon of the DMD gene.

7. A composition comprising a single nucleic acid molecule encoding a pair of guide RNAs and a Cas9, wherein the single nucleic acid molecule comprises:
   a. a first nucleic acid encoding the pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences: SEQ ID NOs: 1 and 3; 16 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20; 17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; 124 and 125; 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and

153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; 158 and 159; 71 and 72; 71 and 73; 71 and 74; 71 and 75; 71 and 76; 71 and 77; 71 and 78; 71 and 84; 71 and 85; 71 and 86; 71 and 87; 71 and 88; 71 and 89; 71 and 90; 71 and 91; 71 and 92; 71 and 93; 71 and 94; 71 and 95; 71 and 96; 71 and 97; 71 and 98; 71 and 99; 71 and 100; 71 and 101; 71 and 102; 72 and 73; 72 and 74; 72 and 75; 72 and 76; 72 and 77; 72 and 78; 72 and 84; 72 and 85; 72 and 86; 72 and 87; 72 and 88; 72 and 89; 72 and 90; 72 and 91; 72 and 92; 72 and 93; 72 and 94; 72 and 95; 72 and 96; 72 and 97; 72 and 98; 72 and 99; 72 and 100; 72 and 101; 72 and 102; 73 and 74; 73 and 75; 73 and 76; 73 and 77; 73 and 78; 73 and 84; 73 and 85; 73 and 86; 73 and 87; 73 and 88; 73 and 89; 73 and 90; 73 and 91; 73 and 92; 73 and 93; 73 and 94; 73 and 95; 73 and 96; 73 and 97; 73 and 98; 73 and 99; 73 and 100; 73 and 101; 73 and 102; 74 and 75; 74 and 76; 74 and 77; 74 and 78; 74 and 84; 74 and 85; 74 and 86; 74 and 87; 74 and 88; 74 and 89; 74 and 90; 74 and 91; 74 and 92; 74 and 93; 74 and 94; 74 and 95; 74 and 96; 74 and 97; 74 and 98; 74 and 99; 74 and 100; 74 and 101; 74 and 102; 75 and 76; 75 and 77; 75 and 78; 75 and 84; 75 and 85; 75 and 86; 75 and 87; 75 and 88; 75 and 89; 75 and 90; 75 and 91; 75 and 92; 75 and 93; 75 and 94; 75 and 95; 75 and 96; 75 and 97; 75 and 98; 75 and 99; 75 and 100; 75 and 101; 75 and 102; 76 and 77; 76 and 78; 76 and 84; 76 and 85; 76 and 86; 76 and 87; 76 and 88; 76 and 89; 76 and 90; 76 and 91; 76 and 92; 76 and 93; 76 and 94; 76 and 95; 76 and 96; 76 and 97; 76 and 98; 76 and 99; 76 and 100; 76 and 101; 76 and 102; 77 and 78; 77 and 84; 77 and 85; 77 and 86; 77 and 87; 77 and 88; 77 and 89; 77 and 90; 77 and 91; 77 and 92; 77 and 93; 77 and 94; 77 and 95; 77 and 96; 77 and 97; 77 and 98; 77 and 99; 77 and 100; 77 and 101; 77 and 102; 78 and 84; 78 and 85; 78 and 86; 78 and 87; 78 and 88; 78 and 89; 78 and 90; 78 and 91; 78 and 92; 78 and 93; 78 and 94; 78 and 95; 78 and 96; 78 and 97; 78 and 98; 78 and 99; 78 and 100; 78 and 101; 78 and 102; 84 and 85; 84 and 86; 84 and 87; 84 and 88; 84 and 89; 84 and 90; 84 and 91; 84 and 92; 84 and 93; 84 and 94; 84 and 95; 84 and 96; 84 and 97; 84 and 98; 84 and 99; 84 and 100; 84 and 101; 84 and 102; 85 and 86; 85 and 87; 85 and 88; 85 and 89; 85 and 90; 85 and 91; 85 and 92; 85 and 93; 85 and 94; 85 and 95; 85 and 96; 85 and 97; 85 and 98; 85 and 99; 85 and 100; 85 and 101; 85 and 102; 86 and 87; 86 and 88; 86 and 89; 86 and 90; 86 and 91; 86 and 92; 86 and 93; 86 and 94; 86 and 95; 86 and 96; 86 and 97; 86 and 98; 86 and 99; 86 and 100; 86 and 101; 86 and 102; 87 and 88; 87 and 89; 87 and 90; 87 and 91; 87 and 92; 87 and 93; 87 and 94; 87 and 95; 87 and 96; 87 and 97; 87 and 98; 87 and 99; 87 and 100; 87

and 101; 87 and 102; 88 and 89; 88 and 90; 88 and 91; 88 and 92; 88 and 93; 88 and 94; 88 and 95; 88 and 96; 88 and 97; 88 and 98; 88 and 99; 88 and 100; 88 and 101; 88 and 102; 89 and 90; 89 and 91; 89 and 92; 89 and 93; 89 and 94; 89 and 95; 89 and 96; 89 and 97; 89 and 98; 89 and 99; 89 and 100; 89 and 101; 89 and 102; 90 and 91; 90 and 92; 90 and 93; 90 and 94; 90 and 95; 90 and 96; 90 and 97; 90 and 98; 90 and 99; 90 and 100; 90 and 101; 90 and 102; 91 and 92; 91 and 93; 91 and 94; 91 and 95; 91 and 96; 91 and 97; 91 and 98; 91 and 99; 91 and 100; 91 and 101; 91 and 102; 92 and 93; 92 and 94; 92 and 95; 92 and 96; 92 and 97; 92 and 98; 92 and 99; 92 and 100; 92 and 101; 92 and 102; 93 and 94; 93 and 95; 93 and 96; 93 and 97; 93 and 98; 93 and 99; 93 and 100; 93 and 101; 93 and 102; 94 and 95; 94 and 96; 94 and 97; 94 and 98; 94 and 99; 94 and 100; 94 and 101; 94 and 102; 95 and 96; 95 and 97; 95 and 98; 95 and 99; 95 and 100; 95 and 101; 95 and 102; 96 and 97; 96 and 98; 96 and 99; 96 and 100; 96 and 101; 96 and 102; 97 and 98; 97 and 99; 97 and 100; 97 and 101; 97 and 102; 98 and 99; 98 and 100; 98 and 101; 98 and 102; 99 and 100; 99 and 101; 99 and 102; 100 and 101; 100 and 102; or 101 and 102; and a second nucleic acid encoding a *Staphylococcus aureus* Cas9 (SaCas9); or

b. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences: SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and 203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208; 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232 and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and 239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; 241 and 242; 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and

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c. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences targeting exon 44: SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208; and a second nucleic acid encoding a *Staphylococcus lugdunensis* (SluCas9); or

d. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences targeting exon 50: SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241; and a second nucleic acid encoding a *Staphylococcus lugdunensis* (SluCas9); or

e. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences targeting exon 53: SEQ

ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73; and a second nucleic acid encoding a *Staphylococcus aureus* Cas9 (SaCas9); or

   f. a first nucleic acid encoding a pair of guide RNAs, wherein the pair of guide RNAs comprises any one of the following pairs of guide sequences targeting exon 53: SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292; and a second nucleic acid encoding a *Staphylococcus lugdunensis* (SluCas9).

8. A composition comprising one or more nucleic acid molecules encoding a *Staphylococcus aureus* Cas9 (SaCas9) and a first and a second guide RNA, wherein the first and the second guide RNAs target different sequences in a DMD gene, and wherein the first and the second guide RNAs each comprise a sequence that is at least 90% identical to a first and a second guide sequence selected from any one of the following pairs of first and second guide sequences:

   a. any one of the following pairs of first and second guide sequences targeting exon 53, SEQ ID NOs: 86 and 96; 87 and 96; 88 and 97; 89 and 96; 90 and 97; 92 and 77; 92 and 78; 92 and 96; 92 and 99; 93 and 98; 93 and 102; 94 and 100; 95 and 77; 95 and 78; 95 and 99; 96 and 100; 97 and 98; 97 and 102; 98 and 73; or 102 and 73.

9. A composition comprising one or more nucleic acid molecules encoding a *Staphylococcus lugdunensis* (SluCas9) and a first and a second guide RNA, wherein the first and the second guide RNAs target different sequences in a DMD gene, and wherein the first and the second guide RNAs each comprise a sequence that is at least 90% identical to a first and second guide sequence selected from any one of the following pairs of first and second guide sequences:

   a. any one of the following pairs of first and second guide sequences targeting exon 44, SEQ ID NOs: 200 and 203; 200 and 204; 202 and 203; 202 and 205; 202 and 206; 202 and 207; 204 and 208; 204 and 205; 204 and 206; 204 and 207; or 204 and 208;
   b. any one of the following pairs of first and second guide sequences targeting exon 50, SEQ ID NOs: 231 and 232; 231 and 234; 231 and 236; 231 and 237; 236 and 233; 236 and 235; 236 and 238; 236 and 240; or 236 and 241;
   c. any one of the following pairs of first and second guide sequences targeting exon 53, SEQ ID NOs: 278 and 290; 278 and 292; 281 and 291; 283 and 290; 283 and 292; 287 and 291; 272 and 290; 290 and 291; or 272 and 292.

10. A composition comprising one or more nucleic acid molecules encoding an endonuclease and at least two guide RNAs, wherein the at least two guide RNAs each target a different

sequence in a DMD gene, and wherein the at least two guide RNAs each comprise a sequence that is at least 90% identical to a first and second guide sequence selected from any one of the following pairs of first and second guide sequences:

a. for exon 44, SEQ ID NOs: 1 and 3; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118; 113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; or 124 and 125;

b. for exon 50, SEQ ID NOs: 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; or 158 and 159;

c. for exon 53, SEQ ID NOs: 16 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20;

17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 71 and 72; 71 and 73; 71 and 74; 71 and 75; 71 and 76; 71 and 77; 71 and 78; 71 and 84; 71 and 85; 71 and 86; 71 and 87; 71 and 88; 71 and 89; 71 and 90; 71 and 91; 71 and 92; 71 and 93; 71 and 94; 71 and 95; 71 and 96; 71 and 97; 71 and 98; 71 and 99; 71 and 100; 71 and 101; 71 and 102; 72 and 73; 72 and 74; 72 and 75; 72 and 76; 72 and 77; 72 and 78; 72 and 84; 72 and 85; 72 and 86; 72 and 87; 72 and 88; 72 and 89; 72 and 90; 72 and 91; 72 and 92; 72 and 93; 72 and 94; 72 and 95; 72 and 96; 72 and 97; 72 and 98; 72 and 99; 72 and 100; 72 and 101; 72 and 102; 73 and 74; 73 and 75; 73 and 76; 73 and 77; 73 and 78; 73 and 84; 73 and 85; 73 and 86; 73 and 87; 73 and 88; 73 and 89; 73 and 90; 73 and 91; 73 and 92; 73 and 93; 73 and 94; 73 and 95; 73 and 96; 73 and 97; 73 and 98; 73 and 99; 73 and 100; 73 and 101; 73 and 102; 74 and 75; 74 and 76; 74 and 77; 74 and 78; 74 and 84; 74 and 85; 74 and 86; 74 and 87; 74 and 88; 74 and 89; 74 and 90; 74 and 91; 74 and 92; 74 and 93; 74 and 94; 74 and 95; 74 and 96; 74 and 97; 74 and 98; 74 and 99; 74 and 100; 74 and 101; 74 and 102; 75 and 76; 75 and 77; 75 and 78; 75 and 84; 75 and 85; 75 and 86; 75 and 87; 75 and 88; 75 and 89; 75 and 90; 75 and 91; 75 and 92; 75 and 93; 75 and 94; 75 and 95; 75 and 96; 75 and 97; 75 and 98; 75 and 99; 75 and 100; 75 and 101; 75 and 102; 76 and 77; 76 and 78; 76 and 84; 76 and 85; 76 and 86; 76 and 87; 76 and 88; 76 and 89; 76 and 90; 76 and 91; 76 and 92; 76 and 93; 76 and 94; 76 and 95; 76 and 96; 76 and 97; 76 and 98; 76 and 99; 76 and 100; 76 and 101; 76 and 102; 77 and 78; 77 and 84; 77 and 85; 77 and 86; 77 and 87; 77 and 88; 77 and 89; 77 and 90; 77 and 91; 77 and 92; 77 and 93; 77 and 94; 77 and 95; 77 and 96; 77 and 97; 77 and 98; 77 and 99; 77 and 100; 77 and 101; 77 and 102; 78 and 84; 78 and 85; 78 and 86; 78 and 87; 78 and 88; 78 and 89; 78 and 90; 78 and 91; 78 and 92; 78 and 93; 78 and 94; 78 and 95; 78 and 96; 78 and 97; 78 and 98; 78 and 99; 78 and 100; 78 and 101; 78 and 102; 84 and 85; 84 and 86; 84 and 87; 84 and 88; 84 and 89; 84 and 90; 84 and 91; 84 and 92; 84 and 93; 84 and 94; 84 and 95; 84 and 96; 84 and 97; 84 and 98; 84 and 99; 84 and 100; 84 and 101; 84 and 102; 85 and 86; 85 and 87; 85 and 88; 85 and 89; 85 and 90; 85 and 91; 85 and 92; 85 and 93; 85 and 94; 85 and 95; 85 and 96; 85 and 97; 85 and 98; 85 and 99; 85 and 100; 85 and 101; 85 and 102; 86 and 87; 86 and 88; 86 and 89; 86 and 90; 86 and 91; 86 and 92; 86 and 93; 86 and 94; 86 and 95; 86 and 96; 86 and 97; 86 and 98; 86 and 99; 86 and 100; 86 and 101; 86 and 102; 87 and 88; 87 and 89; 87 and 90; 87 and 91; 87 and 92; 87 and 93;

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a second nucleic acid encoding a SaCas9.

11. A composition comprising a first and a second nucleic acid molecule, wherein the first nucleic acid molecule encodes a *Staphylococcus aureus* Cas9 (SaCas9) endonuclease and optionally a first or a first and second guide RNA, and the second nucleic acid molecule comprises a first or a first and second guide RNA, wherein the first guide RNA comprises a first sequence and the second guide RNA comprises a second sequence from any one the following pairs of first and second sequences: SEQ ID NOs: 1 and 3; 6 and 17; 16 and 18; 16 and 19; 16 and 20; 16 and 21; 16 and 22; 16 and 23; 16 and 24; 16 and 25; 16 and 26; 17 and 18; 17 and 19; 17 and 20; 17 and 21; 17 and 22; 17 and 23; 17 and 24; 17 and 25; 17 and 26; 18 and 19; 18 and 20; 18 and 21; 18 and 22; 18 and 23; 18 and 24; 18 and 25; 18 and 26; 19 and 20; 19 and 21; 19 and 22; 19 and 23; 19 and 24; 19 and 25; 19 and 26; 20 and 21; 20 and 22; 20 and 23; 20 and 24; 20 and 25; 20 and 26; 21 and 22; 21 and 23; 21 and 24; 21 and 25; 21 and 26; 22 and 23; 22 and 24; 22 and 25; 22 and 26; 23 and 24; 23 and 25; 23 and 26; 24 and 25; 24 and 26; 25 and 26; 110 and 120; 110 and 121; 110 and 122; 110 and 123; 110 and 124; 110 and 125; 111 and 112; 111 and 113; 111 and 114; 111 and 115; 111 and 116; 111 and 117; 111 and 118; 111 and 119; 111 and 120; 111 and 121; 111 and 122; 111 and 123; 111 and 124; 111 and 125; 112 and 113; 112 and 114; 112 and 115; 112 and 116; 112 and 117; 112 and 118; 112 and 119; 112 and 120; 112 and 121; 112 and 122; 112 and 123; 112 and 124; 112 and 125; 113 and 114; 113 and 115; 113 and 116; 113 and 117; 113 and 118;

113 and 119; 113 and 120; 113 and 121; 113 and 122; 113 and 123; 113 and 124; 113 and 125; 114 and 115; 114 and 116; 114 and 117; 114 and 118; 114 and 119; 114 and 120; 114 and 121; 114 and 122; 114 and 123; 114 and 124; 114 and 125; 115 and 116; 115 and 117; 115 and 118; 115 and 119; 115 and 120; 115 and 121; 115 and 122; 115 and 123; 115 and 124; 115 and 125; 116 and 117; 116 and 118; 116 and 119; 116 and 120; 116 and 121; 116 and 122; 116 and 123; 116 and 124; 116 and 125; 117 and 118; 117 and 119; 117 and 120; 117 and 121; 117 and 122; 117 and 123; 117 and 124; 117 and 125; 118 and 119; 118 and 120; 118 and 121; 118 and 122; 118 and 123; 118 and 124; 118 and 125; 119 and 120; 119 and 121; 119 and 122; 119 and 123; 119 and 124; 119 and 125; 120 and 121; 120 and 122; 120 and 123; 120 and 124; 120 and 125; 121 and 122; 121 and 123; 121 and 124; 121 and 125; 122 and 123; 122 and 124; 122 and 125; 123 and 124; 123 and 125; 124 and 125; 148 and 149; 148 and 150; 148 and 151; 148 and 152; 148 and 153; 148 and 154; 148 and 155; 148 and 156; 148 and 157; 148 and 158; 148 and 159; 149 and 150; 149 and 151; 149 and 152; 149 and 153; 149 and 154; 149 and 155; 149 and 156; 149 and 157; 149 and 158; 149 and 159; 150 and 151; 150 and 152; 150 and 153; 150 and 154; 150 and 155; 150 and 156; 150 and 157; 150 and 158; 150 and 159; 151 and 152; 151 and 153; 151 and 154; 151 and 155; 151 and 156; 151 and 157; 151 and 158; 151 and 159; 152 and 153; 152 and 154; 152 and 155; 152 and 156; 152 and 157; 152 and 158; 152 and 159; 153 and 154; 153 and 155; 153 and 156; 153 and 157; 153 and 158; 153 and 159; 154 and 155; 154 and 156; 154 and 157; 154 and 158; 154 and 159; 155 and 156; 155 and 157; 155 and 158; 155 and 159; 156 and 157; 156 and 158; 156 and 159; 157 and 158; 157 and 159; 158 and 159; 71 and 72; 71 and 73; 71 and 74; 71 and 75; 71 and 76; 71 and 77; 71 and 78; 71 and 84; 71 and 85; 71 and 86; 71 and 87; 71 and 88; 71 and 89; 71 and 90; 71 and 91; 71 and 92; 71 and 93; 71 and 94; 71 and 95; 71 and 96; 71 and 97; 71 and 98; 71 and 99; 71 and 100; 71 and 101; 71 and 102; 72 and 73; 72 and 74; 72 and 75; 72 and 76; 72 and 77; 72 and 78; 72 and 84; 72 and 85; 72 and 86; 72 and 87; 72 and 88; 72 and 89; 72 and 90; 72 and 91; 72 and 92; 72 and 93; 72 and 94; 72 and 95; 72 and 96; 72 and 97; 72 and 98; 72 and 99; 72 and 100; 72 and 101; 72 and 102; 73 and 74; 73 and 75; 73 and 76; 73 and 77; 73 and 78; 73 and 84; 73 and 85; 73 and 86; 73 and 87; 73 and 88; 73 and 89; 73 and 90; 73 and 91; 73 and 92; 73 and 93; 73 and 94; 73 and 95; 73 and 96; 73 and 97; 73 and 98; 73 and 99; 73 and 100; 73 and 101; 73 and 102; 74 and 75; 74 and 76; 74 and 77; 74 and 78; 74 and 84; 74 and 85; 74 and 86; 74 and 87; 74 and 88; 74 and 89; 74 and 90; 74 and 91; 74 and 92; 74 and 93; 74 and 94; 74 and 95; 74 and 96; 74 and 97; 74 and 98; 74 and 99; 74 and 100; 74 and 101; 74 and 102; 75 and 76; 75 and 77; 75 and 78; 75 and 84; 75 and 85; 75 and 86; 75 and 87; 75 and 88; 75 and 89; 75 and 90; 75 and 91; 75 and 92; 75 and 93; 75 and 94; 75 and 95; 75 and 96; 75 and 97; 75 and 98; 75 and 99; 75 and 100; 75 and 101; 75 and 102; 76 and 77; 76 and 78; 76 and 84; 76 and 85; 76 and 86; 76 and 87; 76 and 88; 76 and 89; 76 and 90; 76 and 91; 76 and 92; 76 and 93; 76 and 94;

76 and 95; 76 and 96; 76 and 97; 76 and 98; 76 and 99; 76 and 100; 76 and 101; 76 and 102; 77 and 78; 77 and 84; 77 and 85; 77 and 86; 77 and 87; 77 and 88; 77 and 89; 77 and 90; 77 and 91; 77 and 92; 77 and 93; 77 and 94; 77 and 95; 77 and 96; 77 and 97; 77 and 98; 77 and 99; 77 and 100; 77 and 101; 77 and 102; 78 and 84; 78 and 85; 78 and 86; 78 and 87; 78 and 88; 78 and 89; 78 and 90; 78 and 91; 78 and 92; 78 and 93; 78 and 94; 78 and 95; 78 and 96; 78 and 97; 78 and 98; 78 and 99; 78 and 100; 78 and 101; 78 and 102; 84 and 85; 84 and 86; 84 and 87; 84 and 88; 84 and 89; 84 and 90; 84 and 91; 84 and 92; 84 and 93; 84 and 94; 84 and 95; 84 and 96; 84 and 97; 84 and 98; 84 and 99; 84 and 100; 84 and 101; 84 and 102; 85 and 86; 85 and 87; 85 and 88; 85 and 89; 85 and 90; 85 and 91; 85 and 92; 85 and 93; 85 and 94; 85 and 95; 85 and 96; 85 and 97; 85 and 98; 85 and 99; 85 and 100; 85 and 101; 85 and 102; 86 and 87; 86 and 88; 86 and 89; 86 and 90; 86 and 91; 86 and 92; 86 and 93; 86 and 94; 86 and 95; 86 and 96; 86 and 97; 86 and 98; 86 and 99; 86 and 100; 86 and 101; 86 and 102; 87 and 88; 87 and 89; 87 and 90; 87 and 91; 87 and 92; 87 and 93; 87 and 94; 87 and 95; 87 and 96; 87 and 97; 87 and 98; 87 and 99; 87 and 100; 87 and 101; 87 and 102; 88 and 89; 88 and 90; 88 and 91; 88 and 92; 88 and 93; 88 and 94; 88 and 95; 88 and 96; 88 and 97; 88 and 98; 88 and 99; 88 and 100; 88 and 101; 88 and 102; 89 and 90; 89 and 91; 89 and 92; 89 and 93; 89 and 94; 89 and 95; 89 and 96; 89 and 97; 89 and 98; 89 and 99; 89 and 100; 89 and 101; 89 and 102; 90 and 91; 90 and 92; 90 and 93; 90 and 94; 90 and 95; 90 and 96; 90 and 97; 90 and 98; 90 and 99; 90 and 100; 90 and 101; 90 and 102; 91 and 92; 91 and 93; 91 and 94; 91 and 95; 91 and 96; 91 and 97; 91 and 98; 91 and 99; 91 and 100; 91 and 101; 91 and 102; 92 and 93; 92 and 94; 92 and 95; 92 and 96; 92 and 97; 92 and 98; 92 and 99; 92 and 100; 92 and 101; 92 and 102; 93 and 94; 93 and 95; 93 and 96; 93 and 97; 93 and 98; 93 and 99; 93 and 100; 93 and 101; 93 and 102; 94 and 95; 94 and 96; 94 and 97; 94 and 98; 94 and 99; 94 and 100; 94 and 101; 94 and 102; 95 and 96; 95 and 97; 95 and 98; 95 and 99; 95 and 100; 95 and 101; 95 and 102; 96 and 97; 96 and 98; 96 and 99; 96 and 100; 96 and 101; 96 and 102; 97 and 98; 97 and 99; 97 and 100; 97 and 101; 97 and 102; 98 and 99; 98 and 100; 98 and 101; 98 and 102; 99 and 100; 99 and 101; 99 and 102; 100 and 101; 100 and 102; or 101 and 102.

12. A composition comprising a first and a second nucleic acid molecule, wherein the first nucleic acid molecule encodes a *Staphylococcus lugdunensis* (SluCas9) endonuclease and optionally a first or a first and second guide RNA, and the second nucleic acid molecule comprises a first or a first and second guide RNA, wherein the first guide RNA comprises a first sequence and the second guide RNAs comprises a second sequence from any one the following pairs of first and second sequences: SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and

203; 202 and 204; 202 and 205; 202 and 206; 202 and 207; 202 and 208; 203 and 204; 203 and 205; 203 and 206; 203 and 207; 203 and 208; 204 and 205; 204 and 206; 204 and 207; 204 and 208; 205 and 206; 205 and 207; 205 and 208; 206 and 207; 206 and 208; 207 and 208; 231 and 232; 231 and 233; 231 and 234; 231 and 235; 231 and 236; 231 and 237; 231 and 238; 231 and 239; 231 and 240; 231 and 241; 231 and 242; 232 and 233; 232 and 234; 232 and 235; 232 and 236; 232 and 237; 232 and 238; 232 and 239; 232 and 240; 232 and 241; 232 and 242; 233 and 234; 233 and 235; 233 and 236; 233 and 237; 233 and 238; 233 and 239; 233 and 240; 233 and 241; 233 and 242; 234 and 235; 234 and 236; 234 and 237; 234 and 238; 234 and 239; 234 and 240; 234 and 241; 234 and 242; 235 and 236; 235 and 237; 235 and 238; 235 and 239; 235 and 240; 235 and 241; 235 and 242; 236 and 237; 236 and 238; 236 and 239; 236 and 240; 236 and 241; 236 and 242; 237 and 238; 237 and 239; 237 and 240; 237 and 241; 237 and 242; 238 and 239; 238 and 240; 238 and 241; 238 and 242; 239 and 240; 239 and 241; 239 and 242; 240 and 241; 240 and 242; 241 and 242; 270 and 271; 270 and 272; 270 and 273; 270 and 274; 270 and 275; 270 and 276; 270 and 277; 270 and 278; 270 and 279; 270 and 280; 270 and 281; 270 and 282; 270 and 283; 270 and 284; 270 and 285; 270 and 286; 270 and 287; 270 and 288; 270 and 289; 270 and 290; 270 and 291; 270 and 292; 271 and 272; 271 and 273; 271 and 274; 271 and 275; 271 and 276; 271 and 277; 271 and 278; 271 and 279; 271 and 280; 271 and 281; 271 and 282; 271 and 283; 271 and 284; 271 and 285; 271 and 286; 271 and 287; 271 and 288; 271 and 289; 271 and 290; 271 and 291; 271 and 292; 272 and 273; 272 and 274; 272 and 275; 272 and 276; 272 and 277; 272 and 278; 272 and 279; 272 and 280; 272 and 281; 272 and 282; 272 and 283; 272 and 284; 272 and 285; 272 and 286; 272 and 287; 272 and 288; 272 and 289; 272 and 290; 272 and 291; 272 and 292; 273 and 274; 273 and 275; 273 and 276; 273 and 277; 273 and 278; 273 and 279; 273 and 280; 273 and 281; 273 and 282; 273 and 283; 273 and 284; 273 and 285; 273 and 286; 273 and 287; 273 and 288; 273 and 289; 273 and 290; 273 and 291; 273 and 292; 274 and 275; 274 and 276; 274 and 277; 274 and 278; 274 and 279; 274 and 280; 274 and 281; 274 and 282; 274 and 283; 274 and 284; 274 and 285; 274 and 286; 274 and 287; 274 and 288; 274 and 289; 274 and 290; 274 and 291; 274 and 292; 275 and 276; 275 and 277; 275 and 278; 275 and 279; 275 and 280; 275 and 281; 275 and 282; 275 and 283; 275 and 284; 275 and 285; 275 and 286; 275 and 287; 275 and 288; 275 and 289; 275 and 290; 275 and 291; 275 and 292; 276 and 277; 276 and 278; 276 and 279; 276 and 280; 276 and 281; 276 and 282; 276 and 283; 276 and 284; 276 and 285; 276 and 286; 276 and 287; 276 and 288; 276 and 289; 276 and 290; 276 and 291; 276 and 292; 277 and 278; 277 and 279; 277 and 280; 277 and 281; 277 and 282; 277 and 283; 277 and 284; 277 and 285; 277 and 286; 277 and 287; 277 and 288; 277 and 289; 277 and 290; 277 and 291; 277 and 292; 278 and 279; 278 and 280; 278 and 281; 278 and 282; 278 and 283; 278 and 284; 278 and 285; 278 and 286; 278 and 287; 278 and 288; 278 and 289; 278 and 290; 278

and 291; 278 and 292; 279 and 280; 279 and 281; 279 and 282; 279 and 283; 279 and 284; 279 and 285; 279 and 286; 279 and 287; 279 and 288; 279 and 289; 279 and 290; 279 and 291; 279 and 292; 280 and 281; 280 and 282; 280 and 283; 280 and 284; 280 and 285; 280 and 286; 280 and 287; 280 and 288; 280 and 289; 280 and 290; 280 and 291; 280 and 292; 281 and 282; 281 and 283; 281 and 284; 281 and 285; 281 and 286; 281 and 287; 281 and 288; 281 and 289; 281 and 290; 281 and 291; 281 and 292; 282 and 283; 282 and 284; 282 and 285; 282 and 286; 282 and 287; 282 and 288; 282 and 289; 282 and 290; 282 and 291; 282 and 292; 283 and 284; 283 and 285; 283 and 286; 283 and 287; 283 and 288; 283 and 289; 283 and 290; 283 and 291; 283 and 292; 284 and 285; 284 and 286; 284 and 287; 284 and 288; 284 and 289; 284 and 290; 284 and 291; 284 and 292; 285 and 286; 285 and 287; 285 and 288; 285 and 289; 285 and 290; 285 and 291; 285 and 292; 286 and 287; 286 and 288; 286 and 289; 286 and 290; 286 and 291; 286 and 292; 287 and 288; 287 and 289; 287 and 290; 287 and 291; 287 and 292; 288 and 289; 288 and 290; 288 and 291; 288 and 292; 289 and 290; 289 and 291; 289 and 292; 290 and 291; 290 and 292; 291 and 292; 924 and 270; 924 and 272; 924 and 273; 924 and 274; 924 and 275; 924 and 276; 924 and 277; 924 and 278; 924 and 279; 924 and 280; 924 and 281; 924 and 282; 924 and 283; 924 and 284; 924 and 285; 924 and 286; 924 and 287; 924 and 288; 924 and 289; 924 and 290; 924 and 291; 924 and 292; 925 and 270; 925 and 272; 925 and 273; 925 and 274; 925 and 275; 925 and 276; 925 and 277; 925 and 278; 925 and 279; 925 and 280; 925 and 281; 925 and 282; 925 and 283; 925 and 284; 925 and 285; 925 and 286; 925 and 287; 925 and 288; 925 and 289; 925 and 290; 925 and 291; 925 and 292; 926 and 270; 926 and 272; 926 and 273; 926 and 274; 926 and 275; 926 and 276; 926 and 277; 926 and 278; 926 and 279; 926 and 280; 926 and 281; 926 and 282; 926 and 283; 926 and 284; 926 and 285; 926 and 286; 926 and 287; 926 and 288; 926 and 289; 926 and 290; 926 and 291; 926 and 292; 927 and 270; 927 and 272; 927 and 273; 927 and 274; 927 and 275; 927 and 276; 927 and 277; 927 and 278; 927 and 279; 927 and 280; 927 and 281; 927 and 282; 927 and 283; 927 and 284; 927 and 285; 927 and 286; 927 and 287; 927 and 288; 927 and 289; 927 and 290; 927 and 291; 927 and 292; 928 and 270; 928 and 272; 928 and 273; 928 and 274; 928 and 275; 928 and 276; 928 and 277; 928 and 278; 928 and 279; 928 and 280; 928 and 281; 928 and 282; 928 and 283; 928 and 284; 928 and 285; 928 and 286; 928 and 287; 928 and 288; 928 and 289; 928 and 290; 928 and 291; 928 and 292; 929 and 270; 929 and 272; 929 and 273; 929 and 274; 929 and 275; 929 and 276; 929 and 277; 929 and 278; 929 and 279; 929 and 280; 929 and 281; 929 and 282; 929 and 283; 929 and 284; 929 and 285; 929 and 286; 929 and 287; 929 and 288; 929 and 289; 929 and 290; 929 and 291; 929 and 292; 930 and 270; 930 and 272; 930 and 273; 930 and 274; 930 and 275; 930 and 276; 930 and 277; 930 and 278; 930 and 279; 930 and 280; 930 and 281; 930 and 282; 930 and 283; 930 and 284; 930 and 285; 930 and 286; 930 and 287; 930 and 288; 930 and 289; 930 and 290; 930 and 291; 930 and 292;

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13. A composition comprising a first and a second nucleic acid molecule, wherein the first nucleic acid molecule encodes a sRGN endonuclease (e.g., sRGN3.1, sRGN3.3, or sRGN4) and optionally a first or a first and second guide RNA, and the second nucleic acid molecule comprises a first or a first and second guide RNA, wherein the first guide RNA comprises a first sequence and the second guide RNAs comprises a second sequence from any one the following pairs of first and second sequences: SEQ ID NOs: 200 and 201; 200 and 202; 200 and 203; 200 and 204; 200 and 205; 200 and 206; 200 and 207; 200 and 208; 201 and 202; 201 and 203; 201 and 204; 201 and 205; 201 and 206; 201 and 207; 201 and 208; 202 and

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14. The composition of claim 13, wherein the sRGN endonuclease comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of any one of SEQ ID Nos: 7024, 7026, or 7027.

15. The composition of claim 13 or 14, wherein the sRGN endonuclease is encoded by a nucleic acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of any one of SEQ ID Nos: 917, 919 or 920.

16. The composition of any one of the preceding claims, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs facilitate a 3n+1 edit of exon 45, 51 or 53 of the dystrophin gene, wherein "n" is any negative whole number (e.g., any whole number between -10 and -75).

17. The composition of any one of the preceding claims, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs target exon 45, 51 or 53 of the dystrophin gene and are capable of excising a nucleic acid that is at least 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62, 65, 68, 71, 74, 77, 80, 83, 86, 89, 92, 95, 98, 101, 104, 107, 110, 113, 116, 119, 122, 125, 128, 131, 134, 137, 140, 143, 146, 149, 152, 155, 158, 161, 164, 167, 170, 173, 176, 179, 182, 185, 188, 191, 194, 197, 200, 203, 206, 209, 212, 215, or 218 nucleotides in length.

18. The composition of any one of the preceding claims, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs facilitate a 3n+2 edit of exon 44 or 50 of the dystrophin gene, wherein "n" is any negative whole number (e.g., any whole number between -10 and -75).

19. The composition of any one of the preceding claims, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs target exon 44 or 50 of the dystrophin gene and are capable of excising a nucleic acid that is at least 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61, 64, 67, 70, 73, 76, 79, 82, 85, 88, 91, 94, 97, 100, 103, 106, 109, 112, 115, 118, 121, 124, 127, 130, 133, 136, 139, 142, 145, 148, 151, 154, 157, 160, 163, 166, 169, 172, 175, 178, 181, 184, 187, 190, 193, 196, 199, 202, 205, 208, 211, 214. or 217 nucleotides in length.

20. The composition of any one of the preceding claims, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs excise a portion of an exon, wherein the size of the excised portion of the exon is between 5 and 250 nucleotides in length.

21. The composition of any one of the preceding claims, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs excise a portion of an exon, wherein the size of the excised portion of the exon is between 5 and 250, 5 and 200, 5 and 150, 5 and 100, 5 and 75, 5 and 50, 5 and 25, 5 and 10, 20 and 250, 20 and 200, 20 and 150, 20 and 100, 20 and 75, 20 and 50, 20 and 25, 50 and 250, 50 and 200, 50 and 150, 50 and 100, and 50 and 75 nucleotides.

22. The composition of any one of the preceding claims, comprising at least two guide RNAs, wherein once expressed in vitro or in vivo in combination with an RNA-guided endonuclease, the at least two guide RNAs excise a portion of the exon, wherein the size of the excised portion of the exon is between 8 and 167 nucleotides.

23. The composition of any one of the preceding claims, wherein the one or more guide RNAs is an sgRNA.

24. The composition of any one of the preceding claims, wherein the one or more guide RNAs is modified.

25. The composition of any one of the preceding claims, wherein the one or more guide RNAs or nucleic acids are in a vector.

26. The composition of claim 25, wherein the vector is a viral vector.

27. The composition of claim 26, wherein the viral vector is an AAV vector.

28. The composition of claim 27, wherein the AAV vector is an AAV9 vector.

29. The composition of any one of the preceding claims, wherein the promoter for the one or more guide RNAs is hU6c.

30. The composition of any one of the preceding claims, wherein the one or more guide RNAs is a guide RNA for SaCas9, and the one or more guide RNAs comprise a scaffold comprising the sequence of SEQ ID NO: 504.

31. The composition of any one of the preceding claims, wherein the one or more guide RNAs is a guide RNA for SluCas9, and the one or more guide RNAs comprise a scaffold comprising the sequence of SEQ ID NO: 901.

32. The composition of any one of the preceding claims, wherein the one or more guide RNAs is in an AAV vector, wherein the vector comprises from 5' to 3' with respect to the plus strand: the reverse complement of a first guide RNA scaffold sequence; the reverse complement of a nucleic acid encoding a first guide RNA sequence; the reverse complement of a promoter for expression of the nucleic acid encoding the first guide RNA sequence; a promoter for expression of a nucleic acid encoding SaCas9, SluCas9, or a sRGN (e.g., CK8e); a nucleic acid encoding a SaCas9, SluCas9, or a sRGN (e.g., sRGN3.1, sRGN3,3, or sRGN4); a polyadenylation sequence; a promoter for expression of a second guide RNA sequence in the same direction as the promoter for SaCas9, SluCas9, or the sRGN; a second RNA guide sequence; and a second guide RNA scaffold sequence.

33. The composition of claim 32, wherein:

iii) the first guide RNA sequence comprises the sequence of SEQ ID NO: 271 or 281, and the second guide RNA sequence comprises the sequence of SEQ ID NO: 275; or

iv) the first guide RNA sequence comprises the sequence of SEQ ID NO: 283, and the second guide RNA sequence comprises the sequence of SEQ ID NO: 290.

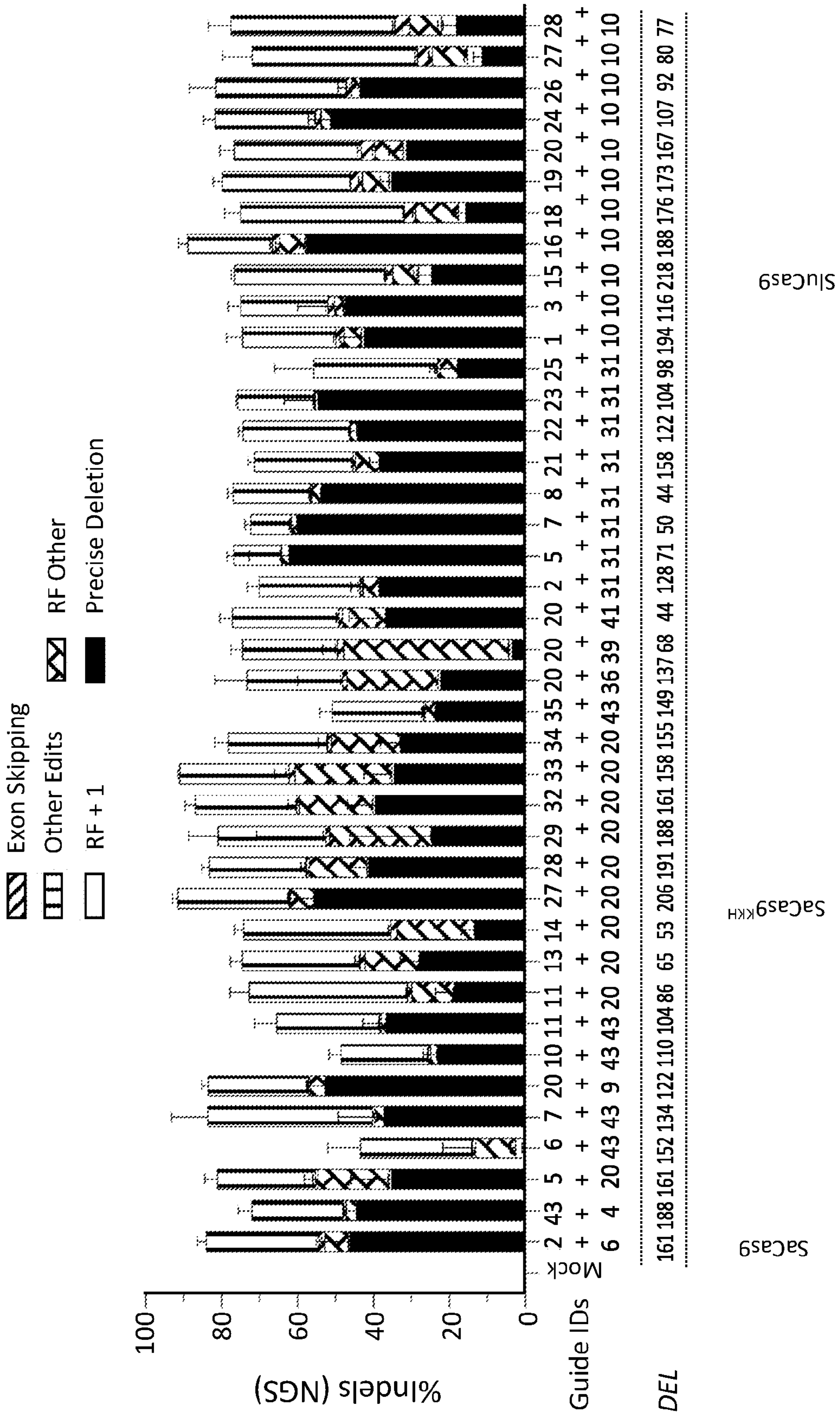
34. The composition of claim 32 or 33, wherein the promoter for expression of a nucleic acid encoding SaCas9, SluCas9, or a sRGN is a promoter for expression of a sRGN; wherein the nucleic acid encoding a SaCas9, SluCas9, or a sRGN encodes for a sRGN, and wherein the sRGN comprises an amino acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of any one of SEQ ID Nos: 7024, 7026, or 7027.

35. The composition of claim 34, wherein the sRGN is encoded by a nucleic acid sequence that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence of any one of SEQ ID Nos: 917, 919 or 920.

36. The composition of any one of claims 1-35, wherein the one or more guide RNA sequences, or the first and/or second guide RNA sequence of the pair of guide RNAs, is no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, or no more than 22 nucleotides in length.

37. A method of treating Duchenne Muscular Dystrophy (DMD), the method comprising delivering to a cell the composition of any one of claims 1-36.

38. A method of excising a portion of the DMD gene, the method comprising delivering to a cell the composition of any one of claims 1-36, wherein the size of the excised portion is less than about 250 nucleotides.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60
40
20
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Guide IDs
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Mock
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43 + 4
5 + 20
6 + 43
7 + 43
20 + 9
10 + 43
11 + 43
11 + 20
13 + 20
14 + 20
27 + 20
28 + 20
29 + 20
32 + 20
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23 + 31
25 + 31
1 + 10
3 + 10
15 + 10
16 + 10
18 + 10
19 + 10
20 + 10
24 + 10
26 + 10
27 + 10
28 + 10
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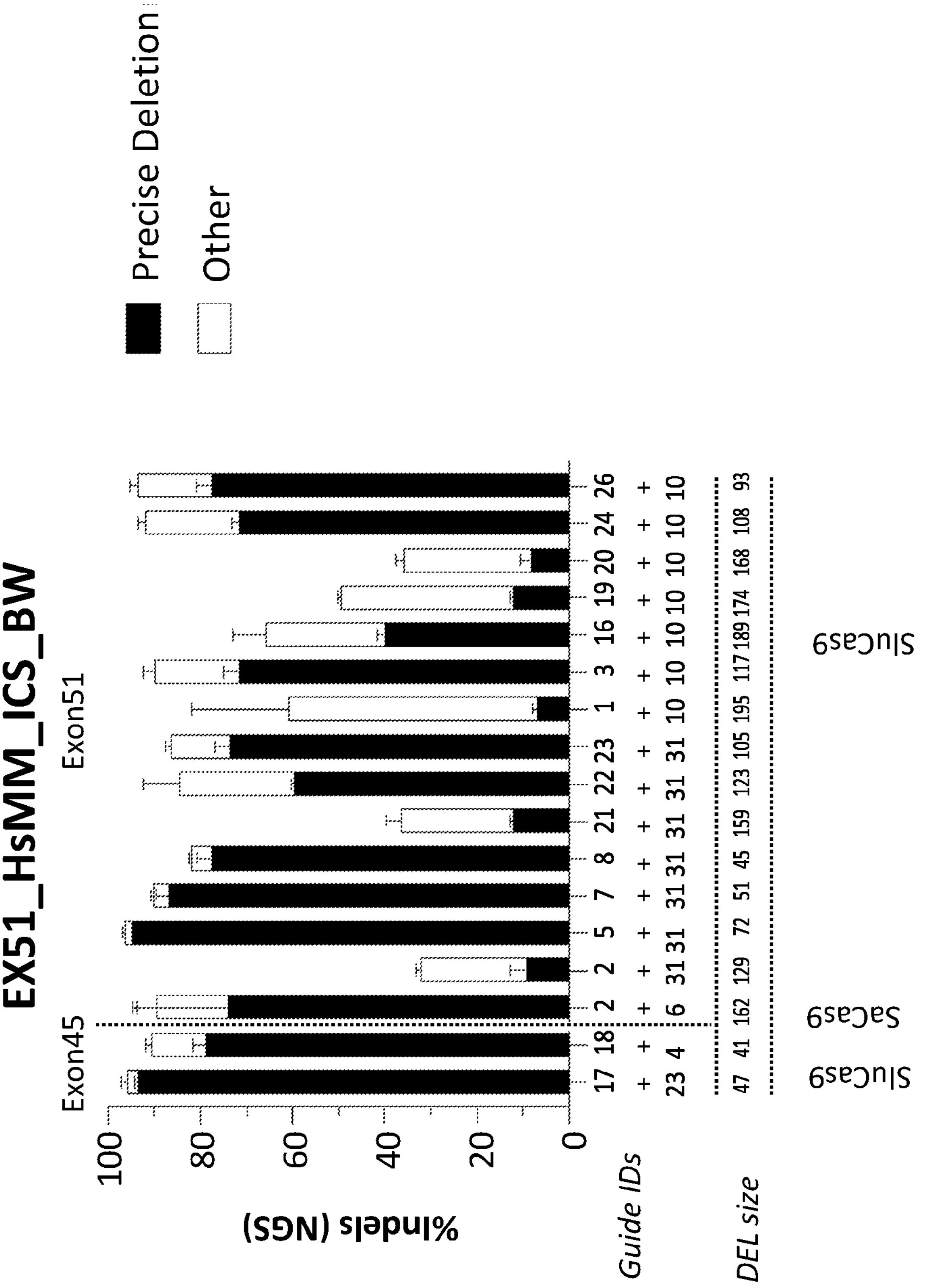
SaCas9
SaCas9KKH
SluCas9

Fig. 1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Precise Deletion
Other
Guide IDs
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+ + + + + + + + + + + + + + + + +
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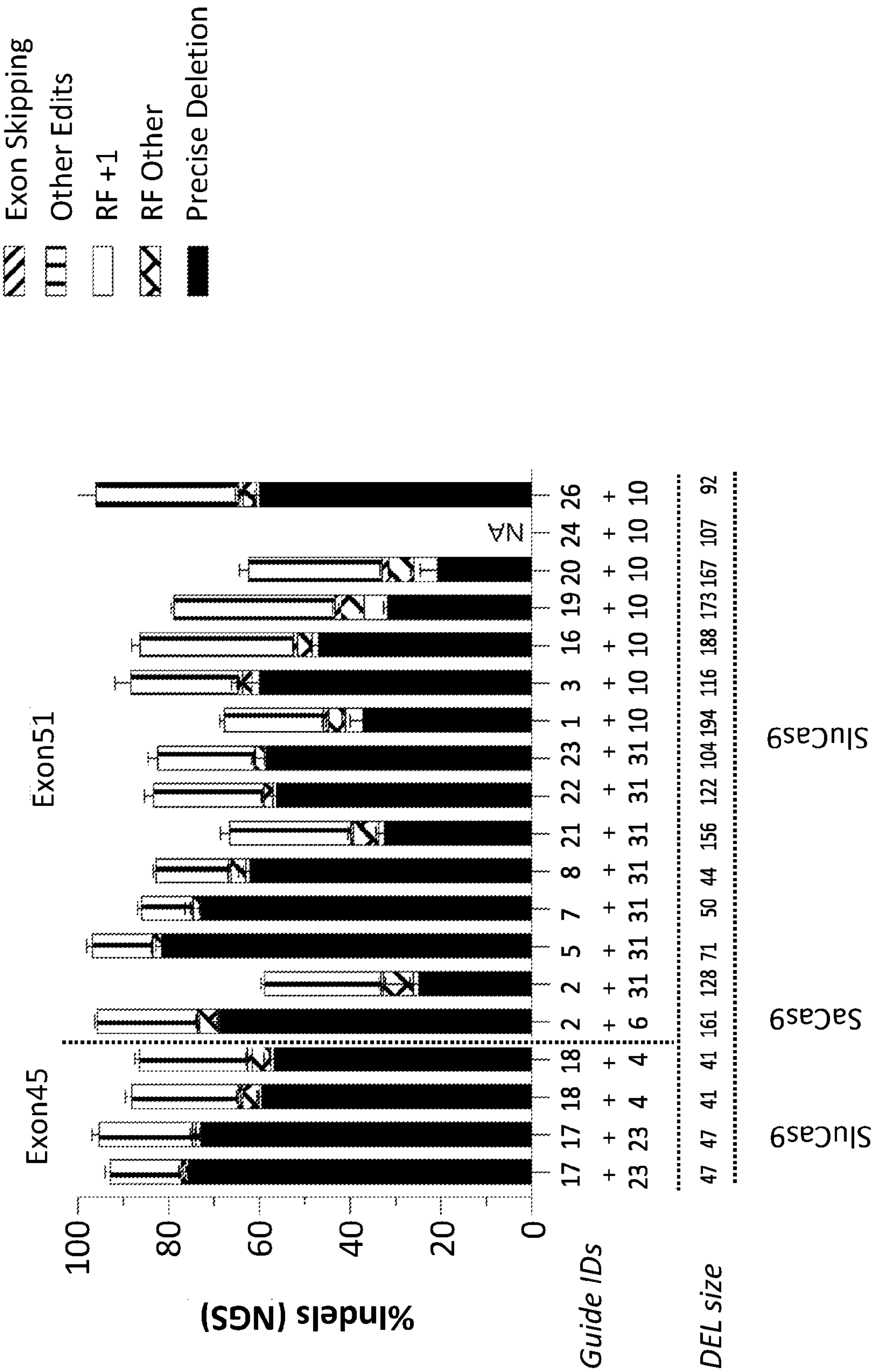
SluCas9
SaCas9
SluCas9

Fig. 2A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80
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40
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NA
Guide IDs
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18 + 4
2 + 6
2 + 31
5 + 31
7 + 31
8 + 31
21 + 31
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19 + 10
20 + 10
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26 + 10
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161
128
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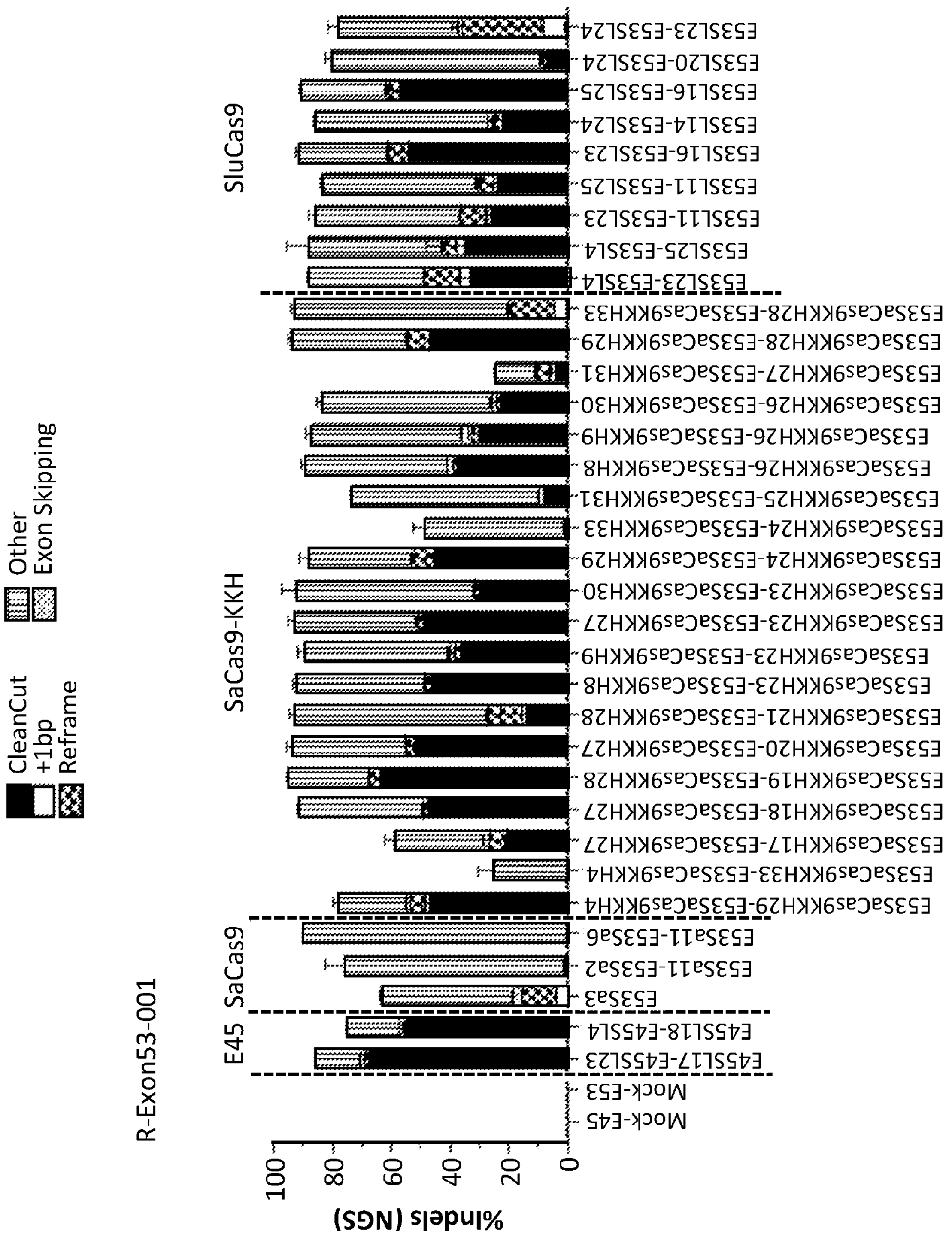
173
167
107
92
SluCas9
SaCas9
SluCas9

Fig. 2B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SaCas9-KKH
SluCas9
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Mock-E53
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E45SL18-E45SL4
E53Sa3
E53Sa11-E53Sa2
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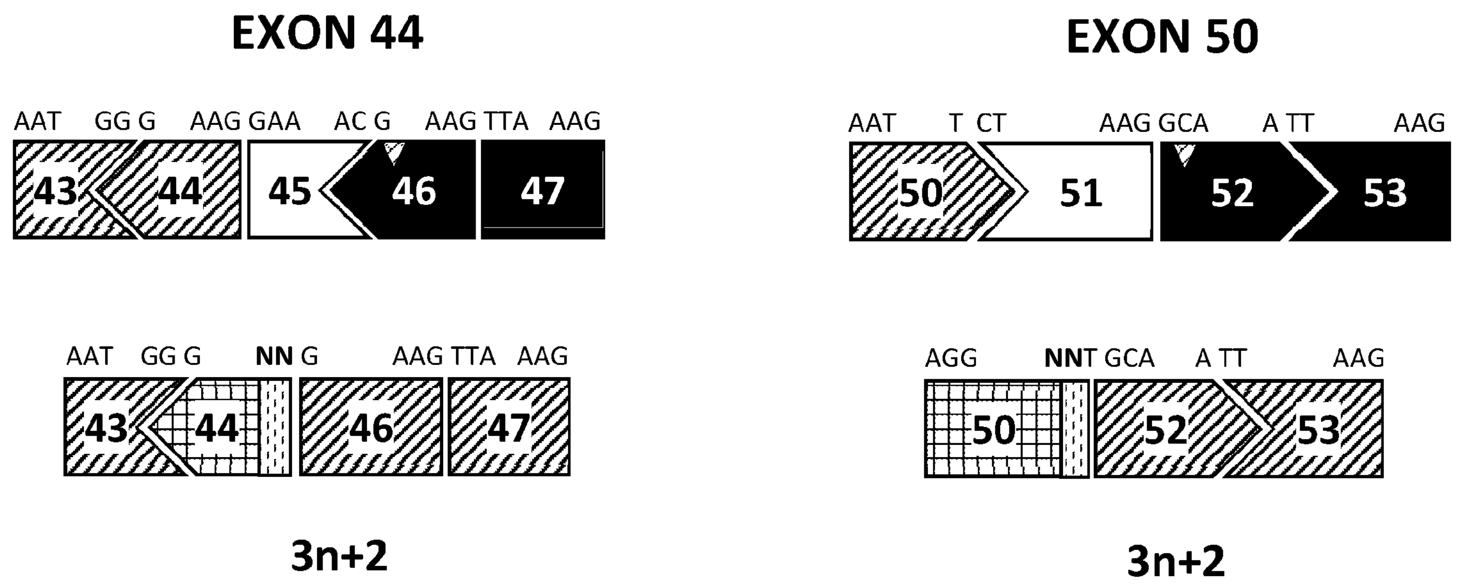
Fig. 3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AC G
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AAG
43
44
46
47
3n+2
EXON 50
AAT
T CT
AAG GCA
A TT
AAG
50
51
52
53
AGG
NNT GCA
A TT
AAG
50
52
53
3n+2

Fig. 4A

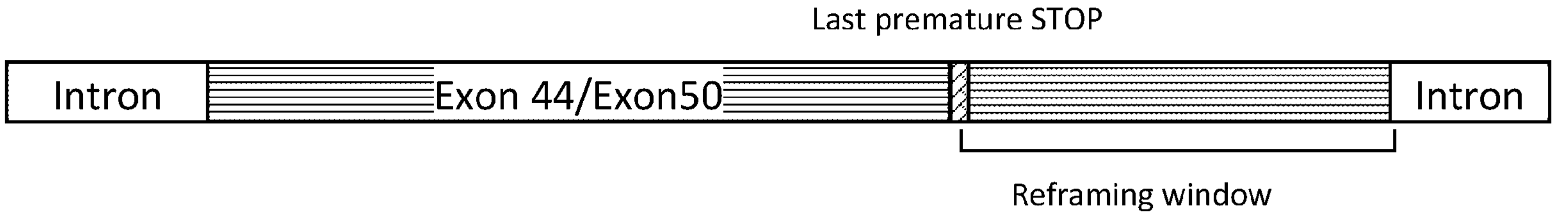

Last premature STOP
Intron
Exon 44/Exon50
Intron
Reframing window

Fig. 4B

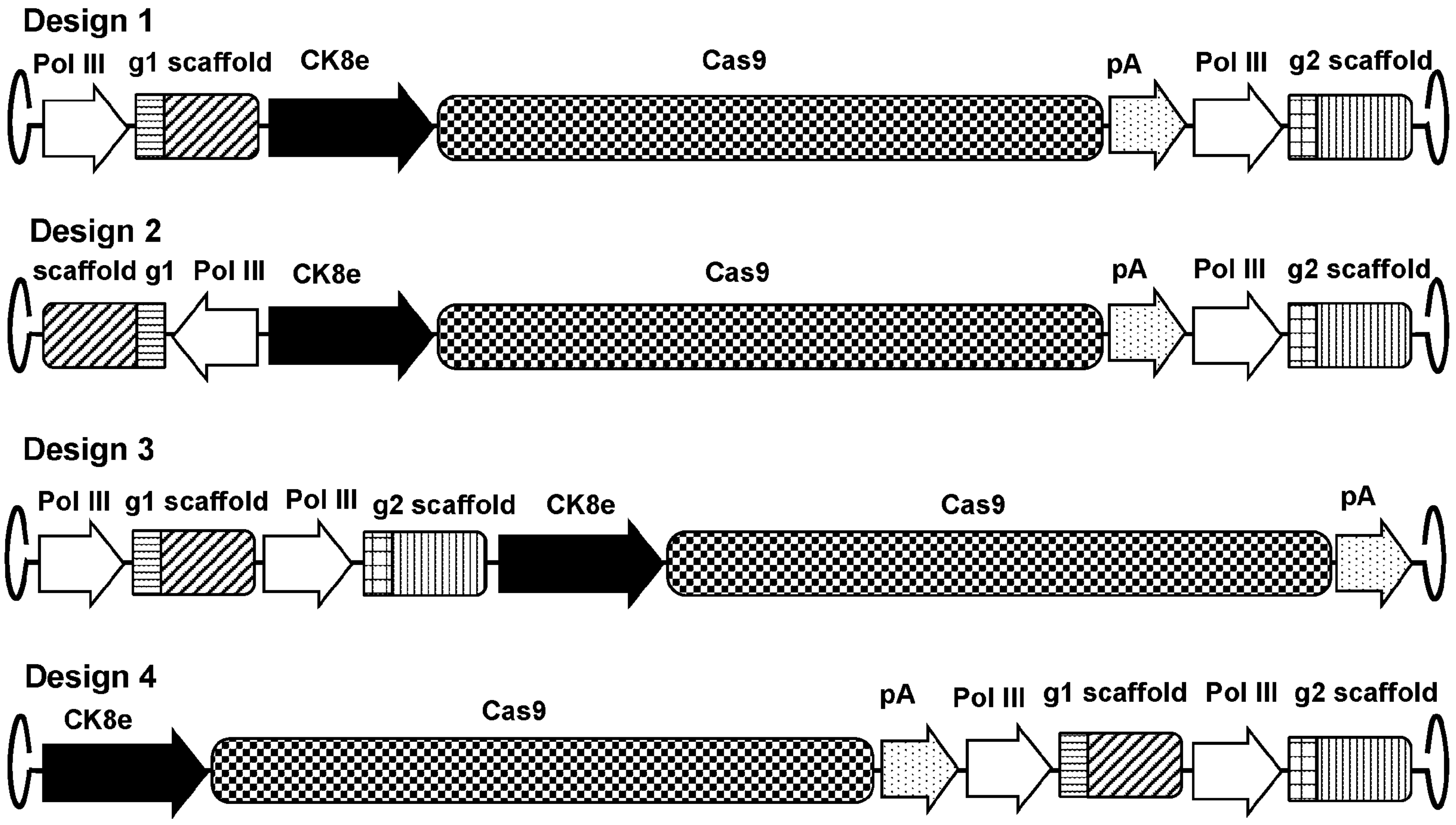

Design 1
Pol III
g1 scaffold
CK8e
Cas9
pA
Pol III
g2 scaffold
Design 2
scaffold g1
Pol III
CK8e
Cas9
pA
Pol III
g2 scaffold
Design 3
Pol III
g1 scaffold
Pol III
g2 scaffold
CK8e
Cas9
pA
Design 4
CK8e
Cas9
pA
Pol III
g1 scaffold
Pol III
g2 scaffold

Fig. 5A

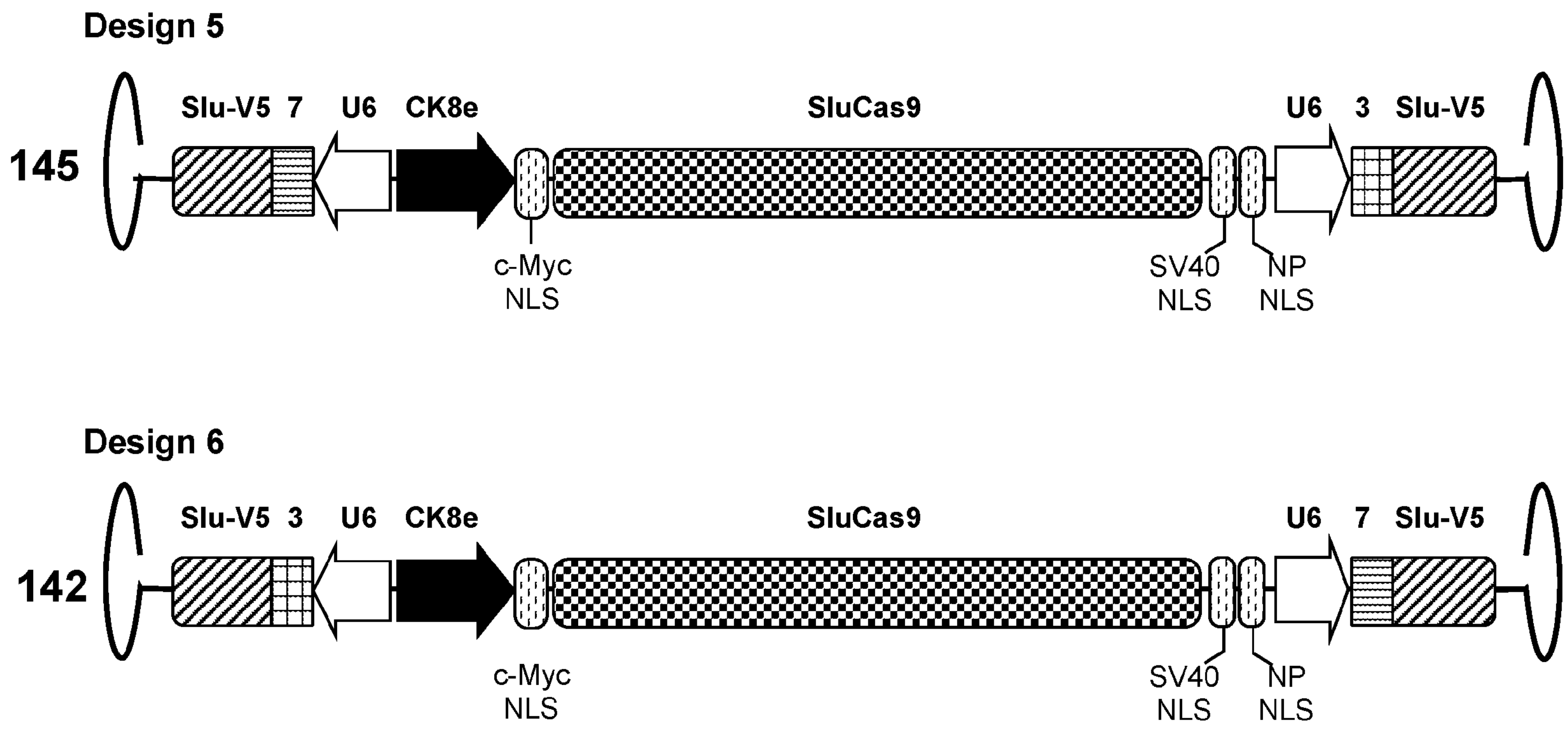

Design 5
145
Slu-V5
7
U6
CK8e
SluCas9
U6
3
Slu-V5
c-Myc NLS
SV40 NLS
NP NLS
Design 6
142
Slu-V5
3
U6
CK8e
SluCas9
U6
7
Slu-V5
c-Myc NLS
SV40 NLS
NP NLS

Fig. 5B

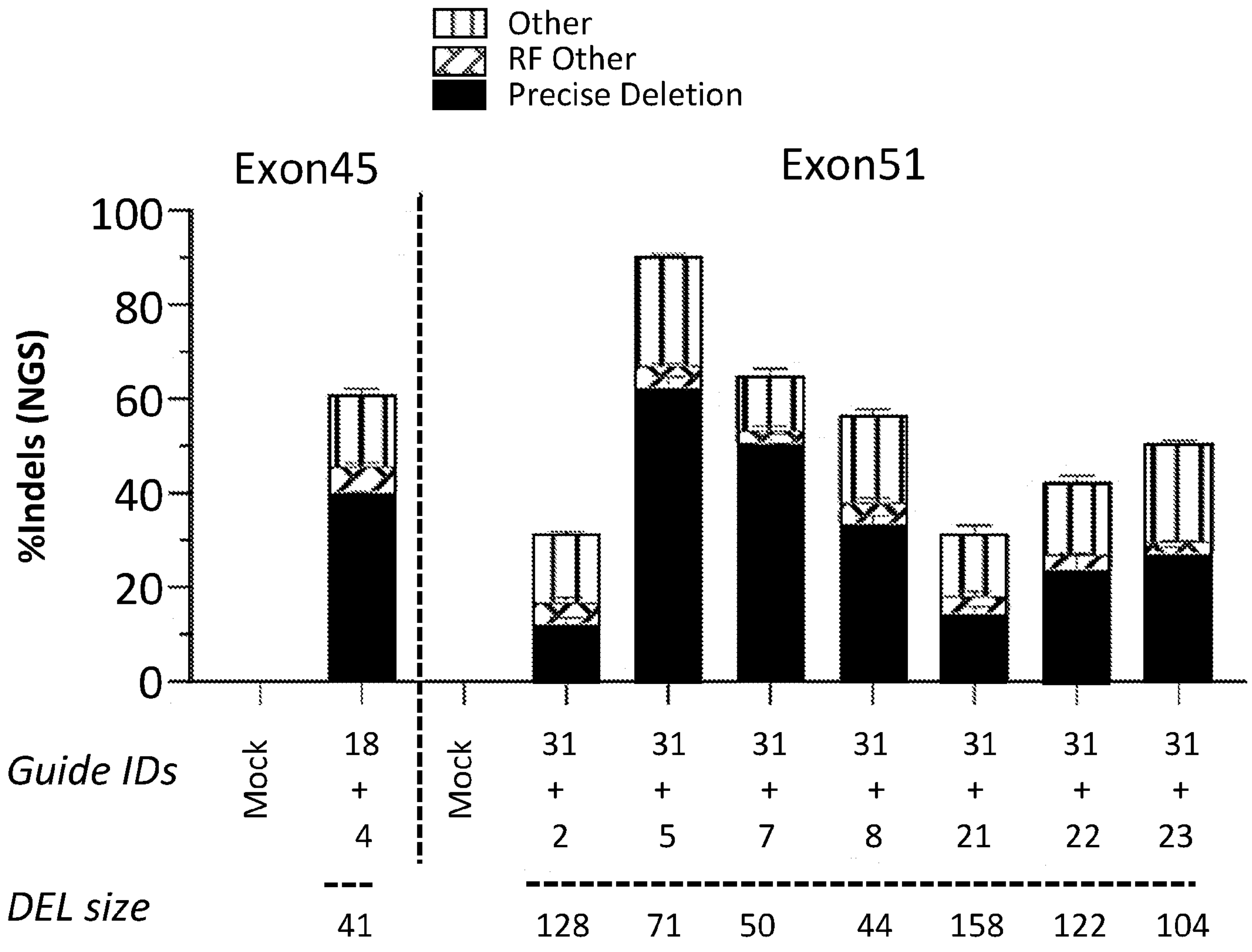

Other
RF Other
Precise Deletion
Exon45
Exon51
%Indels (NGS)
100
80
60
40
20
0
Guide IDs
Mock
18 + 4
Mock
31 + 2
31 + 5
31 + 7
31 + 8
31 + 21
31 + 22
31 + 23
DEL size
41
128
71
50
44
158
122
104

Fig. 6A

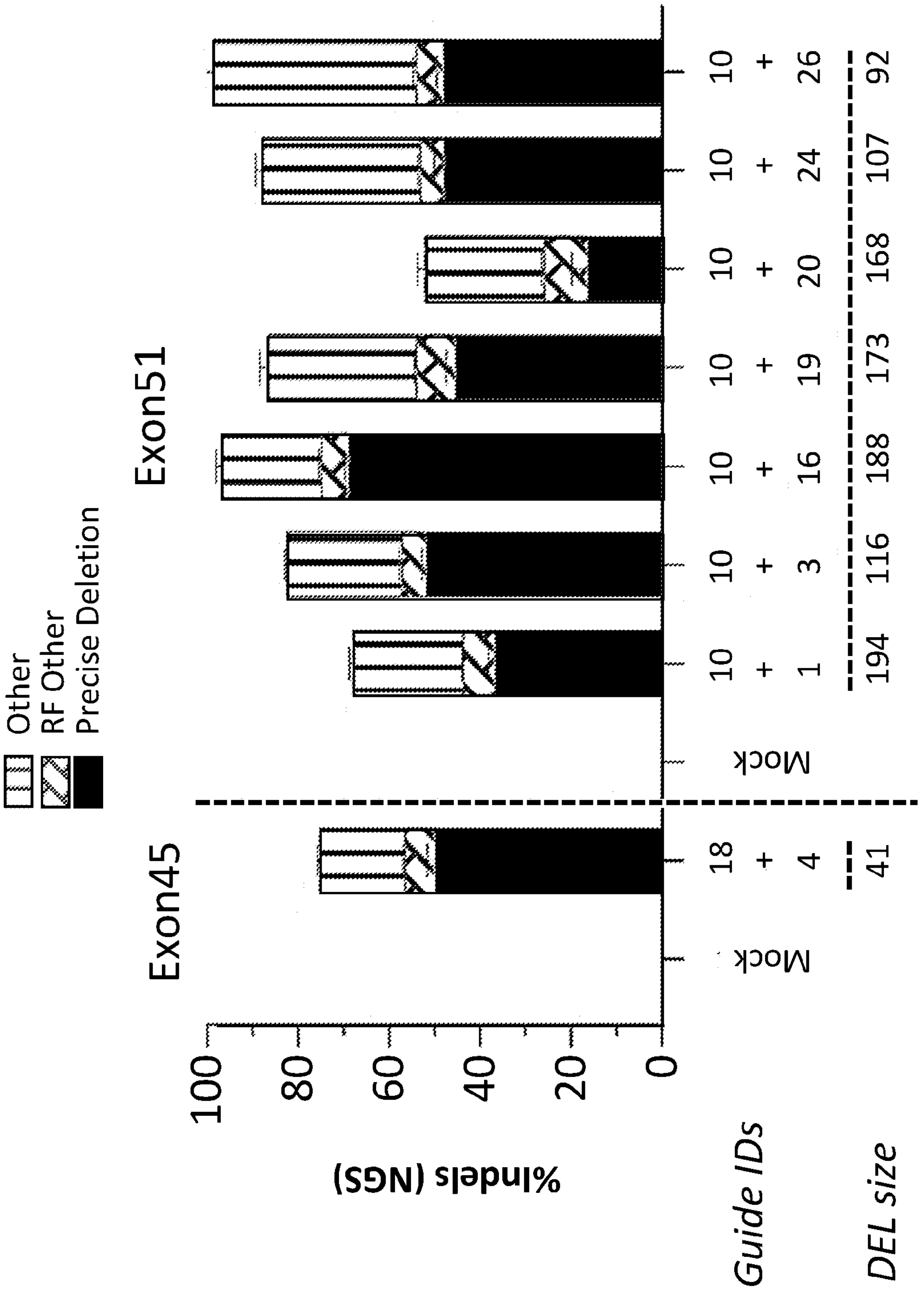
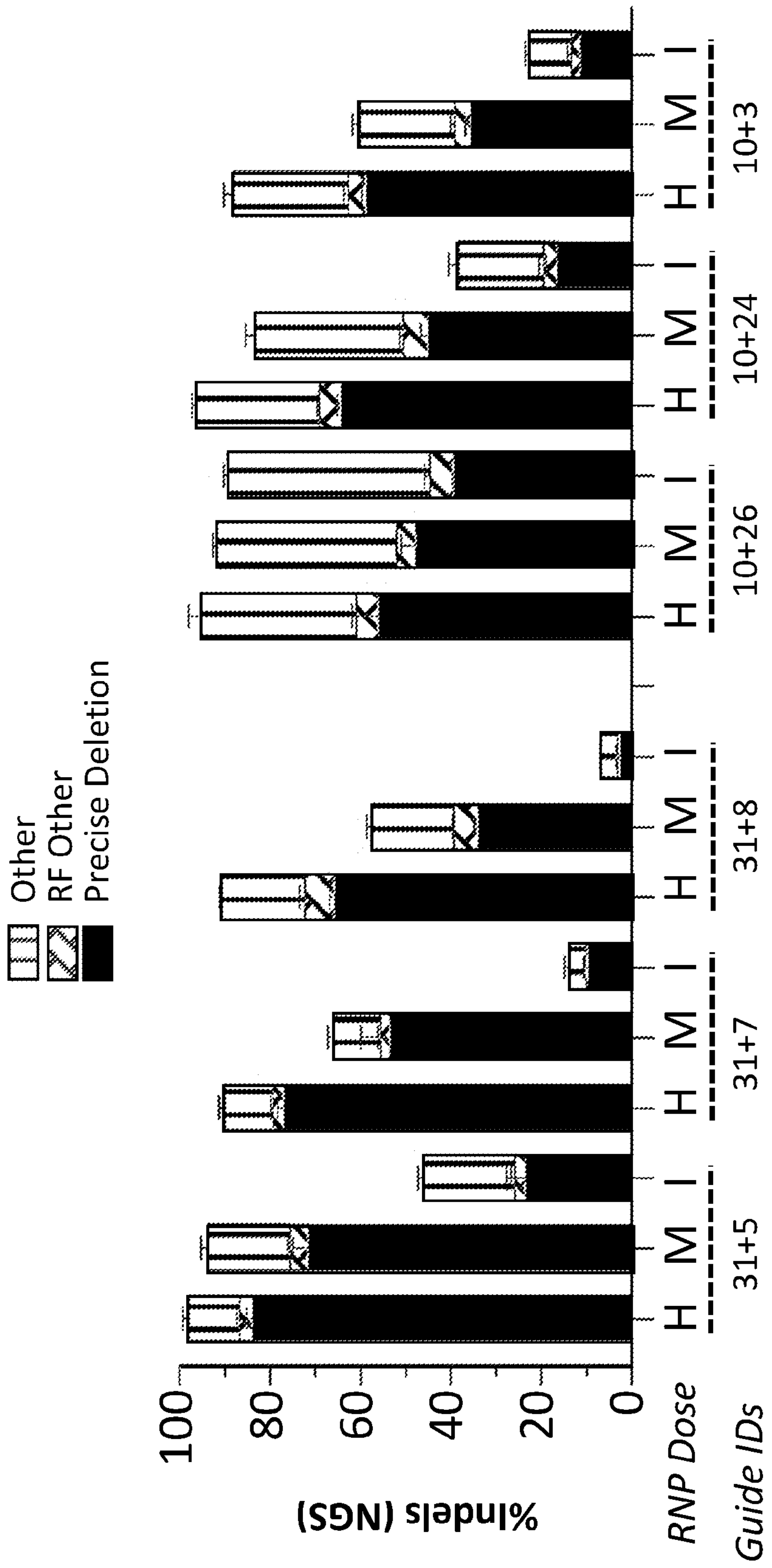

Other
RF Other
Precise Deletion
Exon45
Exon51
%Indels (NGS)
100
80
60
40
20
0
Mock
18
+
4
41
Mock
10
+
1
194
10
+
3
116
10
+
16
188
10
+
19
173
10
+
20
168
10
+
24
107
10
+
26
92
Guide IDs
DEL size

Fig. 6B



Other
RF Other
Precise Deletion
%Indels (NGS)
100
80
60
40
20
0
RNP Dose
Guide IDs
H
M
I
31+5
H
M
I
31+7
H
M
I
31+8
H
M
I
10+26
H
M
I
10+24
H
M
I
10+3

Fig. 7A

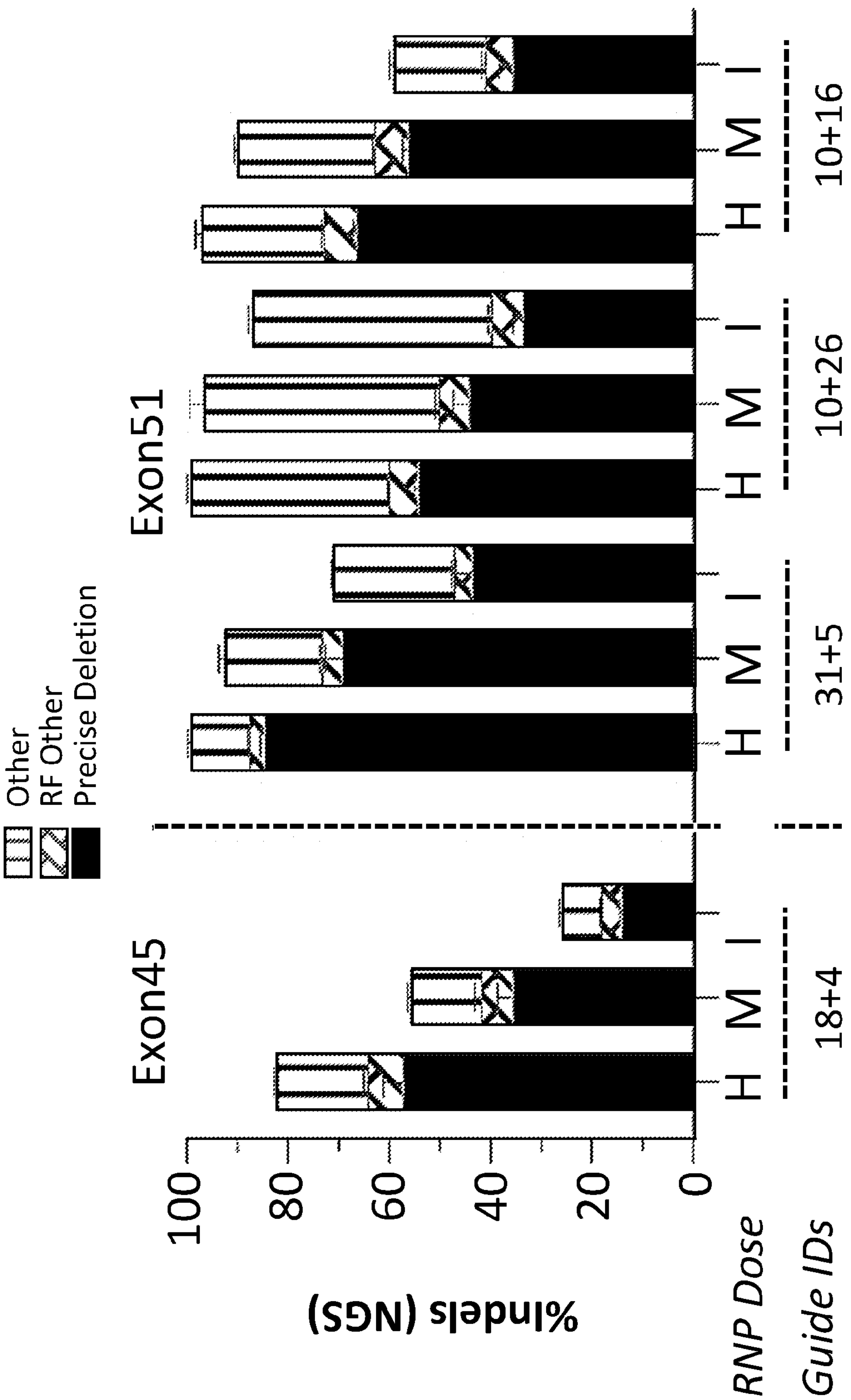

Other
RF Other
Precise Deletion
Exon45
Exon51
%Indels (NGS)
100
80
60
40
20
0
RNP Dose
H
M
I
H
M
I
H
M
I
H
M
I
Guide IDs
18+4
31+5
10+26
10+16

Fig. 7B

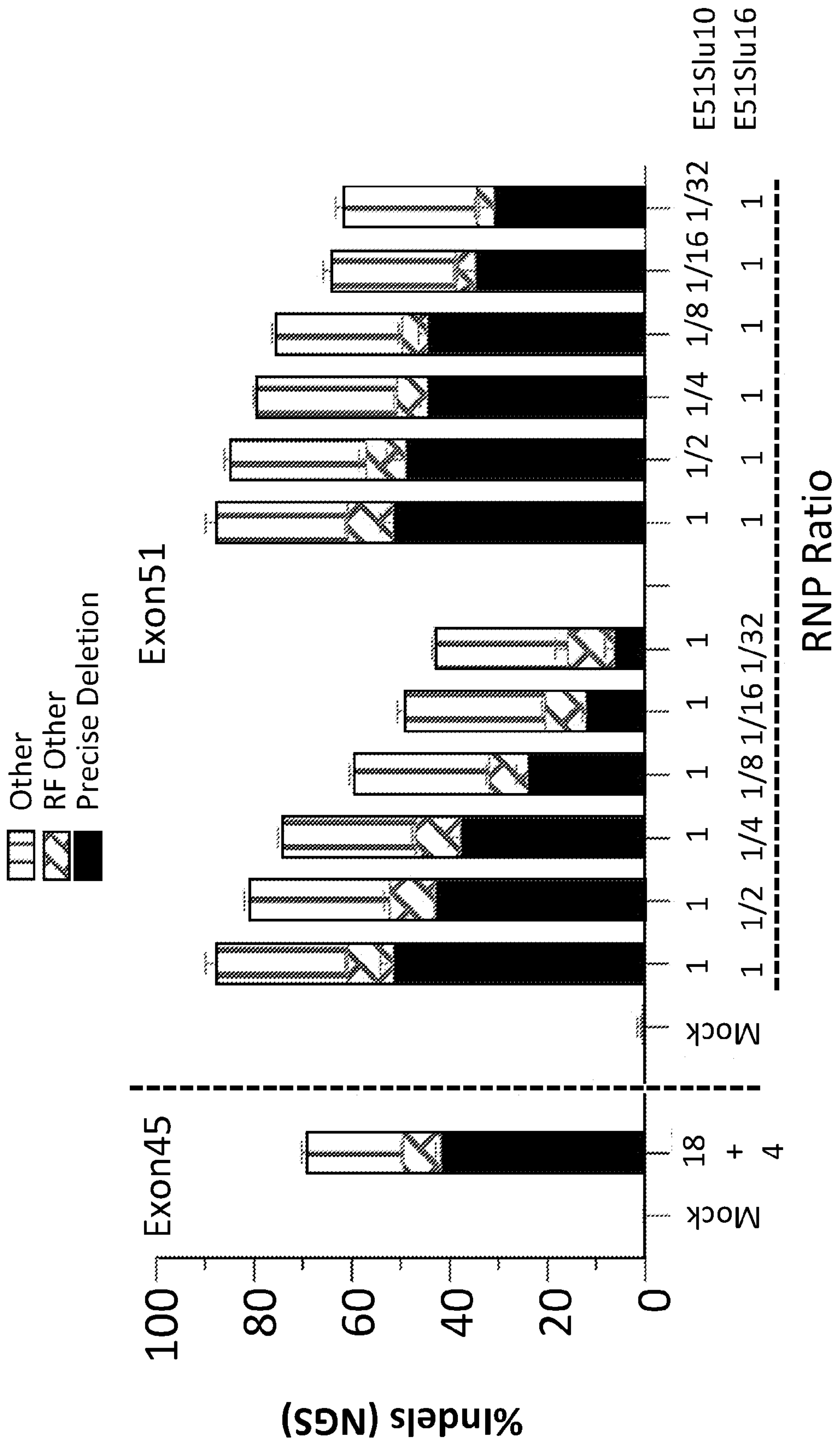

%Indels (NGS)
100
80
60
40
20
0
Exon45
Exon51
▥ Other
▨ RF Other
■ Precise Deletion
Mock
18 + 4
Mock
E51Slu10
E51Slu16
1 1
1/2 1
1/4 1
1/8 1
1/16 1
1/32 1
1 1
1/2 1
1/4 1
1/8 1
1/16 1
1/32 1
RNP Ratio

Fig. 8A

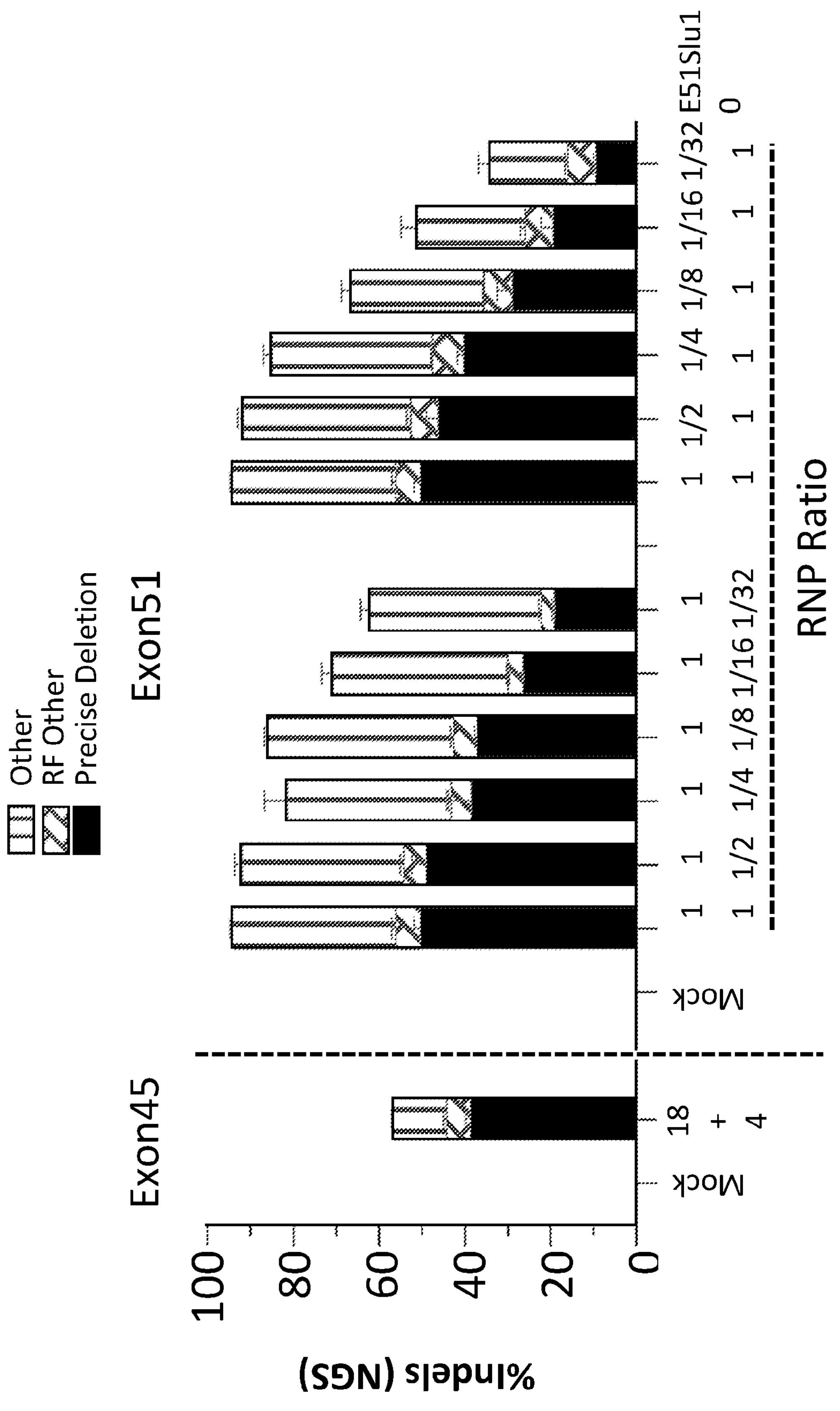

%Indels (NGS)
0
20
40
60
80
100
Exon45
Exon51
Other
RF Other
Precise Deletion
Mock
18
+
4
Mock
1
1
1
1/2
1
1/4
1
1/8
1
1/16
1
1/32
1
1
1/2
1
1/4
1
1/8
1
1/16
1
1/32
1
E51Slu1
0
RNP Ratio

Fig. 8B

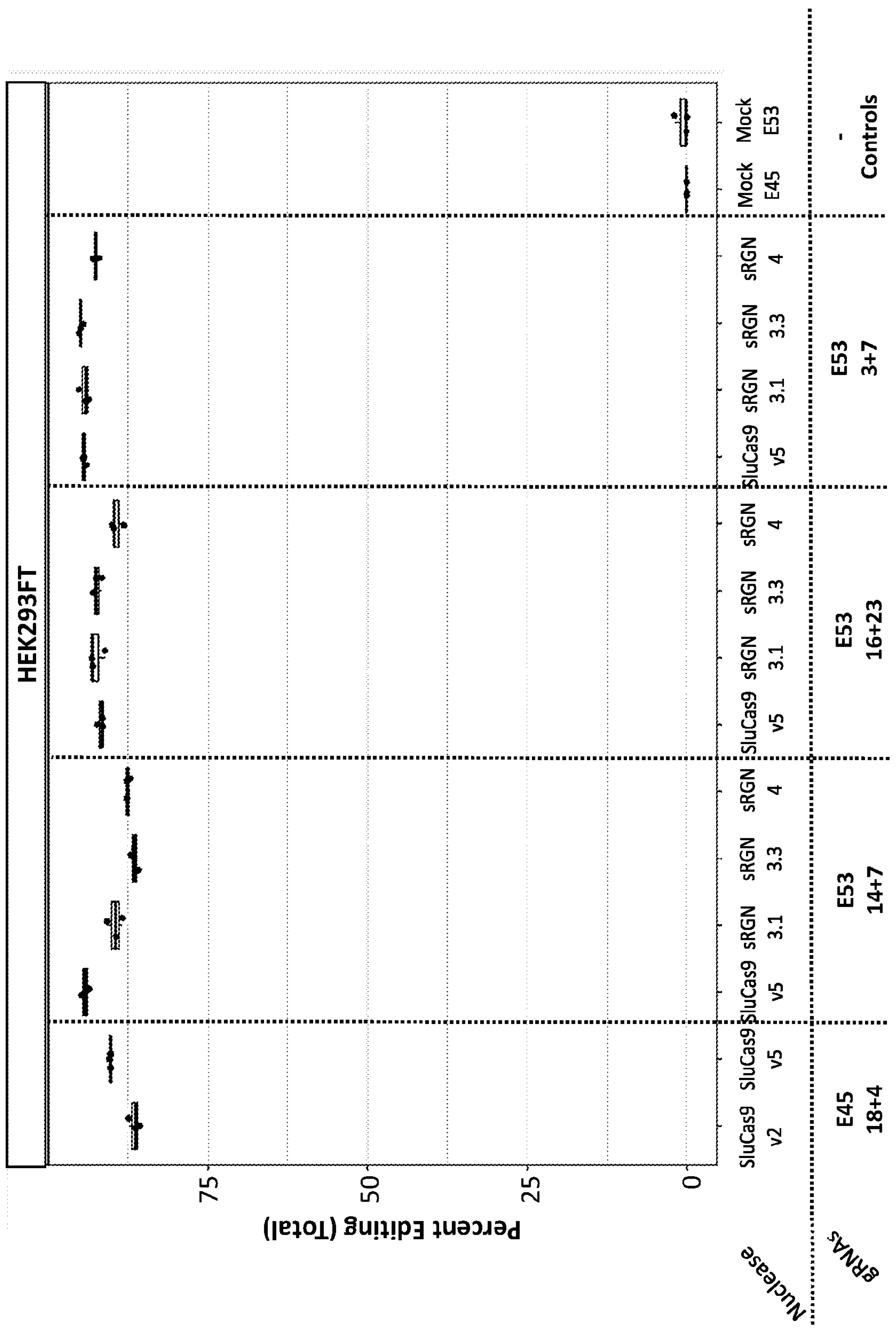

HEK293FT
Percent Editing (Total)
75
50
25
0
Nuclease
gRNAs
SluCas9 v2
SluCas9 v5
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
Mock E45
Mock E53
E45 18+4
E53 14+7
E53 16+23
E53 3+7
- Controls

Fig. 9

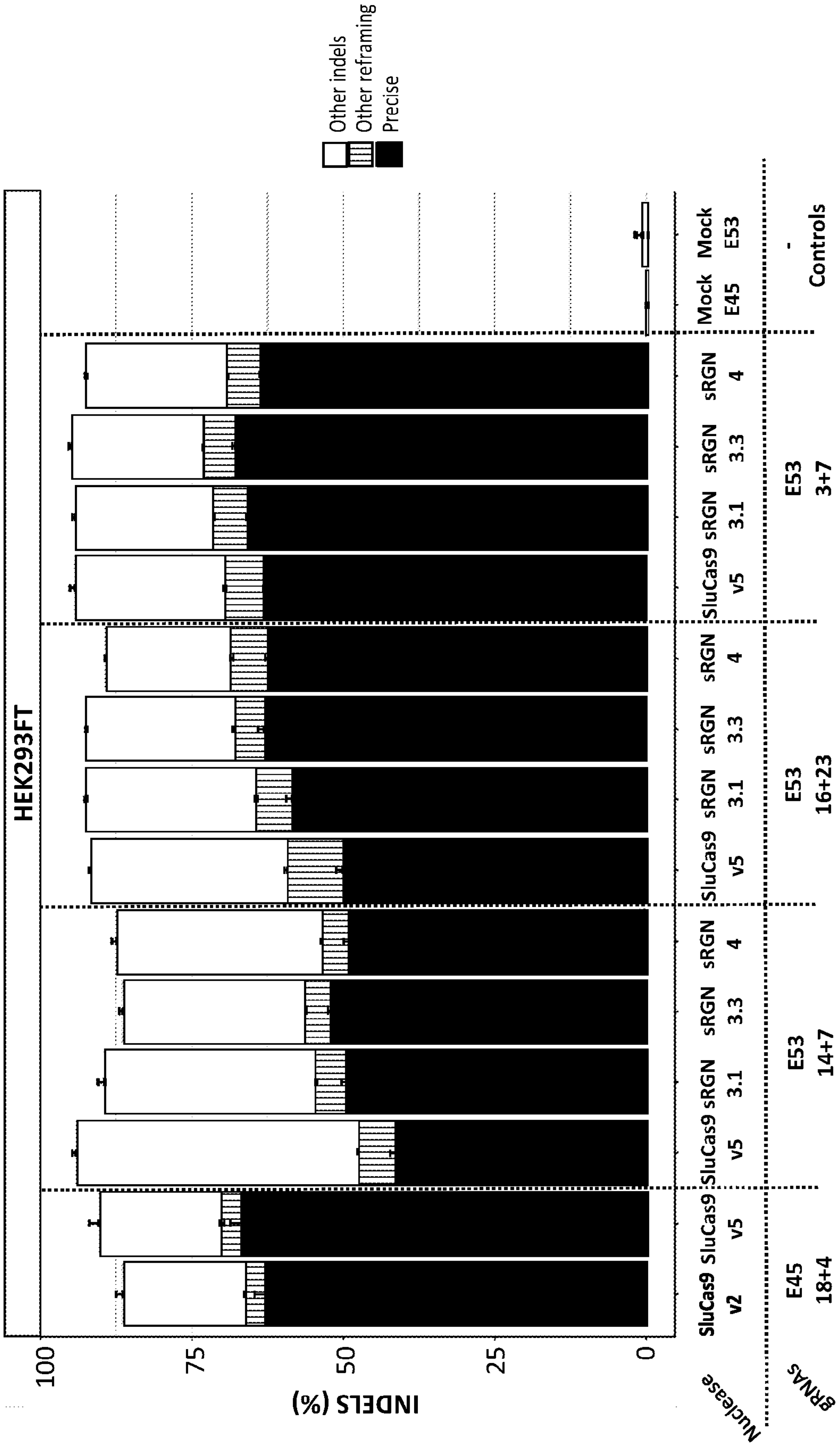

HEK293FT
INDELS (%)
100
75
50
25
0
Other indels
Other reframing
Precise
Nuclease
gRNAs
SluCas9 v2
SluCas9 v5
E45 18+4
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
E53 14+7
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
E53 16+23
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
E53 3+7
Mock E45
Mock E53
-
Controls

Fig. 10

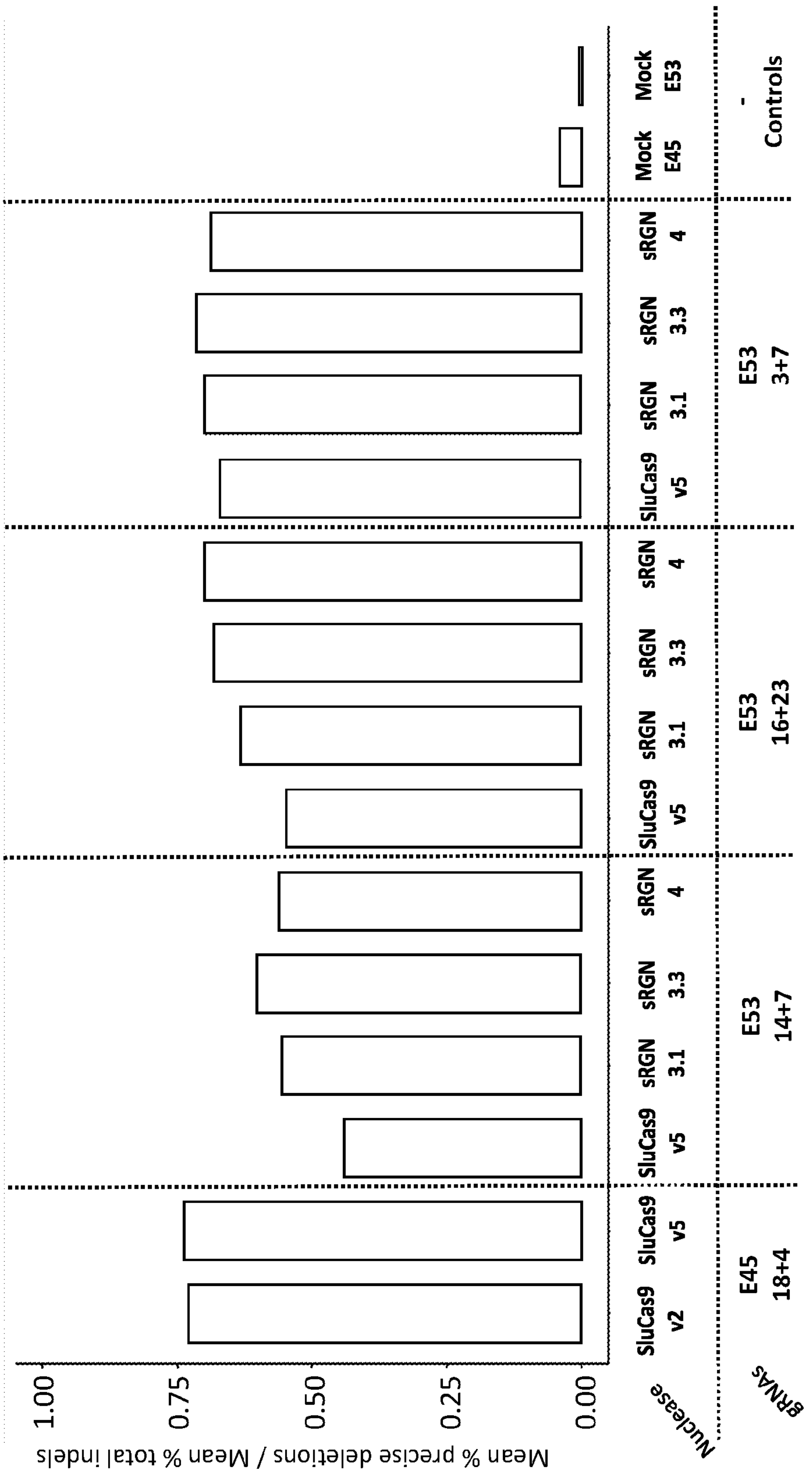

Mean % precise deletions / Mean % total indels
1.00
0.75
0.50
0.25
0.00
Nuclease
gRNAs
SluCas9 v2
SluCas9 v5
E45 18+4
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
E53 14+7
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
E53 16+23
SluCas9 v5
sRGN 3.1
sRGN 3.3
sRGN 4
E53 3+7
Mock E45
Mock E53
- Controls

Fig. 11

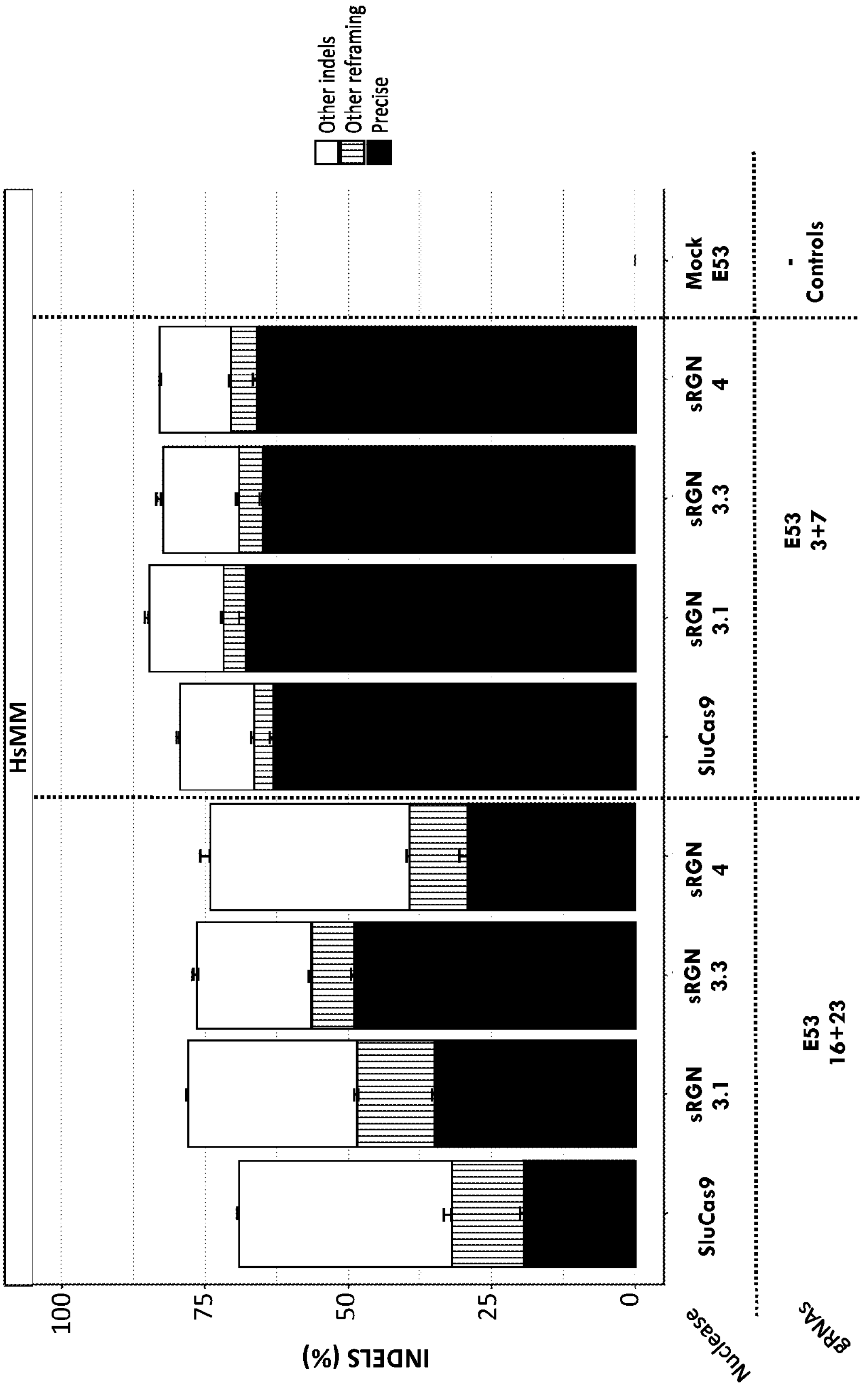

Other indels
Other reframing
Precise
HsMM
INDELS (%)
100
75
50
25
0
Nuclease
gRNAs
SluCas9
sRGN 3.1
sRGN 3.3
sRGN 4
SluCas9
sRGN 3.1
sRGN 3.3
sRGN 4
Mock E53
E53 16+23
E53 3+7
- Controls

Fig. 12

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2023/063885

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/113 A61K31/7105
ADD.

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)
C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, BIOSIS, Sequence Search, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2019/136216 A1 (UNIV TEXAS [US]) 11 July 2019 (2019-07-11) figures 26,62; example 2	1-7,10, 11,18-38
X	WO 2016/161380 A1 (EDITAS MEDICINE INC [US]) 6 October 2016 (2016-10-06) sequences 98955,112829	1,36
X	WO 2017/072590 A1 (CRISPR THERAPEUTICS AG [CH]) 4 May 2017 (2017-05-04) sequences 1013497,1013499,1013489,1013509,1013518 sequences 1013520,1013511,1013488,1410416	1,36
X	WO 2018/098480 A1 (UNIV TEXAS [US]) 31 May 2018 (2018-05-31) sequences 271,203,518,524	1,36

-/--

☒ 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 8 June 2023	Date of mailing of the international search report 09/08/2023
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Romano, Alper

3

International application No.

PCT/US2023/063885

INTERNATIONAL SEARCH REPORT

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.

   b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)).

      ☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2023/063885

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.:
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:

see additional sheet

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 an 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.:

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.:
1-7, 10, 11, 18-38(all partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-7, 10, 11, 18-38(all partially)

   A composition comprising one or more guide RNAs targeting exon 44 from table 6 and pairs of gRNAs from table 1B; and optionally further comprising a SaCas9

   ---

2. claims: 1-7, 10, 11, 16, 17, 20-38(all partially)

   A composition comprising one or more guide RNAs targeting exon 45 from table 6; and optionally further comprising a SaCas9

   ---

3. claims: 1-7, 10, 11, 18-38(all partially)

   A composition comprising one or more guide RNAs targeting exon 50 from table 6 and pairs of gRNAs from table 3B; and optionally further comprising a SaCas9

   ---

4. claims: 1-7, 10, 11, 16, 17, 20-38(all partially)

   A composition comprising one or more guide RNAs targeting exon 51 from table 6; and optionally further comprising a SaCas9

   ---

5. claims: 8(completely); 1-7, 10, 11, 16, 17, 20-38(partially)

   A composition comprising one or more guide RNAs targeting exon 53 from table 6 and pairs of gRNAs from table 5B;and optionally further comprising a SaCas9

   ---

6. claims: 9, 12-15(completely); 1-7, 16-29, 31-38(partially)

   A composition comprising one or more guide RNAs from table 6 and pairs of gRNAs from tables 1D, 3D or 5D; optionally further comprising a SluCas9 or sRGN

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2019/152609 A1 (UNIV TEXAS [US]) 8 August 2019 (2019-08-08) sequences 743,456,2123,457,816,453 -----	1,36
X,P	WO 2022/204476 A1 (UNIV TEXAS [US]) 29 September 2022 (2022-09-29) table 3; sequence 77 -----	1,3,4
X,P	WO 2022/056000 A1 (VERTEX PHARMA [US]) 17 March 2022 (2022-03-17) example 1; table 1A; sequences 6,8 -----	1,3,4
A	XIANG XI ET AL: "Efficient correction of Duchenne muscular dystrophy mutations by SpCas9 and dual gRNAs", MOLECULAR THERAPY-NUCLEIC ACIDS, vol. 24, 1 June 2021 (2021-06-01), pages 403-415, XP093046050, US ISSN: 2162-2531, DOI: 10.1016/j.omtn.2021.03.005 figures 5,6 -----	1-7,10, 11,18-38
A	ZHANG YU ET AL: "A consolidated AAV system for single-cut CRISPR correction of a common Duchenne muscular dystrophy mutation", MOLECULAR THERAPY- METHODS & CLINICAL DEVELOPMENT, vol. 22, 1 September 2021 (2021-09-01), pages 122-132, XP055927102, GB ISSN: 2329-0501, DOI: 10.1016/j.omtm.2021.05.014 the whole document -----	1-7,10, 11,18-38

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2023/063885

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2019136216 A1	11-07-2019	EP 3735462 A1	11-11-2020
		WO 2019136216 A1	11-07-2019
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		AU 2022215178 A1	10-11-2022
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		EP 3545090 A1	02-10-2019
		JP 2019536782 A	19-12-2019
		US 2020046854 A1	13-02-2020
		WO 2018098480 A1	31-05-2018
WO 2019152609 A1	08-08-2019	AU 2019216321 A1	30-07-2020
		BR 112020015617 A2	05-01-2021
		CA 3088547 A1	08-08-2019
		CN 111836893 A	27-10-2020
		EA 202091828 A1	24-05-2021
		EP 3746557 A1	09-12-2020
		IL 276139 A	30-09-2020
		JP 2021511803 A	13-05-2021
		KR 20200116933 A	13-10-2020
		US 2020370042 A1	26-11-2020
		WO 2019152609 A1	08-08-2019
WO 2022204476 A1	29-09-2022	NONE	
WO 2022056000 A1	17-03-2022	TW 202218686 A	16-05-2022
		US 2022096606 A1	31-03-2022
		WO 2022056000 A1	17-03-2022