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(54) Title: GENOME EDITING COMPOSITIONS AND METHODS FOR TREATMENT OF WILSON'S DISEASE

(57) Abstract: Provided herein are compositions and methods of using prime editing systems comprising prime editors and prime editing guide RNAs for treatment of genetic disorders.

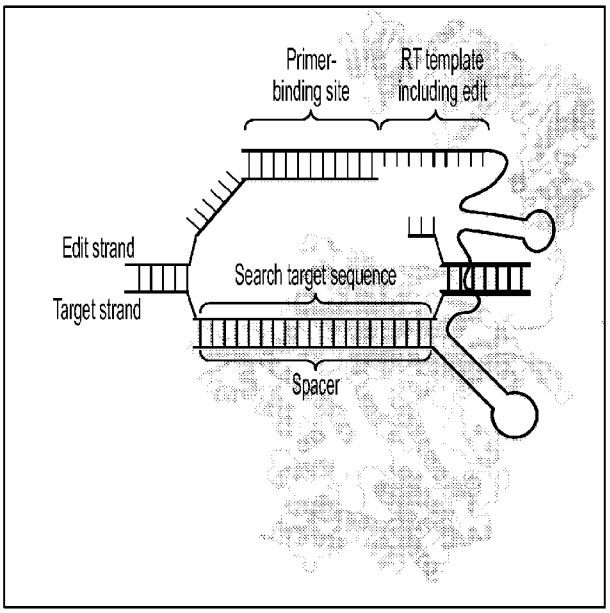


FIG. 1

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GENOME EDITING COMPOSITIONS AND METHODS FOR TREATMENT OF WILSON'S DISEASE

CROSS-REFERENCE

[1] This application claims the benefit of U.S. Provisional Application No. 63/222,480, filed July 16, 2021 which is incorporated herein by reference in its entirety.

SEQUENCE LISTING

[2] The instant application contains a Sequence Listing which has been submitted electronically in XML file format and is hereby incorporated by reference in its entirety. Said XML copy, created on July 14, 2022, is named 59761-722_601_SL.xml and is 13,605,667 bytes in size.

BACKGROUND

[3] Wilson's disease is caused by homozygous or compound heterozygous mutations in the *ATP7B* gene (OMIM# 606882), which is mainly expressed in hepatic and neural tissues and encodes a transmembrane copper-transporting P-type ATPase of the same name. *ATP7B* is located in the human genome on 13q14.3 and contains 20 introns and 21 exons, for a total genomic length of 80 kb. Wilson's disease is an autosomal recessive genetic copper storage disorder caused by mutations in the *ATP7B* gene, which is expressed mainly in hepatocytes and functions in the transmembrane transport of copper. *ATP7B* deficiencies may lead to decreased hepatocellular excretion of copper into bile that may lead to systemic copper buildup, hepatic and neural toxicity, and early demise. The accumulation of copper can be manifested as neurological or psychiatric symptom. Over time without proper treatments, high copper levels can cause life-threatening organ damage.

[4] Current treatment approaches for Wilson's disease are daily oral therapy with chelating agents (such as penicillamine [Cuprimine] and trientine hydrochloride [Syprine]), zinc (to block enterocyte absorption of copper), and tetrathiomolybdate (TM), a copper chelator that forms complexes with albumin in the circulation; all of which require the affected individual to take medicines for their whole life. Furthermore, those treatments may cause side effects, such as drug induced lupus, myasthenia, paradoxical worsening, and do not restore normal copper metabolism. Liver transplantation is curative for Wilson's disease but transplant recipients are required to maintain a constant immune suppression regimen to prevent rejection. Therapeutic strategies, such as gene therapy, that can reverse the underlying metabolic defect would be greatly advantageous. However, the *ATP7B* gene is approximately 4.4 kb, nearing the adeno-associated virus (AAV) packaging size limit and making gene therapy approaches with the full-length gene difficult.

[5] This disclosure provides prime editing methods and compositions for correcting mutations associated with Wilson's disease.

SUMMARY OF THE DISCLOSURE

[6] In one aspect, provided herein is a prime editing guide RNA (PEgRNA) comprising: (a) a spacer that is complementary to a search target sequence on a first strand of an ATP7B gene, wherein the spacer comprises at its 3' end SEQ ID NO: 2128; (b) a gRNA core capable of binding to a Cas9 protein; (c) an extension arm comprising: (i) an editing template that comprises a region of complementarity to an editing target sequence on a second strand of the ATP7B gene, and (ii) a primer binding site that comprises at its 5' end a sequence that is a reverse complement of nucleotides 11-13 of SEQ ID NO: 2128; wherein the first strand and second strand are complementary to each other and wherein the editing target sequence on the second strand is complementary to a portion of the ATP7B gene comprising a c.2333G>T substitution.

[7] In one aspect, provided herein is a prime editing guide RNA (PEgRNA) comprising: (a) a spacer comprising at its 3' end nucleotides SEQ ID NO: 2128; (b) a gRNA core capable of binding to a Cas9 protein, and (c) an extension arm comprising: (i) an editing template comprising at its 3' end any one of SEQ ID NOs: 2152-2161, and (ii) a primer binding site (PBS) comprising at its 5' end a sequence that is a reverse complement of nucleotides 11-13 of SEQ ID NO: 2128.

[8] In some embodiments, the spacer of the PEgRNA is from 16 to 22 nucleotides in length. In some embodiments, the spacer of the PEgRNA comprises at its 3' end any one of SEQ ID NOs: 2129-2134. In some embodiments, the spacer of the PEgRNA comprises at its 3' end SEQ ID NO: 2132. In some embodiments, the spacer of the PEgRNA is 20 nucleotides in length. In some embodiments, the PEgRNA of any one of aspects above, comprising from 5' to 3', the spacer, the gRNA core, the RTT, and the PBS. In some embodiments, the spacer, the gRNA core, the RTT, and the PBS form a contiguous sequence in a single molecule.

[9] In some embodiments, the editing template comprises SEQ ID NO: 2152 at its 3' end and encodes a CGG-to-CTG PAM silencing edit. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2168, 2176, 2190, 2200, 2221, 2225, 2244, 2255, 2262, 2272, 2292, 2305, 2309, 2321, or 2340. In some embodiments, the editing template comprises SEQ ID NO: 2153 at its 3' end and encodes a CGG-to-CTC PAM silencing edit.

In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2173, 2179, 2198, 2202, 2222, 2229, 2236, 2259, 2264, 2276, 2284, 2306, 2316, 2322, or 2339. In some embodiments, the editing template comprises SEQ ID NO: 2154 at its 3' end and encodes a CGG-to-CGT PAM silencing edit. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2166, 2177, 2189, 2204, 2218, 2232, 2242, 2250, 2271, 2280, 2288, 2303, 2311, 2325, or 2336. In some embodiments, the editing template comprises SEQ ID NO: 2155 at its 3' end and encodes a CGG-to-CGA PAM silencing edit. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2167, 2182, 2195, 2211, 2216, 2227, 2245, 2254, 2260, 2282, 2290, 2298, 2319, 2330, or 2337. In some embodiments, the editing template comprises SEQ ID NO: 2156 at its 3' end and encodes a CCGG-to-TCTA PAM silencing edit. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2164, 2187, 2193, 2210, 2217, 2228, 2241, 2251, 2266, 2283, 2287, 2296, 2308, 2327, or 2342.

[10] In some embodiments, the editing template comprises SEQ ID NO: 2157 at its 3' end and encodes a CGG-to-CTT PAM silencing edit. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2174, 2185, 2188, 2205, 2212, 2233, 2237, 2258, 2265, 2274, 2291, 2300, 2310, 2331, or 2332. In some embodiments, the editing template comprises SEQ ID NO: 2158 at its 3' end and encodes a CCGG-to-TCTG PAM silencing edit. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2170, 2178, 2199, 2207, 2219, 2230, 2239, 2248, 2261, 2275, 2294, 2301, 2312, 2323, or 2334.

[11] In some embodiments, the editing template comprises SEQ ID NO: 2159 at its 3' end and encodes a CGG-to-CGC PAM silencing edit. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2165, 2183, 2194, 2201, 2215, 2235, 2240, 2249, 2269, 2277, 2285, 2302, 2318, 2326, or 2333. In some embodiments, the editing template comprises SEQ ID NO: 2160 at its 3' end and encodes a CGG-to-CTA PAM silencing edit.

[12] In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2171, 2186, 2196, 2206, 2214, 2224, 2243, 2252, 2268, 2281, 2293, 2299, 2314, 2329, or 2335. In some embodiments, the editing template comprises SEQ ID NO: 2161 at its 3' end and encodes a CCGG-to-TCTC PAM silencing edit. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2172, 2181, 2197, 2203, 2213, 2231, 2246, 2253, 2267, 2273, 2289, 2304, 2317, 2328, or 2341. In some embodiments, the editing template comprises SEQ ID NO: 2162 at its 3' end. In some embodiments, the editing template comprises at its 3' end SEQ ID NO: 2175, 2180, 2191, 2209, 2223, 2226, 2238, 2256, 2263, 2279, 2295, 2307, 2313, 2324, or 2338. In some embodiments, the editing template has a length of 25 nucleotides or less. In some embodiments, the PBS comprises at its 5' end a sequence that is a reverse complement of

nucleotides 10-13, 9-13, 8-13, 7-13, 6-13, 5-13, 4-13, 3-13, 2-13, or 1-13 of SEQ ID NO: 2128. In some embodiments, the PBS comprises at its 5' end a sequence corresponding to GCTGGAAC, where "T" is a "U".

[13] In some embodiments, the PBS comprises at its 5' end SEQ ID NO: 2142. In some embodiments, the 3' end of the editing template is adjacent to the 5' end of the PBS. In some embodiments, the PEgRNA of any one of aspects above, comprises a pegRNA sequence selected from any one of SEQ ID NOs: 14769, 14770, 14771, 14772, 14773, 14774, 14775, 14776, 14777, 14778, 14779, 14780, 14781, 14782, 14783, 14784, 14785, 14786, 14787, 14788, 14789, 14790, 14791, 14792, 14793, 14794, 14795, 14796, 14797, 14798, or 14799. In some embodiments, the PEgRNA of any one of aspects above, further comprises 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates the presence of a phosphorothioate bond.

[14] In one aspect, the present disclosure provides a prime editing system comprising: (a) the prime editing guide RNA (PEgRNA) of any one of aspects above, or a nucleic acid encoding the PEgRNA; and (b) a nick guide RNA (ngRNA) comprising at its 3' end nucleotides 5-20 of any one of SEQ ID NOs: 63, 88, 1994, 2000, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3245, 3246, 3247, 3248, 3249, 3250, 3251, 3252, 3253, 3254, 3255, 3256, 3257, 3258, 3259, 3260, 3261, 3262, 3263, 3264, 3265, 3266, 3267, 3268, 3269, 3270, 3271, 3272, 3273, 3274, 3275, 3276, 3277, 3278, 3279, 3280, 3281, 3282, 3283, 3284, 3285, 3286, 3287, 3288, 3289, 3290, 3291, 3292, 3293, 3294, 3295, 3296, 3297, 3298, or 3299, and a gRNA core capable of binding to a Cas9 protein, or a nucleic acid encoding the ngRNA.

[15] In some embodiments, the spacer of the ngRNA is from 15 to 22 nucleotides in length.

[16] In some embodiments, the spacer of the ngRNA comprises at its 3' end nucleotides 4-20, 3-20, 2-20, or 1-20 of SEQ ID NO: 63, 88, 1994, 2000, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3245, 3246, 3247, 3248, 3249, 3250, 3251, 3252, 3253, 3254, 3255, 3256, 3257, 3258, 3259, 3260, 3261, 3262, 3263, 3264, 3265, 3266, 3267, 3268, 3269, 3270, 3271, 3272, 3273, 3274, 3275, 3276, 3277, 3278, 3279, 3280, 3281, 3282, 3283, 3284, 3285, 3286, 3287, 3288, 3289, 3290, 3291, 3292, 3293, 3294, 3295, 3296, 3297, 3298, or 3299.

[17] In some embodiments, the spacer of the ngRNA comprises at its 3' end SEQ ID NO: 63, 88, 1994, 2000, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3245, 3246, 3247, 3248, 3249, 3250, 3251, 3252, 3253, 3254, 3255, 3256, 3257, 3258, 3259, 3260, 3261, 3262, 3263, 3264, 3265, 3266, 3267, 3268, 3269, 3270, 3271, 3272, 3273, 3274, 3275, 3276, 3277, 3278, 3279, 3280, 3281, 3282, 3283, 3284, 3285, 3286, 3287, 3288, 3289, 3290, 3291, 3292, 3293, 3294, 3295, 3296, 3297, 3298, or 3299. In some embodiments, the spacer of the

ngRNA is 20 nucleotides in length. In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3269, 3279, 1994, 3247, 3249, 3267, 3288, 3299, 3272, or 3258. In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3269 or 3279 and the editing template of the PEgRNA comprises SEQ ID NO: 2162 at its 3' end. In some embodiments, the spacer of the ngRNA is SEQ ID NO: 1994 and the editing template of the PEgRNA comprises SEQ ID NO: 2162 at its 3' end.

[18] In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3247 and the editing template of the PEgRNA comprises SEQ ID NO: 2154 at its 3' end. In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3249 and the editing template of the PEgRNA comprises SEQ ID NO: 2153 at its 3' end. In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3267 and the editing template of the PEgRNA comprises SEQ ID NO: 2157 at its 3' end. In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3288 and the editing template of the PEgRNA comprises SEQ ID NO: 2152 at its 3' end. In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3299 and the editing template of the PEgRNA comprises SEQ ID NO: 2159 at its 3' end.

[19] In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3272 and the editing template of the PEgRNA comprises SEQ ID NO: 2155 at its 3' end. In some embodiments, the spacer of the ngRNA is SEQ ID NO: 3258 and the editing template of the PEgRNA comprises SEQ ID NO: 2160 at its 3' end. In some embodiments, the prime editing system of any one of aspects above, further comprises: (c) a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain, or a nucleic acid encoding the Cas9 nickase, and a reverse transcriptase, or a nucleic acid encoding the reverse transcriptase. In some embodiments, the Cas9 nickase comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 14831. In some embodiments, the reverse transcriptase comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 14828. In some embodiments, the sequence identities are determined by Needleman-Wunsch alignment of two protein sequences with Gap Costs set to Existence: 11 Extension: 1 where percent identity is calculated by dividing the number of identities by the length of the alignment. In some embodiments, the prime editor is a fusion protein.

[20] In one aspect, the present disclosure provides an LNP comprising the prime editing system of any one of aspects above.

[21] In some embodiments, the PEgRNA, the nucleic acid encoding the Cas9 nickase, and the nucleic acid encoding the reverse transcriptase. In some embodiments, the nucleic acid encoding

the Cas9 nickase and the nucleic acid encoding the reverse transcriptase are mRNA. In some embodiments, the nucleic acid encoding the Cas9 nickase and the nucleic acid encoding the reverse transcriptase are the same molecule. In some embodiments, the LNP of any one of aspects above, further comprises the ngRNA.

[22] In one aspect, provided herein is a method of correcting for editing an ATP7B gene, the method comprising contacting the ATP7B gene with: (A) the PEgRNA of any one of aspects above and a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain and a reverse transcriptase, (B) the prime editing system of any one of aspects above, or (C) the LNP of any one of aspects above.

[23] In some embodiments, the ATP7B gene is in a cell. In some embodiments, the cell is a mammalian cell. In some embodiments, the cell is a human cell. In some embodiments, the cell is a primary cell. In some embodiments, the cell is a hepatocyte. In some embodiments, the cell is in a subject. In some embodiments, the subject is a human. In some embodiments, the cell is from a subject having Wilson's disease. In some embodiments, the method of any one of aspects above, further comprises administering the cell to the subject after incorporation of the intended nucleotide edit.

[24] In one aspect, the present disclosure provides a cell generated by the method of any one of aspects above.

[25] In one aspect, provided herein is a population of cells generated by the method of any one of aspects above.

[26] In one aspect, provided herein is a method for treating Wilson's disease in a subject in need thereof, the method comprising administering to the subject: (a) the PEgRNA of any one of aspects above, (B) the prime editing system of any one of aspects above, or (C) the LNP of any one of aspects above.

[27] In some embodiments, the method of any one of aspects above, comprises administering to the subject the PEgRNA of any one of aspects above and a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain and a reverse transcriptase or one or more nucleic acids encoding the prime editor or its components. In some embodiments, the prime editor is a fusion protein.

[28] In one aspect, provided herein is a prime editing guide RNA (PEgRNA) comprising: (a) a spacer comprising at its 3' end nucleotides 5-20 of a PEgRNA Spacer sequence selected from any one of Tables 1-84; (b) a gRNA core capable of binding to a Cas9 protein, and (c) an extension arm comprising: (i) an editing template comprising at its 3' end an RTT sequence selected from the same Table as the PEgRNA Spacer sequence, and (ii) a primer binding site

(PBS) comprising at its 5' end a PBS sequence selected from the same Table as the PEgRNA Spacer sequence.

[29] In some embodiments, the spacer of the PEgRNA is from 16 to 22 nucleotides in length. In some embodiments, the spacer of the PEgRNA is 20 nucleotides in length. In some embodiments, the PEgRNA of any one of aspects above, comprises from 5' to 3', the spacer, the gRNA core, the editing template, and the PBS. In some embodiments, the spacer, the gRNA core, the editing template, and the PBS form a contiguous sequence in a single molecule. In some embodiments, the PEgRNA of any one of aspects above, comprises a pegRNA sequence selected from the same Table as the PEgRNA Spacer sequence.

[30] In one aspect, provided herein is a prime editing system comprising: (a) the prime editing guide RNA (PEgRNA) of any one of aspects above, or a nucleic acid encoding the PEgRNA; and (b) a nick guide RNA (ngRNA) comprising a spacer comprising at its 3' end nucleotides 5-20 of any ngRNA Spacer sequence selected from the same Table as the PEgRNA Spacer sequence and a gRNA core capable of binding to a Cas9 protein, or a nucleic acid encoding the ngRNA.

[31] In some embodiments, the spacer of the ngRNA is from 16 to 22 nucleotides in length.In some embodiments, the spacer of the ngRNA comprises at its 3' end nucleotides 4-20, 3-20, 2-20, or 1-20 of the ngRNA Spacer sequence selected from the same Table as the PEgRNA Spacer sequence. In some embodiments, the spacer of the ngRNA comprises at its 3' end the ngRNA Spacer sequence selected from the same Table as the PEgRNA Spacer sequence. In some embodiments, the spacer of the ngRNA is 20 nucleotides in length. In some embodiments, the ngRNA comprises a ngRNA sequence selected from the same Table as the PEgRNA Spacer sequence.

[32] In some embodiments, the prime editing system of any one of aspects above, further comprises: (c) a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain, or a nucleic acid encoding the Cas9 nickase, and a reverse transcriptase, or a nucleic acid encoding the reverse transcriptase. In some embodiments, the Cas9 nickase comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 14831. In some embodiments, the reverse transcriptase comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 14828. In some embodiments, the sequence identities are determined by Needleman-Wunsch alignment of two protein sequences with Gap Costs set to Existence: 11 Extension: 1 where percent identity is calculated by dividing the number of

identities by the length of the alignment. In some embodiments, the prime editor is a fusion protein.

[33] In one aspect, provided herein is an LNP comprising the prime editing system of any one of aspects above.

[34] In some embodiments, the PEgRNA, the nucleic acid encoding the Cas9 nickase, and the nucleic acid encoding the reverse transcriptase. In some embodiments, the nucleic acid encoding the Cas9 nickase and the nucleic acid encoding the reverse transcriptase are mRNA. In some embodiments, the nucleic acid encoding the Cas9 nickase and the nucleic acid encoding the reverse transcriptase are the same molecule. In some embodiments, the LNP of any one of aspects above, further comprises the ngRNA.

[35] In one aspect, provided herein is a method of correcting for editing an ATP7B gene, the method comprising contacting the ATP7B gene with: (A) the PEgRNA of any one of aspects above and a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain and a reverse transcriptase, (B) the prime editing system of any one of aspects above, or (C) the LNP of any one of aspects above.

[36] In some embodiments, the ATP7B gene is in a cell. In some embodiments, the cell is a mammalian cell. In some embodiments, the cell is a human cell. In some embodiments, the cell is a primary cell. In some embodiments, the cell is a hepatocyte. In some embodiments, the cell is in a subject. In some embodiments, the subject is a human. In some embodiments, the cell is from a subject having Wilson's disease. In some embodiments, the method of any one of aspects above, further comprises administering the cell to the subject after incorporation of the intended nucleotide edit.

[37] In one aspect, provided herein is a cell generated by the method of any one of aspects above.

[38] In one aspect, provided herein is a population of cells generated by the method of any one of aspects above.

[39] In one aspect, the present disclosure provides a method for treating Wilson's disease in a subject in need thereof, the method comprising administering to the subject: (a) the PEgRNA of any one of aspects above, (B) the prime editing system of any one of aspects above, or (C) the LNP of any one of aspects above.

[40] In some embodiments, the method of any one of aspects above, comprises administering to the subject the PEgRNA of any one of aspects above and a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain and a reverse transcriptase or one or more nucleic acids encoding the prime editor or its components. In some

embodiments, the prime editor is a fusion protein. In some embodiments, the PEgRNA of any one of aspects above comprises, (B) the prime editing system of any one of aspects above, or (C) the LNP of any one of aspects above, wherein the PEgRNA Spacer sequence is selected from Table 9, Table 8, or Table 11. In some embodiments, the PEgRNA Spacer sequence is selected from Table 9.

INCORPORATION BY REFERENCE

[41] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[42] The novel features of the disclosure are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosurewill be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the disclosure are utilized, and the accompanying drawings of which:

[43] **FIG. 1** depicts a schematic of a prime editing guide RNA (PEgRNA) binding to a double stranded target DNA sequence.

[44] **FIG. 2** depicts a PEgRNA architectural overview in an exemplary schematic of PEgRNA designed for a prime editor.

[45] **FIG. 3A** depicts a 3'-to 5' schematic (with the coding strand at the bottom) of an *ATP7B* R778 locus with spacer sequences and an R778L mutation highlighted. Figure 3A discloses SEQ ID NOS 14902-14903, respectively, in order of appearance

[46] **FIG. 3B** depicts a lentiviral screen design schematic.

[47] **FIG. 4** is a schematic showing the spacer and gRNA core part of an exemplary guide RNA, in two separate molecules. The rest of the PEgRNA structure is not shown.

DETAILED DESCRIPTION OF THE DISCLOSURE

[48] Provided herein, in some embodiments, are compositions and methods to edit the target gene *ATP7B* with prime editing. In certain embodiments, provided herein are compositions and methods for correction of mutations in the copper-transporting ATPase 2 (*ATP7B*) gene associated with Wilson's Disease. Compositions provided herein can comprise prime editors (PEs) that may use engineered guide polynucleotides, *e.g.*, prime editing guide RNAs (PEgRNAs), that can direct PEs to specific DNA targets and can encode DNA edits on the target gene *ATP7B* that serve a variety of functions, including direct correction of disease-causing mutations.

[49] The following description and examples illustrate embodiments of the present disclosure in detail. It is to be understood that this disclosure is not limited to the particular embodiments described herein and as such can vary. Those of skill in the art will recognize that there are numerous variations and modifications of this disclosure, which are encompassed within its scope. Although various features of the present disclosure can be described in the context of a single embodiment, the features can also be provided separately or in any suitable combination. Conversely, although the present disclosure can be described herein in the context of separate embodiments for clarity, the present disclosure can also be implemented in a single embodiment.

Definitions

[50] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art.

[51] The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting. As used herein, the singular forms "a", "an" and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise. Furthermore, to the extent that the terms "including", "includes", "having", "has", "with", or variants thereof as used herein mean "comprising".

[52] Unless otherwise specified, the words "comprising", "comprise", "comprises", "having", "have", "has", "including", "includes", "include", "containing", "contains" and "contain" are inclusive or open-ended and do not exclude additional, unrecited elements or method steps.

[53] Reference to "some embodiments", "an embodiment", "one embodiment", or "other embodiments" means that a particular feature or characteristic described in connection with the embodiments is included in at least one or more embodiments, but not necessarily all embodiments, of the present disclosure.

[54] The term "about" or "approximately" means within an acceptable error range for the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, *i.e*, the limitations of the measurement system. For example, "about" can mean within 1 standard deviation, per the practice in the art. Alternatively, "about" can mean a range of up to 20%, up to 10%, up to 5%, or up to 1% of a given value. Alternatively, particularly with respect to biological systems or processes, the term can mean within an order of magnitude, preferably within 5-fold, and more preferably within 2-fold, of a value. Where particular values are described in the application and claims, unless otherwise stated, the term "about" meaning within an acceptable error range for the particular value should be assumed.

[55] As used herein, a "cell" can generally refer to a biological cell. A cell can be the basic structural, functional and/or biological unit of a living organism. A cell can originate from any organism having one or more cells. Some non-limiting examples include: a prokaryotic cell, eukaryotic cell, a bacterial cell, an archaeal cell, a cell of a single-cell eukaryotic organism, a protozoa cell, a cell from a plant, an animal

cell, a cell from an invertebrate animal (*e.g.* fruit fly, cnidarian, echinoderm, nematode, etc.), a cell from a vertebrate animal (*e.g.*, fish, amphibian, reptile, bird, mammal), a cell from a mammal (*e.g.*, a pig, a cow, a goat, a sheep, a rodent, a rat, a mouse, a non-human primate, a human, etc.), et cetera. Sometimes a cell may not originate from a natural organism (*e.g.*, a cell can be synthetically made, sometimes termed an artificial cell).

[56] In some embodiments, the cell is a human cell. A cell can be of or derived from different tissues, organs, and/or cell types. In some embodiments, the cell is a primary cell. As used herein, the term "primary cell" means a cell isolated from an organism, *e.g.*, a mammal, which is grown in tissue culture (*i.e.*, *in vitro*) for the first time before subdivision and transfer to a subculture. In some embodiments, the cell is a stem cell. In some non-limiting examples, mammalian cells, including primary cells and stem cells, can be modified through introduction of one or more polynucleotides, polypeptide, and/or prime editing compositions (e.g., through transfection, transduction, electroporation, and the like) and further passaged. Such modified cells include hepatocytes, fibroblasts, keratinocytes, epithelial cells (*e.g.*, mammary epithelial cells, intestinal epithelial cells), endothelial cells, glial cells, neural cells, formed elements of the blood (*e.g.*, lymphocytes, bone marrow cells), muscle cells and precursors of these somatic cell types. In some embodiments, the cell is a primary hepatocyte. In some embodiments, the cell is a primary human hepatocyte. In some embodiments, the cell is a primary human hepatocyte derived from an induced human pluripotent stem cell (iPSC). In some embodiments, the cell is a neuron. In some embodiments, the cell is a neuron from basal ganglia. In some embodiments, the cell is a neuron from basal ganglia of a subject. In some embodiments, the cell is a stem cell. In some embodiments, the cell is a progenitor cell. In some embodiments, the cell is a pluripotent cell (e.g., a pluripotent stem cell) In some embodiments, the cell (e.g., a stem cell) is an embryonic stem cell, tissue-specific stem cell, mesenchymal stem cell, or an induced pluripotent stem cell. In some embodiments, the cell is an induced pluripotent stem cell (iPSC). In some embodiments, the cell is an embryonic stem cell (ESC). In some embodiments, the cell is a primary hepatocyte. In some embodiments, the cell is a primary human hepatocyte. In some embodiments, the cell is a primary human hepatocyte derived from an induced human pluripotent stem cell (iPSC). In some embodiments, the cell is a neuron. In some embodiments, the cell is a neuron from basal ganglia. In some embodiments, the cell is a neuron from basal ganglia of a subject.

[57] In some embodiments, the cell comprises a prime editor, a PEgRNA, or a prime editing composition disclosed herein. In some embodiments, the cell further comprises an ngRNA. In some embodiments, the cell is from a human subject. In some embodiments, the human subject has a disease or condition, or is at a risk of developing a disease or a condition associated with a mutation to be corrected by prime editing, for example, Wilsons's disease. In some embodiments, the cell is from a human subject, and comprises a prime editor, a PEgRNA, or a prime editing composition for correction of the mutation. In some embodiments, the cell is from the human subject and the mutation has been edited or corrected by prime editing.

[58] The term "substantially" as used herein may refer to a value approaching 100% of a given value. In some embodiments, the term may refer to an amount that may be at least about 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.9%, or 99.99% of a total amount. In some embodiments, the term may refer to an amount that may be about 100% of a total amount.

[59] The terms "protein" and "polypeptide" can be used interchangeably to refer to a polymer of two or more amino acids joined by covalent bonds (*e.g.*, an amide bond) that can adopt a three-dimensional conformation. In some embodiments, a protein or polypeptide comprises at least 10 amino acids, 15 amino acids, 20 amino acids, 30 amino acids or 50 amino acids joined by covalent bonds (*e.g.*, amide bonds). In some embodiments, a protein comprises at least two amide bonds. In some embodiments, a protein comprises multiple amide bonds. In some embodiments, a protein comprises an enzyme, enzyme precursor proteins, regulatory protein, structural protein, receptor, nucleic acid binding protein, a biomarker, a member of a specific binding pair (*e.g.*, a ligand or aptamer), or an antibody. In some embodiments, a protein may be a full-length protein (*e.g.*, a fully processed protein having certain biological function). In some embodiments, a protein may be a variant or a fragment of a full-length protein. For example, in some embodiments, a Cas9 protein domain comprises an H840A amino acid substitution compared to a naturally occurring *S. pyogenes* Cas9 protein. A variant of a protein or enzyme, for example a variant reverse transcriptase, comprises a polypeptide having an amino acid sequence that is about 60% identical, about 70% identical, about 80% identical, about 90% identical, about 95% identical, about 96% identical, about 97% identical, about 98% identical, about 99% identical, about 99.5% identical, or about 99.9% identical to the amino acid sequence of a reference protein.

[60] In some embodiments, a protein comprises one or more protein domains or subdomains. As used herein, the term "polypeptide domain", "protein domain", or "domain" when used in the context of a protein or polypeptide, refers to a polypeptide chain that has one or more biological functions, *e.g.*, a catalytic function, a protein-protein binding function, or a protein-DNA function. In some embodiments, a protein comprises multiple protein domains. In some embodiments, a protein comprises multiple protein domains that are naturally occurring. In some embodiments, a protein comprises multiple protein domains from different naturally occurring proteins. For example, in some embodiments, a prime editor may be a fusion protein comprising a Cas9 protein domain of S. pyogenes and a reverse transcriptase protein domain of a retrovirus (e.g., a Moloney murine leukemia virus) or a variant of the retrovirus. A protein that comprises amino acid sequences from different origins or naturally occurring proteins may be referred to as a fusion, or chimeric protein.

[61] In some embodiments, a protein comprises a functional variant or functional fragment of a full-length wild type protein. A "functional fragment" or "functional portion", as used herein, refers to any portion of a reference protein (*e.g.*, a wild type protein) that encompasses less than the entire amino acid sequence of the reference protein while retaining one or more of the functions, *e.g.*, catalytic or binding functions. For example, a functional fragment of a reverse transcriptase may encompass less than the entire amino acid sequence of a wild type reverse transcriptase but retains the ability under at least one

set of conditions to catalyze the polymerization of a polynucleotide. When the reference protein is a fusion of multiple functional domains, a functional fragment thereof may retain one or more of the functions of at least one of the functional domains. For example, a functional fragment of a Cas9 may encompass less than the entire amino acid sequence of a wild type Cas9 but retains its DNA binding ability and lacks its nuclease activity partially or completely.

[62] A "functional variant" or "functional mutant", as used herein, refers to any variant or mutant of a reference protein (*e.g.*, a wild type protein) that encompasses one or more alterations to the amino acid sequence of the reference protein while retaining one or more of the functions, *e.g.*, catalytic or binding functions. In some embodiments, the one or more alterations to the amino acid sequence comprises amino acid substitutions, insertions or deletions, or any combination thereof. In some embodiments, the one or more alterations to the amino acid sequence comprises amino acid substitutions. For example, a functional variant of a reverse transcriptase may comprise one or more amino acid substitutions compared to the amino acid sequence of a wild type reverse transcriptase but retains the ability under at least one set of conditions to catalyze the polymerization of a polynucleotide. When the reference protein is a fusion of multiple functional domains, a functional variant thereof may retain one or more of the functions of at least one of the functional domains. For example, in some embodiments, a functional fragment of a Cas9 may comprise one or more amino acid substitutions in a nuclease domain, *e.g.*, an H840A amino acid substitution, compared to the amino acid sequence of a wild type Cas9, but retains the DNA binding ability and lacks the nuclease activity partially or completely.

[63] The term "function" and its grammatical equivalents as used herein may refer to a capability of operating, having, or serving an intended purpose. Functional may comprise any percent from baseline to 100% of an intended purpose. For example, functional may comprise or comprise about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or up to about 100% of an intended purpose. In some embodiments, the term functional may mean over or over about 100% of normal function, for example, 125%, 150%, 175%, 200%, 250%, 300%, 400%, 500%, 600%, 700% or up to about 1000% of an intended purpose.

[64] In some embodiments, a protein or polypeptides includes naturally occurring amino acids (*e.g.*, one of the twenty amino acids commonly found in peptides synthesized in nature, and known by the one letter abbreviations A, R, N, C, D, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y and V). In some embodiments, a protein or polypeptides includes non-naturally occurring amino acids (*e.g.*, amino acids which is not one of the twenty amino acids commonly found in peptides synthesized in nature, including synthetic amino acids, amino acid analogs, and amino acid mimetics). In some embodiments, a protein or polypeptide is modified.

[65] In some embodiments, a protein comprises an isolated polypeptide. The term "isolated" means free or removed to varying degrees from components which normally accompany it as found in the natural state or environment. For example, a polypeptide naturally present in a living animal is not

isolated, and the same polypeptide partially or completely separated from the coexisting materials of its natural state is isolated.

[66] In some embodiments, a protein is present within a cell, a tissue, an organ, or a virus particle. In some embodiments, a protein is present within a cell or a part of a cell (*e.g.*, a bacteria cell, a plant cell, or an animal cell). In some embodiments, the cell is in a tissue, in a subject, or in a cell culture. In some embodiments, the cell is a microorganism (*e.g.*, a bacterium, fungus, protozoan, or virus). In some embodiments, a protein is present in a mixture of analytes (*e.g.*, a lysate). In some embodiments, the protein is present in a lysate from a plurality of cells or from a lysate of a single cell.

[67] The terms "homologous," "homology," or "percent homology" as used herein refer to the degree of sequence identity between an amino acid and a corresponding reference amino acid sequence, or a polynucleotide sequence and a corresponding reference polynucleotide sequence. "Homology" can refer to polymeric sequences, *e.g.,* polypeptide or DNA sequences that are similar. Homology can mean, for example, nucleic acid sequences with at least about: 50%, 55%, 60%, 65%, 70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity. In other embodiments, a "homologous sequence" of nucleic acid sequences may exhibit 93%, 95% or 98% sequence identity to the reference nucleic acid sequence. For example, a "region of homology to a genomic region" can be a region of DNA that has a similar sequence to a given genomic region in the genome. A region of homology can be of any length that is sufficient to promote binding of a spacer, a primer binding site, or a protospacer sequence to the genomic region. For example, the region of homology can comprise at least 5, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, 2500, 2600, 2700, 2800, 2900, 3000, 3100 or more bases in length such that the region of homology has sufficient homology to undergo binding with the corresponding genomic region.

[68] When a percentage of sequence homology or identity is specified, in the context of two nucleic acid sequences or two polypeptide sequences, the percentage of homology or identity generally refers to the alignment of two or more sequences across a portion of their length when compared and aligned for maximum correspondence. When a position in the compared sequence can be occupied by the same base or amino acid, then the molecules can be homologous at that position. Unless stated otherwise, sequence homology or identity is assessed over the specified length of the nucleic acid, polypeptide or portion thereof. In some embodiments, the homology or identity is assessed over a functional portion or specified portion of the length.

[69] Alignment of sequences for assessment of sequence homology can be conducted by algorithms known in the art, such as the Basic Local Alignment Search Tool (BLAST) algorithm, which is described in Altschul et al, J. Mol. Biol. 215:403- 410, 1990. A publicly available, internet interface, for performing BLAST analyses is accessible through the National Center for Biotechnology Information. Additional known algorithms include those published in: Smith & Waterman, "Comparison of Biosequences", Adv.

Appl. Math. 2:482, 1981; Needleman & Wunsch, "A general method applicable to the search for similarities in the amino acid sequence of two proteins" J. Mol. Biol. 48:443, 1970; Pearson & Lipman "Improved tools for biological sequence comparison", Proc. Natl. Acad. Sci. USA 85:2444, 1988; or by automated implementation of these or similar algorithms. Global alignment programs may also be used to align similar sequences of roughly equal size. Examples of global alignment programs include NEEDLE (available at www.ebi.ac.uk/Tools/psa/emboss_needle/) which is part of the EMBOSS package (Rice P et al., Trends Genet., 2000; 16: 276-277), and the GGSEARCH program https://fasta.bioch.virginia.edu/fasta_www2/, which is part of the FASTA package (Pearson W and Lipman D, 1988, Proc. Natl. Acad. Sci. USA, 85: 2444-2448). Both of these programs are based on the Needleman-Wunsch algorithm which is used to find the optimum alignment (including gaps) of two sequences along their entire length. A detailed discussion of sequence analysis can also be found in Unit 19.3 of Ausubel et al ("Current Protocols in Molecular Biology" John Wiley & Sons Inc, 1994-1998, Chapter 15, 1998). In some embodiments, alignment between a query sequence and a reference sequence is performed with Needleman-Wunsch alignment with Gap Costs set to Existence: 11 Extension: 1 where percent identity is calculated by dividing the number of identities by the length of the alignment, as further described in Altschul et al.("Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402, 1997) and Altschul et al, ("Protein database searches using compositionally adjusted substitution matrices", FEBS J. 272:5101-5109, 2005).

[70] A skilled person understands that amino acid (or nucleotide) positions may be determined in homologous sequences based on alignment, for example, "H840" in a reference Cas9 sequence may correspond to H839, or another position in a Cas9 homolog.

[71] The term "polynucleotide" or "nucleic acid molecule" can be any polymeric form of nucleotides, including DNA, RNA, a hybridization thereof, or RNA-DNA chimeric molecules. In some embodiments, a polynucleotide comprises cDNA, genomic DNA, mRNA, tRNA, rRNA, or microRNA. In some embodiments, a polynucleotide is double stranded, *e.g.*, a double-stranded DNA in a gene. In some embodiments, a polynucleotide is single-stranded or substantially single-stranded, *e.g.*, single-stranded DNA or an mRNA. In some embodiments, a polynucleotide is a cell-free nucleic acid molecule. In some embodiments, a polynucleotide circulates in blood. In some embodiments, a polynucleotide is a cellular nucleic acid molecule. In some embodiments, a polynucleotide is a cellular nucleic acid molecule in a cell circulating in blood.

[72] Polynucleotides can have any three-dimensional structure. The following are nonlimiting examples of polynucleotides: a gene or gene fragment (for example, a probe, primer, EST or SAGE tag), an exon, an intron, intergenic DNA (including, without limitation, heterochromatic DNA), messenger RNA (mRNA), transfer RNA (tRNA), ribosomal RNA (rRNA), a ribozyme, cDNA, a recombinant polynucleotide, a branched polynucleotide, a plasmid, a vector, isolated DNA, isolated RNA, sgRNA, guide RNA, a nucleic acid probe, a primer, an snRNA, a long non-coding RNA, a snoRNA, a siRNA, a

miRNA, a tRNA-derived small RNA (tsRNA), an antisense RNA, an shRNA, or a small rDNA-derived RNA (srRNA).

[73] In some embodiments, a polynucleotide comprises deoxyribonucleotides, ribonucleotides or analogs thereof. In some embodiments, a polynucleotide comprises modified nucleotides, such as methylated nucleotides and nucleotide analogs. If present, modifications to the nucleotide structure can be imparted before or after assembly of the polynucleotide. The sequence of nucleotides can be interrupted by non-nucleotide components. A polynucleotide can be further modified after polymerization, such as by conjugation with a labeling component.

[74] In some embodiments, a polynucleotide is composed of a specific sequence of four nucleotide bases: adenine (A); cytosine (C); guanine (G); thymine (T); and uracil (U) for thymine when the polynucleotide is RNA. In some embodiments, the polynucleotide may comprise one or more other nucleotide bases, such as inosine (I), which is read by the translation machinery as guanine (G).

[75] In some embodiments, a polynucleotide may be modified. As used herein, the terms "modified" or "modification" refers to chemical modification with respect to the A, C, G, T and U nucleotides. In some embodiments, modifications may be on the nucleoside base and/or sugar portion of the nucleosides that comprise the polynucleotide. In some embodiments, the modification may be on the internucleoside linkage (*e.g.*, phosphate backbone). In some embodiments, multiple modifications are included in the modified nucleic acid molecule. In some embodiments, a single modification is included in the modified nucleic acid molecule.

[76] The term "complement", "complementary", or "complementarity" as used herein, refers to the ability of two polynucleotide molecules to base pair with each other. Complementary polynucleotides may base pair via hydrogen bonding, which may be Watson Crick, Hoogsteen or reversed Hoogsteen hydrogen bonding. For example, an adenine on one polynucleotide molecule will base pair to a thymine or uracil on a second polynucleotide molecule and a cytosine on one polynucleotide molecule will base pair to a guanine on a second polynucleotide molecule. Two polynucleotide molecules are complementary to each other when a first polynucleotide molecule comprising a first nucleotide sequence can base pair with a second polynucleotide molecule comprising a second nucleotide sequence. For instance, the two DNA molecules 5'-ATGC-3' and 5'-GCAT-3' are complementary, and the complement of the DNA molecule 5'-ATGC-3' is 5'-GCAT-3'. A percentage of complementarity indicates the percentage of nucleotides in a polynucleotide molecule which can base pair with a second polynucleotide molecule (*e.g.*, 5, 6, 7, 8, 9, 10 out of 10 being 50%, 60%, 70%, 80%, 90%, and 100% complementary, respectively). "Perfectly complementary" means that all the contiguous nucleotides of a polynucleotide molecule will base pair with the same number of contiguous nucleotides in a second polynucleotide molecule. "Substantially complementary" as used herein refers to a degree of complementarity that can be 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98%, or 99% over all or a portion of two polynucleotide molecules. In some embodiments, the portion of complementarity may be a region of 10, 15, 20, 25, 30, 35, 40, 45, 50, or more nucleotides. "Substantial complementary" can also refer to a

100% complementarity over a portion or region of two polynucleotide molecules. In some embodiments, the portion or region of complementarity between the two polynucleotide molecules is at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98%, or 99% of the length of at least one of the two polynucleotide molecules or a functional or defined portion thereof.

[77] As used herein, "expression" refers to the process by which polynucleotides are transcribed into mRNA and/or the process by which polynucleotides, e.g., the transcribed mRNA translated into peptides, polypeptides, or proteins. If the polynucleotide is derived from genomic DNA, expression may include splicing of the mRNA in a eukaryotic cell. In some embodiments, expression of a polynucleotide, *e.g.*, a gene or a DNA encoding a protein, is determined by the amount of the protein encoded by the gene after transcription and translation of the gene. In some embodiments, expression of a polynucleotide, *e.g.*, a gene or a DNA encoding a protein, is determined by the amount of a functional form of the protein encoded by the gene after transcription and translation of the gene. In some embodiments, expression of a gene is determined by the amount of the mRNA, or transcript, that is encoded by the gene after transcription the gene. In some embodiments, expression of a polynucleotide, *e.g.*, an mRNA, is determined by the amount of the protein encoded by the mRNA after translation of the mRNA. In some embodiments, expression of a polynucleotide, e.g., a mRNA or coding RNA, is determined by the amount of a functional form of the protein encoded by the polypeptide after translation of the polynucleotide.

[78] The term "sequencing" as used herein, may comprise capillary sequencing, bisulfite-free sequencing, bisulfite sequencing, TET-assisted bisulfite (TAB) sequencing, ACE-sequencing, high-throughput sequencing, Maxam-Gilbert sequencing, massively parallel signature sequencing, Polony sequencing, 454 pyrosequencing, Sanger sequencing, Illumina sequencing, SOLiD sequencing, Ion Torrent semiconductor sequencing, DNA nanoball sequencing, Heliscope single molecule sequencing, single molecule real time (SMRT) sequencing, nanopore sequencing, shot gun sequencing, RNA sequencing, or any combination thereof.

[79] The terms "equivalent" or "biological equivalent" are used interchangeably when referring to a particular molecule, or biological or cellular material, and means a molecule having minimal homology to another molecule while still maintaining a desired structure or functionality.

[80] The term "encode" as it is applied to polynucleotides refers to a polynucleotide which is said to "encode" another polynucleotide, a polypeptide, or an amino acid if, in its native state or when manipulated by methods well known to those skilled in the art, it can be used as polynucleotide synthesis template, *e.g.*, transcribed into an RNA, reverse transcribed into a DNA or cDNA, and/or translated to produce an amino acid, or a polypeptide or fragment thereof. In some embodiments, a polynucleotide comprising three contiguous nucleotides form a codon that encodes a specific amino acid. In some embodiments, a polynucleotide comprises one or more codons that encode a polypeptide. In some embodiments, a polynucleotide comprising one or more codons comprises a mutation in a codon compared to a wild-type reference polynucleotide. In some embodiments, the mutation in the codon

encodes an amino acid substitution in a polypeptide encoded by the polynucleotide as compared to a wild-type reference polypeptide.

[81] The term "mutation" as used herein refers to a change and/or alteration in an amino acid sequence of a protein or nucleic acid sequence of a polynucleotide. Such changes and/or alterations may comprise the substitution, insertion, deletion and/or truncation of one or more amino acids, in the case of an amino acid sequence, and/or nucleotides, in the case of nucleic acid sequence, compared to a reference amino acid or a reference nucleic acid sequence. In some embodiments, the reference sequence is a wild-type sequence. In some embodiments, a mutation in a nucleic acid sequence of a polynucleotide encodes a mutation in the amino acid sequence of a polypeptide. In some embodiments, the mutation in the amino acid sequence of the polypeptide or the mutation in the nucleic acid sequence of the polynucleotide is a mutation associated with a disease state.

[82] The term "subject" and its grammatical equivalents as used herein may refer to a human or a non-human. A subject may be a mammal. A human subject may be male or female. A human subject may be of any age. A subject may be a human embryo. A human subject may be a newborn, an infant, a child, an adolescent, or an adult. A human subject may be up to about 100 years of age. A human subject may be in need of treatment for a genetic disease or disorder.

[83] The terms "treatment" or "treating" and their grammatical equivalents may refer to the medical management of a subject with an intent to cure, ameliorate, or ameliorate a symptom of, a disease, condition, or disorder. Treatment may include active treatment, that is, treatment directed specifically toward the improvement of a disease, condition, or disorder. Treatment may include causal treatment, that is, treatment directed toward removal of the cause of the associated disease, condition, or disorder. In addition, this treatment may include palliative treatment, that is, treatment designed for the relief of symptoms rather than the curing of the disease, condition, or disorder. Treatment may include supportive treatment, that is, treatment employed to supplement another specific therapy directed toward the improvement of the disease, condition, or disorder. In some embodiments, a condition may be pathological. In some embodiments, a treatment may not completely cure or prevent a disease, condition, or disorder. In some embodiments, a treatment ameliorates, but does not completely cure or prevent a disease, condition, or disorder. In some embodiments, a subject may be treated for 12 hours, 24 hours, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 2 weeks, 3 weeks, 4 weeks, 2 months, 3 months, 4 months, 5 months, 6 months, 1 year, 2 years, 3 years, 4 years, 5 years, 6 years, indefinitely, or life of the subject.

[84] The term "ameliorate" and its grammatical equivalents means to decrease, suppress, attenuate, diminish, arrest, or stabilize the development or progression of a disease.

[85] The terms "prevent" or "preventing" means delaying, forestalling, or avoiding the onset or development of a disease, condition, or disorder for a period of time. Prevent also means reducing risk of developing a disease, disorder, or condition. Prevention includes minimizing or partially or completely inhibiting the development of a disease, condition, or disorder. In some embodiments, a composition, *e.g.* a pharmaceutical composition, prevents a disorder by delaying the onset of the disorder for 12 hours, 24

hours, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 2 weeks, 3 weeks, 4 weeks, 2 months, 3 months, 4 months, 5 months, 6 months, 1 year, 2 years, 3 years, 4 years, 5 years, 6 years, indefinitely, or life of a subject.

[86] The term "effective amount" or "therapeutically effective amount" refers to a quantity of a composition, for example a prime editing composition comprising a construct, that can be sufficient to result in a desired activity upon introduction into a subject as disclosed herein. An effective amount of the prime editing compositions can be provided to the target gene or cell, whether the cell is *ex vivo* or *in vivo*. An effective amount can be the amount to induce, for example, at least about a 2-fold change (increase or decrease) or more in the amount of target nucleic acid modulation (*e.g.*, expression of ATP7B gene to produce functional ATP7B protein) observed relative to a negative control. An effective amount or dose can induce, for example, about 2-fold increase, about 3-fold increase, about 4-fold increase, about 5-fold increase, about 6-fold increase, about 7-fold increase, about 8-fold increase, about 9-fold increase, about 10-fold increase, about 25-fold increase, about 50-fold increase, about 100-fold increase, about 200-fold increase, about 500-fold increase, about 700-fold increase, about 1000-fold increase, about 5000-fold increase, or about 10,000-fold increase in target gene modulation (*e.g.*, expression of a target *ATP7B* gene to produce functional ATP7B protein). The amount of target gene modulation may be measured by any suitable method known in the art. In some embodiments, the "effective amount" or "therapeutically effective amount" is the amount of a composition that is required to ameliorate the symptoms of a disease relative to an untreated patient. In some embodiments, an effective amount is the amount of a composition sufficient to introduce an alteration in a gene of interest in a cell (*e.g.*, a cell *in vitro* or *in vivo*).

[87] An effective amount can be an amount to induce, when administered to a population of cells, a certain percentage of the population of cells to have a correction of a mutation. For example, in some embodiments, an effective amount can be the amount to induce, when administered to or introduced to a population of cells, installation of one or more intended nucleotide edits that correct a mutation in the target *ATP7B* gene, in at least about 1%, 2%, 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 99% of the population of cells.

[88] As used herein, the terms "Wilson's disease," "Wilsons disease," and "Wilson disease" are used interchangeably. Wilson's disease is a monogenic autosomal-recessive disorder caused by pathogenic variants in ATP7B that decrease ATP7B function in hepatocytes and reduce excretion of excess copper into bile, leading to systemic copper buildup, hepatic and neural toxicity, and early demise. In some embodiments, mutations in the *ATP7B* gene are associated with diseases including Wilson's disease. The *ATP7B* gene codes for a copper transporter expressed in hepatic and neural tissues. The gene product is synthesized in the endoplasmic reticulum, then relocated to the trans Golgi network (TGN) within hepatocytes. *ATP7B* is most highly expressed in the liver, but is also found in the kidney, placenta, mammary glands, brain, and lung. Alternate names for ATP7B include: ATPase Copper Transporting

Beta, Copper-Transporting ATPase, Copper Pump, ATPase, Cu++ Transporting, Beta Polypeptide, Wilson Disease-Associated Protein, PWD, WC1, WND, ATPase, Cu++ Transporting, Beta Polypeptide (Wilson Disease) 2, ATPase, Cu(2+)- Transporting, Beta Polypeptide, Copper-Transporting Protein ATP7B, Wilson Disease, EC 3.6.3.4, EC 7.2.2.8, EC 3.6.3, WD. In the human genome the *ATP7B* gene is located on 13q14.3 and contains 20 introns and 21 exons, for a total genomic length of 80 kb (chr13:51,930,436-52,012,130(GRCh38/hg38)).

[89] More than 600 pathogenic variants in *ATP7B* have been identified, with single-nucleotide missense and nonsense mutations being the most common, followed by insertions, deletions, and splice site mutations. Individuals with the arginine to leucine substitution at amino acid 778 (p.R778L) (caused by c.2333G>T) in *ATP7B* have been shown to have an earlier onset of disease and predominantly hepatic presentation (*See* Wu Z-Y, Lin MT, Murong SX, et al. Molecular diagnosis and prophylactic therapy for presymptomatic Chinese patients with Wilson disease. Arch Neurol. 2003;60(5):737–741). Geographically, the p.Arg778Leu mutation has been reported to be the most common mutation in Far East Asian countries. The p.R778L mutation has a population allelic frequency of about 10-40% (*e.g.*, about 38% among Korean patients with Wilson's Disease; *see* Kim EK, Yoo OJ, Song KY, et al. Identification of three novel mutations and a high frequency of the Arg778Leu mutation in Korean patients with Wilson disease. Hum Mutat. 1998;11(4):275–278.) The p.R778L mutation has been shown to affect mutation affects transmembrane transport of copper. *See* Dmitriev OY, Bhattacharjee A, Nokhrin S, *et al.*

Prime Editing

[90] The term "prime editing" refers to programmable editing of a target DNA using a prime editor complexed with a PEgRNA to incorporate an intended nucleotide edit (also referred to herein as a nucleotide change) into the target DNA through target-primed DNA synthesis. A target gene of prime editing may comprise a double stranded DNA molecule having two complementary strands: a first strand that may be referred to as a "target strand" or a "non-edit strand", and a second strand that may be referred to as a "non-target strand," or an "edit strand." In some embodiments, in a prime editing guide RNA (PEgRNA), a spacer sequence is complementary or substantially complementary to a specific sequence on the target strand, which may be referred to as a "search target sequence". In some embodiments, the spacer sequence anneals with the target strand at the search target sequence. The target strand may also be referred to as the "non-Protospacer Adjacent Motif (non-PAM strand)." In some embodiments, the non-target strand may also be referred to as the "PAM strand". In some embodiments, the PAM strand comprises a protospacer sequence and optionally a protospacer adjacent motif (PAM) sequence. In prime editing using a Cas-protein-based prime editor, a PAM sequence refers to a short DNA sequence immediately adjacent to the protospacer sequence on the PAM strand of the target gene. A PAM sequence may be specifically recognized by a programmable DNA binding protein, e.g., a Cas nickase or a Cas nuclease. In some embodiments, a specific PAM is characteristic of a specific

programmable DNA binding protein, e.g., a Cas nickase or a Cas nuclease. A protospacer sequence refers to a specific sequence in the PAM strand of the target gene that is complementary to the search target sequence. In a PEgRNA, a spacer sequence may have a substantially identical sequence as the protospacer sequence on the edit strand of a target gene, except that the spacer sequence may comprise Uracil (U) and the protospacer sequence may comprise Thymine (T).

[91] In some embodiments, the double stranded target DNA comprises a nick site on the PAM strand (or non-target strand). As used herein, a "nick site" refers to a specific position in between two nucleotides or two base pairs of the double stranded target DNA. In some embodiments, the position of a nick site is determined relative to the position of a specific PAM sequence. In some embodiments, the nick site is the particular position where a nick will occur when the double stranded target DNA is contacted with a nickase, for example, a Cas nickase, that recognizes a specific PAM sequence. In some embodiments, the nick site is upstream of a specific PAM sequence on the PAM strand of the double stranded target DNA. In some embodiments, the nick site is downstream of a specific PAM sequence on the PAM strand of the double stranded target DNA. In some embodiments, the nick site is upstream of a PAM sequence recognized by a Cas9 nickase, wherein the Cas9 nickase comprises a nuclease active RuvC domain and a nuclease inactive HNH domain. In some embodiments, the nick site is 3 nucleotides upstream of the PAM sequence, and the PAM sequence is recognized by a Streptococcus pyogenes Cas9 nickase, a *P. lavamentivorans* Cas9 nickase, a *C. diphtheriae* Cas9 nickase, a *N. cinerea* Cas9, a *S. aureus* Cas9, or a *N. lari* Cas9 nickase.

[92] In some embodiments, the nick site is 3 base pairs upstream of the PAM sequence, and the PAM sequence is recognized by a Cas9 nickase, wherein the Cas9 nickase that comprises a nuclease active HNH domain and a nuclease inactive RuvC domain. In some embodiments, the nick site is 2 nucleotides upstream of the PAM sequence, and the PAM sequence is recognized by a *S. thermophilus* Cas9 nickase that comprises a nuclease active RuvC domain and a nuclease inactive HNH domain.

[93] A "primer binding site" (PBS or primer binding site sequence) is a single-stranded portion of the PEgRNA that comprises a region of complementarity to the PAM strand (i.e., the non-target strand or the edit strand). The PBS is complementary or substantially complementary to a sequence on the PAM strand of the double stranded target DNA that is immediately upstream of the nick site. In some embodiments, in the process of prime editing, the PEgRNA complexes with and directs a prime editor to bind the search target sequence on the target strand of the double stranded target DNA and generates a nick at the nick site on the non-target strand of the double stranded target DNA. In some embodiments, the PBS is complementary to or substantially complementary to, and can anneal to, a free 3′ end on the non-target strand of the double stranded target DNA at the nick site. In some embodiments, the PBS annealed to the free 3′ end on the non-target strand can initiate target-primed DNA synthesis.

[94] An "editing template" of a PEgRNA is a single-stranded portion of the PEgRNA that is 5′ of the PBS and comprises a region of complementarity to the PAM strand (i.e., the non-target strand or the edit strand), and comprises one or more intended nucleotide edits compared to the endogenous sequence of

the double stranded target DNA. In some embodiments, the editing template and the PBS are immediately adjacent to each other. Accordingly, in some embodiments, a PEgRNA in prime editing comprises a single-stranded portion that comprises the PBS and the editing template immediately adjacent to each other. In some embodiments, the single stranded portion of the PEgRNA comprising both the PBS and the editing template is complementary or substantially complementary to an endogenous sequence on the PAM strand (i.e., the non-target strand or the edit strand) of the double stranded target DNA except for one or more non-complementary nucleotides at the intended nucleotide edit positions. As used herein, regardless of relative 5′-3′ positioning in other context, the relative positions as between the PBS and the editing template, and the relative positions as among elements of a PEgRNA, are determined by the 5′ to 3′ order of the PEgRNA as a single molecule regardless of the position of sequences in the double stranded target DNA that may have complementarity or identity to elements of the PEgRNA. In some embodiments, the editing template is complementary or substantially complementary to a sequence on the PAM strand that is immediately downstream of the nick site, except for one or more non-complementary nucleotides at the intended nucleotide edit positions. The endogenous, *e.g.*, genomic, sequence that is complementary or substantially complementary to the editing template, except for the one or more non-complementary nucleotides at the position corresponding to the intended nucleotide edit, may be referred to as an "editing target sequence". In some embodiments, the editing template has identity or substantial identity to a sequence on the target strand that is complementary to, or having the same position in the genome as, the editing target sequence, except for one or more insertions, deletions, or substitutions at the intended nucleotide edit positions. In some embodiments, the editing template encodes a single stranded DNA, wherein the single stranded DNA has identity or substantial identity to the editing target sequence except for one or more insertions, deletions, or substitutions at the positions of the one or more intended nucleotide edits.

[95] In some embodiments, a PEgRNA complexes with and directs a prime editor to bind to the search target sequence of the target gene. In some embodiments, the bound prime editor generates a nick on the edit strand (PAM strand) of the target gene at the nick site. In some embodiments, a primer binding site (PBS) of the PEgRNA anneals with a free 3' end formed at the nick site, and the prime editor initiates DNA synthesis from the nick site, using the free 3' end as a primer. Subsequently, a single-stranded DNA encoded by the editing template of the PEgRNA is synthesized. In some embodiments, the newly synthesized single-stranded DNA comprises one or more intended nucleotide edits compared to an endogenous target gene sequence. Accordingly, in some embodiments, the editing template of a PEgRNA is complementary to a sequence in the edit strand except for one or more mismatches at the intended nucleotide edit positions in the editing template. The endogenous, *e.g.*, genomic, sequence that is partially complementary to the editing template may be referred to as an "editing target sequence". Accordingly, in some embodiments, the newly synthesized single stranded DNA has identity or substantial identity to a sequence in the editing target sequence, except for one or more insertions, deletions, or substitutions at the intended nucleotide edit positions.

[96] In some embodiments, the newly synthesized single-stranded DNA equilibrates with the editing target on the edit strand of the target gene for pairing with the target strand of the target gene. In some embodiments, the editing target sequence of the target gene is excised by a flap endonuclease (FEN), for example, FEN1. In some embodiments, the FEN is an endogenous FEN, for example, in a cell comprising the target gene. In some embodiments, the FEN is provided as part of the prime editor, either linked to other components of the prime editor or provided in *trans*. In some embodiments, the newly synthesized single stranded DNA, which comprises the intended nucleotide edit, replaces the endogenous single stranded editing target sequence on the edit strand of the target gene. In some embodiments, the newly synthesized single stranded DNA and the endogenous DNA on the target strand form a heteroduplex DNA structure at the region corresponding to the editing target sequence of the target gene. In some embodiments, the newly synthesized single-stranded DNA comprising the nucleotide edit is paired in the heteroduplex with the target strand of the target DNA that does not comprise the nucleotide edit, thereby creating a mismatch between the two otherwise complementary strands. In some embodiments, the mismatch is recognized by DNA repair machinery, *e.g.*, an endogenous DNA repair machinery. In some embodiments, through DNA repair, the intended nucleotide edit is incorporated into the target gene.

Prime Editor

[97] The term "prime editor (PE)" refers to the polypeptide or polypeptide components involved in prime editing, or any polynucleotide(s) encoding the polypeptide or polypeptide components. In various embodiments, a prime editor includes a polypeptide domain having DNA binding activity and a polypeptide domain having DNA polymerase activity. In some embodiments, the prime editor further comprises a polypeptide domain having nuclease activity. In some embodiments, the polypeptide domain having DNA binding activity comprises a nuclease domain or nuclease activity. In some embodiments, the polypeptide domain having nuclease activity comprises a nickase, or a fully active nuclease. As used herein, the term "nickase" refers to a nuclease capable of cleaving only one strand of a double-stranded DNA target. In some embodiments, the prime editor comprises a polypeptide domain that is an inactive nuclease. In some embodiments, the polypeptide domain having programmable DNA binding activity comprises a nucleic acid guided DNA binding domain, for example, a CRISPR-Cas protein, for example, a Cas9 nickase, a Cpf1 nickase, or another CRISPR-Cas nuclease. In some embodiments, the polypeptide domain having DNA polymerase activity comprises a template-dependent DNA polymerase, for example, a DNA-dependent DNA polymerase or an RNA-dependent DNA polymerase. In some embodiments, the DNA polymerase is a reverse transcriptase. In some embodiments, the prime editor comprises additional polypeptides involved in prime editing, for example, a polypeptide domain having a 5' endonuclease activity, *e.g.*, a 5' endogenous DNA flap endonucleases (*e.g.*, FEN1), for helping to drive the prime editing process towards the edited product formation. In some embodiments, the prime editor further comprises an RNA-protein recruitment polypeptide, for example, a MS2 coat protein.

[98] A prime editor may be engineered. In some embodiments, the polypeptide components of a prime editor do not naturally occur in the same organism or cellular environment. In some embodiments, the polypeptide components of a prime editor may be of different origins or from different organisms. In some embodiments, a prime editor comprises a DNA binding domain and a DNA polymerase domain that are derived from different species. In some embodiments, a prime editor comprises a Cas polypeptide (DNA binding domain) and a reverse transcriptase polypeptide (DNA polymerase) that are derived from different species. For example, a prime editor may comprise a *S.pyogenes* Cas9 polypeptide and a Moloney murine leukemia virus (M-MLV) reverse transcriptase polypeptide.

[99] In some embodiments, polypeptide domains of a prime editor may be fused or linked by a peptide linker to form a fusion protein. In other embodiments, a prime editor comprises one or more polypeptide domains provided in *trans* as separate proteins, which are capable of being associated to each other through non-peptide linkages or through aptamers or recruitment sequences. For example, a prime editor may comprise a DNA binding domain and a reverse transcriptase domain associated with each other by an RNA-protein recruitment aptamer, *e.g.*, a MS2 aptamer, which may be linked to a PEgRNA. Prime editor polypeptide components may be encoded by one or more polynucleotides in whole or in part. In some embodiments, a single polynucleotide, construct, or vector encodes the prime editor fusion protein. In some embodiments, multiple polynucleotides, constructs, or vectors each encode a polypeptide domain or portion of a domain of a prime editor, or a portion of a prime editor fusion protein. For example, a prime editor fusion protein may comprise an N-terminal portion fused to an intein-N and a C-terminal portion fused to an intein-C, each of which is individually encoded by an AAV vector.

Prime Editor Nucleotide Polymerase Domain

[100] In some embodiments, a prime editor comprises a nucleotide polymerase domain, *e.g.*, a DNA polymerase domain. The DNA polymerase domain may be a wild-type DNA polymerase domain, a full-length DNA polymerase protein domain, or may be a functional mutant, a functional variant, or a functional fragment thereof. In some embodiments, the polymerase domain is a template dependent polymerase domain. For example, the DNA polymerase may rely on a template polynucleotide strand, *e.g.*, the editing template sequence, for new strand DNA synthesis. In some embodiments, the prime editor comprises a DNA-dependent DNA polymerase. For example, a prime editor having a DNA-dependent DNA polymerase can synthesize a new single stranded DNA using a PEgRNA editing template that comprises a DNA sequence as a template. In such cases, the PEgRNA is a chimeric or hybrid PEgRNA, and comprising an extension arm comprising a DNA strand. The chimeric or hybrid PEgRNA may comprise an RNA portion (including the spacer and the gRNA core) and a DNA portion (the extension arm comprising the editing template that includes a strand of DNA).

[101] The DNA polymerases can be wild type polymerases from eukaryotic, prokaryotic, archaeal, or viral organisms, and/or the polymerases may be modified by genetic engineering, mutagenesis, or directed

evolution-based processes. The polymerases can be a T7 DNA polymerase, T5 DNA polymerase, T4 DNA polymerase, Klenow fragment DNA polymerase, DNA polymerase III and the like. The polymerases can be thermostable, and can include Taq, Tne, Tma, Pfu, Tfl, Tth, Stoffel fragment, VENT® and DEEPVENT® DNA polymerases, KOD, Tgo, JDF3, and mutants, variants and derivatives thereof.

[102] In some embodiments, the DNA polymerase is a bacteriophage polymerase, for example, a T4, T7, or phi29 DNA polymerase. In some embodiments, the DNA polymerase is an archaeal polymerase, for example, pol I type archaeal polymerase or a pol II type archaeal polymerase. In some embodiments, the DNA polymerase comprises a thermostable archaeal DNA polymerase. In some embodiments, the DNA polymerase comprises a eubacterial DNA polymerase, for example, Pol I, Pol II, or Pol III polymerase. In some embodiments, the DNA polymerase is a Pol I family DNA polymerase. In some embodiments, the DNA polymerase is a E.coli Pol I DNA polymerase. In some embodiments, the DNA polymerase is a Pol II family DNA polymerase. In some embodiments, the DNA polymerase is a *Pyrococcus furiosus* (Pfu) Pol II DNA polymerase. In some embodiments, the DNA Polymerase is a Pol IV family DNA polymerase. In some embodiments, the DNA polymerase is a E.coli Pol IV DNA polymerase. In some embodiments, the DNA polymerase comprises a eukaryotic DNA polymerase. In some embodiments, the DNA polymerase is a Pol-beta DNA polymerase, a Pol-lambda DNA polymerase, a Pol-sigma DNA polymerase, or a Pol-mu DNA polymerase. In some embodiments, the DNA polymerase is a Pol-alpha DNA polymerase. In some embodiments, the DNA polymerase is a POLA1 DNA polymerase. In some embodiments, the DNA polymerase is a POLA2 DNA polymerase. In some embodiments, the DNA polymerase is a Pol-delta DNA polymerase. In some embodiments, the DNA polymerase is a POLD1 DNA polymerase. In some embodiments, the DNA polymerase is a POLD2 DNA polymerase. In some embodiments, the DNA polymerase is a human POLD1 DNA polymerase. In some embodiments, the DNA polymerase is a human POLD2 DNA polymerase In some embodiments, the DNA polymerase is a POLD3 DNA polymerase. In some embodiments, the DNA polymerase is a POLD4 DNA polymerase. In some embodiments, the DNA polymerase is a Pol-epsilon DNA polymerase. In some embodiments, the DNA polymerase is a POLE1 DNA polymerase. In some embodiments, the DNA polymerase is a POLE2 DNA polymerase. In some embodiments, the DNA polymerase is a POLE3 DNA polymerase. In some embodiments, the DNA polymerase is a Pol-eta (POLH) DNA polymerase. In some embodiments, the DNA polymerase is a Pol-iota (POLI) DNA polymerase. In some embodiments, the DNA polymerase is a Pol-kappa (POLK) DNA polymerase. In some embodiments, the DNA polymerase is a Rev1 DNA polymerase. In some embodiments, the DNA polymerase is a human Rev1 DNA polymerase. In some embodiments, the DNA polymerase is a viral DNA-dependent DNA polymerase. In some embodiments, the DNA polymerase is a B family DNA polymerases. In some embodiments, the DNA polymerase is a herpes simplex virus (HSV) UL30 DNA polymerase. In some embodiments, the DNA polymerase is a cytomegalovirus (CMV) UL54 DNA polymerase.

[103] In some embodiments, the DNA polymerase is an archaeal polymerase. In some embodiments, the DNA polymerase is a Family B/pol I type DNA polymerase. For example, in some embodiments, the DNA polymerase is a homolog of Pfu from *Pyrococcus furiosus*. In some embodiments, the DNA polymerase is a pol II type DNA polymerase. For example, in some embodiments, the DNA polymerase is a homolog of *P. furiosus* DP1/DP2 2-subunit polymerase. In some embodiments, the DNA polymerase lacks 5′ to 3′ nuclease activity. Suitable DNA polymerases (pol I or pol II) can be derived from archaea with optimal growth temperatures that are similar to the desired assay temperatures.

[104] In some embodiments, the DNA polymerase comprises a thermostable archaeal DNA polymerase. In some embodiments, the thermostable DNA polymerase is isolated or derived from *Pyrococcus* species (furiosus, species GB-D, w*oesii, abysii, horikoshii*), *Thermococcus* species (kodakaraensis KOD1, litoralis, species 9 degrees North-7, species JDF-3, gorgonarius), *Pyrodictium occultum*, and *Archaeoglobus fulgidus*.

[105] Polymerases may also be from eubacterial species. In some embodiments, the DNA polymerase is a Pol I family DNA polymerase. In some embodiments, the DNA polymerase is an *E.coli* Pol I DNA polymerase. In some embodiments, the DNA polymerase is a Pol II family DNA polymerase. In some embodiments, the DNA polymerase is a *Pyrococcus furiosus* (Pfu) Pol II DNA polymerase. In some embodiments, the DNA Polymerase is a Pol III family DNA polymerase. In some embodiments, the DNA Polymerase is a Pol IV family DNA polymerase. In some embodiments, the DNA polymerase is an *E.coli* Pol IV DNA polymerase. In some embodiments, the Pol I DNA polymerase is a DNA polymerase functional variant that lacks or has reduced 5′ to 3′ exonuclease activity.

[106] Suitable thermostable pol I DNA polymerases can be isolated from a variety of thermophilic eubacteria, including *Thermus* species and *Thermotoga maritima* such as *Thermus aquaticus* (Taq), *Thermus thermophilus* (Tth) and *Thermotoga maritima* (Tma UlTma).

[107] In some embodiments, a prime editor comprises an RNA-dependent DNA polymerase domain, for example, a reverse transcriptase (RT). A RT or an RT domain may be a wild type RT domain, a full-length RT domain, or may be a functional mutant, a functional variant, or a functional fragment thereof. An RT or an RT domain of a prime editor may comprise a wild-type RT, or may be engineered or evolved to contain specific amino acid substitutions, truncations, or variants. An engineered RT may comprise sequences or amino acid changes different from a naturally occurring RT. In some embodiments, the engineered RT may have improved reverse transcription activity over a naturally occurring RT or RT domain. In some embodiments, the engineered RT may have improved features over a naturally occurring RT, for example, improved thermostability, reverse transcription efficiency, or target fidelity. In some embodiments, a prime editor comprising the engineered RT has improved prime editing efficiency over a prime editor having a reference naturally occurring RT.

[108] In some embodiments, a prime editor comprises a virus RT, for example, a retrovirus RT. Non-limiting examples of virus RT include Moloney murine leukemia virus (M-MLV or MLVRT or M-MLV RT); human T-cell leukemia virus type 1 (HTLV-1) RT; bovine leukemia virus (BLV) RT; Rous

Sarcoma Virus (RSV) RT; human immunodeficiency virus (HIV) RT, M-MFV RT, Avian Sarcoma-Leukosis Virus (ASLV) RT, Rous Sarcoma Virus (RSV) RT, Avian Myeloblastosis Virus (AMV) RT, Avian Erythroblastosis Virus (AEV) Helper Virus MCAV RT, Avian Myelocytomatosis Virus MC29 Helper Virus MCAV RT, Avian Reticuloendotheliosis Virus (REV-T) Helper Virus REV-A RT, Avian Sarcoma Virus UR2 Helper Virus (UR2AV) RT, Avian Sarcoma Virus Y73 Helper Virus YAV RT, Rous Associated Virus (RAV) RT, and Myeloblastosis Associated Virus (MAV) RT, all of which may be suitably used in the methods and composition described herein.

[109] In some embodiments, the prime editor comprises a wild-type M-MLV RT, a functional mutant, a functional variant, or a functional fragment thereof. In some embodiments, the prime editor comprises a reference M-MLV RT, a functional mutant, a functional variant, or a functional fragment thereof. In some embodiments, the RT domain or a RT is a M-MLV RT (e.g., wild-type M-MLV RT, a functional mutant, a functional variant, or a functional fragment thereof). In some embodiments, the RT domain or a RT is a M-MLV RT (e.g., a reference M-MLV RT, a functional mutant, a functional variant, or a functional fragment thereof). In some embodiments, a MMLV RT, e.g., reference MMLV RT, comprises a sequence as disclosed in SEQ ID NO: 14827.

[110] In some embodiments, a reference M-MLV RT is a wild-type M-MLV RT. An exemplary sequence of a reference M-MLV RT is provided in SEQ ID NO: 14826. In some embodiments, the prime editor comprises a wild type M-MLV RT. An exemplary sequence of a wild type M-MLV RT is provided in SEQ ID NO: 14826.

[111] TLNIEDEHRLHETSKEPDVSLGSTWLSDFPQAWAETGGMGLAVRQAPLIIPLKATSTPVSI
KQYPMSQEARLGIKPHIQRLLDQGILVPCQSPWNTPLLPVKKPGTNDYRPVQDLREVNKRVEDI
HPTVPNPYNLLSGLPPSHQWYTVLDLKDAFFCLRLHPTSQPLFAFEWRDPEMGISGQLTWTRLP
QGFKNSPTLFDEALHRDLADFRIQHPDLILLQYVDDLLLAATSELDCQQGTRALLQTLGNLGYR
ASAKKAQICQKQVKYLGYLLKEGQRWLTEARKETVMGQPTPKTPRQLREFLGTAGFCRLWIPG
FAEMAAPLYPLTKTGTLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYAKG
VLTQKLGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPLVILAPHAVE
ALVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLPLPEEGLQHNCLDILAEAHG
TRPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGAAVTTETEVIWAKALPAGTSAQRAELIALTQ
ALKMAEGKKLNVYTDSRYAFATAHIHGEIYRRRGLLTSEGKEIKNKDEILALLKALFLPKRLSIIH
CPGHQKGHSAEARGNRMADQAARKAAITETPDTSTLLIENSSP (SEQ ID NO: 14826)

[112] In some embodiments, the prime editor comprises a reference M-MLV RT. An exemplary amino acid sequence of a reference M-MLV RT is provided in SEQ ID NO: 14827

[113] TLNIEDEYRLHETSKEPDVSLGSTWLSDFPQAWAETGGMGLAVRQAPLIIPLKATSTPVSI
KQYPMSQEARLGIKPHIQRLLDQGILVPCQSPWNTPLLPVKKPGTNDYRPVQDLREVNKRVEDI
HPTVPNPYNLLSGLPPSHQWYTVLDLKDAFFCLRLHPTSQPLFAFEWRDPEMGISGQLTWTRLP
QGFKNSPTLFDEALHRDLADFRIQHPDLILLQYVDDLLLAATSELDCQQGTRALLQTLGNLGYR
ASAKKAQICQKQVKYLGYLLKEGQRWLTEARKETVMGQPTPKTPRQLREFLGTAGFCRLWIPG

FAEMAAPLYPLTKTGTLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYAKG
VLTQKLGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPLVILAPHAVE
ALVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLPLPEEGLQHNCLDILAEAHG
TRPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGAAVTTETEVIWAKALPAGTSAQRAELIALTQ
ALKMAEGKKLNVYTDSRYAFATAHIHGEIYRRRGLLTSEGKEIKNKDEILALLKALFLPKRLSIIH
CPGHQKGHSAEARGNRMADQAARKAAITETPDTSTLLIENSSP (SEQ ID NO: 14827)

[114] In some embodiments, the prime editor comprises a M-MLV RT comprising one or more of amino acid substitutions P51X, S67X, E69X, L139X, T197X, D200X, H204X, F209X, E302X, T306X, F309X, W313X, T330X, L345X, L435X, N454X, D524X, E562X, D583X, H594X, L603X, E607X, or D653X as compared to the reference M-MLV RT as set forth in SEQ ID NO: 14827, where X is any amino acid other than the original amino acid in the reference M-MLV RT. In some embodiments, the prime editor comprises a M-MLV RT comprising one or more of amino acid substitutions P51L, S67K, E69K, L139P, T197A, D200N, H204R, F209N, E302K, E302R, T306K, F309N, W313F, T330P, L345G, L435G, N454K, D524G, E562Q, D583N, H594Q, L603W, E607K, and D653N as compared to the reference M-MLV RT as set forth in SEQ ID NO: 14827. In some embodiments, the prime editor comprises a M-MLV RT comprising one or more amino acid substitutions D200N, T330P, L603W, T306K, and W313F as compared to the wild type M-MLV RT (e.g., SEQ ID NO: 14826), e.g., as set forth in SEQ ID NO: 14828(MMLV-RT^{5M}). In some embodiments, the prime editor comprises a reference M-MLV RT, having an amino acid sequence as set forth in SEQ ID NO: 14828.

[115] TLNIEDEYRLHETSKEPDVSLGSTWLSDFPQAWAETGGMGLAVRQAPLIIPLKATSTPVSI
KQYPMSQEARLGIKPHIQRLLDQGILVPCQSPWNTPLLPVKKPGTNDYRPVQDLREVNKRVEDI
HPTVPNPYNLLSGLPPSHQWYTVLDLKDAFFCLRLHPTSQPLFAFEWRDPEMGISGQLTWTRLP
QGFKNSPTLFNEALHRDLADFRIQHPDLILLQYVDDLLLAATSELDCQQGTRALLQTLGNLGYR
ASAKKAQICQKQVKYLGYLLKEGQRWLTEARKETVMGQPTPKTPRQLREFLGKAGFCRLFIPGF
AEMAAPLYPLTKPGTLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYAKGV
LTQKLGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPLVILAPHAVEA
LVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLPLPEEGLQHNCLDILAEAHGT
RPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGAAVTTETEVIWAKALPAGTSAQRAELIALTQ
ALKMAEGKKLNVYTDSRYAFATAHIHGEIYRRRGWLTSEGKEIKNKDEILALLKALFLPKRLSII
HCPGHQKGHSAEARGNRMADQAARKAAITETPDTSTLLIENSSP (SEQ ID NO: 14828)

[116] In some embodiments, the prime editor comprises a M-MLV RT comprising amino acid substitutions D200N, T330P, L603W, T306K, and W313F as compared to the reference M-MLV RT (e.g., SEQ ID NO: 14827) as set forth in SEQ ID NO: 14828. In some embodiments, a prime editor may comprise amino acid substitutions D200N, T330P, L603W, T306K, and W313F as compared to a reference M-MLV RT.

In some embodiments, an RT variant may be a functional fragment of a reference RT that has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 21, 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, or up to 100, or up to 200, or up to 300, or up to 400, or up to 500 or more amino acid changes compared to a a wild type RT. In some embodiments, the RT variant comprises a fragment of a wild type RT, such that the fragment is about 70% identical, about 80% identical, about 90% identical, about 95% identical, about 96% identical, about 97% identical, about 98% identical, about 99% identical, about 99.5% identical, or about 99.9% identical to the corresponding fragment of the wild type RT (e.g., SEQ ID NO: 14826). In some embodiments, the fragment is 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% identical, 96%, 97%, 98%, 99%, or 99.5% of the amino acid length of a corresponding type RT (M-MLV reverse transcriptase) (*e.g.*, SEQ ID NO: 14826). In some embodiments, the RT variant comprises a fragment of a reference RT, such that the fragment is about 70% identical, about 80% identical, about 90% identical, about 95% identical, about 96% identical, about 97% identical, about 98% identical, about 99% identical, about 99.5% identical, or about 99.9% identical to the corresponding fragment of the reference RT, e.g., SEQ ID NO: 14827. In some embodiments, the fragment is 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% identical, 96%, 97%, 98%, 99%, or 99.5% of the amino acid length of a reference RT (M-MLV reverse transcriptase) (*e.g.*, SEQ ID NO: 14827.

[117] In some embodiments, the fragment is 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% identical, 96%, 97%, 98%, 99%, or 99.5% of the amino acid length of a corresponding type RT (M-MLV reverse transcriptase) (*e.g.*, SEQ ID NO: 14828).

[118] In some embodiments, the RT functional fragment is at least 100 amino acids in length. In some embodiments, the fragment is at least 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, or up to 600 or more amino acids in length.

[119] In still other embodiments, the functional RT variant is truncated at the N-terminus or the C-terminus, or both, by a certain number of amino acids which results in a truncated variant which still retains sufficient DNA polymerase function. In some embodiments, the RT truncated variant has a truncation of at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, or 250 amino acids at the N-terminal end compared to a reference RT, e.g., a wild type RT. In some embodiments, the reference RT is a wild type M-MLV RT. In other embodiments, the RT truncated variant has a truncation of at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, or 250 amino acids at the C-terminal end compared to a reference RT, e.g., a wild type RT. In some embodiments, the reference RT is a wild type M-MLV RT. In still other embodiments, the RT truncated variant has a truncation at the N-

terminal and the C-terminal end compared to a reference RT, e.g., a wild type RT. In some embodiments, the N-terminal truncation and the C-terminal truncation are of the same length. In some embodiments, the N-terminal truncation and the C-terminal truncation are of different lengths.

[120] For example, the prime editors disclosed herein may include a functional variant of a wild type M-MLV reverse transcriptase. In some embodiments, the prime editor comprises a functional variant of a wild type M-MLV RT, wherein the functional variant of M-MLV RT is truncated after amino acid position 502 compared to a wild type M-MLV RT as set forth in SEQ ID NO: 14827. In some embodiments, the functional variant of M-MLV RT further comprises a D200X, T306X, W313X, and/or T330X amino acid substitution compared to compared to a wild type M-MLV RT as set forth in SEQ ID NO: 14827, wherein X is any amino acid other than the original amino acid. In some embodiments, the functional variant of M-MLV RT further comprises a D200N, T306K, W313F, and/or T330P amino acid substitution compared to a wild type M-MLV RT as set forth in SEQ ID NO: 14827, wherein X is any amino acid other than the original amino acid. In some embodiments, the nucleotide polymerase domain is a polynucleotide polymerase domain. In some embodiments, the polynucleotide (e.g., a DNA polynucleotide, a RNA polynucleotide, e.g., an mRNA polynucleotide) encodes a MMLV-RT polypeptide that comprises an amino acid sequences that has at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity with an amino acid sequence as set forth in any of the SEQ ID NOs:14826-14829.

[121] In some embodiments, a prime editor comprises a eukaryotic RT, for example, a yeast, drosophila, rodent, or primate RT. In some embodiments, the prime editor comprises a Group II intron RT, for example, a. *Geobacillus stearothermophilus* Group II Intron (GsI-IIC) RT or a Eubacterium rectale group II intron (Eu.re.I2) RT. In some embodiments, the prime editor comprises a retron RT.

[122] In some embodiments, a prime editor comprises a eukaryotic RT, for example, a yeast, drosophila, rodent, or primate RT. In some embodiments, the prime editor comprises a Group II intron RT, for example, a. Geobacillus stearothermophilus Group II Intron (GsI-IIC) RT or a Eubacterium rectale group II intron (Eu.re.I2) RT. In some embodiments, the prime editor comprises a retron RT.

Programmable DNA binding domain

[123] In some embodiments, the DNA-binding domain of a prime editor is a programmable DNA binding domain. In some embodiments, the prime editors provided herein comprise a DNA binding domain comprising an amino acid sequence that is at least 50%, at least 60%, at least 70%, at least 75%, at least 80%, 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to any one of the sequences set forth in SEQ ID NOs: 14829-14855 or 14876. In some embodiments, the DNA binding domain comprises an amino acid sequence that has no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 differences e.g., mutations e.g., deletions, substitutions and/or insertions compared to any one of the amino acid sequences set forth in SEQ ID

NOs: 14829-14855 or 14876. In some embodiments, the DNA-binding domain of a prime editor is a programmable DNA binding domain. A programmable DNA binding domain refers to a protein domain that is designed to bind a specific nucleic acid sequence, *e.g.*, a target DNA or a target RNA. In some embodiments, the DNA-binding domain is a polynucleotide programmable DNA-binding domain that can associate with a guide polynucleotide (*e.g.*, a PEgRNA) that guides the DNA-binding domain to a specific DNA sequence, *e.g.*, a search target sequence in a target gene. In some embodiments, the polynucleotide (e.g., a DNA polynucleotide, a RNA polynucleotide, e.g., an mRNA polynucleotide) encodes a Cas polypeptide that comprises an amino acid sequences that has at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity with an amino acid sequence as set forth in any of the SEQ ID NOs: 14829-14855, 14876, 14970-14974, or 14908-14910. In some embodiments, the DNA-binding domain comprises a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) Associated (Cas) protein. A Cas protein may comprise any Cas protein described herein or a functional fragment or functional variant thereof. In some embodiments, a DNA-binding domain may also comprise a zinc-finger protein domain. In other cases, a DNA-binding domain comprises a transcription activator-like effector domain (TALE). In some embodiments, the DNA-binding domain comprises a DNA nuclease. For example, the DNA-binding domain of a prime editor may comprise an RNA-guided DNA endonuclease, *e.g.*, a Cas protein. In some embodiments, the DNA-binding domain comprises a zinc finger nuclease (ZFN) or a transcription activator like effector domain nuclease (TALEN), where one or more zinc finger motifs or TALE motifs are associated with one or more nucleases, *e.g.*, a Fok I nuclease domain.

[124] In some embodiments, the DNA-binding domain comprises a nuclease activity. In some embodiments, the DNA-binding domain of a prime editor comprises an endonuclease domain having single strand DNA cleavage activity. For example, the endonuclease domain may comprise a FokI nuclease domain. In some embodiments, the DNA-binding domain of a prime editor comprises a nuclease having full nuclease activity. In some embodiments, the DNA-binding domain of a prime editor comprises a nuclease having modified or reduced nuclease activity as compared to a wild type endonuclease domain. For example, the endonuclease domain may comprise one or more amino acid substitutions as compared to a wild type endonuclease domain. In some embodiments, the DNA-binding domain of a prime editor has nickase activity. In some embodiments, the DNA-binding domain of a prime editor comprises a Cas protein domain that is a nickase. In some embodiments, compared to a wild type Cas protein, the Cas nickase comprises one or more amino acid substitutions in a nuclease domain that reduces or abolishes its double strand nuclease activity but retains DNA binding activity. In some embodiments, the Cas nickase comprises an amino acid substitution in a HNH domain. In some embodiments, the Cas nickase comprises an amino acid substitution in a RuvC domain.

[125] In some embodiments, the DNA-binding domain comprises a CRISPR associated protein (Cas protein) domain. A Cas protein may be a Class 1 or a Class 2 Cas protein. A Cas protein can be a type I, type II, type III, type IV, type V Cas protein, or a type VI Cas protein. Non-limiting examples of Cas

proteins include Casl, Cas1B, Cas2, Cas3, Cas4, Cas5, Cas5d, Cas5t, Cas5h, Cas5a, Cas6, Cas7, Cas8, Cas8a, Cas8b, Cas8c, Cas9 (e.g., Csnl or Csx12), Cas10, CaslOd, Cas12a/Cpfl, Cas12b/C2c1, Cas12c/C2c3, Cas12d/CasY, Cas12e/CasX, Cas12g, Cas12h, Cas12i, Csyl , Csy2, Csy3, Csy4, Csel, Cse2, Cse3, Cse4, Cse5e, Cscl, Csc2, Csa5, Csnl, Csn2, Csml, Csm2, Csm3, Csm4, Csm5, Csm6, Cmrl, Cmr3, Cmr4, Cmr5, Cmr6, Csbl, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CsaX, Csx3, Csxl, Csx1S, Csx11, Csfl, Csf2, CsO, Csf4, Csdl, Csd2, Cstl, Cst2, Cshl, Csh2, Csal, Csa2, Csa3, Csa4, Csa5, Type II Cas effector proteins, Type V Cas effector proteins, Type VI Cas effector proteins, CARF, DinG, Cpfl, Cas12b/C2c1, Cas12c/C2c3, Cas12b/C2c1, Cas12c/C2c3, SpCas9(K855A), eSpCas9(1.1), SpCas9-HF1, hyper accurate Cas9 variant (HypaCas9), Cas Φ, and homologues, modified or engineered variants, mutants, and/or functional fragments thereof. A Cas protein can be a chimeric Cas protein that is fused to other proteins or polypeptides. A Cas protein can be a chimera of various Cas proteins, for example, comprising domains of Cas proteins from different organisms.

[126] A Cas protein, *e.g.*, Cas9, can be from any suitable organism. In some aspects, the organism is *Streptococcus pyogenes* (*S. pyogenes*). In some aspects, the organism is *Staphylococcus aureus* (*S. aureus*). In some aspects, the organism is *Streptococcus thermophilus* (*S. thermophilus*). In some embodiments, the organism is *Staphylococcus lugdunensis*. Non-limiting examples of suitable organism include Streptococcus pyogenes, Streptococcus thermophilus, Streptococcus sp., Staphylococcus aureus, Nocardiopsis dassonvillei, Streptomyces pristinae spiralis, Streptomyces viridochromo genes, Streptomyces viridochromogenes, Streptosporangium roseum, Streptosporangium roseum, AlicyclobacHlus acidocaldarius, Bacillus pseudomycoides, Bacillus selenitireducens, Exiguobacterium sibiricum, Lactobacillus delbrueckii, Lactobacillus salivarius, Microscilla marina, Burkholderiales bacterium, Polaromonas naphthalenivorans, Polaromonas sp., Crocosphaera watsonii, Cyanothece sp., Microcystis aeruginosa, Pseudomonas aeruginosa, Synechococcus sp., Acetohalobium arabaticum, Ammonifex degensii, Caldicelulosiruptor becscii, Candidatus Desulforudis, Clostridium botulinum, Clostridium difficile, Finegoldia magna, Natranaerobius thermophilus, Pelotomaculum thermopropionicum, Acidithiobacillus caldus, Acidithiobacillus ferrooxidans , Allochromatium vinosum, Marinobacter sp., Nitrosococcus halophilus, Nitrosococcus watsoni, Pseudoalteromonas haloplanktis, Ktedonobacter racemifer, Methanohalobium evestigatum, Anabaena variabilis, Nodularia spumigena, Nostoc sp., Arthrospira maxima, Arthrospira platensis, Arthrospira sp., Lyngbya sp., Microcoleus chthonoplastes, Oscillatoria sp., Petrotoga mobilis, Thermosipho africanus, Acaryochloris marina, Leptotrichia shahii, and Francisella novicida. In some embodiments, the organism is Streptococcus pyogenes (S. pyogenes). In some embodiments, the organism is Staphylococcus aureus (S. aureus). In some embodiments, the organism is Streptococcus thermophilus (S. thermophilus). In some embodiments, the organism is Staphylococcus lugdunensis (S. lugdunensis).

[127] In some embodiments, a Cas protein can be derived from a variety of bacterial species including, but not limited to, Veillonella atypical, Fusobacterium nucleatum, Filifactor alocis, Solobacterium moorei, Coprococcus catus, Treponema denticola, Peptoniphilus duerdenii, Catenibacterium mitsuokai,

Streptococcus mutans, Listeria innocua, Staphylococcus pseudintermedius, Acidaminococcus intestine, Olsenella uli, Oenococcus kitaharae, Bifidobacterium bifidum, Lactobacillus rhamnosus, Lactobacillus gasseri, Finegoldia magna, Mycoplasma mobile, Mycoplasma gallisepticum, Mycoplasma ovipneumoniae, Mycoplasma canis, Mycoplasma synoviae, Eubacterium rectale, Streptococcus thermophilus, Eubacterium dolichum, Lactobacillus coryniformis subsp. Torquens, Ilyobacter polytropus, Ruminococcus albus, Akkermansia muciniphila, Acidothermus cellulolyticus, Bifidobacterium longum, Bifidobacterium dentium, Corynebacterium diphtheria, Elusimicrobium minutum, Nitratifractor salsuginis, Sphaerochaeta globus, Fibrobacter succinogenes subsp. Succinogenes, Bacteroides fragilis, Capnocytophaga ochracea, Rhodopseudomonas palustris, Prevotella micans, Prevotella ruminicola, Flavobacterium columnare, Aminomonas paucivorans, Rhodospirillum rubrum, Candidatus Puniceispirillum marinum, Verminephrobacter eiseniae, Ralstonia syzygii, Dinoroseobacter shibae, Azospirillum, Nitrobacter hamburgensis, Bradyrhizobium, Wolinella succinogenes, Campylobacter jejuni subsp. Jejuni, Helicobacter mustelae, Bacillus cereus, Acidovorax ebreus, Clostridium perfringens, Parvibaculum lavamentivorans, Roseburia intestinalis, Neisseria meningitidis, Pasteurella multocida subsp. Multocida, Sutterella wadsworthensis, proteobacterium, Legionella pneumophila, Parasutterella excrementihominis, Wolinella succinogenes, and Francisella novicida.

[128] In some embodiments, a Cas protein, *e.g.*, Cas9, can be a wild type or a modified form of a Cas protein. In some embodiments, a Cas protein, *e.g.*, Cas9, can be a nuclease active variant, nuclease inactive variant, a nickase, or a functional variant or functional fragment of a wild type Cas protein. In some embodiments, a Cas protein, *e.g.*, Cas9, can be a wild type or a modified form of a Cas protein. A Cas protein, *e.g.*, Cas9, can be a nuclease active variant, nuclease inactive variant, a nickase, or a functional variant or functional fragment of a wild type Cas protein. A Cas protein, *e.g.*, Cas9, can comprise an amino acid change such as a deletion, insertion, substitution, fusion, chimera, or any combination thereof relative to a corresponding wild-type version of the Cas protein. In some embodiments, a Cas protein can be a polypeptide with at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity or sequence similarity to a wild type exemplary Cas protein.

[129] A Cas protein, *e.g.*, Cas9, may comprise one or more domains. Non-limiting examples of Cas domains include, guide nucleic acid recognition and/or binding domain, nuclease domains (*e.g.*, DNase or RNase domains, RuvC, HNH), DNA binding domain, RNA binding domain, helicase domains, protein-protein interaction domains, and dimerization domains. In various embodiments, a Cas protein comprises a guide nucleic acid recognition and/or binding domain can interact with a guide nucleic acid, and one or more nuclease domains that comprise catalytic activity for nucleic acid cleavage.

[130] In some embodiments, a Cas protein, *e.g.*, Cas9, comprises one or more nuclease domains. A Cas protein can comprise an amino acid sequence having at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a nuclease domain (*e.g.*, RuvC domain, HNH domain) of a wild-type Cas protein. In some embodiments, a Cas protein comprises

a single nuclease domain. For example, a Cpf1 may comprise a RuvC domain but lacks HNH domain. In some embodiments, a Cas protein comprises two nuclease domains, *e.g.*, a Cas9 protein can comprise an HNH nuclease domain and a RuvC nuclease domain.

[131] In some embodiments, a prime editor comprises a Cas protein, *e.g.*, Cas9, wherein all nuclease domains of the Cas protein are active. In some embodiments, a prime editor comprises a Cas protein having one or more inactive nuclease domains. One or a plurality of the nuclease domains (*e.g.*, RuvC, HNH) of a Cas protein can be deleted or mutated so that they are no longer functional or comprise reduced nuclease activity. In some embodiments, a Cas protein, *e.g.*, Cas9, comprising mutations in a nuclease domain has reduced (*e.g.* nickase) or abolished nuclease activity while maintaining its ability to target a nucleic acid locus at a search target sequence when complexed with a guide nucleic acid, *e.g.* a PEgRNA.

[132] In some embodiments, a prime editor comprises a Cas nickase that can bind to the target gene in a sequence-specific manner and generate a single-strand break at a protospacer within double-stranded DNA in the target gene, but not a double-strand break. For example, the Cas nickase can cleave the edit strand or the non-edit strand of the target gene, but may not cleave both. In some embodiments, a prime editor comprises a Cas nickase comprising two nuclease domains (*e.g.*, Cas9), with one of the two nuclease domains modified to lack catalytic activity or deleted. In some embodiments, the Cas nickase of a prime editor comprises a nuclease inactive RuvC domain and a nuclease active HNH domain. In some embodiments, the Cas nickase of a prime editor comprises a nuclease inactive HNH domain and a nuclease active RuvC domain. In some embodiments, a prime editor comprises a Cas9 nickase having an amino acid substitution in the RuvC domain e.g., an amino acid substitution that reduces or abolishes nuclease activity of the RuvC domain. In some embodiments, the Cas9 nickase comprises a D10X amino acid substitution compared to a wild type S. pyogenes Cas9, wherein X is any amino acid other than D. In some embodiments, a prime editor comprises a Cas9 nickase having an amino acid substitution in the HNH domain, e.g., an amino acid substitution that reduces or abolishes nuclease activity of the HNH domain. In some embodiments, the Cas9 nickase comprises a H840X amino acid substitution compared to a wild type S. pyogenes Cas9, wherein X is any amino acid other than H.

[133] In some embodiments, a prime editor comprises a Cas protein that can bind to the target gene in a sequence-specific manner but lacks or has abolished nuclease activity and may not cleave either strand of a double stranded DNA in a target gene. Abolished activity or lacking activity can refer to an enzymatic activity less than 1%, less than 2%, less than 3%, less than 4%, less than 5%, less than 6%, less than 7%, less than 8%, less than 9%, or less than 10% activity compared to a wild-type exemplary activity (*e.g.*, wild-type Cas9 nuclease activity). In some embodiments, a Cas protein of a prime editor completely lacks nuclease activity. A nuclease, *e.g.*, Cas9, that lacks nuclease activity may be referred to as nuclease inactive or "nuclease dead" (abbreviated by "d"). A nuclease dead Cas protein (*e.g.*, dCas, dCas9) can bind to a target polynucleotide but may not cleave the target polynucleotide. In some aspects, a dead Cas protein is a dead Cas9 protein. In some embodiments, a prime editor comprises a nuclease

dead Cas protein wherein all of the nuclease domains (*e.g.*, both RuvC and HNH nuclease domains in a Cas9 protein; RuvC nuclease domain in a Cpf1 protein) are mutated to lack catalytic activity, or are deleted.

[134] A Cas protein can be modified. A Cas protein, *e.g.*, Cas9, can be modified to increase or decrease nucleic acid binding affinity, nucleic acid binding specificity, and/or enzymatic activity. Cas proteins can also be modified to change any other activity or property of the protein, such as stability. For example, one or more nuclease domains of the Cas protein can be modified, deleted, or inactivated, or a Cas protein can be truncated to remove domains that are not essential for the function of the protein or to optimize (*e.g.*, enhance or reduce) the activity of the Cas protein.

[135] A Cas protein can be a fusion protein. For example, a Cas protein can be fused to a cleavage domain, an epigenetic modification domain, a transcriptional regulation domain, or a polymerase domain. A Cas protein can also be fused to a heterologous polypeptide providing increased or decreased stability. The fused domain or heterologous polypeptide can be located at the N-terminus, the C-terminus, or internally within the Cas protein.

[136] In some embodiments, the Cas protein of a prime editor is a Class 2 Cas protein. In some embodiments, the Cas protein is a type II Cas protein. In some embodiments, the Cas protein is a Cas9 protein, a modified version of a Cas9 protein, a Cas9 protein homolog, mutant, variant, or a functional fragment thereof. As used herein, a Cas9, Cas9 protein, Cas9 polypeptide or a Cas9 nuclease refers to an RNA guided nuclease comprising one or more Cas9 nuclease domains and a Cas9 gRNA binding domain having the ability to bind a guide polynucleotide, *e.g.*, a PEgRNA. A Cas9 protein may refer to a wild type Cas9 protein from any organism or a homolog, ortholog, or paralog from any organisms; any functional mutants or functional variants thereof; or any functional fragments or domains thereof. In some embodiments, a prime editor comprises a full-length Cas9 protein. In some embodiments, the Cas9 protein can generally comprises at least about 50%, 60%, 70%, 80%, 90%, 100% sequence identity to a wild type reference Cas9 protein (*e.g.*, Cas9 from *S. pyogenes*). In some embodiments, the Cas9 comprises an amino acid change such as a deletion, insertion, substitution, fusion, chimera, or any combination thereof as compared to a wild type reference Cas9 protein.

[137] In some embodiments, a Cas9 protein may comprise a Cas9 protein from *Streptococcus pyogenes* (Sp), *Staphylococcus aureus* (Sa), *Streptococcus canis* (Sc), *Streptococcus thermophilus* (St), *Staphylococcus lugdunensis* (Slu), *Neisseria meningitidis* (Nm), *Campylobacter jejuni* (Cj), *Francisella novicida* (Fn), or *Treponema denticola* (Td), or any Cas9 homolog or ortholog from an organism known in the art. In some embodiments, a Cas9 polypeptide is a SpCas9 polypeptide, e.g., comprising an amino acid sequence as set forth in NCBI Accession No. WP_038431314 or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a SaCas9 polypeptide, e.g., comprising an amino acid sequence as set forth in Uniprot Accession No. J7RUA5 or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a ScCas9 polypeptide, e.g., comprising an amino acid sequence as set forth in Uniprot Accession No. A0A3P5YA78 or a fragment or variant thereof. In some

embodiments, a Cas9 polypeptide is a StCas9 polypeptide, e.g., comprising an amino acid sequence as set forth in NCBI Accession No. WP_007896501.1 or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a SluCas9 polypeptide, e.g., comprising an amino acid sequence as set forth in any of NCBI Accession No. WP_230580236.1 or WP_250638315.1 or WP_242234150.1, WP_241435384.1, WP_002460848.1, KAK58371.1, or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a NmCas9 polypeptide, e.g., comprising an amino acid sequence as set forth in any of NCBI Accession No. WP_002238326.1 or WP_061704949.1 or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a CjCas9 polypeptide, e.g., comprising an amino acid sequence as set forth in any of NCBI Accession No. WP_100612036.1, WP_116882154.1, WP_116560509.1, WP_116484194.1, WP_116479303.1, WP_115794652.1, WP_100624872.1, or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a FnCas9 polypeptide, e.g., comprising the amino acid sequence as set forth in Uniprot Accession No. A0Q5Y3 or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a TdCas9 polypeptide, e.g., comprising the amino acid sequence as set forth in NCBI Accession No. WP_147625065.1 or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a chimera comprising domains from two or more of the organisms described herein or those known in the art. In some embodiments, a Cas9 polypeptide is a Cas9 polypeptide from *Streptococcus macacae*, e.g., comprising the amino acid sequence as set forth in NCBI Accession No. WP_003079701.1 or a fragment or variant thereof. In some embodiments, a Cas9 polypeptide is a Cas9 polypeptide generated by replacing a PAM interaction domain of a SpCas9 with that of a *Streptococcus macacae* Cas9 (Spy-mac Cas9). Exemplary Cas sequences are provided in Table 86 below. . In some embodiments, a prime editor comprises a Cas9 protein, lacking a N-terminus methionine having an amino acid sequence as according to any of the SEQ ID NOs: 14970-14974 or 14908-14910.

[138] In some embodiments, a Cas9 protein comprises a Cas9 protein from *Streptococcus pyogenes* (Sp), e.g., as according to NC_002737.2:854751-858857 or the protein encoded by UniProt Q99ZW2, e.g., as according to SEQ ID NO: 14829. In some embodiments, the Cas9 protein is a SpCas9. In some embodiments, a SpCas9 can be a wild type SpCas9, a SpCas9 variant, or a nickase SpCas9. In some embodiments, the SpCas9 lacks the N-terminus methionine relative to a corresponding SpCas9 (e.g., wild type SpCas9, a SpCas9 variant or a nickase SpCas9). In some embodiments, a prime editor comprises a Cas9 protein, having an amino acid sequence as according to SEQ ID NO: 14829, not including the N-terminus methionine. In some embodiments, a wild type SpCas9 comprises an amino acid sequence set forth in SEQ ID NO: 14829. In some embodiments, a prime editor comprises a Cas9 protein, having an amino acid sequence as according to SEQ ID NO: 14829, not including the N-terminus methionine. . In some embodiments, a prime editor comprises a Cas9 protein, lacking a N-terminus methionine having an amino acid sequence as according to SEQ ID NO: 14970. In some embodiments, a prime editor comprises a Cas9 protein comprising one or more mutations (e.g., amino acid substitutions, insertions and/or deletions relative to a corresponding wild type Cas9 protein (e.g., wild type SpCas9). In some

embodiments, the Cas9 protein comprising one or mutations relative to a wild type Cas9 protein comprises an amino acid sequence set forth in SEQ ID NO: 14830. In some embodiments, the SpCas9 lacks the N-terminus methionine relative to a corresponding SpCas9 (e.g., a nickase SpCas9, e.g., as set forth in SEQ ID NO: 14830), e.g., as set forth in SEQ ID NO: 14831. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid H840A as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid H839A as compared to a wild type SpCas9 (as set forth in SEQ ID NO: 14829) lacking a N-terminal methionine, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid H839A as compared to a wild type SpCas9 (as set forth in SEQ ID NO: 14970).

[139] Exemplary *Streptococcus pyogenes* Cas9 (SpCas9) amino acid sequences useful in the prime editors disclosed herein are provided below in SEQ ID NOs: 14829-14831, 14838-14846, 14853-14855, 14876, 14970-14971, 14972, or 14910.

[140] In some embodiments, a prime editor comprises a Cas protein, *e.g.*, Cas9 variant, e.g., a Cas protein comprising one or more mutations. In some embodiments, a Cas9 protein comprises a variant Cas9 protein containing one or more amino acid substitutions. An exemplary Cas9 variant comprising one or more mutations comprises an amino acid sequence as set forth in SEQ ID NO. 14876.

[141] In some embodiments, a prime editor comprises a Cas9 protein as according to any of the SEQ ID NOS 14832-14834 or a variant thereof. In some embodiments, a prime editor comprises a Cas9 protein from *Staphylococcus lugdunensis* (Slu Cas9) e.g., as according to any of the SEQ ID NOS 14832-14834 or a variant thereof. In some embodiments, a sluCas9 lacks a N-terminal methionine relative to a corresponding sluCas9 (e.g., a wild type sluCas9, a sluCas9 variant, or a nickase sluCas9). In some embodiments, the Cas9 protein is a sluCas9. In some embodiments, a sluCas9 can be a wild type sluCas9, a sluCas9 variant or a nickase sluCas9. In some embodiments, a prime editor comprises a Cas9 protein, having an amino acid sequence as according to SEQ ID NO: 14832, not including the N-terminus methionine. In some embodiments, a prime editor comprises a Cas9 protein, lacking a N-terminus methionine having an amino acid sequence as according to SEQ ID NO: 14973. In some embodiments, a wild type SluCas9 comprises an amino acid sequence set forth in SEQ ID NO: 14832. In some embodiments, a prime editor comprises a Cas9 protein, having an amino acid sequence as according to SEQ ID NO: 14833, not including the N-terminus methionine (e.g., as set forth in SEQ ID NO: 14834). In some embodiments, a prime editor comprises a Cas9 protein comprising one or more mutations (e.g., amino acid substitutions, insertions and/or deletions relative to a corresponding wild type Cas9 protein (e.g., wild type sluCas9). In some embodiments, the Cas9 protein comprising one or mutations relative to a wild type Cas9 protein comprises an amino acid sequence set forth in SEQ ID NOs: 14833 or 14834.

[142] Exemplary Staphylococcus lugdunensis Cas9 (SluCas9) amino acid sequences useful in the prime editors disclosed herein are provided below in SEQ ID NOs: 14832-14834 or 14973.

[143] In some embodiments, a prime editor comprises a Cas9 protein from *Staphylococcus aureus* (SaCas9) e.g., as according to any of the SEQ ID NOS: 14835-14837, or 14974 or a variant thereof. In some embodiments, a SaCas9 may lack a N-terminal methionine. In some embodiments, a SaCas9 may comprise a mutation.

[144] In some embodiments, a prime editor comprises a Cas9 protein as according to any of the SEQ ID NOS: 14835,14836, or 14837, 14974, or a variant thereof. In some embodiments, a SaCas9 lacks a N-terminal methionine relative to a corresponding SaCas9 (e.g., a wild type SaCas9, a SaCas9 variant, or a nickase SaCas9). In some embodiments, the Cas9 protein is a SaCas9. In some embodiments, a SaCas9 can be a wild type SaCas9, a SaCas9 variant or a nickase SaCas9. In some embodiments, a prime editor comprises a Cas9 protein, having an amino acid sequence as according to SEQ ID NO: 14835, not including the N-terminus methionine. In some embodiments, a wild type SaCas9 comprises an amino acid sequence set forth in SEQ ID NO: 14835. In some embodiments, a prime editor comprises a Cas9 protein, having an amino acid sequence as according to SEQ ID NO: 14836, not including the N-terminus methionine (e.g., as set forth in SEQ ID NO: 14837). . In some embodiments, a prime editor comprises a Cas9 protein, lacking a N-terminus methionine having an amino acid sequence as according to SEQ ID NO: 14974. In some embodiments, a prime editor comprises a Cas9 protein comprising one or more mutations (e.g., amino acid substitutions, insertions and/or deletions relative to a corresponding wild type Cas9 protein (e.g., wild type SaCas9). In some embodiments, the Cas9 protein comprising one or mutations relative to a wild type Cas9 protein comprises an amino acid sequence set forth in SEQ ID NOs: 14836 or 14837. Exemplary SaCas9 amino acid sequences useful in the prime editors disclosed herein are provided in SEQ ID NOs: 14835-14837, or 14974.

[145] In some embodiments, a Cas9 is a chimeric Cas9, e.g., modified Cas9; e.g., synthetic RNA-guided nucleases (sRGNs), e.g., modified by DNA family shuffling, e.g., sRGN3.1, sRGN3.3. In some embodiments, the DNA family shuffling comprises, fragmentation and reassembly of parental Cas9 genes, e.g., one or more of Cas9s from Staphylococcus hyicus (Shy), Staphylococcus lugdunensis (Slu), Staphylococcus microti (Smi), and Staphylococcus pasteuri (Spa). In some embodiments, a modified sluCas9 shows increased editing efficiency and/or specificity relative to a sluCas9 that is not modified. In some embodiments, a modified Cas9, e.g., a sRGN shows at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 100%, at least 150%, at least 200%, at least 300%, at least 400%, at least 500%, at least 600%, at least 700%, at least 800%, at least 900%, or at least 1000% increase in editing efficiency compared to a Cas9 that is not modified. In some embodiments, a Cas9, e.g., a sRGN shows at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 100%, at least 150%, at least 200%, at least 300%, at least 400%, at least 500%, at least 600%, at least 700%, at least 800%, at least 900%, or at least 1000% increase in specificity compared to a Cas9 that is not modified. In some embodiments, a Cas9, e.g., a sRGN shows at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 100%, at least 150%, at least

200%, at least 300%, at least 400%, at least 500%, at least 600%, at least 700%, at least 800%, at least 900%, or at least 1000% increase in cleavage activity compared to a Cas9 that is not modified. In some embodiments, a Cas9, e.g., a sRGN shows ability to cleave a 5′-NNGG-3′ PAM-containing target. In some embodiments, a prime editor may comprise a Cas9 (e.g., a chimeric Cas9), e.g., as according any of the sequences selected from 14847-14852, 14908, or 14909 or a variant thereof. Exemplary amino acid sequences of sRGN useful in the prime editors disclosed herein are provided below in SEQ ID NOs: 14847-14852, 14908, or 14909. In some embodiments, a prime editor comprises a Cas9 protein, lacking a N-terminus methionine having an amino acid sequence as according to SEQ ID NO: 14908. In some embodiments, a prime editor comprises a Cas9 protein, lacking a N-terminus methionine having an amino acid sequence as according to SEQ ID NO: 14909.

Table 86: Exemplary Cas sequences

Sequence Description	SEQ ID NO.	Sequence
wtSpCas9	14829	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF DSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFK YFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD
Sp Cas9 nickase H840A	14830	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL

		SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF DSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFK YFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD
met-Cas9 nickase H840A	14831	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRL KRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF DSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFK YFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD
sluCas9	14832	MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL ERVKKLLEDYNLLDQSQIPQSTNPYAIRVKGLSEALSKDELVIALLHIAKRRGIHKIDVIDSNDD VGNELSTKEQLNKNSKLLKDKFVCQIQLERMNEGQVRGEKNRFKTADIIKEIIQLLNVQKNFH QLDENFINKYIELVEMRREYFEGPGKGSPYGWEGDPKAWYETLMGHCTYFPDELRSVKYAY SADLFNALNDLNNLVIQRDGLSKLEYHEKYHIIENVFKQKKKPTLKQIANEINVNPEDIKGYRI TKSGKPQFTEFKLYHDLKSVLFDQSILENEDVLDQIAEILTIYQDKDSIKSKLTELDILLNEEDK

		ENIAQLTGYTGTHRLSLKCIRLVLEEQWYSSRNQMEIFTHLNIKPKKINLTAANKIPKAMIDEFI LSPVVKRTFGQAINLINKIIEKYGVPEDIIIELARENNSKDKQKFINEMQKKNENTRKRINEIIGK YGNQNAKRLVEKIRLHDEQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNKVL VKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKFEV QKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNHGY KHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIESKQLDIQVDSEDNYSEMFIIPKQVQDIK DFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPEKFL MYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNKLGSH LDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDKLKLG KAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEPRIKK TIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN
sluCas9 nickase	14833	MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL ERVKKLLEDYNLLDQSQIPQSTNPYAIRVKGLSEALSKDELVIALLHIAKRRGIHKIDVIDSNDD VGNELSTKEQLNKNSKLLKDKFVCQIQLERMNEGQVRGEKNRFKTADIIKEIIQLLNVQKNFH QLDENFINKYIELVEMRREYFEGPGKGSPYGWEGDPKAWYETLMGHCTYFPDELRSVKYAY SADLFNALNDLNNLVIQRDGLSKLEYHEKYHIIENVFKQKKKPTLKQIANEINVNPEDIKGYRI TKSGKPQFTEFKLYHDLKSVLFDQSILENEDVLDQIAEILTIYQDKDSIKSKLTELDILLNEEDK ENIAQLTGYTGTHRLSLKCIRLVLEEQWYSSRNQMEIFTHLNIKPKKINLTAANKIPKAMIDEFI LSPVVKRTFGQAINLINKIIEKYGVPEDIIIELARENNSKDKQKFINEMQKKNENTRKRINEIIGK YGNQNAKRLVEKIRLHDEQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNKVL VKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKFEV QKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNHGY KHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIESKQLDIQVDSEDNYSEMFIIPKQVQDIK DFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPEKFL MYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNKLGSH LDVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDKLKLG KAIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEPRIKK TIGKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN
met-sluCas9 nickase	14834	NQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLER VKKLLEDYNLLDQSQIPQSTNPYAIRVKGLSEALSKDELVIALLHIAKRRGIHKIDVIDSNDDV GNELSTKEQLNKNSKLLKDKFVCQIQLERMNEGQVRGEKNRFKTADIIKEIIQLLNVQKNFHQ LDENFINKYIELVEMRREYFEGPGKGSPYGWEGDPKAWYETLMGHCTYFPDELRSVKYAYS ADLFNALNDLNNLVIQRDGLSKLEYHEKYHIIENVFKQKKKPTLKQIANEINVNPEDIKGYRIT KSGKPQFTEFKLYHDLKSVLFDQSILENEDVLDQIAEILTIYQDKDSIKSKLTELDILLNEEDKE NIAQLTGYTGTHRLSLKCIRLVLEEQWYSSRNQMEIFTHLNIKPKKINLTAANKIPKAMIDEFIL SPVVKRTFGQAINLINKIIEKYGVPEDIIIELARENNSKDKQKFINEMQKKNENTRKRINEIIGKY GNQNAKRLVEKIRLHDEQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNKVLV KQSEASKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKFEVQ KEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNHGYK HHAEDALIIANADFLFKENKKLKAVNSVLEKPEIESKQLDIQVDSEDNYSEMFIIPKQVQDIKD FRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPEKFLM YQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNKLGSHL DVTHQFKSSTKKLVKLSIKPYRFDVYLTDKGYKFITISYLDVLKKDNYYYIPEQKYDKLKLGK AIDKNAKFIASFYKNDLIKLDGEIYKIIGVNSDTRNMIELDLPDIRYKEYCELNNIKGEPRIKKTI GKKVNSIEKLTTDVLGNVFTNTQYTKPQLLFKRGN

saCas9	1483 5	MKRNYILGLDIGITSVGYGIIDYETRDVIDAGVRLFKEANVENNEGRRSKRGARRLKRRRRHR IQRVKKLLFDYNLLTDHSELSGINPYEARVKGLSQKLSEEEFSAALLHLAKRRGVHNVNEVEE DTGNELSTKEQISRNSKALEEKYVAELQLERLKKDGEVRGSINRFKTSDYVKEAKQLLKVQK AYHQLDQSFIDTYIDLLETRRTYYEGPGEGSPFGWKDIKEWYEMLMGHCTYFPEELRSVKYA YNADLYNALNDLNNLVITRDENEKLEYYEKFQIIENVFKQKKKPTLKQIAKEILVNEEDIKGY RVTSTGKPEFTNLKVYHDIKDITARKEIIENAELLDQIAKILTIYQSSEDIQEELTNLNSELTQEEI EQISNLKGYTGTHNLSLKAINLILDELWHTNDNQIAIFNRLKLVPKKVDLSQQKEIPTTLVDDFI LSPVVKRSFIQSIKVINAIIKKYGLPNDIIIELAREKNSKDAQKMINEMQKRNRQTNERIEEIIRTT GKENAKYLIEKIKLHDMQEGKCLYSLEAIPLEDLLNNPFNYEVDHIIPRSVSFDNSFNNKVLVK QEENSKKGNRTPFQYLSSSDSKISYETFKKHILNLAKGKGRISKTKKEYLLEERDINRFSVQKD FINRNLVDTRYATRGLMNLLRSYFRVNNLDVKVKSINGGFTSFLRRKWKFKKERNKGYKHH AEDALIIANADFIFKEWKKLDKAKKVMENQMFEEKQAESMPEIETEQEYKEIFITPHQIKHIKD FKDYKYSHRVDKKPNRELINDTLYSTRKDDKGNTLIVNNLNGLYDKDNDKLKKLINKSPEKL LMYHHDPQTYQKLKLIMEQYGDEKNPLYKYYEETGNYLTKYSKKDNGPVIKKIKYYGNKLN AHLDITDDYPNSRNKVVKLSLKPYRFDVYLDNGVYKFVTVKNLDVIKKENYYEVNSKCYEE AKKLKKISNQAEFIASFYNNDLIKINGELYRVIGVNNDLLNRIEVNMIDITYREYLENMNDKRP PRIIKTIASKTQSIKKYSTDILGNLYEVKSKKHPQIIKKG
SaCas9 (N580A) nickase	1483 6	MKRNYILGLDIGITSVGYGIIDYETRDVIDAGVRLFKEANVENNEGRRSKRGARRLKRRRRHR IQRVKKLLFDYNLLTDHSELSGINPYEARVKGLSQKLSEEEFSAALLHLAKRRGVHNVNEVEE DTGNELSTKEQISRNSKALEEKYVAELQLERLKKDGEVRGSINRFKTSDYVKEAKQLLKVQK AYHQLDQSFIDTYIDLLETRRTYYEGPGEGSPFGWKDIKEWYEMLMGHCTYFPEELRSVKYA YNADLYNALNDLNNLVITRDENEKLEYYEKFQIIENVFKQKKKPTLKQIAKEILVNEEDIKGY RVTSTGKPEFTNLKVYHDIKDITARKEIIENAELLDQIAKILTIYQSSEDIQEELTNLNSELTQEEI EQISNLKGYTGTHNLSLKAINLILDELWHTNDNQIAIFNRLKLVPKKVDLSQQKEIPTTLVDDFI LSPVVKRSFIQSIKVINAIIKKYGLPNDIIIELAREKNSKDAQKMINEMQKRNRQTNERIEEIIRTT GKENAKYLIEKIKLHDMQEGKCLYSLEAIPLEDLLNNPFNYEVDHIIPRSVSFDNSFNNKVLVK QEEASKKGNRTPFQYLSSSDSKISYETFKKHILNLAKGKGRISKTKKEYLLEERDINRFSVQKD FINRNLVDTRYATRGLMNLLRSYFRVNNLDVKVKSINGGFTSFLRRKWKFKKERNKGYKHH AEDALIIANADFIFKEWKKLDKAKKVMENQMFEEKQAESMPEIETEQEYKEIFITPHQIKHIKD FKDYKYSHRVDKKPNRELINDTLYSTRKDDKGNTLIVNNLNGLYDKDNDKLKKLINKSPEKL LMYHHDPQTYQKLKLIMEQYGDEKNPLYKYYEETGNYLTKYSKKDNGPVIKKIKYYGNKLN AHLDITDDYPNSRNKVVKLSLKPYRFDVYLDNGVYKFVTVKNLDVIKKENYYEVNSKCYEE AKKLKKISNQAEFIASFYNNDLIKINGELYRVIGVNNDLLNRIEVNMIDITYREYLENMNDKRP PRIIKTIASKTQSIKKYSTDILGNLYEVKSKKHPQIIKKG
met-SaCas9 (N579A) nickase	1483 7	KRNYILGLDIGITSVGYGIIDYETRDVIDAGVRLFKEANVENNEGRRSKRGARRLKRRRRHRIQ RVKKLLFDYNLLTDHSELSGINPYEARVKGLSQKLSEEEFSAALLHLAKRRGVHNVNEVEED TGNELSTKEQISRNSKALEEKYVAELQLERLKKDGEVRGSINRFKTSDYVKEAKQLLKVQKA YHQLDQSFIDTYIDLLETRRTYYEGPGEGSPFGWKDIKEWYEMLMGHCTYFPEELRSVKYAY NADLYNALNDLNNLVITRDENEKLEYYEKFQIIENVFKQKKKPTLKQIAKEILVNEEDIKGYR VTSTGKPEFTNLKVYHDIKDITARKEIIENAELLDQIAKILTIYQSSEDIQEELTNLNSELTQEEIE QISNLKGYTGTHNLSLKAINLILDELWHTNDNQIAIFNRLKLVPKKVDLSQQKEIPTTLVDDFIL SPVVKRSFIQSIKVINAIIKKYGLPNDIIIELAREKNSKDAQKMINEMQKRNRQTNERIEEIIRTT GKENAKYLIEKIKLHDMQEGKCLYSLEAIPLEDLLNNPFNYEVDHIIPRSVSFDNSFNNKVLVK QEEASKKGNRTPFQYLSSSDSKISYETFKKHILNLAKGKGRISKTKKEYLLEERDINRFSVQKD FINRNLVDTRYATRGLMNLLRSYFRVNNLDVKVKSINGGFTSFLRRKWKFKKERNKGYKHH

		AEDALIIANADFIFKEWKKLDKAKKVMENQMFEEKQAESMPEIETEQEYKEIFITPHQIKHIKD FKDYKYSHRVDKKPNRELINDTLYSTRKDDKGNTLIVNNLNGLYDKDNDKLKKLINKSPEKL LMYHHDPQTYQKLKLIMEQYGDEKNPLYKYYEETGNYLTKYSKKDNGPVIKKIKYYGNKLN AHLDITDDYPNSRNKVVKLSLKPYRFDVYLDNGVYKFVTVKNLDVIKKENYYEVNSKCYEE AKKLKKISNQAEFIASFYNNDLIKINGELYRVIGVNNDLLNRIEVNMIDITYREYLENMNDKRP PRIIKTIASKTQSIKKYSTDILGNLYEVKSKKHPQIIKKG
spCas9 NG	14838	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESIRPKRNSDKLIARKKDWDPKKYGGF VSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASARFLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPRAFK YFDTTIDRKVYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
spCas9 NG nickase	14839	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV

		WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESIRPKRNSDKLIARKKDWDPKKYGGF VSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASARFLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPRAFK YFDTTIDRKVYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
Met- spCas9 NG nickase	1484 0	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRL KRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF VSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASARFLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPRAFK YFDTTIDRKVYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
spCas9 VRQR	1484 1	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF

		VSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASARELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFK YFDTTIDRKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
spCas9 VRQR nickase	14842	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF VSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASARELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFK YFDTTIDRKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
met-spCas9 VRQR	14843	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRL KRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF VSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL

		PKYSLFELENGRKRMLASARELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFK YFDTTIDRKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
SpRY	14844	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAERTR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESIRPKRNSDKLIARKKDWDPKKYGGF LWPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIK LPKYSLFELENGRKRMLASAKQLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTRLGAPRAF KYFDTTIDPKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
SpRY nickase	14845	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAERTR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESIRPKRNSDKLIARKKDWDPKKYGGF LWPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIK LPKYSLFELENGRKRMLASAKQLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFV

		EQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTRLGAPRAF KYFDTTIDPKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
met- SpRY nickase	14846	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAERTRL KRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESIRPKRNSDKLIARKKDWDPKKYGGF LWPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIK LPKYSLFELENGRKRMLASAKQLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTRLGAPRAF KYFDTTIDPKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
sRGN3.1	14847	MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL ERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKE ETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQM QYYPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVK YAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKG YRITKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLMSE ADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIPTD MIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRI NEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYH NKVLVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDIN KFEVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKER NHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQV QDIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSP EKFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNK LGSHLDVTHQFKSSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYIPKDKYQ ELKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYCEINNIKGE PRIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL
sRGN3.1 (N585A) Nickase	14848	MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL ERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKE ETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQM

		QYYPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVK YAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKG YRITKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLMSE ADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIPTD MIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRI NEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYH NKVLVKQSEASKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDIN KFEVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKER NHGYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQV QDIKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSP EKFLMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNK LGSHLDVTHQFKSSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYIPKDKYQ ELKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYCEINNIKGE PRIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL
Met(-) sRGN3.1 (N584A) Nickase	14849	NQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLER VKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKEET ASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQMQY YPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVKYA YSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKGYRI TKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLMSEAD KQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIPTDMI DDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRINEI IGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNK VLVKQSEASKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKF EVQKEFINRNLVDTRYATRELTNYLKAYFSANNMNVKVKTINGSFTDYLRKVWKFKKERNH GYKHHAEDALIIANADFLFKENKKLKAVNSVLEKPEIETKQLDIQVDSEDNYSEMFIIPKQVQD IKDFRNFKYSHRVDKKPNRQLINDTLYSTRKKDNSTYIVQTIKDIYAKDNTTLKKQFDKSPEKF LMYQHDPRTFEKLEVIMKQYANEKNPLAKYHEETGEYLTKYSKKNNGPIVKSLKYIGNKLGS HLDVTHQFKSSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYIPKDKYQELK EKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYCEINNIKGEPRI KKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL
sRGN3.3	14850	MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL ERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKE ETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQM QYYPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVK YAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKG YRITKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLMSE ADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIPTD MIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRI NEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYH NKVLVKQSENSKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDIN KFEVQKEFINRNLVDTRYATRELTSYLKAYFSANNMDVKVKTINGSFTNHLRKVWRFDKYR NHGYKHHAEDALIIANADFLFKENKKLQNTNKILEKPTIENNTKKVTVEKEEDYNNVFETPKL VEDIKQYRDYKFSHRVDKKPNRQLINDTLYSTRMKDEHDYIVQTITDIYGKDNTNLKKQFNK NPEKFLMYQNDPKTFEKLSIIMKQYSDEKNPLAKYYEETGEYLTKYSKKNNGPIVKKIKLLGN

		KVGNHLDVTNKYENSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYIPKDK YQELKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYCEINNIK GEPRIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL
sRGN3.3 (N585A) Nickase	14851	MNQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRL ERVKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKE ETASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQM QYYPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVK YAYSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKG YRITKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLMSE ADKQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIPTD MIDDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRI NEIIGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYH NKVLVKQSEASKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDIN KFEVQKEFINRNLVDTRYATRELTSYLKAYFSANNMDVKVKTINGSFTNHLRKVWRFDKYR NHGYKHHAEDALIIANADFLFKENKKLQNTNKILEKPTIENNTKKVTVEKEEDYNNVFETPKL VEDIKQYRDYKFSHRVDKKPNRQLINDTLYSTRMKDEHDYIVQTITDIYGKDNTNLKKQFNK NPEKFLMYQNDPKTFEKLSIIMKQYSDEKNPLAKYYEETGEYLTKYSKKNNGPIVKKIKLLGN KVGNHLDVTNKYENSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYIPKDK YQELKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYCEINNIK GEPRIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL
Met(-) sRGN3.3 (N584A) Nickase	14852	NQKFILGLDIGITSVGYGLIDYETKNIIDAGVRLFPEANVENNEGRRSKRGSRRLKRRRIHRLER VKLLLTEYDLINKEQIPTSNNPYQIRVKGLSEILSKDELAIALLHLAKRRGIHNVDVAADKEET ASDSLSTKDQINKNAKFLESRYVCELQKERLENEGHVRGVENRFLTKDIVREAKKIIDTQMQY YPEIDETFKEKYISLVETRREYFEGPGQGSPFGWNGDLKKWYEMLMGHCTYFPQELRSVKYA YSADLFNALNDLNNLIIQRDNSEKLEYHEKYHIIENVFKQKKKPTLKQIAKEIGVNPEDIKGYRI TKSGTPEFTSFKLFHDLKKVVKDHAILDDIDLLNQIAEILTIYQDKDSIVAELGQLEYLMSEAD KQSISELTGYTGTHSLSLKCMNMIIDELWHSSMNQMEVFTYLNMRPKKYELKGYQRIPTDMI DDAILSPVVKRTFIQSINVINKVIEKYGIPEDIIIELARENNSDDRKKFINNLQKKNEATRKRINEI IGQTGNQNAKRIVEKIRLHDQQEGKCLYSLESIPLEDLLNNPNHYEVDHIIPRSVSFDNSYHNK VLVKQSEASKKSNLTPYQYFNSGKSKLSYNQFKQHILNLSKSQDRISKKKKEYLLEERDINKF EVQKEFINRNLVDTRYATRELTSYLKAYFSANNMDVKVKTINGSFTNHLRKVWRFDKYRNH GYKHHAEDALIIANADFLFKENKKLQNTNKILEKPTIENNTKKVTVEKEEDYNNVFETPKLVE DIKQYRDYKFSHRVDKKPNRQLINDTLYSTRMKDEHDYIVQTITDIYGKDNTNLKKQFNKNP EKFLMYQNDPKTFEKLSIIMKQYSDEKNPLAKYYEETGEYLTKYSKKNNGPIVKKIKLLGNKV GNHLDVTNKYENSTKKLVKLSIKNYRFDVYLTEKGYKFVTIAYLNVFKKDNYYYIPKDKYQE LKEKKKIKDTDQFIASFYKNDLIKLNGDLYKIIGVNSDDRNIIELDYYDIKYKDYCEINNIKGEP RIKKTIGKKTESIEKFTTDVLGNLYLHSTEKAPQLIFKRGL
SpG	14853	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT

		FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDHIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF LWPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIK LPKYSLFELENGRKRMLASAKQLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
SpG nickase	14854	MDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATR LKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF LWPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIK LPKYSLFELENGRKRMLASAKQLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
met-SpG nickase	14855	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRL KRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL

		PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF LWPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIK LPKYSLFELENGRKRMLASAKQLQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFV EQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAF KYFDTTIDRKQYRSTKEVLDATLIHQSITGLYETRIDLSQLGGD
Met-SpCAS9 (R221K N394K H840A)	1487 6	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSGETAEATRL KRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVA YHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRKLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKS NFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPL SASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILE KMDGTEELLVKLKREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILT FRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLPNEKVL PKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFK KIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERL KTYAHLFDDKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVI EMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDM YVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVKKMKNYW RQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKHVAQILDSRMNTKYDEN DKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFV YGDYKVYDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIV WDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGF DSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKL PKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVE QHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFK YFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD

[146] In some embodiments, a Cas9 protein comprises a variant Cas9 protein containing one or more amino acid substitutions. In some embodiments, a wildtype Cas9 protein comprises a RuvC domain and an HNH domain. In some embodiments, a prime editor comprises a nuclease active Cas9 protein that may cleave both strands of a double stranded target DNA sequence. In some embodiments, the nuclease active Cas9 protein comprises a functional RuvC domain and a functional HNH domain. In some embodiments, a prime editor comprises a Cas9 nickase that can bind to a guide polynucleotide and

recognize a target DNA, but can cleave only one strand of a double stranded target DNA. In some embodiments, the Cas9 nickase comprises only one functional RuvC domain or one functional HNH domain. In some embodiments, a prime editor comprises a Cas9 that has a non-functional HNH domain and a functional RuvC domain. In some embodiments, the prime editor can cleave the edit strand (i.e., the PAM strand), but not the non-edit strand of a double stranded target DNA sequence. In some embodiments, a prime editor comprises a Cas9 having a non-functional RuvC domain that can cleave the target strand (i.e., the non-PAM strand), but not the edit strand of a double stranded target DNA sequence. In some embodiments, a prime editor comprises a Cas9 that has neither a functional RuvC domain nor a functional HNH domain, which may not cleave any strand of a double stranded target DNA sequence.

[147] In some embodiments, a prime editor comprises a Cas9 having a mutation in the RuvC domain that reduces or abolishes the nuclease activity of the RuvC domain. In some embodiments, the Cas9 comprises a mutation at amino acid D10 as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 comprises a D10A mutation as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid D10, G12, and/or G17 as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a D10A mutation, a G12A mutation, and/or a G17A mutation as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof.

[148] In some embodiments, a prime editor comprises a Cas9 polypeptide having a mutation in the HNH domain that reduces or abolishes the nuclease activity of the HNH domain. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid H840 as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a H840A mutation as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14830, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid E762, D839, H840, N854, N856, N863, H982, H983, A984, D986, and/or a A987 as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a E762A, D839A, H840A, N854A, N856A, N863A, H982A, H983A, A984A, and/or a D986A mutation as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid R221, N394, and/or H840 as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid R220, N393, and/or H839 as compared to a wild type SpCas9 (as set forth in SEQ ID NO: 14829) lacking a N-terminal methionine, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid R221K, N394L, and/or H840A as compared to a wild type SpCas9 as set forth in SEQ ID

NO: 14829, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid R220K, N393K, and/or H839A as compared to a wild type SpCas9 (as set forth in SEQ ID NO: 14829) lacking a N-terminal methionine, or a corresponding mutation thereof. In some embodiments, the Cas9 polypeptide comprises a mutation at amino acid R220K, N393K, and/or H839A as compared to a wild type SpCas9 (as set forth in SEQ ID NO: 14970).

[149] In some embodiments, a prime editor comprises a Cas9 having one or more amino acid substitutions in both the HNH domain and the RuvC domain that reduce or abolish the nuclease activity of both the HNH domain and the RuvC domain. In some embodiments, the prime editor comprises a nuclease inactive Cas9, or a nuclease dead Cas9 (dCas9). In some embodiments, the dCas9 comprises a H840X substitution and a D10X mutation compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829 or corresponding mutations thereof, wherein X is any amino acid other than H for the H840X substitution and any amino acid other than D for the D10X substitution. In some embodiments, the dead Cas9 comprises a H840A and a D10A mutation as compared to a wild type SpCas9 as set forth in SEQ ID NO: 14829, or corresponding mutations thereof.

[150] In some embodiments, the N-terminal methionine is removed from a Cas9 nickase, or from any Cas9 variant, ortholog, or equivalent disclosed or contemplated herein. For example, methionine-minus Cas9 nickases include any one of the sequences set forth in SEQ ID Nos:14831, 14834, 14837, 14840, 14843, 14846, 14849, 14852, 14855, 14876, or a variant thereof having an amino acid sequence that has at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% sequence identity thereto.

[151] Besides dead Cas9 and Cas9 nickase variants, the Cas9 proteins used herein may also include other Cas9 variants having at least about 70% identical, at least about 80% identical, at least about 90% identical, at least about 95% identical, at least about 96% identical, at least about 97% identical, at least about 98% identical, at least about 99% identical, at least about 99.5% identical, or at least about 99.9% identical to any reference Cas9 protein, including any wild type Cas9, or mutant Cas9 (e.g., a dead Cas9 or Cas9 nickase), or fragment Cas9, or circular permutant Cas9, or other variant of Cas9 disclosed herein or known in the art. In some embodiments, a Cas9 variant may have 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 21, 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 or more amino acid changes compared to a reference Cas9, e.g., a wild type Cas9. In some embodiments, the Cas9 variant comprises a fragment of a reference Cas9 (*e.g.*, a gRNA binding domain or a DNA-cleavage domain), such that the fragment is at least about 70% identical, at least about 80% identical, at least about 90% identical, at least about 95% identical, at least about 96% identical, at least about 97% identical, at least about 98% identical, at least about 99% identical, at least about 99.5% identical, or at least about 99.9% identical to the corresponding fragment of the reference Cas9, e.g., a wild type Cas9. In some embodiments, the fragment is 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% identical, at least 96%, at least

97%, at least 98%, at least 99%, or at least 99.5% of the amino acid length of a corresponding wild type Cas9.

[152] In some embodiments, a Cas9 fragment is a functional fragment that retains one or more Cas9 activities. In some embodiments, the Cas9 fragment is at least 100 amino acids in length. In some embodiments, the fragment is at least 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, or at least 1300 amino acids in length.

[153] In some embodiments, a prime editor comprises a Cas protein, *e.g.*, Cas9, containing modifications that allow altered PAM recognition. In prime editing using a Cas-protein-based prime editor, a "*protospacer* adjacent motif (PAM)", PAM sequence, or PAM-like motif, may be used to refer to a short DNA sequence immediately following the protospacer sequence on the PAM strand of the target gene. In some embodiments, the PAM is recognized by the Cas nuclease in the prime editor during prime editing. In certain embodiments, the PAM is required for target binding of the Cas protein. The specific PAM sequence required for Cas protein recognition may depend on the specific type of the Cas protein. A PAM can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more nucleotides in length. In some embodiments, a PAM is between 2-6 nucleotides in length. In some embodiments, the PAM can be a 5' PAM (*i.e.*, located upstream of the 5' end of the protospacer). In other embodiments, the PAM can be a 3' PAM (*i.e.*, located downstream of the 5' end of the protospacer).In some embodiments, the Cas protein of a prime editor recognizes a canonical PAM, for example, a SpCas9 recognizes 5'-NGG-3' PAM. In some embodiments, the Cas protein of a prime editor has altered or non-canonical PAM specificities. Exemplary PAM sequences and corresponding Cas variants are described in **Table 87** below. It should be appreciated that for each of the variants provided, the Cas protein comprises one or more of the amino acid substitutions as indicated compared to a wild type Cas protein sequence, for example, the Cas9 as set forth in SEQ ID NO: 14829. The PAM motifs as shown in **Table 87** below are in the order of 5' to 3'. In some embodiments, the Cas proteins of the invention can also be used to direct transcriptional control of target sequences, for example silencing transcription by sequence-specific binding to target sequences. In some embodiments, a Cas protein described herein may have one or mutation in a PAM recognition motif. In some embodiments, a Ca protein described herein may have altered PAM specificity. In some embodiments, the disclosure provides PEgRNA comprising a spacer that correspond to the altered PAM.

[154] As used in PAM sequences in Table 1, "N" refers to any one of nucleotides A, G, C, and T, "R" refers to nucleotide A or G, and "Y" refers to nucleotide C or T.

Table 87: Cas protein variants and corresponding PAM sequences

Variant	PAM
spCas9 (wild type)	NGG, NGA, NAG, NGNGA
spCas9- VRVRFRR R1335V/L1111R/D1135V/G1218R/E1219F/A1322R/T1337R	NG
spCas9-VQR (D1135V/R1335Q/T1337R)	NGA

spCas9-EQR (D1135E/R1335Q/T1337R)	NGA
spCas9-VRER (D1135V/G1218R/R1335E/T1337R)	NGCG
spCas9-VRQR (D1135V, G1218R, R1335Q, T1337R)	NGA
Cas9-NG (L1111R, D1135V, G1218R, E1219F, A1322R, T1337R, R1335V)	NGN
SpG Cas9 (D1135L, S1136W, G1218K, E1219Q, R1335Q, T1337R)	NGN
SyRY Cas9 (A61R, L1111R, N1317R, A1322R, and R1333P)	NRN
xCas9 (E480K, E543D, E1219V, K294R, Q1256K, A262T, S409I, M694I)	NGN
SluCa9	NNGG
sRGN1, sRGN2, sRGN4, sRGN3.1, sRGN3.3	NNGG
saCas9	NNGRRT NNGRRN
saCas9-KKH (E782K, N968K, R1015H)	NNNRRT
spCas9-MQKSER (D1135M, S1136Q, G1218K, E1219S, R1335E, T1337R)	NGCG/NGCN
spCas9-LRKIQK (D1135L, S1136R, G1218K, E1219I, R1335Q, T1337K)	NGTN
spCas9-LRVSQK (D1135L, S1136R, G1218V, E1219S, R1335Q, T1337K)	NGTN
spCas9-LRVSQL(D1135L, S1136R, G1218V, E1219S, R1335Q, T1337L)	NGTN
Cpf1	TTTV
Spy-Mac	NAA
NmCas9	NNNNGATT
StCas9	NNAGAAW
TdCas9	NAAAAC

[155] In some embodiments, a prime editor comprises a Cas9 polypeptide comprising one or mutations selected from the group consisting of: A61R, L111R, D1135V, R221K, A262T, R324L, N394K, S409I, S409I, E427G, E480K, M495V, N497A, Y515N, K526E, F539S, E543D, R654L, R661A, R661L, R691A, N692A, M694A, M694I, Q695A, H698A, R753G, M763I, K848A, K890N, Q926A, K1003A, R1060A, L1111R, R1114G, D1135E, D1135L, D1135N, S1136W, V1139A, D1180G, G1218K, G1218R, G1218S, E1219Q, E1219V, E1219V, Q1221H, P1249S, E1253K, N1317R, A1320V, P1321S, A1322R, I1322V, D1332G, R1332N, A1332R, R1333K, R1333P, R1335L, R1335Q, R1335V, T1337N, T1337R, S1338T, H1349R, and any combinations thereof as compared to a wildtype SpCas9 polypeptide as set forth in SEQ ID NO: 14829.

[156] In some embodiments, a prime editor comprises a SaCas9 polypeptide. In some embodiments, the SaCas9 polypeptide comprises one or more of mutations E782K, N968K, and R1015H as compared to a wild type SaCas9. In some embodiments, a prime editor comprises a FnCas9 polypeptide, for example, a wildtype FnCas9 polypeptide or a FnCas9 polypeptide comprising one or more of mutations

E1369R, E1449H, or R1556A as compared to the wild type FnCas9. In some embodiments, a prime editor comprises a Sc Cas9, for example, a wild type ScCas9 or a ScCas9 polypeptide comprises one or more of mutations I367K, G368D, I369K, H371L, T375S, T376G, and T1227K as compared to the wild type ScCas9. In some embodiments, a prime editor comprises a St1 Cas9 polypeptide, a St3 Cas9 polypeptide, or a Slu Cas9 polypeptide.

[157] In some embodiments, a prime editor comprises a Cas polypeptide that comprises a circular permutant Cas variant. For example, a Cas9 polypeptide of a prime editor may be engineered such that the N-terminus and the C-terminus of a Cas9 protein (*e.g.*, a wild type Cas9 protein, or a Cas9 nickase) are topically rearranged to retain the ability to bind DNA when complexed with a guide RNA (gRNA). An exemplary circular permutant configuration may be N-terminus-[original C-terminus]-[original N-terminus]-C-terminus. Any of the Cas9 proteins described herein, including any variant, ortholog, or naturally occurring Cas9 or equivalent thereof, may be reconfigured as a circular permutant variant.

[158] In various embodiments, the circular permutants of a Cas protein, e.g., a Cas9, may have the following structure: N-terminus–[original C-terminus]–[optional linker]–[original N-terminus]–C-terminus. In some embodiments, a circular permutant Cas9 comprises any one of the following structures (amino acid positions as set forth in SEQ ID NO: 14829):

[159] N-terminus–[1268-1368]–[optional linker]–[1-1267]–C-terminus;

[160] N-terminus–[1168-1368]–[optional linker]–[1-1167]–C-terminus;

[161] N-terminus–[1068-1368]–[optional linker]–[1-1067]–C-terminus;

[162] N-terminus–[968-1368]–[optional linker]–[1-967]–C-terminus;

[163] N-terminus–[868-1368]–[optional linker]–[1-867]–C-terminus;

[164] N-terminus–[768-1368]–[optional linker]–[1-767]–C-terminus;

[165] N-terminus–[668-1368]–[optional linker]–[1-667]–C-terminus;

[166] N-terminus–[568-1368]–[optional linker]–[1-567]–C-terminus;

[167] N-terminus–[468-1368]–[optional linker]–[1-467]–C-terminus;

[168] N-terminus–[368-1368]–[optional linker]–[1-367]–C-terminus;

[169] N-terminus–[268-1368]–[optional linker]–[1-267]–C-terminus;

[170] N-terminus–[168-1368]–[optional linker]–[1-167]–C-terminus;

[171] N-terminus–[68-1368]–[optional linker]–[1-67]–C-terminus;

[172] N-terminus–[10-1368]–[optional linker]–[1-9]–C-terminus, or the corresponding circular permutants of other Cas9 proteins (including other Cas9 orthologs, variants, etc).

[173] In some embodiments, a circular permutant Cas9 comprises any one of the following structures (amino acid positions as set forth in SEQ ID NO: 14829- 1368 amino acids of UniProtKB - Q99ZW2:

[174] N-terminus–[102-1368]–[optional linker]–[1-101]–C-terminus;

[175] N-terminus–[1028-1368]–[optional linker]–[1-1027]–C-terminus;

[176] N-terminus–[1041-1368]–[optional linker]–[1-1043]–C-terminus;

[177] N-terminus–[1249-1368]–[optional linker]–[1-1248]–C-terminus; or

[178] N-terminus–[1300-1368]–[optional linker]–[1-1299]–C-terminus, or the corresponding circular permutants of other Cas9 proteins (including other Cas9 orthologs, variants, etc).

[179] In some embodiments, a circular permutant Cas9 comprises any one of the following structures (amino acid positions as set forth in SEQ ID NO: 14829 - 1368 amino acids of UniProtKB - Q99ZW2 N-terminus–[103-1368]–[optional linker]–[1-102]–C-terminus:

[180] N-terminus–[1029-1368]–[optional linker]–[1-1028]–C-terminus;

[181] N-terminus–[1042-1368]–[optional linker]–[1-1041]–C-terminus;

[182] N-terminus–[1250-1368]–[optional linker]–[1-1249]–C-terminus; or

[183] N-terminus–[1301-1368]–[optional linker]–[1-1300]–C-terminus, or the corresponding circular permutants of other Cas9 proteins (including other Cas9 orthologs, variants, etc).

[184] In some embodiments, the circular permutant can be formed by linking a C-terminal fragment of a Cas9 to an N-terminal fragment of a Cas9, either directly or by using a linker, such as an amino acid linker. In some embodiments, thee C-terminal fragment may correspond to the 95% or more of the C-terminal amino acids of a Cas9 (e.g., amino acids about 1300-1368 as set forth in SEQ ID No: 14829 or corresponding amino acid positions thereof), or the 90%, 85%, 80%, 75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, or 5% or more of the C-terminal amino acids of a Cas9 (e.g., SEQ ID NO: 14829 or a ortholog or a variant thereof). The N-terminal portion may correspond to 95% or more of the N-terminal amino acids of a Cas9 (e.g., amino acids about 1-1300 as set forth in SEQ ID No: 14829or corresponding amino acid positions thereof), or 90%, 85%, 80%, 75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, or 5% or more of the N terminal amino acids of a Cas9 (e.g., as set forth in SEQ ID No: 14829 or corresponding amino acid positions thereof).

[185] In some embodiments, the circular permutant can be formed by linking a C-terminal fragment of a Cas9 to an N-terminal fragment of a Cas9, either directly or by using a linker, such as an amino acid linker. In some embodiments, the C-terminal fragment that is rearranged to the N-terminus includes or corresponds to the C-terminal 30% or less of the amino acids of a Cas9 (e.g., amino acids 1012-1368 as set forth in SEQ ID No: 14829 or corresponding amino acid positions thereof). In some embodiments, the C-terminal fragment that is rearranged to the N-terminus, includes or corresponds to the C-terminal 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%,5%, 4%, 3%, 2%, or 1% of the amino acids of a Cas9 (e.g., as set forth in SEQ ID No: 14829or corresponding amino acid positions thereof). In some embodiments, the C-terminal fragment that is rearranged to the N-terminus, includes or corresponds to the C-terminal 410 residues or less of a Cas9 (e.g., as set forth in SEQ ID No: 14829 or corresponding amino acid positions thereof). In some embodiments, the C-terminal portion that is rearranged to the N-terminus, includes or corresponds to the C-terminal 410, 400, 390, 380, 370, 360, 350, 340, 330, 320, 310, 300, 290, 280, 270, 260, 250, 240, 230, 220, 210, 200, 190, 180, 170, 160, 150, 140, 130, 120, 110, 100, 90, 80, 70, 60, 50, 40, 30, 20, or 10 residues of a Cas9 (e/g/ as set forth in SEQ ID No: 14829 or corresponding amino acid positions thereof). In some embodiments, the C-terminal portion that is rearranged to the N-terminus includes or

corresponds to the C-terminal 357, 341, 328, 120, or 69 residues of a Cas9 (e.g., as set forth in SEQ ID No: 14829 or corresponding amino acid positions thereof).

[186] In other embodiments, circular permutant Cas9 variants may be a topological rearrangement of a Cas9 primary structure based on the following method, which is based on *S. pyogenes* Cas9 of SEQ ID NO: 14829: (a) selecting a circular permutant (CP) site corresponding to an internal amino acid residue of the Cas9 primary structure, which dissects the original protein into two halves: an N-terminal region and a C-terminal region; (b) modifying the Cas9 protein sequence (e.g., by genetic engineering techniques) by moving the original C-terminal region (comprising the CP site amino acid) to precede the original N-terminal region, thereby forming a new N-terminus of the Cas9 protein that now begins with the CP site amino acid residue. The CP site can be located in any domain of the Cas9 protein, including, for example, the helical-II domain, the RuvCIII domain, or the CTD domain. For example, the CP site may be located (as set forth in SEQ ID No: 14829or corresponding amino acid positions thereof) at original amino acid residue 181, 199, 230, 270, 310, 1010, 1016, 1023, 1029, 1041, 1247, 1249, or 1282. Thus, once relocated to the N-terminus, original amino acid 181, 199, 230, 270, 310, 1010, 1016, 1023, 1029, 1041, 1247, 1249, or 1282 would become the new N-terminal amino acid. Nomenclature of these CP-Cas9 proteins may be referred to as Cas9-CP^{181}, Cas9-CP^{199}, Cas9-CP^{230}, Cas9-CP^{270}, Cas9-CP^{310}, Cas9-CP^{1010}, Cas9-CP^{1016}, Cas9-CP^{1023}, Cas9-CP^{1029}, Cas9-CP^{1041}, Cas9-CP^{1247}, Cas9-CP^{1249}, and Cas9-CP^{1282}, respectively. This description is not meant to be limited to making CP variants from SEQ ID NO: 14829 but may be implemented to make CP variants in any Cas9 sequence, either at CP sites that correspond to these positions, or at other CP sites entirely. This description is not meant to limit the specific CP sites in any way. Virtually any CP site may be used to form a CP-Cas9 variant.

[187] In some embodiments, a prime editor comprises a Cas9 functional variant that is of smaller molecular weight than a wild type SpCas9 protein. In some embodiments, a smaller-sized Cas9 functional variant may facilitate delivery to cells, e.g., by an expression vector, nanoparticle, or other means of delivery. In certain embodiments, a smaller-sized Cas9 functional variant is a Class 2 Type II Cas protein. In certain embodiments, a smaller-sized Cas9 functional variant is a Class 2 Type V Cas protein. In certain embodiments, a smaller-sized Cas9 functional variant is a Class 2 Type VI Cas protein.

[188] In some embodiments, a prime editor comprises a SpCas9 that is 1368 amino acids in length and has a predicted molecular weight of 158 kilodaltons. In some embodiments, a prime editor comprises a Cas9 functional variant or functional fragment that is less than 1300 amino acids, less than 1290 amino acids, than less than 1280 amino acids, less than 1270 amino acids, less than 1260 amino acid, less than 1250 amino acids, less than 1240 amino acids, less than 1230 amino acids, less than 1220 amino acids, less than 1210 amino acids, less than 1200 amino acids, less than 1190 amino acids, less than 1180 amino acids, less than 1170 amino acids, less than 1160 amino acids, less than 1150 amino acids, less than 1140 amino acids, less than 1130 amino acids, less than 1120 amino acids, less than 1110 amino acids, less than 1100 amino acids, less than 1050 amino acids, less than 1000 amino acids, less than

950 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800 amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 550 amino acids, or less than 500 amino acids, but at least larger than about 400 amino acids and retaining the one or more functions, e.g., DNA binding function, of the Cas9 protein.

[189] In some embodiments, the Cas protein may include any CRISPR associated protein, including but not limited to, Cas12a, Cas12b1, Cas1, Cas1B, Cas2, Cas3, Cas4, Cas5, Cas6, Cas7, Cas8, Cas9 (also known as Csn1 and Csx12), Cas10, Csy1, Csy2, Csy3, Cse1, Cse2, Csc1, Csc2, Csa5, Csn2, Csm2, Csm3, Csm4, Csm5, Csm6, Cmr1, Cmr3, Cmr4, Cmr5, Cmr6, Csb1, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CsaX, Csx3, Csx1, Csx15, Csf1, Csf2, Csf3, Csf4, homologs thereof, or modified versions thereof, and preferably comprising a nickase mutation (e.g., a mutation corresponding to the D10A mutation of the wild type Cas9 polypeptide of SEQ ID NO: 14829). In various other embodiments, the napDNAbp can be any of the following proteins: a Cas9, a Cas12a (Cpf1), a Cas12e (CasX), a Cas12d (CasY), a Cas12b1 (C2c1), a Cas13a (C2c2), a Cas12c (C2c3), a GeoCas9, a CjCas9, a Cas12g, a Cas12h, a Cas12i, a Cas13b, a Cas13c, a Cas13d, a Cas14, a Csn2, an xCas9, an SpCas9-NG, a circularly permuted Cas9, or an Argonaute (Ago) domain, or a functional variant or fragment thereof.

[190] Exemplary Cas proteins and nomenclature are shown in **Table 88** below:

Table 88: Exemplary Cas proteins and nomenclature

Legacy nomenclature	**Current nomenclature**
type II CRISPR-Cas enzymes	
Cas9	same
type V CRISPR-Cas enzymes	
Cpf1	Cas12a
CasX	Cas12e
C2c1	Cas12b1
Cas12b2	same
C2c3	Cas12c
CasY	Cas12d
C2c4	same
C2c8	same
C2c5	same
C2c10	same
C2c9	same
type VI CRISPR-Cas enzymes	
C2c2	Cas13a
Cas13d	same
C2c7	Cas13c
C2c6	Cas13b

[191] In some embodiments, prime editors described herein may also comprise Cas proteins other than Cas9. For example, in some embodiments, a prime editor as described herein may comprise a Cas12a (Cpf1) polypeptide or functional variants thereof. In some embodiments, the Cas12a polypeptide comprises a mutation that reduces or abolishes the endonuclease domain of the Cas12a polypeptide. In some embodiments, the Cas12a polypeptide is a Cas12a nickase. In some embodiments, the Cas protein

comprises an amino acid sequence that comprises at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a naturally occurring Cas12a polypeptide.

[192] In some embodiments, a prime editor comprises a Cas protein that is a Cas12b (C2c1) or a Cas12c (C2c3) polypeptide. In some embodiments, the Cas protein comprises an amino acid sequence that comprises at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a naturally occurring Cas12b (C2c1) or Cas12c (C2c3) protein. In some embodiments, the Cas protein is a Cas12b nickase or a Cas12c nickase. In some embodiments, the Cas protein is a Cas12e, a Cas12d, a Cas13, Cas14a, Cas14b, Cas14c, Cas14d, Cas14e, Cas14f, Cas14g, Cas14h, Cas14u, or a CasΦ polypeptide. In some embodiments, the Cas protein comprises an amino acid sequence that comprises at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to a naturally-occurring Cas12e, Cas12d, Cas13, Cas14a, Cas14b, Cas14c, Cas14d, Cas14e, Cas14f, Cas14g, Cas14h, Cas14u, or Cas Φ protein. In some embodiments, the Cas protein is a Cas12e, Cas12d, Cas13, or Cas Φ nickase.

Nuclear Localization Sequences

[193] In some embodiments, a prime editor further comprises one or more nuclear localization sequence (NLS). In some embodiments, the NLS helps promote translocation of a protein into the cell nucleus. In some embodiments, a prime editor comprises a fusion protein, *e.g.*, a fusion protein comprising a DNA binding domain and a DNA polymerase, that comprises one or more NLSs. In some embodiments, one or more polypeptides of the prime editor are fused to or linked to one or more NLSs. In some embodiments, the prime editor comprises a DNA binding domain and a DNA polymerase domain that are provided in trans, wherein the DNA binding domain and/or the DNA polymerase domain is fused or linked to one or more NLSs.

[194] In certain embodiments, a prime editor or prime editing complex comprises at least one NLS. In some embodiments, a prime editor or prime editing complex comprises at least two NLSs. In embodiments with at least two NLSs, the NLSs can be the same NLS, or they can be different NLSs.

[195] In some instances, a prime editor may further comprise at least one nuclear localization sequence (NLS). In some cases, a prime editor may further comprise 1 NLS. In some cases, a prime editor may further comprise 2 NLSs. In other cases, a prime editor may further comprise 3 NLSs. In one case, a primer editor can further comprise more than 4, 5, 6, 7, 8, 9 or 10 NLSs.

[196] In addition, the NLSs can be expressed as part of a prime editor complex. In some embodiments, a NLS can be positioned almost anywhere in a protein's amino acid sequence, and generally comprises a short sequence of three or more or four or more amino acids. The location of the NLS fusion can be at the N-terminus, the C-terminus, or positioned anywhere within a sequence of a prime editor or a component thereof (*e.g.*, inserted between the DNA-binding domain and the DNA polymerase domain of a prime editor fusion protein, between the DNA binding domain and a linker sequence, between a DNA

polymerase and a linker sequence, between two linker sequences of a prime editor fusion protein or a component thereof, in either N-terminus to C-terminus or C-terminus to N-terminus order). In some embodiments, a prime editor is fusion protein that comprises an NLS at the N terminus. In some embodiments, a prime editor is fusion protein that comprises an NLS at the C terminus. In some embodiments, a prime editor is fusion protein that comprises at least one NLS at both the N terminus and the C terminus. In some embodiments, the prime editor is a fusion protein that comprises two NLSs at the N terminus and/or the C terminus.

[197] Any NLSs that are known in the art are also contemplated herein. The NLSs may be any naturally occurring NLS, or any non-naturally occurring NLS (*e.g.*, an NLS with one or more mutations relative to a wild-type NLS). In some embodiments, the one or more NLSs of a prime editor comprise bipartite NLSs. In some embodiments, a nuclear localization signal (NLS) is predominantly basic. In some embodiments, the one or more NLSs of a prime editor are rich in lysine and arginine residues. In some embodiments, the one or more NLSs of a prime editor comprise proline residues.

[198] In some embodiments, a nuclear localization signal (NLS) comprises the sequence

[199] MDSLLMNRRKFLYQFKNVRWAKGRRETYLC (SEQ ID NO: 14864), KRTADGSEFESPKKKRKV (SEQ ID NO: 14913), KRTADGSEFEPKKKRKV (SEQ ID NO: 14914), NLSKRPAAIKKAGQAKKKK (SEQ ID NO: 14915), RQRRNELKRSF (SEQ ID NO: 14916), or NQSSNFGPMKGGNFGGRSSGPYGGGGQYFAKPRNQGGY (SEQ ID NO: 14917).

[200] In some embodiments, a NLS is a monopartite NLS. For example, in some embodiments, a NLS is a SV40 large T antigen NLS PKKKRKV (SEQ ID NO: 14862). In some embodiments, a NLS is a bipartite NLS. In some embodiments, a bipartite NLS comprises two basic domains separated by a spacer sequence comprising a variable number of amino acids. In some embodiments, a NLS is a bipartite NLS. In some embodiments, a bipartite NLS consists of two basic domains separated by a spacer sequence comprising a variable number of amino acids. In some embodiments, the spacer amino acid sequence comprises the sequence KRXXXXXXXXXXKKKL (*Xenopus nucleoplasmin* NLS) (SEQ ID NO: 14918), wherein X is any amino acid. In some embodiments, the NLS comprises a nucleoplasmin NLS sequence KRPAATKKAGQAKKKK (SEQ ID NO: 14919). In some embodiments, a NLS is a noncanonical sequences such as M9 of the hnRNP Al protein, the influenza virus nucleoprotein NLS, and the yeast Gal4 protein NLS. In some embodiments, a NLS is a noncanonical sequences such as M9 of the hnRNP Al protein, the influenza virus nucleoprotein NLS, and the yeast Gal4 protein NLS.

[201] In some embodiments, a bipartite NLS consists of two basic domains separated by a spacer sequence comprising a variable number of amino acids. In some embodiments, a NLS comprises an amino acid sequence that is at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOs: 14862-14872. In some embodiments, a NLS comprises an amino acid sequence selected from the group consisting of 14862-14872. In some embodiments, a prime editing composition comprises a

polynucleotide that encodes a NLS that comprises an amino acid sequence that is at least about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of any one of SEQ ID NOs: 14862-14872. In some embodiments, a prime editing composition comprises a polynucleotide that encodes a NLS that comprises an amino acid sequence selected from the group consisting of 14862-14872.

[202] Any NLSs that are known in the art are also contemplated herein. The NLSs may be any naturally occurring NLS, or any non-naturally occurring NLS (*e.g.*, an NLS with one or more mutations relative to a wild-type NLS). In some embodiments, the one or more NLSs of a prime editor comprise bipartite NLSs. In some embodiments, the one or more NLSs of a prime editor are rich in lysine and arginine residues. In some embodiments, the one or more NLSs of a prime editor comprise proline residues. Non-limiting examples of NLS sequences are provided in **Table 89** below.

[203] In addition, the NLSs may be expressed as part of a prime editor composition, fusion protein, or complex. The location of the NLS fusion can be at the N-terminus, the C-terminus, or positioned anywhere within a sequence of a prime editor or a component thereof (*e.g.*, inserted between the DNA binding domain and the DNA polymerase domain of a prime editor fusion protein, between the DNA binding domain and a linker sequence, between a DNA polymerase and a linker sequence, between two linker sequences of a prime editor fusion protein or a component thereof, in either N-terminus to C-terminus or C-terminus to N-terminus order). In some embodiments, a prime editor is a fusion protein that comprises an NLS at the N terminus. In some embodiments, a prime editor is a fusion protein that comprises an NLS at the C terminus. In some embodiments, a prime editor is a fusion protein that comprises at least one NLS at both the N terminus and the C terminus. In some embodiments, the prime editor is a fusion protein that comprises two NLSs at the N terminus and/or the C terminus.

[204] Non-limiting examples of NLS sequences are provided in Table 89 below.

Table 89: Exemplary nuclear localization sequences

Description	Sequence	SEQ ID NO:
NLS of SV40 Large T-AG	PKKKRKV	14862
NLS	MKRTADGSEFESPKKKRKV	14863
NLS	MDSLLMNRRKFLYQFKNVRWAKGRRETYLC	14864
NLS of Nucleoplasmin	AVKRPAATKKAGQAKKKKLD	14865
NLS of EGL-13	MSRRRKANPTKLSENAKKLAKEVEN	14866
NLS of C-Myc	PAAKRVKLD	14867
NLS of Tus-protein	KLKIKRPVK	14868
NLS of polyoma large T-AG	VSRKRPRP	14869
NLS of Hepatitis D virus antigen	EGAPPAKRAR	14870
NLS of murine p53	PPQPKKKPLDGE	14871
C-Terminal linker and NLS of an exemplary prime editor fusion protein	SGGSKRTADGSEFEPKKKRKV	14872

[205] In some embodiments, a prime editing complex comprises a fusion protein comprising a DNA binding domain (*e.g.*, Cas9(H840A)) and a reverse transcriptase (*e.g.*, a variant MMLV RT) having the following structure: [NLS]- [Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K)(W313F)], and a desired PEgRNA. In some embodiments, the prime editing complex comprises a prime editor fusion protein that has the amino acid sequence of SEQ ID NO: 14873,.: Sequence of an exemplary prime editor fusion protein comprising a DNA binding domain (*e.g.*, Cas9(H840A)) and a reverse transcriptase (*e.g.*, a variant MMLV RT) having the following structure: [NLS]- [Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K)(W313F)] and its components are shown in Table 90.

[206] In some embodiments, a prime editing complex comprises a fusion protein comprising a DNA binding domain (*e.g.*, Cas9((R221K N394K H840A)) and a reverse transcriptase (*e.g.*, a variant MMLV RT) having the following structure: [NLS]- [Cas9((R221K N394K H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K)(W313F)], and a desired PEgRNA. In some embodiments, the prime editing complex comprises a prime editor fusion protein that has the amino acid sequence of SEQ ID NO: 14874. Sequence of an exemplary prime editor fusion protein comprising a DNA binding domain (*e.g.*, Cas9(H840A)) and a reverse transcriptase (*e.g.*, a variant MMLV RT) having the following structure: [NLS]- [Cas9 (R221K N394K H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K)(W313F)] and its components are shown in Table 91.

[207] Polypeptides comprising components of a prime editor may be fused via peptide linkers, or may be provided *in trans* relevant to each other. For example, a reverse transcriptase may be expressed, delivered, or otherwise provided as an individual component rather than as a part of a fusion protein with the DNA binding domain. In such cases, components of the prime editor may be associated through non-peptide linkages or co-localization functions. In some embodiments, a prime editor further comprises additional components capable of interacting with, associating with, or capable of recruiting other components of the prime editor or the prime editing system. For example, a prime editor may comprise an RNA-protein recruitment polypeptide that can associate with an RNA-protein recruitment RNA aptamer. In some embodiments, an RNA-protein recruitment polypeptide can recruit, or be recruited by, a specific RNA sequence. Non limiting examples of RNA-protein recruitment polypeptide and RNA aptamer pairs include a MS2 coat protein and a MS2 RNA hairpin, a PCP polypeptide and a PP7 RNA hairpin, a Com polypeptide and a Com RNA hairpin, a Ku protein and a telomerase Ku binding RNA motif, and a Sm7 protein and a telomerase Sm7 binding RNA motif. In some embodiments, the prime editor comprises a DNA binding domain fused or linked to an RNA-protein recruitment polypeptide. In some embodiments, the prime editor comprises a DNA polymerase domain fused or linked to an RNA-protein recruitment polypeptide. In some embodiments, the DNA binding domain and the DNA polymerase domain fused to the RNA-protein recruitment polypeptide, or the DNA binding domain fused to the RNA-protein recruitment polypeptide and the DNA polymerase domain are co-localized by the

corresponding RNA-protein recruitment RNA aptamer of the RNA-protein recruitment polypeptide. In some embodiments, the corresponding RNA-protein recruitment RNA aptamer fused or linked to a portion of the PEgRNA or ngRNA. For example, an MS2 coat protein fused or linked to the DNA polymerase and a MS2 hairpin installed on the PEgRNA for co-localization of the DNA polymerase and the RNA-guided DNA binding domain (*e.g.*, a Cas9 nickase).

[208] In some embodiments, a prime editor comprises a polypeptide domain, an MS2 coat protein (MCP), that recognizes an MS2 hairpin. In some embodiments, the nucleotide sequence of the MS2 hairpin (or equivalently referred to as the "MS2 aptamer") is: GCCAACATGAGGATCACCCATGTCTGCAGGGCC (SEQ ID NO: 14960). In some embodiments, the amino acid sequence of the MCP is: GSASNFTQFVLVDNGGTGDVTVAPSNFANGVAEWISSNSRSQAYKVTCSVRQSSAQNRKYTIK VEVPKVATQTVGGEELPVAGWRSYLNMELTIPIFATNSDCELIVKAMQGLLKDGNPIPSAIA ANSGIY(SEQ ID NO: 14961).

[209] In certain embodiments, components of a prime editor are directly fused to each other. In certain embodiments, components of a prime editor are associated to each other via a linker.

[210] As used herein, a linker can be any chemical group or a molecule linking two molecules or moieties, *e.g.*, a DNA binding domain and a polymerase domain of a prime editor. In some embodiments, a linker is an organic molecule, group, polymer, or chemical moiety. In some embodiments, the linker comprises a non-peptide moiety. The linker may be as simple as a covalent bond, or it may be a polymeric linker many atoms in length, for example, a polynucleotide sequence. In certain embodiments, the linker is a covalent bond (*e.g.*, a carbon-carbon bond, disulfide bond, carbon-heteroatom bond, etc.).

[211] In certain embodiments, two or more components of a prime editor are linked to each other by a peptide linker. In some embodiments, a peptide linker is 5-100 amino acids in length, for example, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 30-35, 35-40, 40-45, 45-50, 50-60, 60-70, 70-80, 80-90, 90-100, 100-150, or 150-200 amino acids in length. In some embodiments, the peptide linker is 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 35, 45, 50, 55, 60, 60, 65, 70, 70, 75, 80, 85, 90, 90, 95, 100, 101, 102, 103, 104, 105, 110, 120, 130, 140,150, 160, 175, 180, 190, or 200 amino acids in length. In some embodiments, the peptide linker is 5-100 amino acids in length. In some embodiments, the peptide linker is 10-80 amino acids in length. In some embodiments, the peptide linker is 15-70 amino acids in length. In some embodiments, the peptide linker is 16 amino acids in length, 24 amino acids in length, 64 amino acids in length, or 96 amino acids in length. In some embodiments, the peptide linker is at least 50 amino acids in length. In some embodiments, the peptide linker is at least 40 amino acids in length. In some embodiments, the peptide linker is at least 30 amino acids in length. In some embodiments, the peptide linker is 46 amino acids in length. In some embodiments, the peptide linker is 92 amino acids in length. In some embodiments, the peptide linker is 16 amino acids in length, 24 amino acids in length, 64 amino acids in length, or 96 amino acids in length.

[212] In some embodiments, the linker comprises the amino acid sequence (GGGGS)n (SEQ ID NO: 14881), (G)n (SEQ ID NO: 14882), (EAAAK)n (SEQ ID NO: 14883), (GGS)n (SEQ ID NO: 14884), (SGGS)n (SEQ ID NO: 14886), (XP)n (SEQ ID NO: 14887), or any combination thereof, wherein n is independently an integer between 1 and 30, and wherein X is any amino acid. In some embodiments, the linker comprises the amino acid sequence (GGS)n (SEQ ID NO: 14904), wherein n is 1, 3, or 7. In some embodiments, the linker comprises the amino acid sequence SGSETPGTSESATPES (SEQ ID NO: 14888). In some embodiments, the linker comprises the amino acid sequence SGGSSGGSSGS ETPGTSESATPESSGGSSGGS (SEQ ID NO: 14889). In some embodiments, the linker comprises the amino acid sequence SGGSGGSGGS (SEQ ID NO: 14891). In some embodiments, the linker comprises the amino acid sequence SGGS (SEQ ID NO: 14892). In other embodiments, the linker comprises the amino acid sequence SGGSSGGSSGSETPGTSESATPESAGSYPYDVPDYAGSAAPAAKKKKLDGSGSGGSSGGS (SEQ ID NO: 14893.

[213] In some embodiments, a linker comprises 1-100 amino acids. In some embodiments, the linker comprises the amino acid sequence SGSETPGTSESATPES (SEQ ID NO: 14888). In some embodiments, the linker comprises the amino acid sequence SGGSSGGSSGSETPGTSESATPESSGGSSGGS (SEQ ID NO: 14889). In some embodiments, the linker comprises the amino acid sequence SGGSGGSGGS (SEQ ID NO: 14891). In some embodiments, the linker comprises the amino acid sequence SGGS (SEQ ID NO: 14892). In some embodiments, the linker comprises the amino acid sequence GGSGGS (SEQ ID NO: 14911), GGSGGSGGS (SEQ ID NO: 14912), SGGSSGGSSGSETPGTSESATPESAGSYPYDVPDYAGSAAPAAKKKKLDGSGSGGSSGGS (SEQ ID NO: 14893), or SGGSSGGSSGSETPGTSESATPESSGGSSGGSS (SEQ ID NO: 14890.

[214] In certain embodiments, two or more components of a prime editor are linked to each other by a non-peptide linker. In some embodiments, the linker is a carbon-nitrogen bond of an amide linkage. In certain embodiments, the linker is a cyclic or acyclic, substituted or unsubstituted, branched or unbranched aliphatic or heteroaliphatic linker. In certain embodiments, the linker is polymeric (*e.g.*, polyethylene, polyethylene glycol, polyamide, polyester, etc.). In certain embodiments, the linker comprises a monomer, dimer, or polymer of aminoalkanoic acid. In certain embodiments, the linker comprises an aminoalkanoic acid (*e.g.*, glycine, ethanoic acid, alanine, beta-alanine, 3- aminopropanoic acid, 4-aminobutanoic acid, 5-pentanoic acid, etc.). In certain embodiments, the linker comprises a monomer, dimer, or polymer of aminohexanoic acid (Ahx). In certain embodiments, the linker is based on a carbocyclic moiety (*e.g.*, cyclopentane, cyclohexane). In other embodiments, the linker comprises a polyethylene glycol moiety (PEG). In certain embodiments, the linker comprises an aryl or heteroaryl moiety. In certain embodiments, the linker is based on a phenyl ring. The linker may include functionalized moieties to facilitate attachment of a nucleophile (*e.g.*, thiol, amino) from the peptide to the linker. Any electrophile may be used as part of the linker. Exemplary electrophiles include, but are

not limited to, activated esters, activated amides, Michael acceptors, alkyl halides, aryl halides, acyl halides, and isothiocyanates.

[215] Components of a prime editor may be connected to each other in any order. In some embodiments, the DNA binding domain and the DNA polymerase domain of a prime editor may be fused to form a fusion protein or may be joined by a peptide or protein linker, in any order from the N terminus to the C terminus. In some embodiments, a prime editor comprises a DNA binding domain fused or linked to the C-terminal end of a DNA polymerase domain. In some embodiments, a prime editor comprises a DNA binding domain fused or linked to the N-terminal end of a DNA polymerase domain. In some embodiments, the prime editor comprises a fusion protein comprising the structure NH2-[DNA binding domain]-[polymerase]-COOH; or NH2-[polymerase]-[DNA binding domain]-COOH, wherein each instance of "]-[" indicates the presence of an optional linker sequence. In some embodiments, a prime editor comprises a fusion protein and a DNA polymerase domain provided in trans, wherein the fusion protein comprises the structure NH2-[DNA binding domain]-[RNA-protein recruitment polypeptide]-COOH. In some embodiments, a prime editor comprises a fusion protein and a DNA binding domain provided in trans, wherein the fusion protein comprises the structure NH2-[DNA polymerase domain]-[RNA-protein recruitment polypeptide]-COOH.

[216] In some embodiments, a prime editor fusion protein, a polypeptide component of a prime editor, or a polynucleotide encoding the prime editor fusion protein or polypeptide component, may be split into an N-terminal half and a C-terminal half or polypeptides that encode the N-terminal half and the C terminal half, and provided to a target DNA in a cell separately. For example, in certain embodiments, a prime editor fusion protein may be split into a N-terminal and a C-terminal half for separate delivery in AAV vectors, and subsequently translated and colocalized in a target cell to reform the complete polypeptide or prime editor protein. In such cases, separate halves of a protein or a fusion protein may each comprise a split-intein to facilitate colocalization and reformation of the complete protein or fusion protein by the mechanism of intein facilitated trans splicing. In some embodiments, a prime editor comprises a N-terminal half fused to an intein-N, and a C-terminal half fused to an intein-C, or polynucleotides or vectors (*e.g.*, AAV vectors) encoding each thereof. When delivered and/or expressed in a target cell, the intein-N and the intein-C can be excised via protein trans-splicing, resulting in a complete prime editor fusion protein in the target cell.

[217] In some embodiments, a prime editor fusion protein comprises a Cas9(H840A) nickase and a wild type M-MLV RT, e.g., "PE1", and a prime editing system or composition may be referred to as PE1 system or PE1 composition . In some embodiments, a prime editor fusion protein comprises a Cas9(H840A) nickase and a M-MLV RT that comprises amino acid substitutions D200N, T330P, T306K, W313F, and L603W compared to a wild type M-MLV RT. In some embodiments, a prime editor fusion protein comprises a Cas9(H840A) nickase and a M-MLV RT that comprises amino acid substitutions D200N, T330P, T306K, W313F, and L603W compared to a wild type M-MLV RT (e.g., "PE2", and a prime editing system or composition referred to as PE2 system or PE2 composition). The

amino acid sequence of an exemplary PE2 and its individual components in shown in **Table 90**. In some embodiments, a prime editor fusion protein comprises a Cas9(R221K N394K H840A) nickase and a M-MLV RT that comprises amino acid substitutions D200N, T330P, T306K, W313F, and L603W compared to a wild type M-MLV RT. The amino acid sequence of an exemplary Prime editor fusion protein and its individual components in shown in **Table 91**. In some embodiments, an exemplary PE fusion protein may lack a methionine at the N-terminus. In some embodiments an exemplary prime editor protein may comprise an amino acid sequence as set forth in any of the SEQ ID NOs. 14874, or 14875, 14899, or 14900.

[218] In various embodiments, a prime editor fusion proteins comprise an amino acid sequence that is at least about 70% identical, at least about 80% identical, at least about 90% identical, at least about 95% identical, at least about 96% identical, at least about 97% identical, at least about 98% identical, at least about 99% identical, at least about 99.5% identical, or at least about 99.9% identical to any of the prime editor fusion sequences described herein or known in the art.

Table 90. lists exemplary prime editor and its components

SEQ ID NO.	DESCRIPTION	SEQUENCE
14874	Exemplary Prime Editor [NLS]- [Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K)(W313F)] - [NLS]	MKRTADGSEFESPKKKRKVDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKV LGNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIF SNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHL RKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIA LSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAK NLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEK YKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDL LRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYY VGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNL PNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLF KTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKD FLDNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRY TGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDI QKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENI VIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEK LYLYYLQNGRDMYVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDK NRGKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELD KAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSKLVS DFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKV YDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGE TGEIVWDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLI ARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIME RSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQK GNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQIS

		EFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYF **DTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGD**SGGSSGGSSGSE **TPGTSESATPESSGGSSGGSS***TLNIEDEYRLHETSKEPDVSLGSTWLSDFPQAWAET* *GGMGLAVRQAPLIIPLKATSTPVSIKQYPMSQEARLGIKPHIQRLLDQGILVPCQSPWN* *TPLLPVKKPGTNDYRPVQDLREVNKRVEDIHPTVPNPYNLLSGLPPSHQWYTVLDLK* *DAFFCLRLHPTSQPLFAFEWRDPEMGISGQLTWTRLPQGFKNSPTLFNEALHRDLAD* *FRIQHPDLILLQYVDDLLLAATSELDCQQGTRALLQTLGNLGYRASAKKAQICQKQVK* *YLGYLLKEGQRWLTEARKETVMGQPTPKTPRQLREFLGKAGFCRLFIPGFAEMAAPL* *YPLTKPGTLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYAKGVL* *TQKLGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPLVILAPH* *AVEALVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLPLPEEGLQHN* *CLDILAEAHGTRPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGAAVTTETEVIWAKA* *LPAGTSAQRAELIALTQALKMAEGKKLNVYTDSRYAFATAHIHGEIYRRRGWLTSEGK* *EIKNKDEILALLKALFLPKRLSIIHCPGHQKGHSAEARGNRMADQAARKAAITETPDTS* *TLLIENSSP*SGGSKRTADGSEFEPKKKRKV KEY: NUCLEAR LOCALIZATION SEQUENCE (NLS) **CAS9(H840A)** **33-AMINO ACID LINKER** *M-MLV REVERSE TRANSCRIPTASE*
14899	Met- Exemplary Prime Editor [NLS]-[Cas9(H840A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K)(W313F)] - [NLS]	KRTADGSEFESPKKKRKV**DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVL** **GNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFS** **NEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLR** **KKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQT** **YNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIAL** **SLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKN** **LSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKY** **KEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLNREDLL** **RKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYYV** **GPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNLP** **NEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLFK** **TNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDF** **LDNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYT** **GWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQ** **KAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIV** **IEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKL** **YLYYLQNGRDMYVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKN** **RGKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDK** **AGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSKLVSD** **FRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVY** **DVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGET** **GEIVWDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIA** **RKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERS**

		SFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGN ELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFS KRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYFDT TIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDSGGSSGGSSGSETP GTSESATPESSGGSSGGSS*TLNIEDEYRLHETSKEPDVSLGSTWLSDFPQAWAETGG MGLAVRQAPLIIPLKATSTPVSIKQYPMSQEARLGIKPHIQRLLDQGILVPCQSPWNTP LLPVKKPGTNDYRPVQDLREVNKRVEDIHPTVPNPYNLLSGLPPSHQWYTVLDLKDA FFCLRLHPTSQPLFAFEWRDPEMGISGQLTWTRLPQGFKNSPTLFNEALHRDLADFR IQHPDLILLQYVDDLLLAATSELDCQQGTRALLQTLGNLGYRASAKKAQICQKQVKYL GYLLKEGQRWLTEARKETVMGQPTPKTPRQLREFLGKAGFCRLFIPGFAEMAAPLYP LTKPGTLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYAKGVLTQ KLGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPLVILAPHAV EALVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLPLPEEGLQHNCL DILAEAHGTRPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGAAVTTETEVIWAKALP AGTSAQRAELIALTQALKMAEGKKLNVYTDSRYAFATAHIHGEIYRRRGWLTSEGKEIK NKDEILALLKALFLPKRLSIIHCPGHQKGHSAEARGNRMADQAARKAAITETPDTSTLL IENSSP***SGGSKRTADGSEFEPKKKRKV

14875	– N-terminal NLS	MKRTADGSEFESPKKKRKV
14831	– CAS9 (H840A)	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSG ETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDK KHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRG HFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRRL ENLIAQLPGEKKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDN LLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDL TLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTE ELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKI LTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNF DKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLL FKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFL DNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTGWGR LSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQVSGQ GDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIEMARENQTT QKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMY VDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVK KMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKH VAQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHA HDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYF FYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLSMPQV NIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVV AKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYS LFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQK QLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIH LFTLTNLGAPAAFKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGG D

14890	-- linker between CAS9 domain and RT domain (33 amino acids)	SGGSSGGSSGSETPGTSESATPESSGGSSGGSS
14828	-- MMLV_RT D200N T330P L603W T306K W313F	TLNIEDEYRLHETSKEPDVSLGSTWLSDFPQAWAETGGMGLAVRQAPLIIPLKAT STPVSIKQYPMSQEARLGIKPHIQRLLDQGILVPCQSPWNTPLLPVKKPGTNDYRP VQDLREVNKRVEDIHPTVPNPYNLLSGLPPSHQWYTVLDLKDAFFCLRLHPTSQ PLFAFEWRDPEMGISGQLTWTRLPQGFKNSPTLFNEALHRDLADFRIQHPDLILL QYVDDLLLAATSELDCQQGTRALLQTLGNLGYRASAKKAQICQKQVKYLGYLL KEGQRWLTEARKETVMGQPTPKTPRQLREFLGKAGFCRLFIPGFAEMAAPLYPL TKPGTLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYAKGV LTQKLGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPL VILAPHAVEALVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLP LPEEGLQHNCLDILAEAHGTRPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGA AVTTETEVIWAKALPAGTSAQRAELIALTQALKMAEGKKLNVYTDSRYAFATA HIHGEIYRRRGWLTSEGKEIKNKDEILALLKALFLPKRLSIIHCPGHQKGHSAEAR GNRMADQAARKAAITETPDTSTLLIENSSP	
14879	-- C- terminal NLS	SGGSKRTADGSEFEPKKKRKV

Table 91. lists exemplary prime editor and its components

SEQ ID NO.	DESCRIPTION	SEQUENCE
14874	Exemplary prime editor [NLS]- [Cas9((R220K) (R393K) (H839A)]- [linker]- [MMLV_RT(D200N)(T330P)(L603W)(T306K)(W313F)] - [NLS]	MKRTADGSEFESPKKKRKVDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKV LGNTDRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIF SNEMAKVDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHL RKKLVDSTDKADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQ TYNQLFEENPINASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIA LSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAK NLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDLTLLKALVRQQLPEK YKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTEELLVKLKREDL LRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKILTFRIPYY VGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNFDKNL PNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLLF KTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKD FLDNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRY TGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDI QKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENI VIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEK LYLYYLQNGRDMYVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDK NRGKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELD KAGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSKLVS DFRKDFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKV YDVRKMIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGE TGEIVWDKGRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLI ARKKDWDPKKYGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIME RSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQK GNELALPSKYVNFLYLASHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQIS EFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIHLFTLTNLGAPAAFKYF DTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGGDSGGSSGGSKRTA DGSEFESPKKKRKVSGGSSGGSTLNIEDEYRLHETSKEPDVSLGSTWLSDFPQAW AETGGMGLAVRQAPLIIPLKATSTPVSIKQYPMSQEARLGIKPHIQRLLDQGILVPCQS PWNTPLLPVKKPGTNDYRPVQDLREVNKRVEDIHPTVPNPYNLLSGLPPSHQWYTVL DLKDAFFCLRLHPTSQPLFAFEWRDPEMGISGQLTWTRLPQGFKNSPTLFNEALHRD LADFRIQHPDLILLQYVDDLLLAATSELDCQQGTRALLQTLGNLGYRASAKKAQICQK QVKYLGYLLKEGQRWLTEARKETVMGQPTPKTPRQLREFLGKAGFCRLFIPGFAEM AAPLYPLTKPGTLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYA KGVLTQKLGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPLVI LAPHAVEALVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLPLPEEGL QHNCLDILAEAHGTRPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGAAVTTETEVIW AKALPAGTSAQRAELIALTQALKMAEGKKLNVYTDSRYAFATAHIHGEIYRRRGWLTSE

		GKEIKNKDEILALLKALFLPKRLSIIHCPGHQKGHSAEARGNRMADQAARKAAITETP DTSTLLIENSSPSGGSKRTADGSEFESPKKKRKVGSGPAAKRVKLD KEY: N-terminal bipartiteSV40NLS **CAS9(R221K N394K H840A)** **SGGSx2-met-bpSV40NLS-SGGSx2 LINKER** *M-MLV D200N T306K W313F T330P L603W REVERSE TRANSCRIPTASE* *C-terminal linker- NLS1* ***C-terminal linker-NLS2***
14900	Met- Exemplary prime editor [NLS]-[Cas9((R220K) (R393K) (H839A)]-[linker]-[MMLV_RT(D200N)(T330P)(L603W)(T306K)(W313F)] - [NLS]	KRTADGSEFESPKKKRKVDKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGN TDRHSIKKNLIGALLFDSGETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAK VDDSFFHRLEESFLVEEDKKHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTD KADLRLIYLALAHMIKFRGHFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPIN ASGVDAKAILSARLSKSRRLENLIAQLPGEKKNGLFGNLIALSLGLTPNFKSNFDL AEDAKLQLSKDTYDDDLDNLLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEIT KAPLSASMIKRYDEHHQDLTLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGA SQEEFYKFIKPILEKMDGTEELLVKLNREDLLRKQRTFDNGSIPHQIHLGELHAIL RRQEDFYPFLKDNREKIEKILTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFE EVVDKGASAQSFIERMTNFDKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEG MRKPAFLSGEQKKAIVDLLFKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFN ASLGTYHDLLKIIKDKDFLDNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFD DKVMKQLKRRRYTGWGRLSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIH DDSLTFKEDIQKAQVSGQGDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMG RHKPENIVIEMARENQTTQKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQ NEKLYLYYLQNGRDMYVDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSD KNRGKSDNVPSEEVVKKMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDK AGFIKRQLVETRQITKHVAQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRK DFQFYKVREINNYHHAHDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRK MIAKSEQEIGKATAKYFFYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDK GRDFATVRKVLSMPQVNIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKK YGGFDSPTVAYSVLVVAKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAK GYKEVKKDLIIKLPKYSLFELENGRKRMLASAGELQKGNELALPSKYVNFLYLA SHYEKLKGSPEDNEQKQLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAY NKHRDKPIREQAENIIHLFTLTNLGAPAAFKYFDTTIDRKRYTSTKEVLDATLIHQ SITGLYETRIDLSQLGGDSGGSSGGSKRTADGSEFESPKKKRKVSGGSSGGSTLNI EDEYRLHETSKEPDVSLGSTWLSDFPQAWAETGGMGLAVRQAPLIIPLKATSTPV SIKQYPMSQEARLGIKPHIQRLLDQGILVPCQSPWNTPLLPVKKPGTNDYRPVQD LREVNKRVEDIHPTVPNPYNLLSGLPPSHQWYTVLDLKDAFFCLRLHPTSQPLFA FEWRDPEMGISGQLTWTRLPQGFKNSPTLFNEALHRDLADFRIQHPDLILLQYVD DLLLAATSELDCQQGTRALLQTLGNLGYRASAKKAQICQKQVKYLGYLLKEGQ RWLTEARKETVMGQPTPKTPRQLREFLGKAGFCRLFIPGFAEMAAPLYPLTKPG TLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYAKGVLTQK LGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPLVILAP HAVEALVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLPLPEEG LQHNCLDILAEAHGTRPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGAAVTTE TEVIWAKALPAGTSAQRAELIALTQALKMAEGKKLNVYTDSRYAFATAHIHGEI YRRRGWLTSEGKEIKNKDEILALLKALFLPKRLSIIHCPGHQKGHSAEARGNRMA DQAARKAAITETPDTSTLLIENSSPSGGSKRTADGSEFESPKKKRKVGSGPAAKR VKLD
14875	-- N-terminal bpSV40NLS	MKRTADGSEFESPKKKRKV
14876	-- CAS9 (R221K N394K H840A)	DKKYSIGLDIGTNSVGWAVITDEYKVPSKKFKVLGNTDRHSIKKNLIGALLFDSG ETAEATRLKRTARRRYTRRKNRICYLQEIFSNEMAKVDDSFFHRLEESFLVEEDK KHERHPIFGNIVDEVAYHEKYPTIYHLRKKLVDSTDKADLRLIYLALAHMIKFRG HFLIEGDLNPDNSDVDKLFIQLVQTYNQLFEENPINASGVDAKAILSARLSKSRKL ENLIAQLPGEKKNGLFGNLIALSLGLTPNFKSNFDLAEDAKLQLSKDTYDDDLDN LLAQIGDQYADLFLAAKNLSDAILLSDILRVNTEITKAPLSASMIKRYDEHHQDL TLLKALVRQQLPEKYKEIFFDQSKNGYAGYIDGGASQEEFYKFIKPILEKMDGTE ELLVKLKREDLLRKQRTFDNGSIPHQIHLGELHAILRRQEDFYPFLKDNREKIEKI LTFRIPYYVGPLARGNSRFAWMTRKSEETITPWNFEEVVDKGASAQSFIERMTNF DKNLPNEKVLPKHSLLYEYFTVYNELTKVKYVTEGMRKPAFLSGEQKKAIVDLL FKTNRKVTVKQLKEDYFKKIECFDSVEISGVEDRFNASLGTYHDLLKIIKDKDFL DNEENEDILEDIVLTLTLFEDREMIEERLKTYAHLFDDKVMKQLKRRRYTGWGR LSRKLINGIRDKQSGKTILDFLKSDGFANRNFMQLIHDDSLTFKEDIQKAQVSGQ GDSLHEHIANLAGSPAIKKGILQTVKVVDELVKVMGRHKPENIVIEMARENQTT QKGQKNSRERMKRIEEGIKELGSQILKEHPVENTQLQNEKLYLYYLQNGRDMY

		VDQELDINRLSDYDVDAIVPQSFLKDDSIDNKVLTRSDKNRGKSDNVPSEEVVK KMKNYWRQLLNAKLITQRKFDNLTKAERGGLSELDKAGFIKRQLVETRQITKH VAQILDSRMNTKYDENDKLIREVKVITLKSKLVSDFRKDFQFYKVREINNYHHA HDAYLNAVVGTALIKKYPKLESEFVYGDYKVYDVRKMIAKSEQEIGKATAKYF FYSNIMNFFKTEITLANGEIRKRPLIETNGETGEIVWDKGRDFATVRKVLSMPQV NIVKKTEVQTGGFSKESILPKRNSDKLIARKKDWDPKKYGGFDSPTVAYSVLVV AKVEKGKSKKLKSVKELLGITIMERSSFEKNPIDFLEAKGYKEVKKDLIIKLPKYS LFELENGRKRMLASAGELQKGNELALPSKYVNFLYLASHYEKLKGSPEDNEQK QLFVEQHKHYLDEIIEQISEFSKRVILADANLDKVLSAYNKHRDKPIREQAENIIH LFTLTNLGAPAAFKYFDTTIDRKRYTSTKEVLDATLIHQSITGLYETRIDLSQLGG D
14877	-- SGGSx2-bpSV40NLS-SGGSx2 linker	SGGSSGGSKRTADGSEFESPKKKRKVSGGSSGGS
14828	-- MMLV_RT D200N T330P L603W T306K W313F	TLNIEDEYRLHETSKEPDVSLGSTWLSDFPQAWAETGGMGLAVRQAPLIIPLKAT STPVSIKQYPMSQEARLGIKPHIQRLLDQGILVPCQSPWNTPLLPVKKPGTNDYRP VQDLREVNKRVEDIHPTVPNPYNLLSGLPPSHQWYTVLDLKDAFFCLRLHPTSQ PLFAFEWRDPEMGISGQLTWTRLPQGFKNSPTLFNEALHRDLADFRIQHPDLILL QYVDDLLLAATSELDCQQGTRALLQTLGNLGYRASAKKAQICQKQVKYLGYLL KEGQRWLTEARKETVMGQPTPKTPRQLREFLGKAGFCRLFIPGFAEMAAPLYPL TKPGTLFNWGPDQQKAYQEIKQALLTAPALGLPDLTKPFELFVDEKQGYAKGV LTQKLGPWRRPVAYLSKKLDPVAAGWPPCLRMVAAIAVLTKDAGKLTMGQPL VILAPHAVEALVKQPPDRWLSNARMTHYQALLLDTDRVQFGPVVALNPATLLP LPEEGLQHNCLDILAEAHGTRPDLTDQPLPDADHTWYTDGSSLLQEGQRKAGA AVTTETEVIWAKALPAGTSAQRAELIALTQALKMAEGKKLNVYTDSRYAFATA HIHGEIYRRRGWLTSEGKEIKNKDEILALLKALFLPKRLSIIHCPGHQKGHSAEAR GNRMADQAARKAAITETPDTSTLLIENSSP
14879	C-terminal linker-NLS	SGGSKRTADGSEFESPKKKRKV
14880	C-terminal linker-NLS2	GSGPAAKRVKLD

PEgRNA for editing of ATP7B gene

[219] The term "prime editing guide RNA", or "PEgRNA", refers to a guide polynucleotide that comprises one or more intended nucleotide edits for incorporation into the target DNA. In some embodiments, the PEgRNA associates with and directs a prime editor to incorporate the one or more intended nucleotide edits into the target gene via prime editing. "Nucleotide edit" or "intended nucleotide edit" refers to a specified deletion of one or more nucleotides at one specific position, insertion of one or more nucleotides at one specific position, substitution of a single nucleotide, or other alterations at one specific position to be incorporated into the sequence of the target gene. Intended nucleotide edit may refer to the edit on the editing template as compared to the sequence on the target strand of the target gene or may refer to the edit encoded by the editing template on the newly synthesized single stranded DNA that replaces the editing target sequence, as compared to the editing target sequence. In some embodiments, a PEgRNA comprises a spacer sequence that is complementary or substantially complementary to a search target sequence on a target strand of the target gene. In some embodiments, the PEgRNA comprises a gRNA core that associates with a DNA binding domain, *e.g.*, a CRISPR-Cas protein domain, of a prime editor. In some embodiments, the PEgRNA further comprises an extended nucleotide sequence comprising one or more intended nucleotide edits compared to the endogenous sequence of the target gene, wherein the extended nucleotide sequence may be referred to as an extension arm.

[220] In certain embodiments, the extension arm comprises a primer binding site sequence (PBS) that can initiate target-primed DNA synthesis. In some embodiments, the PBS is complementary or substantially complementary to a free 3' end on the edit strand of the target gene at a nick site generated by the prime editor. In some embodiments, the extension arm further comprises an editing template that comprises one or more intended nucleotide edits to be incorporated in the target gene by prime editing. In some embodiments, the editing template is a template for an RNA-dependent DNA polymerase domain or polypeptide of the prime editor, for example, a reverse transcriptase domain. The reverse transcriptase editing template may also be referred to herein as an RT template, or RTT. In some embodiments, the editing template comprises partial complementarity to an editing target sequence in the target gene, e.g., an *ATP7B* gene. In some embodiments, the editing template comprises substantial or partial complementarity to the editing target sequence except at the position of the intended nucleotide edits to be incorporated into the target gene. An exemplary architecture of a PEgRNA including its components is as demonstrated in **Fig. 2**.

[221] In some embodiments, a PEgRNA includes only RNA nucleotides and forms an RNA polynucleotide. In some embodiments, a PEgRNA is a chimeric polynucleotide that includes both RNA and DNA nucleotides. For example, a PEgRNA can include DNA in the spacer sequence, the gRNA core, or the extension arm. In some embodiments, a PEgRNA comprises DNA in the spacer sequence. In some embodiments, the entire spacer sequence of a PEgRNA is a DNA sequence. In some embodiments, the PEgRNA comprises DNA in the gRNA core, for example, in a stem region of the gRNA core. In some embodiments, the PEgRNA comprises DNA in the extension arm, for example, in the editing template. An editing template that comprises a DNA sequence may serve as a DNA synthesis template for a DNA polymerase in a prime editor, for example, a DNA-dependent DNA polymerase. Accordingly, the PEgRNA may be a chimeric polynucleotide that comprises RNA in the spacer, gRNA core, and/or the PBS sequences and DNA in the editing template.

[222] Components of a PEgRNA may be arranged in a modular fashion. In some embodiments, the spacer and the extension arm comprising a primer binding site sequence (PBS) and an editing template, *e.g.*, a reverse transcriptase template (RTT), can be interchangeably located in the 5' portion of the PEgRNA, the 3' portion of the PEgRNA, or in the middle of the gRNA core. In some embodiments, a PEgRNA comprises a PBS and an editing template sequence in 5' to 3' order. In some embodiments, the gRNA core of a PEgRNA of this disclosure may be located in between a spacer and an extension arm of the PEgRNA. In some embodiments, the gRNA core of a PEgRNA may be located at the 3' end of a spacer. In some embodiments, the gRNA core of a PEgRNA may be located at the 5' end of a spacer. In some embodiments, the gRNA core of a PEgRNA may be located at the 3' end of an extension arm. In some embodiments, the gRNA core of a PEgRNA may be located at the 5' end of an extension arm. In some embodiments, the PEgRNA comprises, from 5' to 3': a spacer, a gRNA core, and an extension arm. In some embodiments, the PEgRNA comprises, from 5' to 3': a spacer, a gRNA core, an editing template, and a PBS. In some embodiments, the PEgRNA comprises, from 5' to 3': an extension arm, a

spacer, and a gRNA core. In some embodiments, the PEgRNA comprises, from 5' to 3': an editing template, a PBS, a spacer, and a gRNA core.

[223] In some embodiments, a PEgRNA comprises a single polynucleotide molecule that comprises the spacer sequence, the gRNA core, and the extension arm. In some embodiments, a PEgRNA comprises multiple polynucleotide molecules, for example, two polynucleotide molecules. In some embodiments, a PEgRNA comprise a first polynucleotide molecule that comprises the spacer and a portion of the gRNA core, and a second polynucleotide molecule that comprises the rest of the gRNA core and the extension arm. In some embodiments, the gRNA core portion in the first polynucleotide molecule and the gRNA core portion in the second polynucleotide molecule are at least partly complementary to each other. In some embodiments, the PEgRNA may comprise a first polynucleotide comprising the spacer and a first portion of a gRNA core comprising, which may be also be referred to as a crRNA. In some embodiments, the PEgRNA comprise a second polynucleotide comprising a second portion of the gRNA core and the extension arm, wherein the second portion of the gRNA core may also be referred to as a trans-activating crRNA, or tracr RNA. In some embodiments, the crRNA portion and the tracr RNA portion of the gRNA core are at least partially complementary to each other. In some embodiments, the partially complementary portions of the crRNA and the tracr RNA form a lower stem, a bulge, and an upper stem, as exemplified in **FIG. 4**.

[224] In some embodiments, a spacer sequence comprises a region that has substantial complementarity to a search target sequence on the target strand of a double stranded target DNA, *e.g.*, an *AT7B* gene. In some embodiments, the spacer sequence of a PEgRNA is identical or substantially identical to a protospacer sequence on the edit strand of the target gene (except that the protospacer sequence comprises thymine and the spacer sequence may comprise uracil). In some embodiments, the spacer sequence is at least about 70%, 75%, 80%, 85%, 90%, 95%, or 100% complementary to a search target sequence in the target gene. In some embodiments, the spacer comprises is substantially complementary to the search target sequence.

[225] In some embodiments, the length of the spacer varies from about 10 to about 100 nucleotides. In some embodiments, the spacer is 16 nucleotides, 17 nucleotides, 18 nucleotides, 19 nucleotides, 20 nucleotides, 21 nucleotides, 22 nucleotides, 23 nucleotides, 24 nucleotides, or 25 nucleotides in length. In some embodiments, the spacer is from 15 nucleotides to 30 nucleotides in length, 15 to 25 nucleotides in length, 18 to 22 nucleotides in length, 10 to 20 nucleotides in length, or 20 to 30 nucleotides in length. In some embodiments, the spacer is 16 to 22 nucleotides in length. In some embodiments, the spacer is 16 to 20 nucleotides in length. In some embodiments, the spacer is 17 to 18 nucleotides in length. In some embodiments, the spacer is 20 nucleotides in length.

[226] As used herein in a PEgRNA or a nick guide RNA sequence, or fragments thereof such as a spacer, PBS, or RTT sequence, unless indicated otherwise, it should be appreciated that the letter "T" or "thymine" indicates a nucleobase in a DNA sequence that encodes the PEgRNA or guide RNA sequence,

and is intended to refer to a uracil (U) nucleobase of the PEgRNA or guide RNA or any chemically modified uracil nucleobase known in the art, such as 5-methoxyuracil.

[227] The extension arm of a PEgRNA may comprise a primer binding site (PBS) and an editing template (*e.g.*, an RTT). The extension arm may be partially complementary to the spacer. In some embodiments, the editing template (*e.g.*, RTT) is partially complementary to the spacer. In some embodiments, the editing template (*e.g.*, RTT) and the primer binding site (PBS) are each partially complementary to the spacer.

[228] An extension arm of a PEgRNA may comprise a primer binding site sequence (PBS, or PBS sequence) that comprises complementarity to and can hybridize with a free 3' end of a single stranded DNA in the target gene (*e.g.*, the *ATP7B* gene) generated by nicking with a prime editor at the nick site on the PAM strand.

[229] The length of the PBS sequence may vary depending on, *e.g.*, the prime editor components, the search target sequence and other components of the PEgRNA. In some embodiments, the PBS is about 3 to 19 nucleotides in length. in some embodiments, the PBS is about 3 to 17 nucleotides in length. In some embodiments, the PBS is about 4 to 16 nucleotides, about 6 to 16 nucleotides, about 6 to 18 nucleotides, about 6 to 20 nucleotides, about 8 to 20 nucleotides, about 10 to 20 nucleotides, about 12 to 20 nucleotides, about 14 to 20 nucleotides, about 16 to 20 nucleotides, or about 18 to 20 nucleotides in length. In some embodiments, the PBS is 8 to 17 nucleotides in length. In some embodiments, the PBS is 8 to 16 nucleotides in length. In some embodiments, the PBS is 8 to 15 nucleotides in length. In some embodiments, the PBS is 8 to 14 nucleotides in length. In some embodiments, the PBS is 8 to 13 nucleotides in length. In some embodiments, the PBS is 8 to 12 nucleotides in length. In some embodiments, the PBS is 8 to 11 nucleotides in length. In some embodiments, the PBS is 8 to 10 nucleotides in length. In some embodiments, the PBS is 8 or 9 nucleotides in length. In some embodiments, the PBS is 16 or 17 nucleotides in length. In some embodiments, the PBS is 15 to 17 nucleotides in length. In some embodiments, the PBS is 14 to 17 nucleotides in length. In some embodiments, the PBS is 13 to 17 nucleotides in length. In some embodiments, the PBS is 12 to 17 nucleotides in length. In some embodiments, the PBS is 11 to 17 nucleotides in length. In some embodiments, the PBS is 10 to 17 nucleotides in length. In some embodiments, the PBS is 9 to 17 nucleotides in length. In some embodiments, the PBS is about 7 to 15 nucleotides in length. In some embodiments, the PBS is 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, or 19 nucleotides in length. In some embodiments, the PBS is 8, 9, 10, 11, 12, 13, or 14 nucleotides in length.

[230] The PBS may be complementary or substantially complementary to a DNA sequence in the edit strand of the target gene. By annealing with the edit strand at a free hydroxy group, *e.g.*, a free 3' end generated by prime editor nicking, the PBS may initiate synthesis of a new single stranded DNA encoded by the editing template at the nick site. In some embodiments, the PBS is at least about 70%, 75%, 80%, 85%, 90%, 95%, or 100% complementary to a region of the edit strand of the target gene (*e.g.*, the

ATP7B gene). In some embodiments, the PBS is perfectly complementary, or 100% complementary, to a region of the edit strand of the target gene (*e.g.*, the ATP7B gene).

[231] An extension arm of a PEgRNA may comprise an editing template that serves as a DNA synthesis template for the DNA polymerase in a prime editor during prime editing.

[232] The length of an editing template may vary depending on, *e.g.*, the prime editor components, the search target sequence and other components of the PEgRNA. In some embodiments, the editing template serves as a DNA synthesis template for a reverse transcriptase, and the editing template is referred to as a reverse transcription editing template (RTT).

[233] The editing template (*e.g.*, RTT), in some embodiments, is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleotides in length. In some embodiments, the RTT is 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleotides in length. In some embodiments, the RTT is 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 nucleotides in length. In some embodiments, the RTT is 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 nucleotides in length.

[234] In some embodiments, the editing template (*e.g.*, RTT) sequence is about 70%, 75%, 80%, 85%, 90%, 95%, or 99% complementary to the editing target sequence on the edit strand of the target gene. In some embodiments, the editing template sequence (*e.g.*, RTT) is substantially complementary to the editing target sequence. In some embodiments, the editing template sequence (*e.g.*, RTT) is complementary to the editing target sequence except at positions of the intended nucleotide edits to be incorporated int the target gene. In some embodiments, the editing template comprises a nucleotide sequence comprising about 85% to about 95% complementarity to an editing target sequence in the edit strand in the target gene (*e.g.*, the *ATP7B* gene). In some embodiments, the editing template comprises about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, or about 99% complementarity to an editing target sequence in the edit strand of the target gene (*e.g.*, the *ATP7B* gene).

[235] An intended nucleotide edit in an editing template of a PEgRNA may comprise various types of alterations as compared to the target gene sequence. In some embodiments, the nucleotide edit is a single nucleotide substitution as compared to the target gene sequence. In some embodiments, the nucleotide edit is a deletion as compared to the target gene sequence. In some embodiments, the nucleotide edit is an insertion as compared to the target gene sequence. In some embodiments, the editing template comprises one to ten intended nucleotide edits as compared to the target gene sequence. In some embodiments, the editing template comprises one or more intended nucleotide edits as compared to the target gene sequence. In some embodiments, the editing template comprises two or more intended nucleotide edits as compared to the target gene sequence. In some embodiments, the editing template comprises three or more intended nucleotide edits as compared to the target gene sequence. In some embodiments, the

editing template comprises four or more, five or more, or six or more intended nucleotide edits as compared to the target gene sequence. In some embodiments, the editing template comprises two single nucleotide substitutions, insertions, deletions, or any combination thereof, as compared to the target gene sequence. In some embodiments, the editing template comprises three single nucleotide substitutions, insertions, deletions, or any combination thereof, as compared to the target gene sequence. In some embodiments, the editing template comprises four, five, or six single nucleotide substitutions, insertions, deletions, or any combination thereof, as compared to the target gene sequence. In some embodiments, a nucleotide substitution comprises an adenine (A)-to-thymine (T) substitution. In some embodiments, a nucleotide substitution comprises an A-to-guanine (G) substitution. In some embodiments, a nucleotide substitution comprises an A-to-cytosine (C) substitution. In some embodiments, a nucleotide substitution comprises a T-A substitution. In some embodiments, a nucleotide substitution comprises a T-G substitution. In some embodiments, a nucleotide substitution comprises a T-C substitution. In some embodiments, a nucleotide substitution comprises a G-to-A substitution. In some embodiments, a nucleotide substitution comprises a G-to-T substitution. In some embodiments, a nucleotide substitution comprises a G-to-C substitution. In some embodiments, a nucleotide substitution comprises a C-to-A substitution. In some embodiments, a nucleotide substitution comprises a C-to-T substitution. In some embodiments, a nucleotide substitution comprises a C-to-G substitution.

[236] In some embodiments, a nucleotide insertion is at least 5 nucleotides, at least 6 nucleotides, at least 7 nucleotides, at least 8 nucleotides, at least 9 nucleotides, at least 10 nucleotides, at least 11 nucleotides, at least 12 nucleotides, at least 13 nucleotides, at least 14 nucleotides, at least 15 nucleotides, at least 16 nucleotides, at least 17 nucleotides, at least 18 nucleotides, at least 19 nucleotides, or at least 20 nucleotides in length. In some embodiments, a nucleotide insertion is from 1 to 2 nucleotides, from 1 to 3 nucleotides, from 1 to 4 nucleotides, from 1 to 5 nucleotides, form 2 to 5 nucleotides, from 3 to 5 nucleotides, from 3 to 6 nucleotides, from 3 to 8 nucleotides, from 4 to 9 nucleotides, from 5 to 10 nucleotides, from 6 to 11 nucleotides, from 7 to 12 nucleotides, from 8 to 13 nucleotides, from 9 to 14 nucleotides, from 10 to 15 nucleotides, from 11 to 16 nucleotides, from 12 to 17 nucleotides, from 13 to 18 nucleotides, from 14 to 19 nucleotides, from 15 to 20 nucleotides in length. In some embodiments, a nucleotide insertion is a single nucleotide insertion. In some embodiments, a nucleotide insertion comprises insertion of two nucleotides.

[237] The editing template of a PEgRNA may comprise one or more intended nucleotide edits, compared to the ATP7B gene to be edited. Position of the intended nucleotide edit(s) relevant to other components of the PEgRNA, or to particular nucleotides (*e.g.*, mutations) in the ATP7B target gene may vary. In some embodiments, the nucleotide edit is in a region of the PEgRNA corresponding to or homologous to the protospacer sequence. In some embodiments, the nucleotide edit is in a region of the PEgRNA corresponding to a region of the ATP7B gene outside of the protospacer sequence.

[238] In some embodiments, the position of a nucleotide edit incorporation in the target gene may be determined based on position of the protospacer adjacent motif (PAM). For instance, the intended

nucleotide edit may be installed in a sequence corresponding to the protospacer adjacent motif (PAM) sequence. In some embodiments, a nucleotide edit in the editing template is at a position corresponding to the 5' most nucleotide of the PAM sequence. In some embodiments, a nucleotide edit in the editing template is at a position corresponding to the 3' most nucleotide of the PAM sequence. In some embodiments, position of an intended nucleotide edit in the editing template may be referred to by aligning the editing template with the partially complementary edit strand of the target gene, and referring to nucleotide positions on the editing strand where the intended nucleotide edit is incorporated. In some embodiments, a nucleotide edit is incorporated at a position corresponding to about 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 nucleotides upstream of the 5' most nucleotide of the PAM sequence in the edit strand of the target gene. By 0 base pair upstream or downstream of a reference position, it is meant that the intended nucleotide is immediately upstream or downstream of the reference position. In some embodiments, a nucleotide edit is incorporated at a position corresponding to about 0 to 2 nucleotides, 0 to 4 nucleotides, 0 to 6 nucleotides, 0 to 8 nucleotides, 0 to 10 nucleotides, , 2 to 4 nucleotides, 2 to 6 nucleotides, 2 to 8 nucleotides, 2 to 10 nucleotides, 2 to 12 nucleotides, 4 to 6 nucleotides, 4 to 8 nucleotides, 4 to 10 nucleotides, 4 to 12 nucleotides, 4 to 14 nucleotides, 6 to 8 nucleotides, 6 to 10 nucleotides, 6 to 12 nucleotides, 6 to 14 nucleotides, 6 to16 nucleotides, 8 to 10 nucleotides, 8 to 12 nucleotides, 8 to 14 nucleotides, 8 to 16 nucleotides, 8 to 18 nucleotides, 10 to 12 nucleotides, 10 to 14 nucleotides, 10 to 16 nucleotides, 10 to 18 nucleotides, 10 to 20 nucleotides, 12 to 14 nucleotides, 12 to 16 nucleotides, 12 to 18 nucleotides, 12 to 20 nucleotides, 12 to 22 nucleotides, 14 to 16 nucleotides, 14 to 18 nucleotides, 14 to 20 nucleotides, 14 to 22 nucleotides, 14 to 24 nucleotides, 16 to 18 nucleotides, 16 to 20 nucleotides, 16 to 22 nucleotides, 16 to 24 nucleotides, 16 to 26 nucleotides, 18 to 20 nucleotides, 18 to 22 nucleotides, 18 to 24 nucleotides, 18 to 26 nucleotides, 18 to 28 nucleotides, 20 to 22 nucleotides, 20 to 24 nucleotides, 20 to 26 nucleotides, 20 to 28 nucleotides, or 20 to 30 nucleotides upstream of the 5' most nucleotide of the PAM sequence. In some embodiments, the nucleotide edit is incorporated at a position corresponding to 3 nucleotides upstream of the 5' most nucleotide of the PAM sequence. In some embodiments, the nucleotide edit in is incorporated at a position corresponding to 4 nucleotides upstream of the 5' most nucleotide of the PAM sequence. In some embodiments, the nucleotide edit is incorporated at a position corresponding to 5 nucleotides upstream of the 5' most nucleotide of the PAM sequence. In some embodiments, the nucleotide edit in the editing template is at a position corresponding to 6 nucleotides upstream of the 5' most nucleotide of the PAM sequence.

[239] In some embodiments, an intended nucleotide edit is incorporated at a position corresponding to about 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 nucleotides downstream of the 5' most nucleotide of the PAM sequence in the edit strand of the target gene. In some embodiments, a nucleotide edit is incorporated at a position corresponding to about 0 to 2 nucleotides, 0 to 4 nucleotides, 0 to 6 nucleotides, 0 to 8 nucleotides, 0 to 10 nucleotides, , 2 to 4 nucleotides, 2 to 6 nucleotides, 2 to 8 nucleotides, 2 to 10

nucleotides, 2 to 12 nucleotides, 4 to 6 nucleotides, 4 to 8 nucleotides, 4 to 10 nucleotides, 4 to 12 nucleotides, 4 to 14 nucleotides, 6 to 8 nucleotides, 6 to 10 nucleotides, 6 to 12 nucleotides, 6 to 14 nucleotides, 6 to16 nucleotides, 8 to 10 nucleotides, 8 to 12 nucleotides, 8 to 14 nucleotides, 8 to 16 nucleotides, 8 to 18 nucleotides, 10 to 12 nucleotides, 10 to 14 nucleotides, 10 to 16 nucleotides, 10 to 18 nucleotides, 10 to 20 nucleotides, 12 to 14 nucleotides, 12 to 16 nucleotides, 12 to 18 nucleotides, 12 to 20 nucleotides, 12 to 22 nucleotides, 14 to 16 nucleotides, 14 to 18 nucleotides, 14 to 20 nucleotides, 14 to 22 nucleotides, 14 to 24 nucleotides, 16 to 18 nucleotides, 16 to 20 nucleotides, 16 to 22 nucleotides, 16 to 24 nucleotides, 16 to 26 nucleotides, 18 to 20 nucleotides, 18 to 22 nucleotides, 18 to 24 nucleotides, 18 to 26 nucleotides, 18 to 28 nucleotides, 20 to 22 nucleotides, 20 to 24 nucleotides, 20 to 26 nucleotides, 20 to 28 nucleotides, or 20 to 30 nucleotides downstream of the 5' most nucleotide of the PAM sequence. In some embodiments, a nucleotide edit is incorporated at a position corresponding to 3 nucleotides downstream of the 5' most nucleotide of the PAM sequence. In some embodiments, a nucleotide edit is incorporated at a position corresponding to 4 nucleotides downstream of the 5' most nucleotide of the PAM sequence. In some embodiments, a nucleotide edit is incorporated at a position corresponding to 5 nucleotides downstream of the 5' most nucleotide of the PAM sequence. In some embodiments, a nucleotide edit is incorporated at a position corresponding to 6 nucleotides downstream of the 5' most nucleotide of the PAM sequence. By "upstream" and "downstream" it is intended to define relevant positions at least two regions or sequences in a nucleic acid molecule orientated in a 5′-to-3′ direction. For example, a first sequence is upstream of a second sequence in a DNA molecule where the first sequence is positioned 5' to the second sequence. Accordingly, the second sequence is downstream of the first sequence.

[240] In some embodiments, the position of a nucleotide edit incorporation in the target gene can be determined based on position of the nick site. In some embodiments, position of an intended nucleotide edit is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, or 150 nucleotides apart from the nick site. In some embodiments, position of an intended nucleotide edit is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, or 150 nucleotides downstream of the nick site on the PAM strand (or the non-target strand, or the edit strand) of the double stranded target DNA. In some embodiments, position of the intended nucleotide edit in the editing template can be referred to by aligning the editing template with the partially complementary editing target sequence on the edit strand and referring to nucleotide positions on the editing strand where the intended nucleotide edit is incorporated. Accordingly, in some embodiments, a nucleotide edit in an editing template is at a position corresponding to a position about 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, or 150 nucleotides apart from the nick site. In some embodiments, a nucleotide edit in an editing template is

at a position corresponding to a position about 0 to 2 nucleotides, 0 to 4 nucleotides, 0 to 6 nucleotides, 0 to 8 nucleotides, 0 to 10 nucleotides, , 2 to 4 nucleotides, 2 to 6 nucleotides, 2 to 8 nucleotides, 2 to 10 nucleotides, 2 to 12 nucleotides, 4 to 6 nucleotides, 4 to 8 nucleotides, 4 to 10 nucleotides, 4 to 12 nucleotides, 4 to 14 nucleotides, 6 to 8 nucleotides, 6 to 10 nucleotides, 6 to 12 nucleotides, 6 to 14 nucleotides, 6 to16 nucleotides, 8 to 10 nucleotides, 8 to 12 nucleotides, 8 to 14 nucleotides, 8 to 16 nucleotides, 8 to 18 nucleotides, 10 to 12 nucleotides, 10 to 14 nucleotides, 10 to 16 nucleotides, 10 to 18 nucleotides, 10 to 20 nucleotides, 12 to 14 nucleotides, 12 to 16 nucleotides, 12 to 18 nucleotides, 12 to 20 nucleotides, 12 to 22 nucleotides, 14 to 16 nucleotides, 14 to 18 nucleotides, 14 to 20 nucleotides, 14 to 22 nucleotides, 14 to 24 nucleotides, 16 to 18 nucleotides, 16 to 20 nucleotides, 16 to 22 nucleotides, 16 to 24 nucleotides, 16 to 26 nucleotides, 18 to 20 nucleotides, 18 to 22 nucleotides, 18 to 24 nucleotides, 18 to 26 nucleotides, 18 to 28 nucleotides, 20 to 22 nucleotides, 20 to 24 nucleotides, 20 to 26 nucleotides, 20 to 28 nucleotides, 20 to 30 nucleotides, 30 to 40 nucleotides, 40 to 50 nucleotides, 50 to 60 nucleotides, 60 to 70 nucleotides, 70 to 80 nucleotides, 80 to 90 nucleotides, 90 to 100 nucleotides, 100 to 110 nucleotides, 110 to 120 nucleotides, 120 to 130 nucleotides, 130 to 140 nucleotides, or 140 to 150 nucleotides apart from the nick site. In some embodiments, when referred to in the context of the PAM strand (or the non-target strand, or the edit strand), a nucleotide edit in an editing template is at a position corresponding to a position about 0 to 2 nucleotides, 0 to 4 nucleotides, 0 to 6 nucleotides, 0 to 8 nucleotides, 0 to 10 nucleotides, , 2 to 4 nucleotides, 2 to 6 nucleotides, 2 to 8 nucleotides, 2 to 10 nucleotides, 2 to 12 nucleotides, 4 to 6 nucleotides, 4 to 8 nucleotides, 4 to 10 nucleotides, 4 to 12 nucleotides, 4 to 14 nucleotides, 6 to 8 nucleotides, 6 to 10 nucleotides, 6 to 12 nucleotides, 6 to 14 nucleotides, 6 to16 nucleotides, 8 to 10 nucleotides, 8 to 12 nucleotides, 8 to 14 nucleotides, 8 to 16 nucleotides, 8 to 18 nucleotides, 10 to 12 nucleotides, 10 to 14 nucleotides, 10 to 16 nucleotides, 10 to 18 nucleotides, 10 to 20 nucleotides, 12 to 14 nucleotides, 12 to 16 nucleotides, 12 to 18 nucleotides, 12 to 20 nucleotides, 12 to 22 nucleotides, 14 to 16 nucleotides, 14 to 18 nucleotides, 14 to 20 nucleotides, 14 to 22 nucleotides, 14 to 24 nucleotides, 16 to 18 nucleotides, 16 to 20 nucleotides, 16 to 22 nucleotides, 16 to 24 nucleotides, 16 to 26 nucleotides, 18 to 20 nucleotides, 18 to 22 nucleotides, 18 to 24 nucleotides, 18 to 26 nucleotides, 18 to 28 nucleotides, 20 to 22 nucleotides, 20 to 24 nucleotides, 20 to 26 nucleotides, 20 to 28 nucleotides, 20 to 30 nucleotides, 30 to 40 nucleotides, 40 to 50 nucleotides, 50 to 60 nucleotides, 60 to 70 nucleotides, 70 to 80 nucleotides, 80 to 90 nucleotides, 90 to 100 nucleotides, 100 to 110 nucleotides, 110 to 120 nucleotides, 120 to 130 nucleotides, 130 to 140 nucleotides, or 140 to 150 nucleotides downstream from the nick site. The relative positions of the intended nucleotide edit(s) and nick site may be referred to by numbers. For example, in some embodiments, the nucleotide immediately downstream of the nick site on a PAM strand (or the non-target strand, or the edit strand) may be referred to as at position 0. The nucleotide immediately upstream of the nick site on the PAM strand (or the non-target strand, or the edit strand) may be referred to as at position -1. The nucleotides downstream of position 0 on the PAM strand can be referred to as at positions +1, +2, +3, +4, … +n, and the nucleotides upstream of position -1 on the PAM strand may be referred to as at positions -2, -3, -4,

…, -n. Accordingly, in some embodiments, the nucleotide in the editing template that corresponds to position 0 when the editing template is aligned with the partially complementary editing target sequence by complementarity can also be referred to as position 0 in the editing template, the nucleotides in the editing template corresponding to the nucleotides at positions +1, +2, +3, +4, …, +n on the PAM strand of the double stranded target DNA can also be referred to as at positions +1, +2, +3, +4, …, +n in the editing template, and the nucleotides in the editing template corresponding to the nucleotides at positions -1, -2, -3, -4, …, -n on the PAM strand on the double stranded target DNA may also be referred to as at positions -1, -2, -3, -4, …, -n on the editing template, even though when the PEgRNA is viewed as a standalone nucleic acid, positions +1, +2, +3, +4, …, +n are 5′ of position 0 and positions -1, -2, -3, -4, …-n are 3′ of position 0 in the editing template. In some embodiments, an intended nucleotide edit is at position +n of the editing template relative to position 0. Accordingly, the intended nucleotide edit may be incorporated at position +n of the PAM strand of the double stranded target DNA (and subsequently, the target strand of the double stranded target DNA) by prime editing. The number n may be referred to as the nick to edit distance.

[241] When referred to within the PEgRNA, positions of the one or more intended nucleotide edits may be referred to relevant to components of the PEgRNA. For example, an intended nucleotide edit may be 5' or 3' to the PBS. In some embodiments, a PEgRNA comprises the structure, from 5' to 3': a spacer, a gRNA core, an editing template, and a PBS. In some embodiments, the intended nucleotide edit is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 nucleotides upstream to the 5' most nucleotide of the PBS. In some embodiments, the intended nucleotide edit is 0 to 2 nucleotides, 0 to 4 nucleotides, 0 to 6 nucleotides, 0 to 8 nucleotides, 0 to 10 nucleotides, 2 to 4 nucleotides, 2 to 6 nucleotides, 2 to 8 nucleotides, 2 to 10 nucleotides, 2 to 12 nucleotides, 4 to 6 nucleotides, 4 to 8 nucleotides, 4 to 10 nucleotides, 4 to 12 nucleotides, 4 to 14 nucleotides, 6 to 8 nucleotides, 6 to 10 nucleotides, 6 to 12 nucleotides, 6 to 14 nucleotides, 6 to16 nucleotides, 8 to 10 nucleotides, 8 to 12 nucleotides, 8 to 14 nucleotides, 8 to 16 nucleotides, 8 to 18 nucleotides, 10 to 12 nucleotides, 10 to 14 nucleotides, 10 to 16 nucleotides, 10 to 18 nucleotides, 10 to 20 nucleotides, 12 to 14 nucleotides, 12 to 16 nucleotides, 12 to 18 nucleotides, 12 to 20 nucleotides, 12 to 22 nucleotides, 14 to 16 nucleotides, 14 to 18 nucleotides, 14 to 20 nucleotides, 14 to 22 nucleotides, 14 to 24 nucleotides, 16 to 18 nucleotides, 16 to 20 nucleotides, 16 to 22 nucleotides, 16 to 24 nucleotides, 16 to 26 nucleotides, 18 to 20 nucleotides, 18 to 22 nucleotides, 18 to 24 nucleotides, 18 to 26 nucleotides, 18 to 28 nucleotides, 20 to 22 nucleotides, 20 to 24 nucleotides, 20 to 26 nucleotides, 20 to 28 nucleotides, or 20 to 30 nucleotides upstream to the 5' most nucleotide of the PBS.

[242] The corresponding positions of the intended nucleotide edit incorporated in the target gene may also be referred to based on the nicking position (i.e., the nick site) generated by a prime editor based on sequence homology and complementarity. For example, in embodiments, the distance between the intended nucleotide edit to be incorporated into the target ATP7B gene and the nick site (also referred to

as the "nick to edit distanc") may be determined by the position of the nick site and the position of the nucleotide(s) corresponding to the intended nucleotide edit(s), for example, by identifying sequence complementarity between the spacer and the search target sequence and sequence complementarity between the editing template and the editing target sequence. In certain embodiments, the position of the nucleotide edit can be in any position downstream of the nick site on the edit strand (or the PAM strand) generated by the prime editor, such that the distance between the nick site and the intended nucleotide edit is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. In some embodiments, the position of the nucleotide edit is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides upstream of the nick site on the edit strand. In some embodiments, the position of the nucleotide edit is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides downstream of the nick site on the edit strand. In some embodiments, the position of the nucleotide edit is 0 base pair from the nick site on the edit strand, that is, the editing position is at the same position as the nick site. As used herein, the distance between the nick site and the nucleotide edit, for example, where the nucleotide edit comprises an insertion or deletion, refers to the 5' most position of the nucleotide edit for a nick that creates a 3' free end on the edit strand (i.e., the "near position" of the nucleotide edit to the nick site). Similarly, as used herein, the distance between the nick site and a PAM position edit, for example, where the nucleotide edit comprises an insertion, deletion, or substitution of two or more contiguous nucleotides, refers to the 5' most position of the nucleotide edit and the 5' most position of the PAM sequence.

[243] In some embodiments, the editing template extends beyond a nucleotide edit to be incorporated to the target ATP7B gene sequence. For example, in some embodiments, the editing template comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 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 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence.

[244] In some embodiments, the editing template can comprise a second editing sequence comprising a second mutation relative to a target sequence. The second mutation can be designed to mutate or otherwise silence a PAM sequence such that a corresponding nucleic acid guided nuclease or CRISPR nuclease is no longer able to cleave the target sequence. In some embodiments, this mutation or silencing of a PAM can serve as a method for selecting transformants in which the first editing sequence has been incorporated. In some embodiments, the mutation is in at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more nucleic acids in a PAM motif.

[245] In some embodiments, the editing template comprises 1 to 2 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template

comprises 1 to 3 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 4 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 5 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 6 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 7 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 8 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 9 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 10 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 11 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 12 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 13 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 14 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 15 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 16 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 17 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 18 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 19 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 20 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 21 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 22 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 23 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 24 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 25 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 26 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 27 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene

sequence. In some embodiments, the editing template comprises 1 to 28 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 29 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 30 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 31 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 32 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 33 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 34 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 35 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 36 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 37 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 38 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 39 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 40 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 41 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 42 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 43 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 44 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 45 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 46 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 47 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 48 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 49 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 50 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 51 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 52 nucleotides 3' to the nucleotide

edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 53 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 54 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 55 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 56 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 57 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 58 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 59 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 60 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 61 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 62 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 63 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 64 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 65 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 66 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 67 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 68 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 69 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 70 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 71 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 72 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 73 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 74 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 75 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 76 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template

comprises 1 to 77 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 1 to 78 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 3 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 5 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 6 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 7 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 8 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 9 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 10 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 11 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 12 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 13 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 14 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 15 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 16 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 17 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 18 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 19 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 20 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 21 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 22 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 23 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 24 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene

sequence. In some embodiments, the editing template comprises 25 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 26 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 27 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 28 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 29 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 30 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 31 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 32 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 33 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 34 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 35 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 36 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 37 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 38 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 39 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 40 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 41 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 42 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 43 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 44 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 45 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 46 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 47 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 48 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 49 to 80 nucleotides 3' to the nucleotide

edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 50 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 51 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 52 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 53 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 54 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 55 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 56 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 57 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 58 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 59 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 60 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 61 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 62 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 63 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 64 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 65 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 66 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 67 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 68 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 69 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 70 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 71 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 72 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 73 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template

comprises 74 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 75 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 76 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 77 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 78 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 79 to 80 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence.

[246] In some embodiments, the editing template comprises 2 to 40 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 38 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 36 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 34 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 32 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 30 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 25 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 20 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 15 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 10 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 2 to 5 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 25 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 20 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 25 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 15 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 10 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 10 to 15 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 10 to 20 nucleotides 3' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 10 to 30 nucleotides 3' to the nucleotide

edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 30 nucleotides 5' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 25 nucleotides 5' to the nucleotide edit to be incorporated to the target ATP7B gene sequence. In some embodiments, the editing template comprises 4 to 20 nucleotides 5' to the nucleotide edit to be incorporated to the target ATP7B gene sequence.

[247] In some embodiments, the length of the editing template is at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 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 nucleotides longer than the nick to edit distance. In some embodiments, for example, the nick to edit distance is 8 nucleotides, and the editing template is 10 to 15, 10 to 20, 10 to 25, 10 to 30, 10 to 35, 10 to 40, 10 to 45, 10 to 50, 10 to 55, 10 to 60, 10 to 65, 10 to 70, 10 to 75, or 10 to 80 nucleotides in length. In some embodiments, the nick to edit distance is 22 nucleotides, and the editing template is 24 to 28, 24 to 30, 24 to 32, 24 to 34, 24 to 36, 24 to 37, 24 to 38, 24 to 40, 24 to 45, 24 to 50, 24 to 55, 24 to 60, 24 to 65, 24 to 70, 24 to 75, 24 to 80, 24 to 85, 24 to 90, 24 to 95, 24 to 100, 24 to 105, 24 to 100, 24 to 105, or 24 to 110 nucleotides in length.

[248] In some embodiments, the editing template comprises an adenine at the first nucleobase position (*e.g.*, for a PEgRNA following 5'-spacer-gRNA core-RTT-PBS-3' orientation, the 5' most nucleobase is the "first base"). In some embodiments, the editing template comprises a guanine at the first nucleobase position (*e.g.*, for a PEgRNA following 5'-spacer-gRNA core-RTT-PBS-3' orientation, the 5' most nucleobase is the "first base"). In some embodiments, the editing template comprises an uracil at the first nucleobase position (*e.g.*, for a PEgRNA following 5'-spacer-gRNA core-RTT-PBS-3' orientation, the 5' most nucleobase is the "first base"). In some embodiments, the editing template comprises a cytosine at the first nucleobase position (*e.g.*, for a PEgRNA following 5'-spacer-gRNA core-RTT-PBS-3' orientation, the 5' most nucleobase is the "first base"). In some embodiments, the editing template does not comprise a cytosine at the first nucleobase position (*e.g.*, for a PEgRNA following 5'-spacer-gRNA core-RTT-PBS-3' orientation, the 5' most nucleobase is the "first base").

[249] The editing template of a PEgRNA may encode a new single stranded DNA (*e.g.*, by reverse transcription) to replace a editing target sequence in the target gene. In some embodiments, the editing target sequence in the edit strand of the target gene is replaced by the newly synthesized strand, and the nucleotide edit(s) are incorporated in the region of the target gene. In some embodiments, the target gene is an *ATP7B* gene. In some embodiments, the editing template of the PEgRNA encodes a newly synthesized single stranded DNA that comprises a wild type *APT7B* gene sequence. In some embodiments, the newly synthesized DNA strand replaces the editing target sequence in the target *ATP7B* gene, wherein the editing target sequence (or the endogenous sequence complementary to the editing target sequence on the target strand of the *ATP7B* gene) comprises a mutation compared to a wild type *ATP7B* gene. In some embodiments, the mutation is associated with Wilson's disease.

[250] In some embodiments, the editing target sequence comprises a mutation in exon 1, exon 2, exon 3, exon 4, exon 5, exon 6, exon 7, exon 8, exon 9, exon 10, exon 11, exon 12, exon 13, exon 14, exon 15, exon 16, exon 17, exon 18, exon 19, exon 20, or exon 21 of the *ATP7B* gene as compared to a wild type *ATP7B* gene. In some embodiments, the editing target sequence comprises a mutation in exon 8, exon 13, exon 14, exon 15, or exon 17 of the *ATP7B* gene as compared to a wild type ATP7B gene. In some embodiments, the editing target sequence comprises a mutation in exon 14 of the *ATP7B* gene as compared to a wild type *ATP7B* gene. In some embodiments, the editing target sequence comprises a mutation in exon 3 of the *ATP7B* gene as compared to a wild type *ATP7B* gene. In some embodiments, the editing target sequence comprises a mutation that is located in exon 8 of the *ATP7B* gene as compared to a wild type *ATP7B* gene. In some embodiments, the mutation is not a c.1288dup duplication. In some embodiments, the editing target sequence comprises a mutation that is located between positions 51932669 and 52012130 of human chromosome 13 as set forth in human genome assembly consortium Human build 38 (GRCh38), GenBank accession GCA_000001405.15. In some embodiments, the editing target sequence comprises a mutation that is located between positions 51958233 and 51958433 of human chromosome 13 as set forth in human genome assembly consortium Human build 38 (GRCh38), GenBank accession GCA_000001405.15. In some embodiments, the editing target sequence comprises a mutation that encodes an amino acid substitution R778L relative to a wild type ATP7B polypeptide set forth in SEQ ID NO: 14897. In some embodiments, the editing target sequence comprises a G>T mutation at position 51958333 in human chromosome 13 as set forth in human genome assembly consortium Human build 38 (GRCh38), GenBank accession GCA_000001405.15. As used herein, unless otherwise noted, reference to positions in human genome is as set forth in human genome assembly consortium Human build 38 (GRCh38), GenBank accession GCA_000001405.15.

Wild **Wild-type ATP7B protein sequence (SEQ ID NO: 14897)**

>sp|P35670|ATP7B_HUMAN Copper-transporting ATPase 2 OS=Homo sapiens OX=9606 GN=ATP7B PE=1 SV=4

MPEQERQITAREGASRKILSKLSLPTRAWEPAMKKSFAFDNVGYEGGLDGLGPSSQVATS
TVRILGMTCQSCVKSIEDRISNLKGIISMKVSLEQGSATVKYVPSVVCLQQVCHQIGDMG
FEASIAEGKAASWPSRSLPAQEAVVKLRVEGMTCQSCVSSIEGKVRKLQGVVRVKVSLSN
QEAVITYQPYLIQPEDLRDHVNDMGFEAAIKSKVAPLSLGPIDIERLQSTNPKRPLSSAN
QNFNNSETLGHQGSHVVTLQLRIDGMHCKSCVLNIEENIGQLLGVQSIQVSLENKTAQVK
YDPSCTSPVALQRAIEALPPGNFKVSLPDGAEGSGTDHRSSSSHSPGSPPRNQVQGTCST
TLIAIAGMTCASCVHSIEGMISQLEGVQQISVSLAEGTATVLYNPSVISPEELRAAIEDM
GFEASVVSESCSTNPLGNHSAGNSMVQTTDGTPTSVQEVAPHTGRLPANHAPDILAKSPQ
STRAVAPQKCFLQIKGMTCASCVSNIERNLQKEAGVLSVLVALMAGKAEIKYDPEVIQPL
EIAQFIQDLGFEAAVMEDYAGSDGNIELTITGMTCASCVHNIESKLTRTNGITYASVALA
TSKALVKFDPEIIGPRDIIKIIEEIGFHASLAQRNPNAHHLDHKMEIKQWKKSFLCSLVF
GIPVMALMIYMLIPSNEPHQSMVLDHNIIPGLSILNLIFFILCTFVQLLGGWYFYVQAYK
SLRHRSANMDVLIVLATSIAYVYSLVILVVAVAEKAERSPVTFFDTPPMLFVFIALGRWL
EHLAKSKTSEALAKLMSLQATEATVVTLGEDNLIIREEQVPMELVQRGDIVKVVPGGKFP
VDGKVLEGNTMADESLITGEAMPVTKKPGSTVIAGSINAHGSVLIKATHVGNDTTLAQIV
KLVEEAQMSKAPIQQLADRFSGYFVPFIIIMSTLTLVVWIVIGFIDFGVVQRYFPNPNKH
ISQTEVIIRFAFQTSITVLCIACPCSLGLATPTAVMVGTGVAAQNGILIKGGKPLEMAHK

IKTVMFDKTGTITHGVPRVMRVLLLGDVATLPLRKVLAVVGTAEASSEHPLGVAVTKYCK
EELGTETLGYCTDFQAVPGCGIGCKVSNVEGILAHSERPLSAPASHLNEAGSLPAEKDAV
PQTFSVLIGNREWLRRNGLTISSDVSDAMTDHEMKGQTAILVAIDGVLCGMIAIADAVKQ
EAALAVHTLQSMGVDVVLITGDNRKTARAIATQVGINKVFAEVLPSHKVAKVQELQNKGK
KVAMVGDGVNDSPALAQADMGVAIGTGTDVAIEAADVVLIRNDLLDVVASIHLSKRTVRR
IRINLVLALIYNLVGIPIAAGVFMPIGIVLQPWMGSAAMAASSVSVVLSSLQLKCYKKPD
LERYEAQAHGHMKPLTASQVSVHIGMDDRWRDSPRATPWDQVSYVSQVSLSSLTSDKPSR
HSAAADDDGDKWSLLLNGRDEEQYI

[251] In some embodiments, the editing template comprises one or more intended nucleotide edits compared to the sequence on the target strand of the *ATP7B* gene that is complementary to the editing target sequence. In some embodiments, the editing template encodes a single stranded DNA that comprises one or more intended nucleotide edits compared to the editing target sequence. In some embodiments, the single stranded DNA replaces the editing target sequence by prime editing, thereby incorporating the one or more intended nucleotide edits.

[252] In some embodiments, incorporation of the one or more intended nucleotide edits corrects the mutation in the editing target sequence to wild type nucleotides at corresponding positions in the *ATP7B* gene. As used herein, "correcting" a mutation means restoring a wild type sequence at the place of the mutation in the double stranded target DNA, e.g., target gene, by prime editing. In some embodiments, the editing template comprises and/or encodes a wild type *ATP7B* gene sequence.

[253] In some embodiments, incorporation of the one or more intended nucleotide edits does not correct the mutation in the editing target sequence to wild type sequence, but allows for expression of a functional ATP7B protein encoded by the *ATP7B* gene.

[254] In some embodiments, the editing template comprises one or more intended nucleotide edits compared to the sequence on the target strand of the *ATP7B* gene that is complementary to the editing target sequence, wherein the one or more intended nucleotide edits is a single nucleotide substitution, polynucleotide substitution, nucleotide insertion, or nucleotide deletion. In some embodiments, the intended nucleotide edit in the editing template comprises a single nucleotide substitution, polynucleotide substitution, nucleotide insertion, or nucleotide deletion compared to the sequence on the target strand of the *ATP7B* gene that is complementary to the editing target at a position corresponding to a mutation in *ATP7B* located between positions 51932669 and 52012130 of human chromosome 13, wherein the editing target sequence is on the sense strand of the *ATP7B* gene. In some embodiments, the intended nucleotide edit in the editing template comprises a single nucleotide substitution, polynucleotide substitution, nucleotide insertion, or nucleotide deletion compared to the sequence on the target strand of the *ATP7B* gene that is complementary to the editing target at a position corresponding to a mutation in *ATP7B* located between positions 51932669 and 52012130 of human chromosome 13, wherein the editing target sequence is on the antisense strand of the *ATP7B* gene. In some embodiments, the editing template (RTT) comprises an RTT as provided in **Tables 1-Table 84**.

[255] A guide RNA core (also referred to herein as the gRNA core, gRNA scaffold, or gRNA backbone sequence) of a PEgRNA may contain a polynucleotide sequence that binds to a DNA binding domain (*e.g.*, Cas9) of a prime editor. The gRNA core may interact with a prime editor as described herein, for example, by association with a DNA binding domain, such as a DNA nickase of the prime editor.

[256] One of skill in the art will recognize that different prime editors having different DNA binding domains from different DNA binding proteins may require different gRNA core sequences specific to the DNA binding protein. In some embodiments, the gRNA core is capable of binding to a Cas9-based prime editor. In some embodiments, the gRNA core is capable of binding to a Cpf1-based prime editor. In some embodiments, the gRNA core is capable of binding to a Cas12b-based prime editor.

[257] In some embodiments, the gRNA core comprises regions and secondary structures involved in binding with specific CRISPR Cas proteins. For example, in a Cas9 based prime editing system, the gRNA core of a PEgRNA may comprise one or more regions of a base paired "lower stem" adjacent to the spacer sequence and a base paired "upper stem" following the lower stem, where the lower stem and upper stem may be connected by a "bulge" comprising unpaired RNAs. The gRNA core may further comprise a "nexus" distal from the spacer sequence, followed by a hairpin structure, *e.g.*, at the 3' end, as exemplified in **FIG. 4**. In some embodiments, the gRNA core comprises modified nucleotides as compared to a wild type gRNA core in the lower stem, upper stem, and/or the hairpin. For example, nucleotides in the lower stem, upper stem, an/or the hairpin regions may be modified, deleted, or replaced. In some embodiments, RNA nucleotides in the lower stem, upper stem, an/or the hairpin regions may be replaced with one or more DNA sequences. In some embodiments, the gRNA core comprises unmodified or wild type RNA sequences in the nexus and/or the bulge regions. In some embodiments, the gRNA core does not include long stretches of A-T pairs, for example, a GUUUU-AAAAC pairing element. In some embodiments, a prime editing system comprises a prime editor and a PEgRNA, wherein the prime editor comprises a SpCas9 nickase or a variant thereof, and the gRNA core of the PEgRNA comprises the sequence:
GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAG UGGCACCGAGUCGGUGC (SEQ ID NO: 14905);
GUUUGAGAGCUAGAAAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAG UGGGACCGAGUCGGUCC (SEQ ID NO: 14906), or
GUUUAAGAGCUAUGCUGGAAACAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAA CUUGAAAAAGUGGCACCGAGUCGGUGC (SEQ ID NO: 14907). In some embodiments, the gRNA core comprises the sequence
GUUUUAGAGCUAGAAAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAG UGGCACCGAGUCGGUGC (SEQ ID NO: 14905). Any gRNA core sequences known in the art are also contemplated in the prime editing compositions described herein.

[258] A PEgRNA may also comprise optional modifiers, *e.g.*, 3′ end modifier region and/or an 5′ end modifier region. In some embodiments, a PEgRNA comprises at least one nucleotide that is not part of a spacer, a gRNA core, or an extension arm. The optional sequence modifiers could be positioned within or between any of the other regions shown, and not limited to being located at the 3′ and 5′ ends. In certain embodiments, the PEgRNA comprises secondary RNA structure, such as, but not limited to, aptamers, hairpins, stem/loops, toeloops, and/or RNA-binding protein recruitment domains (*e.g.*, the MS2 aptamer which recruits and binds to the MS2cp protein). In some embodiments, a PEgRNA comprises a short stretch of uracil at the 5' end or the 3' end. For example, in some embodiments, a PEgRNA comprising a 3' extension arm comprises a "UUU" sequence at the 3' end of the extension arm. In some embodiments, a PEgRNA comprises a toeloop sequence at the 3' end. In some embodiments, the PEgRNA comprises a 3' extension arm and a toeloop sequence at the 3' end of the extension arm. In some embodiments, the PEgRNA comprises a 5' extension arm and a toeloop sequence at the 5' end of the extension arm. In some embodiments, the PEgRNA comprises a toeloop element having the sequence 5'-GAAANNNNN-3', wherein N is any nucleobase. In some embodiments, the secondary RNA structure is positioned within the spacer. In some embodiments, the secondary structure is positioned within the extension arm. In some embodiments, the secondary structure is positioned within the gRNA core. In some embodiments, the secondary structure is positioned between the spacer and the gRNA core, between the gRNA core and the extension arm, or between the spacer and the extension arm. In some embodiments, the secondary structure is positioned between the PBS and the editing template. In some embodiments the secondary structure is positioned at the 3' end or at the 5' end of the PEgRNA. In some embodiments, the PEgRNA comprises a transcriptional termination signal at the 3′ end of the PEgRNA. In addition to secondary RNA structures, the PEgRNA may comprise a chemical linker or a poly(N) linker or tail, where "N" can be any nucleobase. In some embodiments, the chemical linker may function to prevent reverse transcription of the gRNA core.

[259] In some embodiments, a PEgRNA or a nick guide RNA (ngRNA) can be chemically synthesized, or can be assembled or cloned and transcribed from a DNA sequence, e.g., a plasmid DNA sequence, or by any RNA oligonucleotide synthesis method known in the art. In some embodiments, DNA sequence that encodes a PEgRNA (or ngRNA) can be designed to append one or more nucleotides at the 5′ end or the 3′ end of the PEgRNA (or nick guide RNA) encoding sequence to enhance PEgRNA transcription. For example, in some embodiments, a DNA sequence that encodes a PEgRNA (or nick guide RNA) (or an ngRNA) can be designed to append a nucleotide G at the 5′ end. Accordingly, in some embodiments, the PEgRNA (or nick guide RNA) can comprise an appended nucleotide G at the 5′ end. In some embodiments, a DNA sequence that encodes a PEgRNA (or nick guide RNA) can be designed to append a sequence that enhances transcription, e.g., a Kozak sequence, at the 5′ end. In some embodiments, a DNA sequence that encodes a PEgRNA (or nick guide RNA) can be designed to append the sequence CACC or CCACC at the 5′ end. Accordingly, in some embodiments, the PEgRNA (or nick guide RNA) can comprise an appended sequence CACC or CCACC at the 5′ end. In some embodiments, a DNA

sequence that encodes a PEgRNA (or nick guide RNA) can be designed to append the sequence TTT, TTTT, TTTTT, TTTTTT, TTTTTTT at the 3′ end. Accordingly, in some embodiments, the PEgRNA (or nick guide RNA) can comprise an appended sequence UUU, UUUU, UUUUU, UUUUUU, or UUUUUUU at the 3′ end. In some embodiments, a PEgRNA or ngRNA may include a modifying sequence at the 3′ end having the sequence AACAUUGACGCGUCUCUACGUGGGGGCGCG (SEQ ID NO: 14920).

[260] In some embodiments, a prime editing system or composition further comprises a nick guide polynucleotide, such as a nick guide RNA (ngRNA). Without wishing to be bound by any particular theory, the non-edit strand of a double stranded target DNA in the target gene may be nicked by a CRISPR-Cas nickase directed by an ngRNA. In some embodiments, the nick on the non-edit strand directs endogenous DNA repair machinery to use the edit strand as a template for repair of the non-edit strand, which may increase efficiency of prime editing. In some embodiments, the non-edit strand is nicked by a prime editor localized to the non-edit strand by the ngRNA. Accordingly, also provided herein are PEgRNA systems comprising at least one PEgRNA and at least one ngRNA.

[261] In some embodiments, the ngRNA is a guide RNA which contains a variable spacer sequence and a guide RNA scaffold or core region that interacts with the DNA binding domain, *e.g.*, Cas9 of the prime editor. In some embodiments, the ngRNA comprises a spacer sequence (referred to herein as an ng spacer, or a second spacer) that is substantially complementary to a second search target sequence (or ng search target sequence), which is located on the edit strand, or the non-target strand. Thus, in some embodiments, the ng search target sequence recognized by the ng spacer and the search target sequence recognized by the spacer sequence of the PEgRNA are on opposite strands of the double stranded target DNA of target gene, *e.g.*, the *ATP7B* gene. In some embodiments, a prime editing system or complex comprising a ngRNA may be referred to as a "PE3" prime editing system or PE3 prime editing complex. In some embodiments, an ng spacer sequence is complementary to, and may hybridize with the second search target sequence only after an intended nucleotide edit has been incorporated on the edit strand, by the editing template of a PEgRNA, e.g., a "PE3b" prime editing system or composition.

Table 1

Sequence Number	Sequence	Description
1	SEQ ID NO: 1	PEgRNA spacer (TGG;TG PAM)
2	SEQ ID NO: 2	PEgRNA spacer (TGG;TG PAM)
3	SEQ ID NO: 3	PEgRNA spacer (TGG;TG PAM)
4	SEQ ID NO: 4	PEgRNA spacer (TGG;TG PAM)
5	SEQ ID NO: 5	PEgRNA spacer (TGG;TG PAM)
6	SEQ ID NO: 6	PEgRNA spacer (TGG;TG PAM)
7	SEQ ID NO: 7	PEgRNA spacer (TGG;TG PAM)
8	TGA	PBS
9	TGAC	PBS
10	TGACC	PBS
11	TGACCA	PBS
12	TGACCA G	PBS
13	TGACCA GA	PBS
14	TGACCA GAG	PBS
15	SEQ ID NO: 15	PBS
16	SEQ ID NO: 16	PBS
17	SEQ ID NO: 17	PBS
18	SEQ ID NO: 18	PBS
19	SEQ ID NO: 19	PBS
20	SEQ ID NO: 20	PBS
21	SEQ ID NO: 21	PBS
22	SEQ ID NO: 22	PBS
23	SEQ ID NO: 23	PBS
24	SEQ ID NO: 24	PBS
25	SEQ ID NO: 25	RTT
26	SEQ ID NO: 26	RTT*83 (PAM silencing)
27	SEQ ID NO: 27	RTT*80 (PAM silencing)
28	SEQ ID NO: 28	RTT*82 (PAM silencing)
29	SEQ ID NO: 29	RTT*81 (PAM silencing)
30	SEQ ID NO: 30	RTT*82 (PAM silencing)
31	SEQ ID NO: 31	RTT*80 (PAM silencing)
32	SEQ ID NO: 32	RTT*83 (PAM silencing)
33	SEQ ID NO: 33	RTT
34	SEQ ID NO: 34	RTT*81 (PAM silencing)
35	SEQ ID NO: 35	RTT*83 (PAM silencing)
36	SEQ ID NO: 36	RTT
37	SEQ ID NO: 37	RTT*81 (PAM silencing)
38	SEQ ID NO: 38	RTT*82 (PAM silencing)
39	SEQ ID NO: 39	RTT*80 (PAM silencing)
40	SEQ ID NO: 40	RTT*82 (PAM silencing)
41	SEQ ID NO: 41	RTT*80 (PAM silencing)
42	SEQ ID NO: 42	RTT
43	SEQ ID NO: 43	RTT*81 (PAM silencing)
44	SEQ ID NO: 44	RTT*83 (PAM silencing)
45	SEQ ID NO: 45	RTT*82 (PAM silencing)
46	SEQ ID NO: 46	RTT*81 (PAM silencing)
47	SEQ ID NO: 47	RTT*83 (PAM silencing)
48	SEQ ID NO: 48	RTT*80 (PAM silencing)
49	SEQ ID NO: 49	RTT
50	SEQ ID NO: 50	RTT*83 (PAM silencing)
51	SEQ ID NO: 51	RTT*82 (PAM silencing)
52	SEQ ID NO: 52	RTT*80 (PAM silencing)
53	SEQ ID NO: 53	RTT
54	SEQ ID NO: 54	RTT*81 (PAM silencing)
55	SEQ ID NO: 55	RTT
56	SEQ ID NO: 56	RTT*80 (PAM silencing)
57	SEQ ID NO: 57	RTT*83 (PAM silencing)
58	SEQ ID NO: 58	RTT*82 (PAM silencing)
59	SEQ ID NO: 59	RTT*81 (PAM silencing)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
66	SEQ ID NO: 66	PE3b*83 ngRNA spacer (TG PAM)
67	SEQ ID NO: 67	PE3 ngRNA spacer (AG;AGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (TG;TGG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
71	SEQ ID NO: 71	PE3 ngRNA spacer (GG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
73	SEQ ID NO: 73	PE3b*81 ngRNA spacer (TG PAM)
74	SEQ ID NO: 74	PE3b*82 ngRNA spacer (GG PAM)
75	SEQ ID NO: 75	PE3 ngRNA spacer (TG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
80	SEQ ID NO: 80	PE3b*82 ngRNA spacer (TG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
82	SEQ ID NO: 82	PE3b*81 ngRNA spacer

Sequence Number	Sequence	Description
		(GG PAM)
83	SEQ ID NO: 83	PE3b*83 ngRNA spacer (AG;GG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
86	SEQ ID NO: 86	PE3b*82 ngRNA spacer (AG;AGG PAM)
87	SEQ ID NO: 87	PE3b*80 ngRNA spacer (TG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
89	SEQ ID NO: 89	PE3b*83 ngRNA spacer (AAG;AG; AGG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
94	SEQ ID NO: 94	PE3b*81 ngRNA spacer (AG;AGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)

Sequence Number	Sequence	Description
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
106	SEQ ID NO: 106	ngRNA (AG;AGG PAM)
111	SEQ ID NO: 111	ngRNA (AG;AGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)

Sequence Number	Sequence	Description
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)

Table 2

Sequence Number	Sequence	Description
119	SEQ ID NO: 119	PEgRNA spacer (TGG;TG PAM)
120	SEQ ID NO: 120	PEgRNA spacer (TGG;TG PAM)
121	SEQ ID NO: 121	PEgRNA spacer (TGG;TG PAM)
122	SEQ ID NO: 122	PEgRNA spacer (TGG;TG PAM)
123	SEQ ID NO: 123	PEgRNA spacer (TGG;TG PAM)
124	SEQ ID NO: 124	PEgRNA spacer (TGG;TG PAM)
125	SEQ ID NO: 125	PEgRNA spacer (TGG;TG PAM)
126	GGA	PBS
127	GGAT	PBS
128	GGATG	PBS
129	GGATGA	PBS
130	GGATGAC	PBS
131	GGATGACC	PBS
132	GGATGACCA	PBS
133	SEQ ID NO: 133	PBS
134	SEQ ID NO: 134	PBS
135	SEQ ID NO: 135	PBS
136	SEQ ID NO: 136	PBS
137	SEQ ID NO: 137	PBS
138	SEQ ID NO: 138	PBS
139	SEQ ID NO: 139	PBS
140	SEQ ID NO: 140	PBS
141	SEQ ID NO: 141	PBS
142	SEQ ID NO: 142	PBS
143	SEQ ID NO: 143	RTT*110 (PAM silencing)
144	SEQ ID NO: 144	RTT*108 (PAM silencing)
145	SEQ ID NO: 145	RTT
146	SEQ ID NO: 146	RTT*109 (PAM silencing)
147	SEQ ID NO: 147	RTT*109 (PAM silencing)
148	SEQ ID NO: 148	RTT*110 (PAM silencing)
149	SEQ ID NO: 149	RTT
150	SEQ ID NO: 150	RTT*108 (PAM silencing)
151	SEQ ID NO: 151	RTT*110 (PAM silencing)
152	SEQ ID NO: 152	RTT
153	SEQ ID NO: 153	RTT*108 (PAM silencing)
154	SEQ ID NO: 154	RTT*109 (PAM silencing)
155	SEQ ID NO: 155	RTT
156	SEQ ID NO: 156	RTT*110 (PAM silencing)
157	SEQ ID NO: 157	RTT*108 (PAM silencing)
158	SEQ ID NO: 158	RTT*109 (PAM silencing)
159	SEQ ID NO: 159	RTT*110 (PAM silencing)
160	SEQ ID NO: 160	RTT*108 (PAM silencing)
161	SEQ ID NO: 161	RTT
162	SEQ ID NO: 162	RTT*109 (PAM silencing)
163	SEQ ID NO: 163	RTT*108 (PAM silencing)
164	SEQ ID NO: 164	RTT*109 (PAM silencing)
165	SEQ ID NO: 165	RTT*110 (PAM silencing)
166	SEQ ID NO: 166	RTT
167	SEQ ID NO: 167	RTT*108 (PAM silencing)
168	SEQ ID NO: 168	RTT*110 (PAM silencing)
169	SEQ ID NO: 169	RTT*109 (PAM silencing)
170	SEQ ID NO: 170	RTT
171	SEQ ID NO: 171	RTT*110 (PAM silencing)
172	SEQ ID NO: 172	RTT
173	SEQ ID NO: 173	RTT*108 (PAM silencing)
174	SEQ ID NO: 174	RTT*109 (PAM silencing)
175	SEQ ID NO: 175	RTT*108 (PAM silencing)
176	SEQ ID NO: 176	RTT
177	SEQ ID NO: 177	RTT*110 (PAM silencing)
178	SEQ ID NO: 178	RTT*109 (PAM silencing)
179	SEQ ID NO: 179	RTT*110 (PAM silencing)
180	SEQ ID NO: 180	RTT*109 (PAM silencing)
181	SEQ ID NO: 181	RTT*108 (PAM silencing)
182	SEQ ID NO: 182	RTT
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
183	SEQ ID NO: 183	PE3b*109 ngRNA spacer

Sequence Number	Sequence	Description
		(AG;AGG PAM)
184	SEQ ID NO: 184	PE3b*110 ngRNA spacer (AG;AGG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
185	SEQ ID NO: 185	PE3b*110 ngRNA spacer (GG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
67	SEQ ID NO: 67	PE3 ngRNA spacer (AG;AGG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
186	SEQ ID NO: 186	PE3b*108 ngRNA spacer (TG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
187	SEQ ID NO: 187	PE3b*108 ngRNA spacer (AG;AGG PAM)
188	SEQ ID NO: 188	PE3b*108 ngRNA spacer (GG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
71	SEQ ID NO: 71	PE3 ngRNA spacer (GG PAM)
75	SEQ ID NO: 75	PE3 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
190	SEQ ID NO: 190	PE3b*109 ngRNA spacer (GG PAM)
191	SEQ ID NO: 191	PE3b*109 ngRNA spacer (TG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
192	SEQ ID NO: 192	PE3b*110 ngRNA spacer (TG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
106	SEQ ID NO: 106	ngRNA (AG;AGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)

Sequence Number	Sequence	Description
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
111	SEQ ID NO: 111	ngRNA (AG;AGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)

Table 3

Sequence Number	Sequence	Description
193	SEQ ID NO: 193	PEgRNA spacer (TGG;TG PAM)
194	SEQ ID NO: 194	PEgRNA spacer (TGG;TG PAM)
195	SEQ ID NO: 195	PEgRNA spacer (TGG;TG PAM)
196	SEQ ID NO: 196	PEgRNA spacer (TGG;TG PAM)
197	SEQ ID NO: 197	PEgRNA spacer (TGG;TG PAM)
198	SEQ ID NO: 198	PEgRNA spacer (TGG;TG PAM)
199	SEQ ID NO: 199	PEgRNA spacer (TGG;TG PAM)
200	CAA	PBS
201	CAAC	PBS
202	CAACC	PBS
203	CAACCA	PBS
204	CAACCAC	PBS
205	CAACCACC	PBS
206	CAACCACCA	PBS
207	SEQ ID NO: 207	PBS
208	SEQ ID NO: 208	PBS
209	SEQ ID NO: 209	PBS
210	SEQ ID NO: 210	PBS
211	SEQ ID NO: 211	PBS
212	SEQ ID NO: 212	PBS
213	SEQ ID NO: 213	PBS
214	SEQ ID NO: 214	PBS
215	SEQ ID NO: 215	PBS
216	SEQ ID NO: 216	PBS
217	SEQ ID NO: 217	RTT*110 (PAM silencing)
218	SEQ ID NO: 218	RTT*108 (PAM silencing)
219	SEQ ID NO: 219	RTT*109 (PAM silencing)
220	SEQ ID NO: 220	RTT
221	SEQ ID NO: 221	RTT*110 (PAM silencing)
222	SEQ ID NO: 222	RTT
223	SEQ ID NO: 223	RTT*109 (PAM silencing)
224	SEQ ID NO: 224	RTT*108 (PAM silencing)
225	SEQ ID NO: 225	RTT*108 (PAM silencing)
226	SEQ ID NO: 226	RTT*109 (PAM silencing)
227	SEQ ID NO: 227	RTT*110 (PAM silencing)
228	SEQ ID NO: 228	RTT
229	SEQ ID NO: 229	RTT*109 (PAM silencing)
230	SEQ ID NO: 230	RTT*110 (PAM silencing)
231	SEQ ID NO: 231	RTT*108 (PAM silencing)
232	SEQ ID NO: 232	RTT
233	SEQ ID NO: 233	RTT*110 (PAM silencing)
234	SEQ ID NO: 234	RTT*108 (PAM silencing)
235	SEQ ID NO: 235	RTT*109 (PAM silencing)
236	SEQ ID NO: 236	RTT
237	SEQ ID NO: 237	RTT*110 (PAM silencing)
238	SEQ ID NO: 238	RTT*109 (PAM silencing)
239	SEQ ID NO: 239	RTT*108 (PAM silencing)
240	SEQ ID NO: 240	RTT
241	SEQ ID NO: 241	RTT
242	SEQ ID NO: 242	RTT*108 (PAM silencing)
243	SEQ ID NO: 243	RTT*109 (PAM silencing)
244	SEQ ID NO: 244	RTT*110 (PAM silencing)
245	SEQ ID NO: 245	RTT*108 (PAM silencing)
246	SEQ ID NO: 246	RTT*110 (PAM silencing)
247	SEQ ID NO: 247	RTT
248	SEQ ID NO: 248	RTT*109 (PAM silencing)
249	SEQ ID NO: 249	RTT*108 (PAM silencing)
250	SEQ ID NO: 250	RTT*110 (PAM silencing)
251	SEQ ID NO: 251	RTT
252	SEQ ID NO: 252	RTT*109 (PAM silencing)
253	SEQ ID NO: 253	RTT
254	SEQ ID NO: 254	RTT*110 (PAM silencing)

Sequence Number	Sequence	Description
255	SEQ ID NO: 255	RTT*109 (PAM silencing)
256	SEQ ID NO: 256	RTT*108 (PAM silencing)
257	SEQ ID NO: 257	RTT
258	SEQ ID NO: 258	RTT*110 (PAM silencing)
259	SEQ ID NO: 259	RTT*108 (PAM silencing)
260	SEQ ID NO: 260	RTT*109 (PAM silencing)
261	SEQ ID NO: 261	RTT*109 (PAM silencing)
262	SEQ ID NO: 262	RTT
263	SEQ ID NO: 263	RTT*108 (PAM silencing)
264	SEQ ID NO: 264	RTT*110 (PAM silencing)
265	SEQ ID NO: 265	RTT*109 (PAM silencing)
266	SEQ ID NO: 266	RTT*110 (PAM silencing)
267	SEQ ID NO: 267	RTT*108 (PAM silencing)
268	SEQ ID NO: 268	RTT
269	SEQ ID NO: 269	RTT
270	SEQ ID NO: 270	RTT*110 (PAM silencing)
271	SEQ ID NO: 271	RTT*109 (PAM silencing)
272	SEQ ID NO: 272	RTT*108 (PAM silencing)
273	SEQ ID NO: 273	RTT*109 (PAM silencing)
274	SEQ ID NO: 274	RTT*110 (PAM silencing)
275	SEQ ID NO: 275	RTT*108 (PAM silencing)
276	SEQ ID NO: 276	RTT
277	SEQ ID NO: 277	RTT*108 (PAM silencing)
278	SEQ ID NO: 278	RTT*110 (PAM silencing)
279	SEQ ID NO: 279	RTT*109 (PAM silencing)
280	SEQ ID NO: 280	RTT
281	SEQ ID NO: 281	RTT*109 (PAM silencing)
282	SEQ ID NO: 282	RTT*108 (PAM silencing)
283	SEQ ID NO: 283	RTT*110 (PAM silencing)
284	SEQ ID NO: 284	RTT
285	SEQ ID NO: 285	RTT*108 (PAM silencing)
286	SEQ ID NO: 286	RTT*110 (PAM silencing)
287	SEQ ID NO: 287	RTT
288	SEQ ID NO: 288	RTT*109 (PAM silencing)
289	SEQ ID NO: 289	RTT
290	SEQ ID NO: 290	RTT*110 (PAM silencing)
291	SEQ ID NO: 291	RTT*108 (PAM silencing)
292	SEQ ID NO: 292	RTT*109 (PAM silencing)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
295	SEQ ID NO: 295	PE3b*109 ngRNA spacer (AG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
296	SEQ ID NO: 296	PE3b*108 ngRNA spacer (AG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(GG;GGG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
297	SEQ ID NO: 297	PE3b*110 ngRNA spacer (AG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)

Table 4

Sequence Number	Sequence	Description
298	SEQ ID NO: 298	PEgRNA spacer (AGG;AG PAM)
299	SEQ ID NO: 299	PEgRNA spacer (AGG;AG PAM)
300	SEQ ID NO: 300	PEgRNA spacer (AGG;AG PAM)
301	SEQ ID NO: 301	PEgRNA spacer (AGG;AG PAM)
302	SEQ ID NO: 302	PEgRNA spacer (AGG;AG PAM)
303	SEQ ID NO: 303	PEgRNA spacer (AGG;AG PAM)
304	SEQ ID NO: 304	PEgRNA spacer (AGG;AG PAM)
305	CAG	PBS
306	CAGC	PBS
307	CAGCC	PBS
308	CAGCCA	PBS
309	CAGCCAC	PBS
310	CAGCCACA	PBS
311	CAGCCACAG	PBS
312	SEQ ID NO: 312	PBS
313	SEQ ID NO: 313	PBS
314	SEQ ID NO: 314	PBS
315	SEQ ID NO: 315	PBS
316	SEQ ID NO: 316	PBS
317	SEQ ID NO: 317	PBS
318	SEQ ID NO: 318	PBS
319	SEQ ID NO: 319	PBS
320	SEQ ID NO: 320	PBS
321	SEQ ID NO: 321	PBS
322	SEQ ID NO: 322	RTT
323	SEQ ID NO: 323	RTT*40 (PAM silencing)
324	SEQ ID NO: 324	RTT
325	SEQ ID NO: 325	RTT*40 (PAM silencing)
326	SEQ ID NO: 326	RTT
327	SEQ ID NO: 327	RTT*40 (PAM silencing)
328	SEQ ID NO: 328	RTT*40 (PAM silencing)
329	SEQ ID NO: 329	RTT
330	SEQ ID NO: 330	RTT

Sequence Number	Sequence	Description
331	SEQ ID NO: 331	RTT*40 (PAM silencing)
332	SEQ ID NO: 332	RTT*40 (PAM silencing)
333	SEQ ID NO: 333	RTT
334	SEQ ID NO: 334	RTT
335	SEQ ID NO: 335	RTT*40 (PAM silencing)
336	SEQ ID NO: 336	RTT*40 (PAM silencing)
337	SEQ ID NO: 337	RTT
338	SEQ ID NO: 338	RTT
339	SEQ ID NO: 339	RTT*40 (PAM silencing)
340	SEQ ID NO: 340	RTT
341	SEQ ID NO: 341	RTT*40 (PAM silencing)
342	SEQ ID NO: 342	RTT
343	SEQ ID NO: 343	RTT*40 (PAM silencing)
344	SEQ ID NO: 344	RTT
345	SEQ ID NO: 345	RTT*40 (PAM silencing)
346	SEQ ID NO: 346	RTT*40 (PAM silencing)
347	SEQ ID NO: 347	RTT
348	SEQ ID NO: 348	RTT*40 (PAM silencing)
349	SEQ ID NO: 349	RTT
350	SEQ ID NO: 350	RTT
351	SEQ ID NO: 351	RTT*40 (PAM silencing)
352	SEQ ID NO: 352	RTT
353	SEQ ID NO: 353	RTT*40 (PAM silencing)
354	SEQ ID NO: 354	RTT*40 (PAM silencing)
355	SEQ ID NO: 355	RTT
356	SEQ ID NO: 356	RTT
357	SEQ ID NO: 357	RTT*40 (PAM silencing)
358	SEQ ID NO: 358	RTT*40 (PAM silencing)
359	SEQ ID NO: 359	RTT
360	SEQ ID NO: 360	RTT*40 (PAM silencing)
361	SEQ ID NO: 361	RTT
362	SEQ ID NO: 362	RTT*40 (PAM silencing)
363	SEQ ID NO: 363	RTT
364	SEQ ID NO: 364	RTT
365	SEQ ID NO: 365	RTT*40 (PAM silencing)
366	SEQ ID NO: 366	RTT
367	SEQ ID NO: 367	RTT*40 (PAM silencing)
368	SEQ ID NO: 368	RTT
369	SEQ ID NO: 369	RTT*40 (PAM silencing)
370	SEQ ID NO: 370	RTT
371	SEQ ID NO: 371	RTT*40 (PAM silencing)
372	SEQ ID NO: 372	RTT*40 (PAM silencing)
373	SEQ ID NO: 373	RTT
374	SEQ ID NO: 374	RTT
375	SEQ ID NO: 375	RTT*40 (PAM silencing)
376	SEQ ID NO: 376	RTT*40 (PAM silencing)
377	SEQ ID NO: 377	RTT
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer
		(GG;GGG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)

Sequence Number	Sequence	Description
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
379	SEQ ID NO: 379	PE3b*40 ngRNA spacer
		(AG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)

Table 5

Sequence Number	Sequence	Description
380	SEQ ID NO: 380	PEgRNA spacer (CGG;CG PAM)
381	SEQ ID NO: 381	PEgRNA spacer (CGG;CG PAM)
382	SEQ ID NO: 382	PEgRNA spacer (CGG;CG PAM)
383	SEQ ID NO: 383	PEgRNA spacer (CGG;CG PAM)
384	SEQ ID NO: 384	PEgRNA spacer (CGG;CG PAM)
385	SEQ ID NO: 385	PEgRNA spacer (CGG;CG PAM)
386	SEQ ID NO: 386	PEgRNA spacer (CGG;CG PAM)
387	TCT	PBS
388	TCTC	PBS
389	TCTCA	PBS
390	TCTCAG	PBS
391	TCTCAG C	PBS
392	TCTCAG CC	PBS
393	TCTCAG CCA	PBS
394	SEQ ID NO: 394	PBS
395	SEQ ID NO: 395	PBS
396	SEQ ID NO: 396	PBS
397	SEQ ID NO: 397	PBS
398	SEQ ID NO: 398	PBS
399	SEQ ID NO: 399	PBS
400	SEQ ID NO: 400	PBS
401	SEQ ID NO: 401	PBS
402	SEQ ID NO: 402	PBS
403	SEQ ID NO: 403	PBS
404	SEQ ID NO: 404	RTT*76 (PAM silencing)
405	SEQ ID NO: 405	RTT*71 (PAM silencing)
406	SEQ ID NO: 406	RTT*72 (PAM silencing)
407	SEQ ID NO: 407	RTT
408	SEQ ID NO: 408	RTT*76 (PAM silencing)

Sequence Number	Sequence	Description
409	SEQ ID NO: 409	RTT
410	SEQ ID NO: 410	RTT*72 (PAM silencing)
411	SEQ ID NO: 411	RTT*71 (PAM silencing)
412	SEQ ID NO: 412	RTT*72 (PAM silencing)
413	SEQ ID NO: 413	RTT
414	SEQ ID NO: 414	RTT*71 (PAM silencing)
415	SEQ ID NO: 415	RTT*76 (PAM silencing)
416	SEQ ID NO: 416	RTT*76 (PAM silencing)
417	SEQ ID NO: 417	RTT*72 (PAM silencing)
418	SEQ ID NO: 418	RTT*71 (PAM silencing)
419	SEQ ID NO: 419	RTT
420	SEQ ID NO: 420	RTT*76 (PAM silencing)
421	SEQ ID NO: 421	RTT*71 (PAM silencing)
422	SEQ ID NO: 422	RTT*72 (PAM silencing)
423	SEQ ID NO: 423	RTT
424	SEQ ID NO: 424	RTT*71 (PAM silencing)
425	SEQ ID NO: 425	RTT*76 (PAM silencing)
426	SEQ ID NO: 426	RTT*72 (PAM silencing)
427	SEQ ID NO: 427	RTT
428	SEQ ID NO: 428	RTT*72 (PAM silencing)
429	SEQ ID NO: 429	RTT
430	SEQ ID NO: 430	RTT*76 (PAM silencing)
431	SEQ ID NO: 431	RTT*71 (PAM silencing)
432	SEQ ID NO: 432	RTT
433	SEQ ID NO: 433	RTT*71 (PAM silencing)
434	SEQ ID NO: 434	RTT*76 (PAM silencing)
435	SEQ ID NO: 435	RTT*72 (PAM silencing)
436	SEQ ID NO: 436	RTT*72 (PAM silencing)
437	SEQ ID NO: 437	RTT*71 (PAM silencing)
438	SEQ ID NO: 438	RTT
439	SEQ ID NO: 439	RTT*76 (PAM silencing)
440	SEQ ID NO: 440	RTT*72 (PAM silencing)
441	SEQ ID NO: 441	RTT*76 (PAM silencing)
442	SEQ ID NO: 442	RTT
443	SEQ ID NO: 443	RTT*71 (PAM silencing)
444	SEQ ID NO: 444	RTT*76 (PAM silencing)
445	SEQ ID NO: 445	RTT*72 (PAM silencing)
446	SEQ ID NO: 446	RTT*71 (PAM silencing)
447	SEQ ID NO: 447	RTT
448	SEQ ID NO: 448	RTT*71 (PAM silencing)
449	SEQ ID NO: 449	RTT*72 (PAM silencing)
450	SEQ ID NO: 450	RTT
451	SEQ ID NO: 451	RTT*76 (PAM silencing)
452	SEQ ID NO: 452	RTT
453	SEQ ID NO: 453	RTT*76 (PAM silencing)
454	SEQ ID NO: 454	RTT*71 (PAM silencing)
455	SEQ ID NO: 455	RTT*72 (PAM silencing)
456	SEQ ID NO: 456	RTT*72 (PAM silencing)
457	SEQ ID NO: 457	RTT
458	SEQ ID NO: 458	RTT*76 (PAM silencing)
459	SEQ ID NO: 459	RTT*71 (PAM silencing)
460	SEQ ID NO: 460	RTT*72 (PAM silencing)
461	SEQ ID NO: 461	RTT*71 (PAM silencing)
462	SEQ ID NO: 462	RTT
463	SEQ ID NO: 463	RTT*76 (PAM silencing)
464	SEQ ID NO: 464	RTT*72 (PAM silencing)
465	SEQ ID NO: 465	RTT*71 (PAM silencing)
466	SEQ ID NO: 466	RTT*76 (PAM silencing)
467	SEQ ID NO: 467	RTT
468	SEQ ID NO: 468	RTT*76 (PAM silencing)
469	SEQ ID NO: 469	RTT*72 (PAM silencing)
470	SEQ ID NO: 470	RTT
471	SEQ ID NO: 471	RTT*71 (PAM silencing)
472	SEQ ID NO: 472	RTT*76 (PAM silencing)
473	SEQ ID NO: 473	RTT
474	SEQ ID NO: 474	RTT*71 (PAM silencing)
475	SEQ ID NO: 475	RTT*72 (PAM silencing)
476	SEQ ID NO: 476	RTT
477	SEQ ID NO: 477	RTT*72 (PAM silencing)
478	SEQ ID NO: 478	RTT*71 (PAM silencing)
479	SEQ ID NO: 479	RTT*76 (PAM silencing)
480	SEQ ID NO: 480	RTT*71 (PAM silencing)

Sequence Number	Sequence	Description
481	SEQ ID NO: 481	RTT*76 (PAM silencing)
482	SEQ ID NO: 482	RTT
483	SEQ ID NO: 483	RTT*72 (PAM silencing)
484	SEQ ID NO: 484	RTT*76 (PAM silencing)
485	SEQ ID NO: 485	RTT*72 (PAM silencing)
486	SEQ ID NO: 486	RTT
487	SEQ ID NO: 487	RTT*71 (PAM silencing)
488	SEQ ID NO: 488	RTT*71 (PAM silencing)
489	SEQ ID NO: 489	RTT*72 (PAM silencing)
490	SEQ ID NO: 490	RTT*76 (PAM silencing)
491	SEQ ID NO: 491	RTT
492	SEQ ID NO: 492	RTT
493	SEQ ID NO: 493	RTT*72 (PAM silencing)
494	SEQ ID NO: 494	RTT*76 (PAM silencing)
495	SEQ ID NO: 495	RTT*71 (PAM silencing)
496	SEQ ID NO: 496	RTT*71 (PAM silencing)
497	SEQ ID NO: 497	RTT
498	SEQ ID NO: 498	RTT*72 (PAM silencing)
499	SEQ ID NO: 499	RTT*76 (PAM silencing)
500	SEQ ID NO: 500	RTT*71 (PAM silencing)
501	SEQ ID NO: 501	RTT
502	SEQ ID NO: 502	RTT*76 (PAM silencing)
503	SEQ ID NO: 503	RTT*72 (PAM silencing)
504	SEQ ID NO: 504	RTT*71 (PAM silencing)
505	SEQ ID NO: 505	RTT*76 (PAM silencing)
506	SEQ ID NO: 506	RTT
507	SEQ ID NO: 507	RTT*72 (PAM silencing)
508	SEQ ID NO: 508	RTT
509	SEQ ID NO: 509	RTT*76 (PAM silencing)
510	SEQ ID NO: 510	RTT*71 (PAM silencing)
511	SEQ ID NO: 511	RTT*72 (PAM silencing)
512	SEQ ID NO: 512	RTT*72 (PAM silencing)
513	SEQ ID NO: 513	RTT*76 (PAM silencing)
514	SEQ ID NO: 514	RTT
515	SEQ ID NO: 515	RTT*71 (PAM silencing)
516	SEQ ID NO: 516	RTT*72 (PAM silencing)
517	SEQ ID NO: 517	RTT*71 (PAM silencing)
518	SEQ ID NO: 518	RTT*76 (PAM silencing)
519	SEQ ID NO: 519	RTT
520	SEQ ID NO: 520	RTT*72 (PAM silencing)
521	SEQ ID NO: 521	RTT
522	SEQ ID NO: 522	RTT*71 (PAM silencing)
523	SEQ ID NO: 523	RTT*76 (PAM silencing)
524	SEQ ID NO: 524	RTT
525	SEQ ID NO: 525	RTT*72 (PAM silencing)
526	SEQ ID NO: 526	RTT*71 (PAM silencing)
527	SEQ ID NO: 527	RTT*76 (PAM silencing)
98	SEQ ID NO: 98	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(GG;GGG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer

Sequence Number	Sequence	Description
		(GG;GGG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(TG;TGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)

Table 6

Sequence Number	Sequence	Description
528	SEQ ID NO: 528	PEgRNA spacer (AGG;AG PAM)
529	SEQ ID NO: 529	PEgRNA spacer (AGG;AG PAM)

Sequence Number	Sequence	Description
530	SEQ ID NO: 530	PEgRNA spacer (AGG;AG PAM)
531	SEQ ID NO: 531	PEgRNA spacer (AGG;AG PAM)
532	SEQ ID NO: 532	PEgRNA spacer (AGG;AG PAM)
533	SEQ ID NO: 533	PEgRNA spacer (AGG;AG PAM)
534	SEQ ID NO: 534	PEgRNA spacer (AGG;AG PAM)
535	CGC	PBS
536	CGCC	PBS
537	CGCCT	PBS
538	CGCCTT	PBS
539	CGCCTTC	PBS
540	CGCCTTCT	PBS
541	CGCCTTCTC	PBS
542	SEQ ID NO: 542	PBS
543	SEQ ID NO: 543	PBS
544	SEQ ID NO: 544	PBS
545	SEQ ID NO: 545	PBS
546	SEQ ID NO: 546	PBS
547	SEQ ID NO: 547	PBS
548	SEQ ID NO: 548	PBS
549	SEQ ID NO: 549	PBS
550	SEQ ID NO: 550	PBS
551	SEQ ID NO: 551	PBS
552	SEQ ID NO: 552	RTT*41 (PAM silencing)
553	SEQ ID NO: 553	RTT*42 (PAM silencing)
554	SEQ ID NO: 554	RTT*44 (PAM silencing)
555	SEQ ID NO: 555	RTT*43 (PAM silencing)
556	SEQ ID NO: 556	RTT

Sequence Number	Sequence	Description
557	SEQ ID NO: 557	RTT*42 (PAM silencing)
558	SEQ ID NO: 558	RTT
559	SEQ ID NO: 559	RTT*44 (PAM silencing)
560	SEQ ID NO: 560	RTT*43 (PAM silencing)
561	SEQ ID NO: 561	RTT*41 (PAM silencing)
562	SEQ ID NO: 562	RTT*43 (PAM silencing)
563	SEQ ID NO: 563	RTT*44 (PAM silencing)
564	SEQ ID NO: 564	RTT*41 (PAM silencing)
565	SEQ ID NO: 565	RTT
566	SEQ ID NO: 566	RTT*42 (PAM silencing)
567	SEQ ID NO: 567	RTT*42 (PAM silencing)
568	SEQ ID NO: 568	RTT*44 (PAM silencing)
569	SEQ ID NO: 569	RTT
570	SEQ ID NO: 570	RTT*43 (PAM silencing)
571	SEQ ID NO: 571	RTT*41 (PAM silencing)
572	SEQ ID NO: 572	RTT*41 (PAM silencing)
573	SEQ ID NO: 573	RTT*42 (PAM silencing)
574	SEQ ID NO: 574	RTT*44 (PAM silencing)
575	SEQ ID NO: 575	RTT*43 (PAM silencing)
576	SEQ ID NO: 576	RTT
577	SEQ ID NO: 577	RTT*42 (PAM silencing)
578	SEQ ID NO: 578	RTT*44 (PAM silencing)
579	SEQ ID NO: 579	RTT
580	SEQ ID NO: 580	RTT*43 (PAM silencing)
581	SEQ ID NO: 581	RTT*41 (PAM silencing)
582	SEQ ID NO: 582	RTT*43 (PAM silencing)
583	SEQ ID NO: 583	RTT
584	SEQ ID NO: 584	RTT*42 (PAM silencing)
585	SEQ ID NO: 585	RTT*41 (PAM silencing)
586	SEQ ID NO: 586	RTT*44 (PAM silencing)
587	SEQ ID NO: 587	RTT*43 (PAM silencing)
588	SEQ ID NO: 588	RTT*42 (PAM silencing)
589	SEQ ID NO: 589	RTT*41 (PAM silencing)
590	SEQ ID NO: 590	RTT
591	SEQ ID NO: 591	RTT*44 (PAM silencing)
592	SEQ ID NO: 592	RTT*42 (PAM silencing)
593	SEQ ID NO: 593	RTT*44 (PAM silencing)
594	SEQ ID NO: 594	RTT
595	SEQ ID NO: 595	RTT*41 (PAM silencing)
596	SEQ ID NO: 596	RTT*43 (PAM silencing)
597	SEQ ID NO: 597	RTT
598	SEQ ID NO: 598	RTT*43 (PAM silencing)
599	SEQ ID NO: 599	RTT*42 (PAM silencing)
600	SEQ ID NO: 600	RTT*44 (PAM silencing)
601	SEQ ID NO: 601	RTT*41 (PAM silencing)
602	SEQ ID NO: 602	RTT*44 (PAM silencing)
603	SEQ ID NO: 603	RTT
604	SEQ ID NO: 604	RTT*42 (PAM silencing)
605	SEQ ID NO: 605	RTT*43 (PAM silencing)
606	SEQ ID NO: 606	RTT*41 (PAM silencing)
607	SEQ ID NO: 607	RTT*41 (PAM silencing)
608	SEQ ID NO: 608	RTT
609	SEQ ID NO: 609	RTT*44 (PAM silencing)
610	SEQ ID NO: 610	RTT*42 (PAM silencing)
611	SEQ ID NO: 611	RTT*43 (PAM silencing)
612	SEQ ID NO: 612	RTT*43 (PAM silencing)
613	SEQ ID NO: 613	RTT*44 (PAM silencing)
614	SEQ ID NO: 614	RTT
615	SEQ ID NO: 615	RTT*41 (PAM silencing)
616	SEQ ID NO: 616	RTT*42 (PAM silencing)
617	SEQ ID NO: 617	RTT*42 (PAM silencing)
618	SEQ ID NO: 618	RTT*43 (PAM silencing)
619	SEQ ID NO: 619	RTT
620	SEQ ID NO: 620	RTT*41 (PAM silencing)
621	SEQ ID NO: 621	RTT*44 (PAM silencing)
622	SEQ ID NO: 622	RTT
623	SEQ ID NO: 623	RTT*42 (PAM silencing)
624	SEQ ID NO: 624	RTT*41 (PAM silencing)
625	SEQ ID NO: 625	RTT*44 (PAM silencing)
626	SEQ ID NO: 626	RTT*43 (PAM silencing)
627	SEQ ID NO: 627	RTT*43 (PAM silencing)
628	SEQ ID NO: 628	RTT

Sequence Number	Sequence	Description
629	SEQ ID NO: 629	RTT*42 (PAM silencing)
630	SEQ ID NO: 630	RTT*41 (PAM silencing)
631	SEQ ID NO: 631	RTT*44 (PAM silencing)
632	SEQ ID NO: 632	RTT*44 (PAM silencing)
633	SEQ ID NO: 633	RTT
634	SEQ ID NO: 634	RTT*42 (PAM silencing)
635	SEQ ID NO: 635	RTT*43 (PAM silencing)
636	SEQ ID NO: 636	RTT*41 (PAM silencing)
637	SEQ ID NO: 637	RTT*44 (PAM silencing)
638	SEQ ID NO: 638	RTT*41 (PAM silencing)
639	SEQ ID NO: 639	RTT*43 (PAM silencing)
640	SEQ ID NO: 640	RTT
641	SEQ ID NO: 641	RTT*42 (PAM silencing)
642	SEQ ID NO: 642	RTT*44 (PAM silencing)
643	SEQ ID NO: 643	RTT
644	SEQ ID NO: 644	RTT*42 (PAM silencing)
645	SEQ ID NO: 645	RTT*41 (PAM silencing)
646	SEQ ID NO: 646	RTT*43 (PAM silencing)
647	SEQ ID NO: 647	RTT*42 (PAM silencing)
648	SEQ ID NO: 648	RTT
649	SEQ ID NO: 649	RTT*44 (PAM silencing)
650	SEQ ID NO: 650	RTT*41 (PAM silencing)
651	SEQ ID NO: 651	RTT*43 (PAM silencing)
652	SEQ ID NO: 652	RTT*44 (PAM silencing)
653	SEQ ID NO: 653	RTT*41 (PAM silencing)
654	SEQ ID NO: 654	RTT
655	SEQ ID NO: 655	RTT*43 (PAM silencing)
656	SEQ ID NO: 656	RTT*42 (PAM silencing)
657	SEQ ID NO: 657	RTT*44 (PAM silencing)
658	SEQ ID NO: 658	RTT*43 (PAM silencing)
659	SEQ ID NO: 659	RTT*41 (PAM silencing)
660	SEQ ID NO: 660	RTT
661	SEQ ID NO: 661	RTT*42 (PAM silencing)
662	SEQ ID NO: 662	RTT
663	SEQ ID NO: 663	RTT*44 (PAM silencing)
664	SEQ ID NO: 664	RTT*43 (PAM silencing)
665	SEQ ID NO: 665	RTT*42 (PAM silencing)
666	SEQ ID NO: 666	RTT*41 (PAM silencing)
667	SEQ ID NO: 667	RTT*42 (PAM silencing)
668	SEQ ID NO: 668	RTT*44 (PAM silencing)
669	SEQ ID NO: 669	RTT*41 (PAM silencing)
670	SEQ ID NO: 670	RTT*43 (PAM silencing)
671	SEQ ID NO: 671	RTT
672	SEQ ID NO: 672	RTT*43 (PAM silencing)
673	SEQ ID NO: 673	RTT*44 (PAM silencing)
674	SEQ ID NO: 674	RTT
675	SEQ ID NO: 675	RTT*41 (PAM silencing)
676	SEQ ID NO: 676	RTT*42 (PAM silencing)
677	SEQ ID NO: 677	RTT*44 (PAM silencing)
678	SEQ ID NO: 678	RTT
679	SEQ ID NO: 679	RTT*42 (PAM silencing)
680	SEQ ID NO: 680	RTT*41 (PAM silencing)
681	SEQ ID NO: 681	RTT*43 (PAM silencing)
682	SEQ ID NO: 682	RTT
683	SEQ ID NO: 683	RTT*42 (PAM silencing)
684	SEQ ID NO: 684	RTT*43 (PAM silencing)
685	SEQ ID NO: 685	RTT*44 (PAM silencing)
686	SEQ ID NO: 686	RTT*41 (PAM silencing)
687	SEQ ID NO: 687	RTT*42 (PAM silencing)
688	SEQ ID NO: 688	RTT*41 (PAM silencing)
689	SEQ ID NO: 689	RTT*44 (PAM silencing)
690	SEQ ID NO: 690	RTT
691	SEQ ID NO: 691	RTT*43 (PAM silencing)
692	SEQ ID NO: 692	RTT*41 (PAM silencing)
693	SEQ ID NO: 693	RTT*42 (PAM silencing)
694	SEQ ID NO: 694	RTT
695	SEQ ID NO: 695	RTT*44 (PAM silencing)
696	SEQ ID NO: 696	RTT*43 (PAM silencing)
697	SEQ ID NO: 697	RTT
698	SEQ ID NO: 698	RTT*42 (PAM silencing)
699	SEQ ID NO: 699	RTT*41 (PAM silencing)

Sequence Number	Sequence	Description
700	SEQ ID NO: 700	RTT*43 (PAM silencing)
701	SEQ ID NO: 701	RTT*44 (PAM silencing)
702	SEQ ID NO: 702	RTT*41 (PAM silencing)
703	SEQ ID NO: 703	RTT
704	SEQ ID NO: 704	RTT*42 (PAM silencing)
705	SEQ ID NO: 705	RTT*44 (PAM silencing)
706	SEQ ID NO: 706	RTT*43 (PAM silencing)
707	SEQ ID NO: 707	RTT*41 (PAM silencing)
708	SEQ ID NO: 708	RTT
709	SEQ ID NO: 709	RTT*44 (PAM silencing)
710	SEQ ID NO: 710	RTT*43 (PAM silencing)
711	SEQ ID NO: 711	RTT*42 (PAM silencing)
712	SEQ ID NO: 712	RTT
713	SEQ ID NO: 713	RTT*44 (PAM silencing)
714	SEQ ID NO: 714	RTT*41 (PAM silencing)
715	SEQ ID NO: 715	RTT*43 (PAM silencing)
716	SEQ ID NO: 716	RTT*42 (PAM silencing)
717	SEQ ID NO: 717	RTT*41 (PAM silencing)
718	SEQ ID NO: 718	RTT*43 (PAM silencing)
719	SEQ ID NO: 719	RTT*42 (PAM silencing)
720	SEQ ID NO: 720	RTT
721	SEQ ID NO: 721	RTT*44 (PAM silencing)
722	SEQ ID NO: 722	RTT
723	SEQ ID NO: 723	RTT*41 (PAM silencing)
724	SEQ ID NO: 724	RTT*42 (PAM silencing)
725	SEQ ID NO: 725	RTT*43 (PAM silencing)
726	SEQ ID NO: 726	RTT*44 (PAM silencing)
727	SEQ ID NO: 727	RTT*43 (PAM silencing)
728	SEQ ID NO: 728	RTT
729	SEQ ID NO: 729	RTT*44 (PAM silencing)
730	SEQ ID NO: 730	RTT*41 (PAM silencing)
731	SEQ ID NO: 731	RTT*42 (PAM silencing)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)

Sequence Number	Sequence	Description
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)

Table 7

Sequence Number	Sequence	Description
734	SEQ ID NO: 734	PEgRNA spacer (TGG;TG; TGGG PAM)
735	SEQ ID NO: 735	PEgRNA spacer (TGG;TG; TGGG PAM)
736	SEQ ID NO: 736	PEgRNA spacer (TGG;TG; TGGG PAM)
737	SEQ ID NO: 737	PEgRNA spacer (TGG;TG; TGGG PAM)
738	SEQ ID NO: 738	PEgRNA spacer (TGG;TG; TGGG PAM)
739	SEQ ID NO: 739	PEgRNA spacer (TGG;TG; TGGG PAM)
740	SEQ ID NO: 740	PEgRNA spacer (TGG;TG; TGGG PAM)
200	CAA	PBS
741	CAAT	PBS
742	CAATG	PBS
743	CAATGA	PBS
744	CAATGA A	PBS
745	CAATGA AC	PBS
746	CAATGA ACA	PBS
747	SEQ ID NO: 747	PBS
748	SEQ ID NO: 748	PBS
749	SEQ ID NO: 749	PBS
750	SEQ ID NO: 750	PBS
751	SEQ ID NO: 751	PBS
752	SEQ ID NO: 752	PBS
753	SEQ ID NO: 753	PBS
754	SEQ ID NO: 754	PBS
755	SEQ ID NO: 755	PBS
756	SEQ ID NO: 756	PBS
757	SEQ ID NO: 757	RTT*83 (PAM silencing)
758	SEQ ID NO: 758	RTT*81 (PAM silencing)
759	SEQ ID NO: 759	RTT
760	SEQ ID NO: 760	RTT*80 (PAM silencing)
761	SEQ ID NO: 761	RTT*82 (PAM silencing)
762	SEQ ID NO: 762	RTT*80 (PAM silencing)
763	SEQ ID NO: 763	RTT*82 (PAM silencing)
764	SEQ ID NO: 764	RTT
765	SEQ ID NO: 765	RTT*83 (PAM silencing)
766	SEQ ID NO: 766	RTT*81 (PAM silencing)
767	SEQ ID NO: 767	RTT
768	SEQ ID NO: 768	RTT*83 (PAM silencing)
769	SEQ ID NO: 769	RTT*81 (PAM silencing)
770	SEQ ID NO: 770	RTT*80 (PAM silencing)
771	SEQ ID NO: 771	RTT*82 (PAM silencing)
772	SEQ ID NO: 772	RTT*82 (PAM silencing)

Sequence Number	Sequence	Description
773	SEQ ID NO: 773	RTT*80 (PAM silencing)
774	SEQ ID NO: 774	RTT
775	SEQ ID NO: 775	RTT*81 (PAM silencing)
776	SEQ ID NO: 776	RTT*83 (PAM silencing)
777	SEQ ID NO: 777	RTT
778	SEQ ID NO: 778	RTT*83 (PAM silencing)
779	SEQ ID NO: 779	RTT*81 (PAM silencing)
780	SEQ ID NO: 780	RTT*80 (PAM silencing)
781	SEQ ID NO: 781	RTT*82 (PAM silencing)
782	SEQ ID NO: 782	RTT*80 (PAM silencing)
783	SEQ ID NO: 783	RTT*82 (PAM silencing)
784	SEQ ID NO: 784	RTT*81 (PAM silencing)
785	SEQ ID NO: 785	RTT
786	SEQ ID NO: 786	RTT*83 (PAM silencing)
787	SEQ ID NO: 787	RTT*83 (PAM silencing)
788	SEQ ID NO: 788	RTT
789	SEQ ID NO: 789	RTT*81 (PAM silencing)
790	SEQ ID NO: 790	RTT*82 (PAM silencing)
791	SEQ ID NO: 791	RTT*80 (PAM silencing)
792	SEQ ID NO: 792	RTT*83 (PAM silencing)
793	SEQ ID NO: 793	RTT*80 (PAM silencing)
794	SEQ ID NO: 794	RTT*82 (PAM silencing)
795	SEQ ID NO: 795	RTT*81 (PAM silencing)
796	SEQ ID NO: 796	RTT
797	SEQ ID NO: 797	RTT
798	SEQ ID NO: 798	RTT*80 (PAM silencing)
799	SEQ ID NO: 799	RTT*83 (PAM silencing)
800	SEQ ID NO: 800	RTT*81 (PAM silencing)
801	SEQ ID NO: 801	RTT*82 (PAM silencing)
802	SEQ ID NO: 802	RTT
803	SEQ ID NO: 803	RTT*81 (PAM silencing)
804	SEQ ID NO: 804	RTT*82 (PAM silencing)
805	SEQ ID NO: 805	RTT*80 (PAM silencing)
806	SEQ ID NO: 806	RTT*83 (PAM silencing)
807	SEQ ID NO: 807	RTT*80 (PAM silencing)
808	SEQ ID NO: 808	RTT*82 (PAM silencing)
809	SEQ ID NO: 809	RTT
810	SEQ ID NO: 810	RTT*81 (PAM silencing)
811	SEQ ID NO: 811	RTT*83 (PAM silencing)
812	SEQ ID NO: 812	RTT
813	SEQ ID NO: 813	RTT*82 (PAM silencing)
814	SEQ ID NO: 814	RTT*80 (PAM silencing)
815	SEQ ID NO: 815	RTT*83 (PAM silencing)
816	SEQ ID NO: 816	RTT*81 (PAM silencing)
817	SEQ ID NO: 817	RTT*80 (PAM silencing)
818	SEQ ID NO: 818	RTT*81 (PAM silencing)
819	SEQ ID NO: 819	RTT*83 (PAM silencing)
820	SEQ ID NO: 820	RTT*82 (PAM silencing)
821	SEQ ID NO: 821	RTT
822	SEQ ID NO: 822	RTT*83 (PAM silencing)
823	SEQ ID NO: 823	RTT
824	SEQ ID NO: 824	RTT*80 (PAM silencing)
825	SEQ ID NO: 825	RTT*82 (PAM silencing)
826	SEQ ID NO: 826	RTT*81 (PAM silencing)
827	SEQ ID NO: 827	RTT*80 (PAM silencing)
828	SEQ ID NO: 828	RTT*82 (PAM silencing)
829	SEQ ID NO: 829	RTT
830	SEQ ID NO: 830	RTT*81 (PAM silencing)
831	SEQ ID NO: 831	RTT*83 (PAM silencing)
832	SEQ ID NO: 832	RTT*82 (PAM silencing)
833	SEQ ID NO: 833	RTT
834	SEQ ID NO: 834	RTT*81 (PAM silencing)
835	SEQ ID NO: 835	RTT*83 (PAM silencing)
836	SEQ ID NO: 836	RTT*80 (PAM silencing)
837	SEQ ID NO: 837	RTT*83 (PAM silencing)
838	SEQ ID NO: 838	RTT*82 (PAM silencing)
839	SEQ ID NO: 839	RTT*80 (PAM silencing)
840	SEQ ID NO: 840	RTT
841	SEQ ID NO: 841	RTT*81 (PAM silencing)
842	SEQ ID NO: 842	RTT*83 (PAM silencing)
843	SEQ ID NO: 843	RTT*82 (PAM silencing)

Sequence Number	Sequence	Description
844	SEQ ID NO: 844	RTT*81 (PAM silencing)
845	SEQ ID NO: 845	RTT
846	SEQ ID NO: 846	RTT*80 (PAM silencing)
847	SEQ ID NO: 847	RTT*82 (PAM silencing)
848	SEQ ID NO: 848	RTT
849	SEQ ID NO: 849	RTT*83 (PAM silencing)
850	SEQ ID NO: 850	RTT*80 (PAM silencing)
851	SEQ ID NO: 851	RTT*81 (PAM silencing)
852	SEQ ID NO: 852	RTT*82 (PAM silencing)
853	SEQ ID NO: 853	RTT*80 (PAM silencing)
854	SEQ ID NO: 854	RTT
855	SEQ ID NO: 855	RTT*83 (PAM silencing)
856	SEQ ID NO: 856	RTT*81 (PAM silencing)
857	SEQ ID NO: 857	RTT
858	SEQ ID NO: 858	RTT*81 (PAM silencing)
859	SEQ ID NO: 859	RTT*80 (PAM silencing)
860	SEQ ID NO: 860	RTT*83 (PAM silencing)
861	SEQ ID NO: 861	RTT*82 (PAM silencing)
862	SEQ ID NO: 862	RTT
863	SEQ ID NO: 863	RTT*80 (PAM silencing)
864	SEQ ID NO: 864	RTT*83 (PAM silencing)
865	SEQ ID NO: 865	RTT*81 (PAM silencing)
866	SEQ ID NO: 866	RTT*82 (PAM silencing)
867	SEQ ID NO: 867	RTT*80 (PAM silencing)
868	SEQ ID NO: 868	RTT*83 (PAM silencing)
869	SEQ ID NO: 869	RTT*82 (PAM silencing)
870	SEQ ID NO: 870	RTT
871	SEQ ID NO: 871	RTT*81 (PAM silencing)
872	SEQ ID NO: 872	RTT*81 (PAM silencing)
873	SEQ ID NO: 873	RTT*83 (PAM silencing)
874	SEQ ID NO: 874	RTT
875	SEQ ID NO: 875	RTT*82 (PAM silencing)
876	SEQ ID NO: 876	RTT*80 (PAM silencing)
877	SEQ ID NO: 877	RTT*82 (PAM silencing)
878	SEQ ID NO: 878	RTT*80 (PAM silencing)
879	SEQ ID NO: 879	RTT*81 (PAM silencing)
880	SEQ ID NO: 880	RTT*83 (PAM silencing)
881	SEQ ID NO: 881	RTT
882	SEQ ID NO: 882	RTT*82 (PAM silencing)
883	SEQ ID NO: 883	RTT*80 (PAM silencing)
884	SEQ ID NO: 884	RTT*83 (PAM silencing)
885	SEQ ID NO: 885	RTT*81 (PAM silencing)
886	SEQ ID NO: 886	RTT
887	SEQ ID NO: 887	RTT*80 (PAM silencing)
888	SEQ ID NO: 888	RTT*81 (PAM silencing)
889	SEQ ID NO: 889	RTT*82 (PAM silencing)
890	SEQ ID NO: 890	RTT
891	SEQ ID NO: 891	RTT*83 (PAM silencing)
892	SEQ ID NO: 892	RTT*82 (PAM silencing)
893	SEQ ID NO: 893	RTT*81 (PAM silencing)
894	SEQ ID NO: 894	RTT*83 (PAM silencing)
895	SEQ ID NO: 895	RTT*80 (PAM silencing)
896	SEQ ID NO: 896	RTT
897	SEQ ID NO: 897	RTT*83 (PAM silencing)
898	SEQ ID NO: 898	RTT*81 (PAM silencing)
899	SEQ ID NO: 899	RTT*82 (PAM silencing)
900	SEQ ID NO: 900	RTT
901	SEQ ID NO: 901	RTT*80 (PAM silencing)
902	SEQ ID NO: 902	RTT*81 (PAM silencing)
903	SEQ ID NO: 903	RTT
904	SEQ ID NO: 904	RTT*82 (PAM silencing)
905	SEQ ID NO: 905	RTT*80 (PAM silencing)
906	SEQ ID NO: 906	RTT*83 (PAM silencing)
907	SEQ ID NO: 907	RTT*80 (PAM silencing)
908	SEQ ID NO: 908	RTT*83 (PAM silencing)
909	SEQ ID NO: 909	RTT*81 (PAM silencing)
910	SEQ ID NO: 910	RTT
911	SEQ ID NO: 911	RTT*82 (PAM silencing)
912	SEQ ID NO: 912	RTT*83 (PAM silencing)
913	SEQ ID NO: 913	RTT*82 (PAM silencing)
914	SEQ ID NO: 914	RTT
915	SEQ ID NO: 915	RTT*81 (PAM silencing)

Sequence Number	Sequence	Description
916	SEQ ID NO: 916	RTT*80 (PAM silencing)
917	SEQ ID NO: 917	RTT
918	SEQ ID NO: 918	RTT*81 (PAM silencing)
919	SEQ ID NO: 919	RTT*83 (PAM silencing)
920	SEQ ID NO: 920	RTT*80 (PAM silencing)
921	SEQ ID NO: 921	RTT*82 (PAM silencing)
922	SEQ ID NO: 922	RTT*82 (PAM silencing)
923	SEQ ID NO: 923	RTT*81 (PAM silencing)
924	SEQ ID NO: 924	RTT
925	SEQ ID NO: 925	RTT*83 (PAM silencing)
926	SEQ ID NO: 926	RTT*80 (PAM silencing)
927	SEQ ID NO: 927	RTT*80 (PAM silencing)
928	SEQ ID NO: 928	RTT
929	SEQ ID NO: 929	RTT*81 (PAM silencing)
930	SEQ ID NO: 930	RTT*83 (PAM silencing)
931	SEQ ID NO: 931	RTT*82 (PAM silencing)
932	SEQ ID NO: 932	RTT*80 (PAM silencing)
933	SEQ ID NO: 933	RTT*83 (PAM silencing)
934	SEQ ID NO: 934	RTT*82 (PAM silencing)
935	SEQ ID NO: 935	RTT*81 (PAM silencing)
936	SEQ ID NO: 936	RTT
937	SEQ ID NO: 937	RTT
938	SEQ ID NO: 938	RTT*81 (PAM silencing)
939	SEQ ID NO: 939	RTT*82 (PAM silencing)
940	SEQ ID NO: 940	RTT*80 (PAM silencing)
941	SEQ ID NO: 941	RTT*83 (PAM silencing)
942	SEQ ID NO: 942	RTT*82 (PAM silencing)
943	SEQ ID NO: 943	RTT*83 (PAM silencing)
944	SEQ ID NO: 944	RTT*81 (PAM silencing)
945	SEQ ID NO: 945	RTT*80 (PAM silencing)
946	SEQ ID NO: 946	RTT
947	SEQ ID NO: 947	RTT*81 (PAM silencing)
948	SEQ ID NO: 948	RTT*83 (PAM silencing)
949	SEQ ID NO: 949	RTT*82 (PAM silencing)
950	SEQ ID NO: 950	RTT
951	SEQ ID NO: 951	RTT*80 (PAM silencing)
952	SEQ ID NO: 952	RTT*80 (PAM silencing)
953	SEQ ID NO: 953	RTT*83 (PAM silencing)
954	SEQ ID NO: 954	RTT*82 (PAM silencing)
955	SEQ ID NO: 955	RTT*81 (PAM silencing)
956	SEQ ID NO: 956	RTT
957	SEQ ID NO: 957	RTT
958	SEQ ID NO: 958	RTT*80 (PAM silencing)
959	SEQ ID NO: 959	RTT*83 (PAM silencing)
960	SEQ ID NO: 960	RTT*81 (PAM silencing)
961	SEQ ID NO: 961	RTT*82 (PAM silencing)
962	SEQ ID NO: 962	RTT*83 (PAM silencing)
963	SEQ ID NO: 963	RTT
964	SEQ ID NO: 964	RTT*80 (PAM silencing)
965	SEQ ID NO: 965	RTT*82 (PAM silencing)
966	SEQ ID NO: 966	RTT*81 (PAM silencing)
967	SEQ ID NO: 967	RTT
968	SEQ ID NO: 968	RTT*80 (PAM silencing)
969	SEQ ID NO: 969	RTT*82 (PAM silencing)
970	SEQ ID NO: 970	RTT*81 (PAM silencing)
971	SEQ ID NO: 971	RTT*83 (PAM silencing)
972	SEQ ID NO: 972	RTT
973	SEQ ID NO: 973	RTT*81 (PAM silencing)
974	SEQ ID NO: 974	RTT*80 (PAM silencing)
975	SEQ ID NO: 975	RTT*82 (PAM silencing)
976	SEQ ID NO: 976	RTT*83 (PAM silencing)
977	SEQ ID NO: 977	RTT*82 (PAM silencing)
978	SEQ ID NO: 978	RTT*83 (PAM silencing)
979	SEQ ID NO: 979	RTT*80 (PAM silencing)
980	SEQ ID NO: 980	RTT*81 (PAM silencing)
981	SEQ ID NO: 981	RTT
982	SEQ ID NO: 982	RTT*80 (PAM silencing)
983	SEQ ID NO: 983	RTT*81 (PAM silencing)
984	SEQ ID NO: 984	RTT*82 (PAM silencing)
985	SEQ ID NO: 985	RTT
986	SEQ ID NO: 986	RTT*83 (PAM silencing)
987	SEQ ID NO: 987	RTT

Sequence Number	Sequence	Description
988	SEQ ID NO: 988	RTT*83 (PAM silencing)
989	SEQ ID NO: 989	RTT*81 (PAM silencing)
990	SEQ ID NO: 990	RTT*82 (PAM silencing)
991	SEQ ID NO: 991	RTT*80 (PAM silencing)
992	SEQ ID NO: 992	RTT*81 (PAM silencing)
993	SEQ ID NO: 993	RTT
994	SEQ ID NO: 994	RTT*82 (PAM silencing)
995	SEQ ID NO: 995	RTT*83 (PAM silencing)
996	SEQ ID NO: 996	RTT*80 (PAM silencing)
997	SEQ ID NO: 997	RTT*81 (PAM silencing)
998	SEQ ID NO: 998	RTT*83 (PAM silencing)
999	SEQ ID NO: 999	RTT*82 (PAM silencing)
1000	SEQ ID NO: 1000	RTT
1001	SEQ ID NO: 1001	RTT*80 (PAM silencing)
1002	SEQ ID NO: 1002	RTT*81 (PAM silencing)
1003	SEQ ID NO: 1003	RTT*82 (PAM silencing)
1004	SEQ ID NO: 1004	RTT*80 (PAM silencing)
1005	SEQ ID NO: 1005	RTT*83 (PAM silencing)
1006	SEQ ID NO: 1006	RTT
1007	SEQ ID NO: 1007	RTT*82 (PAM silencing)
1008	SEQ ID NO: 1008	RTT*80 (PAM silencing)
1009	SEQ ID NO: 1009	RTT
1010	SEQ ID NO: 1010	RTT*83 (PAM silencing)
1011	SEQ ID NO: 1011	RTT*81 (PAM silencing)
1012	SEQ ID NO: 1012	RTT*81 (PAM silencing)
1013	SEQ ID NO: 1013	RTT*82 (PAM silencing)
1014	SEQ ID NO: 1014	RTT
1015	SEQ ID NO: 1015	RTT*83 (PAM silencing)
1016	SEQ ID NO: 1016	RTT*80 (PAM silencing)
1017	SEQ ID NO: 1017	RTT*80 (PAM silencing)
1018	SEQ ID NO: 1018	RTT
1019	SEQ ID NO: 1019	RTT*81 (PAM silencing)
1020	SEQ ID NO: 1020	RTT*82 (PAM silencing)
1021	SEQ ID NO: 1021	RTT*83 (PAM silencing)
1022	SEQ ID NO: 1022	RTT*80 (PAM silencing)
1023	SEQ ID NO: 1023	RTT
1024	SEQ ID NO: 1024	RTT*83 (PAM silencing)
1025	SEQ ID NO: 1025	RTT*81 (PAM silencing)
1026	SEQ ID NO: 1026	RTT*82 (PAM silencing)
1027	SEQ ID NO: 1027	RTT
1028	SEQ ID NO: 1028	RTT*80 (PAM silencing)
1029	SEQ ID NO: 1029	RTT*81 (PAM silencing)
1030	SEQ ID NO: 1030	RTT*83 (PAM silencing)
1031	SEQ ID NO: 1031	RTT*82 (PAM silencing)
1032	SEQ ID NO: 1032	RTT
1033	SEQ ID NO: 1033	RTT*80 (PAM silencing)
1034	SEQ ID NO: 1034	RTT*81 (PAM silencing)
1035	SEQ ID NO: 1035	RTT*83 (PAM silencing)
1036	SEQ ID NO: 1036	RTT*82 (PAM silencing)
1037	SEQ ID NO: 1037	RTT*82 (PAM silencing)
1038	SEQ ID NO: 1038	RTT
1039	SEQ ID NO: 1039	RTT*81 (PAM silencing)
1040	SEQ ID NO: 1040	RTT*80 (PAM silencing)
1041	SEQ ID NO: 1041	RTT*83 (PAM silencing)
1042	SEQ ID NO: 1042	RTT*81 (PAM silencing)
1043	SEQ ID NO: 1043	RTT
1044	SEQ ID NO: 1044	RTT*80 (PAM silencing)
1045	SEQ ID NO: 1045	RTT*82 (PAM silencing)
1046	SEQ ID NO: 1046	RTT*83 (PAM silencing)
1047	SEQ ID NO: 1047	RTT*82 (PAM silencing)
1048	SEQ ID NO: 1048	RTT
1049	SEQ ID NO: 1049	RTT*81 (PAM silencing)
1050	SEQ ID NO: 1050	RTT*80 (PAM silencing)
1051	SEQ ID NO: 1051	RTT*83 (PAM silencing)
1052	SEQ ID NO: 1052	RTT
1053	SEQ ID NO: 1053	RTT*81 (PAM silencing)
1054	SEQ ID NO: 1054	RTT*80 (PAM silencing)
1055	SEQ ID NO: 1055	RTT*82 (PAM silencing)
1056	SEQ ID NO: 1056	RTT*83 (PAM silencing)
1057	SEQ ID NO: 1057	RTT*80 (PAM silencing)
1058	SEQ ID NO: 1058	RTT

Sequence Number	Sequence	Description
1059	SEQ ID NO: 1059	RTT*83 (PAM silencing)
1060	SEQ ID NO: 1060	RTT*82 (PAM silencing)
1061	SEQ ID NO: 1061	RTT*81 (PAM silencing)
1062	SEQ ID NO: 1062	RTT*82 (PAM silencing)
1063	SEQ ID NO: 1063	RTT
1064	SEQ ID NO: 1064	RTT*83 (PAM silencing)
1065	SEQ ID NO: 1065	RTT*81 (PAM silencing)
1066	SEQ ID NO: 1066	RTT*80 (PAM silencing)
1067	SEQ ID NO: 1067	RTT
1068	SEQ ID NO: 1068	RTT*80 (PAM silencing)
1069	SEQ ID NO: 1069	RTT*82 (PAM silencing)
1070	SEQ ID NO: 1070	RTT*83 (PAM silencing)
1071	SEQ ID NO: 1071	RTT*81 (PAM silencing)
1072	SEQ ID NO: 1072	RTT*80 (PAM silencing)
1073	SEQ ID NO: 1073	RTT*83 (PAM silencing)
1074	SEQ ID NO: 1074	RTT*82 (PAM silencing)
1075	SEQ ID NO: 1075	RTT*81 (PAM silencing)
1076	SEQ ID NO: 1076	RTT
1077	SEQ ID NO: 1077	RTT*82 (PAM silencing)
1078	SEQ ID NO: 1078	RTT*80 (PAM silencing)
1079	SEQ ID NO: 1079	RTT*81 (PAM silencing)
1080	SEQ ID NO: 1080	RTT
1081	SEQ ID NO: 1081	RTT*83 (PAM silencing)
1082	SEQ ID NO: 1082	RTT*82 (PAM silencing)
1083	SEQ ID NO: 1083	RTT*83 (PAM silencing)
1084	SEQ ID NO: 1084	RTT*81 (PAM silencing)
1085	SEQ ID NO: 1085	RTT
1086	SEQ ID NO: 1086	RTT*80 (PAM silencing)
1087	SEQ ID NO: 1087	RTT*81 (PAM silencing)
1088	SEQ ID NO: 1088	RTT
1089	SEQ ID NO: 1089	RTT*83 (PAM silencing)
1090	SEQ ID NO: 1090	RTT*80 (PAM silencing)
1091	SEQ ID NO: 1091	RTT*82 (PAM silencing)
1092	SEQ ID NO: 1092	RTT*83 (PAM silencing)
1093	SEQ ID NO: 1093	RTT*82 (PAM silencing)
1094	SEQ ID NO: 1094	RTT*81 (PAM silencing)
1095	SEQ ID NO: 1095	RTT*80 (PAM silencing)
1096	SEQ ID NO: 1096	RTT
1097	SEQ ID NO: 1097	RTT*82 (PAM silencing)
1098	SEQ ID NO: 1098	RTT*83 (PAM silencing)
1099	SEQ ID NO: 1099	RTT
1100	SEQ ID NO: 1100	RTT*80 (PAM silencing)
1101	SEQ ID NO: 1101	RTT*81 (PAM silencing)
1102	SEQ ID NO: 1102	RTT*83 (PAM silencing)
1103	SEQ ID NO: 1103	RTT*82 (PAM silencing)
1104	SEQ ID NO: 1104	RTT
1105	SEQ ID NO: 1105	RTT*80 (PAM silencing)
1106	SEQ ID NO: 1106	RTT*81 (PAM silencing)
1107	SEQ ID NO: 1107	RTT
1108	SEQ ID NO: 1108	RTT*82 (PAM silencing)
1109	SEQ ID NO: 1109	RTT*80 (PAM silencing)
1110	SEQ ID NO: 1110	RTT*83 (PAM silencing)
1111	SEQ ID NO: 1111	RTT*81 (PAM silencing)
1112	SEQ ID NO: 1112	RTT*80 (PAM silencing)
1113	SEQ ID NO: 1113	RTT
1114	SEQ ID NO: 1114	RTT*82 (PAM silencing)
1115	SEQ ID NO: 1115	RTT*81 (PAM silencing)
1116	SEQ ID NO: 1116	RTT*83 (PAM silencing)
1117	SEQ ID NO: 1117	RTT
1118	SEQ ID NO: 1118	RTT*80 (PAM silencing)
1119	SEQ ID NO: 1119	RTT*82 (PAM silencing)
1120	SEQ ID NO: 1120	RTT*83 (PAM silencing)
1121	SEQ ID NO: 1121	RTT*81 (PAM silencing)
1122	SEQ ID NO: 1122	RTT*82 (PAM silencing)
1123	SEQ ID NO: 1123	RTT*83 (PAM silencing)
1124	SEQ ID NO: 1124	RTT
1125	SEQ ID NO: 1125	RTT*81 (PAM silencing)
1126	SEQ ID NO: 1126	RTT*80 (PAM silencing)
1127	SEQ ID NO: 1127	RTT*82 (PAM silencing)
1128	SEQ ID NO: 1128	RTT
1129	SEQ ID NO: 1129	RTT*80 (PAM silencing)

Sequence Number	Sequence	Description
1130	SEQ ID NO: 1130	RTT*81 (PAM silencing)
1131	SEQ ID NO: 1131	RTT*83 (PAM silencing)
1132	SEQ ID NO: 1132	RTT*82 (PAM silencing)
1133	SEQ ID NO: 1133	RTT
1134	SEQ ID NO: 1134	RTT*81 (PAM silencing)
1135	SEQ ID NO: 1135	RTT*80 (PAM silencing)
1136	SEQ ID NO: 1136	RTT*83 (PAM silencing)
1137	SEQ ID NO: 1137	RTT*80 (PAM silencing)
1138	SEQ ID NO: 1138	RTT*82 (PAM silencing)
1139	SEQ ID NO: 1139	RTT*83 (PAM silencing)
1140	SEQ ID NO: 1140	RTT
1141	SEQ ID NO: 1141	RTT*81 (PAM silencing)
1142	SEQ ID NO: 1142	RTT*80 (PAM silencing)
1143	SEQ ID NO: 1143	RTT*83 (PAM silencing)
1144	SEQ ID NO: 1144	RTT*81 (PAM silencing)
1145	SEQ ID NO: 1145	RTT*82 (PAM silencing)
1146	SEQ ID NO: 1146	RTT
1147	SEQ ID NO: 1147	RTT*83 (PAM silencing)
1148	SEQ ID NO: 1148	RTT*82 (PAM silencing)
1149	SEQ ID NO: 1149	RTT*80 (PAM silencing)
1150	SEQ ID NO: 1150	RTT*81 (PAM silencing)
1151	SEQ ID NO: 1151	RTT
1152	SEQ ID NO: 1152	RTT*80 (PAM silencing)
1153	SEQ ID NO: 1153	RTT*83 (PAM silencing)
1154	SEQ ID NO: 1154	RTT*82 (PAM silencing)
1155	SEQ ID NO: 1155	RTT
1156	SEQ ID NO: 1156	RTT*81 (PAM silencing)
1157	SEQ ID NO: 1157	RTT*82 (PAM silencing)
1158	SEQ ID NO: 1158	RTT*80 (PAM silencing)
1159	SEQ ID NO: 1159	RTT*83 (PAM silencing)
1160	SEQ ID NO: 1160	RTT*81 (PAM silencing)
1161	SEQ ID NO: 1161	RTT
1162	SEQ ID NO: 1162	RTT
1163	SEQ ID NO: 1163	RTT*80 (PAM silencing)
1164	SEQ ID NO: 1164	RTT*83 (PAM silencing)
1165	SEQ ID NO: 1165	RTT*81 (PAM silencing)
1166	SEQ ID NO: 1166	RTT*82 (PAM silencing)
1167	SEQ ID NO: 1167	RTT
1168	SEQ ID NO: 1168	RTT*80 (PAM silencing)
1169	SEQ ID NO: 1169	RTT*81 (PAM silencing)
1170	SEQ ID NO: 1170	RTT*83 (PAM silencing)
1171	SEQ ID NO: 1171	RTT*82 (PAM silencing)
1172	SEQ ID NO: 1172	RTT*82 (PAM silencing)
1173	SEQ ID NO: 1173	RTT*81 (PAM silencing)
1174	SEQ ID NO: 1174	RTT*83 (PAM silencing)
1175	SEQ ID NO: 1175	RTT
1176	SEQ ID NO: 1176	RTT*80 (PAM silencing)
1177	SEQ ID NO: 1177	RTT*80 (PAM silencing)
1178	SEQ ID NO: 1178	RTT*83 (PAM silencing)
1179	SEQ ID NO: 1179	RTT*82 (PAM silencing)
1180	SEQ ID NO: 1180	RTT*81 (PAM silencing)
1181	SEQ ID NO: 1181	RTT
1182	SEQ ID NO: 1182	RTT*83 (PAM silencing)
1183	SEQ ID NO: 1183	RTT*81 (PAM silencing)
1184	SEQ ID NO: 1184	RTT*82 (PAM silencing)
1185	SEQ ID NO: 1185	RTT*80 (PAM silencing)
1186	SEQ ID NO: 1186	RTT
1187	SEQ ID NO: 1187	RTT*81 (PAM silencing)
1188	SEQ ID NO: 1188	RTT*83 (PAM silencing)
1189	SEQ ID NO: 1189	RTT
1190	SEQ ID NO: 1190	RTT*80 (PAM silencing)
1191	SEQ ID NO: 1191	RTT*82 (PAM silencing)
1192	SEQ ID NO: 1192	RTT*82 (PAM silencing)
1193	SEQ ID NO: 1193	RTT
1194	SEQ ID NO: 1194	RTT*81 (PAM silencing)
1195	SEQ ID NO: 1195	RTT*83 (PAM silencing)
1196	SEQ ID NO: 1196	RTT*80 (PAM silencing)
1197	SEQ ID NO: 1197	RTT*82 (PAM silencing)
1198	SEQ ID NO: 1198	RTT*81 (PAM silencing)
1199	SEQ ID NO: 1199	RTT
1200	SEQ ID NO: 1200	RTT*83 (PAM silencing)

Sequence Number	Sequence	Description
1201	SEQ ID NO: 1201	RTT*80 (PAM silencing)
1202	SEQ ID NO: 1202	RTT*81 (PAM silencing)
1203	SEQ ID NO: 1203	RTT*80 (PAM silencing)
1204	SEQ ID NO: 1204	RTT*83 (PAM silencing)
1205	SEQ ID NO: 1205	RTT
1206	SEQ ID NO: 1206	RTT*82 (PAM silencing)
1207	SEQ ID NO: 1207	RTT
1208	SEQ ID NO: 1208	RTT*82 (PAM silencing)
1209	SEQ ID NO: 1209	RTT*80 (PAM silencing)
1210	SEQ ID NO: 1210	RTT*83 (PAM silencing)
1211	SEQ ID NO: 1211	RTT*81 (PAM silencing)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
1215	SEQ ID NO: 1215	PE3b*81 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
1216	SEQ ID NO: 1216	PE3 ngRNA spacer (GAG;GA GG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
1217	SEQ ID NO: 1217	PE3 ngRNA
		spacer (TG PAM)
1218	SEQ ID NO: 1218	PE3b*80 ngRNA spacer (TG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
1219	SEQ ID NO: 1219	PE3b*83 ngRNA spacer (TG PAM)
1220	SEQ ID NO: 1220	PE3 ngRNA spacer (TG;TGA G PAM)
1221	SEQ ID NO: 1221	PE3b*83 ngRNA spacer (AG;AGG; GG;GGG PAM)
1222	SEQ ID NO: 1222	PE3 ngRNA spacer (GG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG;AGG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAG;CA GG PAM)
1225	SEQ ID NO: 1225	PE3b*82 ngRNA spacer (AG;AGG; AGGG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
1226	SEQ ID NO: 1226	PE3b*80 ngRNA spacer (AAG;AA GG;AG;A GG;AGG G PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAG;CA GG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
1230	SEQ ID NO: 1230	PE3b*82 ngRNA spacer (GG;GGG PAM)
1231	SEQ ID NO: 1231	PE3b*80 ngRNA spacer (GG PAM)
1232	SEQ ID NO: 1232	PE3b*81 ngRNA spacer (GG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG;GGA G PAM)
1235	SEQ ID NO: 1235	PE3b*82 ngRNA spacer (GG PAM)
1236	SEQ ID NO: 1236	PE3b*81 ngRNA spacer (AG;AGG; AGGG PAM)

Sequence Number	Sequence	Description
1237	SEQ ID NO: 1237	PE3b*81 ngRNA spacer (GG;GGG PAM)
1238	SEQ ID NO: 1238	PE3 ngRNA spacer (AG;AGA G PAM)
1239	SEQ ID NO: 1239	PE3 ngRNA spacer (AG;AGG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG;AGT G PAM)
1240	SEQ ID NO: 1240	PE3 ngRNA spacer (AG PAM)
1241	SEQ ID NO: 1241	PE3b*82 ngRNA spacer (TG PAM)
1242	SEQ ID NO: 1242	PE3b*83 ngRNA spacer (GG PAM)
1243	SEQ ID NO: 1243	PE3 ngRNA spacer (AG;AGT G PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG; AGGG PAM)
1244	SEQ ID NO: 1244	PE3 ngRNA spacer (AAG;AA GG PAM)
1247	SEQ ID NO: 1247	PEgRNA (TGG;TG; TGGG PAM)
1248	SEQ ID NO: 1248	PEgRNA (TGG;TG; TGGG PAM)
1246	SEQ ID NO: 1246	PEgRNA (TGG;TG; TGGG PAM)
1245	SEQ ID NO: 1245	PEgRNA (TGG;TG; TGGG PAM)
1249	SEQ ID NO: 1249	PEgRNA (TGG;TG; TGGG PAM)
1252	SEQ ID NO: 1252	PEgRNA (TGG;TG; TGGG PAM)
1251	SEQ ID NO: 1251	PEgRNA (TGG;TG; TGGG PAM)
1250	SEQ ID NO: 1250	PEgRNA (TGG;TG; TGGG PAM)
1256	SEQ ID NO: 1256	PEgRNA (TGG;TG; TGGG PAM)
1253	SEQ ID NO: 1253	PEgRNA (TGG;TG; TGGG PAM)
1254	SEQ ID NO: 1254	PEgRNA (TGG;TG; TGGG PAM)
1255	SEQ ID NO: 1255	PEgRNA (TGG;TG; TGGG PAM)
1260	SEQ ID NO: 1260	PEgRNA (TGG;TG; TGGG PAM)
1262	SEQ ID NO: 1262	PEgRNA (TGG;TG; TGGG PAM)
1259	SEQ ID NO: 1259	PEgRNA (TGG;TG; TGGG PAM)
1264	SEQ ID NO: 1264	PEgRNA (TGG;TG; TGGG PAM)
1258	SEQ ID NO: 1258	PEgRNA (TGG;TG; TGGG PAM)
1257	SEQ ID NO: 1257	PEgRNA (TGG;TG; TGGG PAM)
1263	SEQ ID NO: 1263	PEgRNA (TGG;TG; TGGG PAM)
1261	SEQ ID NO: 1261	PEgRNA (TGG;TG; TGGG PAM)
1275	SEQ ID NO: 1275	PEgRNA (TGG;TG; TGGG PAM)
1269	SEQ ID NO: 1269	PEgRNA (TGG;TG; TGGG PAM)
1267	SEQ ID NO: 1267	PEgRNA (TGG;TG; TGGG PAM)
1271	SEQ ID NO: 1271	PEgRNA (TGG;TG; TGGG PAM)
1266	SEQ ID NO: 1266	PEgRNA (TGG;TG; TGGG PAM)
1273	SEQ ID NO: 1273	PEgRNA (TGG;TG; TGGG PAM)
1274	SEQ ID NO: 1274	PEgRNA (TGG;TG; TGGG PAM)
1272	SEQ ID NO: 1272	PEgRNA (TGG;TG; TGGG PAM)
1265	SEQ ID NO: 1265	PEgRNA (TGG;TG; TGGG PAM)
1270	SEQ ID NO: 1270	PEgRNA (TGG;TG; TGGG PAM)
1276	SEQ ID NO: 1276	PEgRNA (TGG;TG; TGGG PAM)
1268	SEQ ID NO: 1268	PEgRNA (TGG;TG; TGGG PAM)
1279	SEQ ID NO: 1279	PEgRNA (TGG;TG; TGGG PAM)
1281	SEQ ID NO: 1281	PEgRNA (TGG;TG; TGGG PAM)
1288	SEQ ID NO: 1288	PEgRNA (TGG;TG;

Sequence Number	Sequence	Description
		TGGG PAM)
1280	SEQ ID NO: 1280	PEgRNA (TGG;TG; TGGG PAM)
1287	SEQ ID NO: 1287	PEgRNA (TGG;TG; TGGG PAM)
1278	SEQ ID NO: 1278	PEgRNA (TGG;TG; TGGG PAM)
1277	SEQ ID NO: 1277	PEgRNA (TGG;TG; TGGG PAM)
1284	SEQ ID NO: 1284	PEgRNA (TGG;TG; TGGG PAM)
1282	SEQ ID NO: 1282	PEgRNA (TGG;TG; TGGG PAM)
1283	SEQ ID NO: 1283	PEgRNA (TGG;TG; TGGG PAM)
1285	SEQ ID NO: 1285	PEgRNA (TGG;TG; TGGG PAM)
1286	SEQ ID NO: 1286	PEgRNA (TGG;TG; TGGG PAM)
1294	SEQ ID NO: 1294	PEgRNA (TGG;TG; TGGG PAM)
1298	SEQ ID NO: 1298	PEgRNA (TGG;TG; TGGG PAM)
1299	SEQ ID NO: 1299	PEgRNA (TGG;TG; TGGG PAM)
1295	SEQ ID NO: 1295	PEgRNA (TGG;TG; TGGG PAM)
1293	SEQ ID NO: 1293	PEgRNA (TGG;TG; TGGG PAM)
1297	SEQ ID NO: 1297	PEgRNA (TGG;TG; TGGG PAM)
1300	SEQ ID NO: 1300	PEgRNA (TGG;TG; TGGG PAM)

Sequence Number	Sequence	Description
1292	SEQ ID NO: 1292	PEgRNA (TGG;TG; TGGG PAM)
1289	SEQ ID NO: 1289	PEgRNA (TGG;TG; TGGG PAM)
1291	SEQ ID NO: 1291	PEgRNA (TGG;TG; TGGG PAM)
1290	SEQ ID NO: 1290	PEgRNA (TGG;TG; TGGG PAM)
1296	SEQ ID NO: 1296	PEgRNA (TGG;TG; TGGG PAM)
1301	SEQ ID NO: 1301	PEgRNA (TGG;TG; TGGG PAM)
1303	SEQ ID NO: 1303	PEgRNA (TGG;TG; TGGG PAM)
1313	SEQ ID NO: 1313	PEgRNA (TGG;TG; TGGG PAM)
1311	SEQ ID NO: 1311	PEgRNA (TGG;TG; TGGG PAM)
1310	SEQ ID NO: 1310	PEgRNA (TGG;TG; TGGG PAM)
1304	SEQ ID NO: 1304	PEgRNA (TGG;TG; TGGG PAM)
1306	SEQ ID NO: 1306	PEgRNA (TGG;TG; TGGG PAM)
1305	SEQ ID NO: 1305	PEgRNA (TGG;TG; TGGG PAM)
1307	SEQ ID NO: 1307	PEgRNA (TGG;TG; TGGG PAM)
1315	SEQ ID NO: 1315	PEgRNA (TGG;TG; TGGG PAM)
1314	SEQ ID NO: 1314	PEgRNA (TGG;TG; TGGG PAM)
1312	SEQ ID NO: 1312	PEgRNA (TGG;TG;

Sequence Number	Sequence	Description
		TGGG PAM)
1309	SEQ ID NO: 1309	PEgRNA (TGG;TG; TGGG PAM)
1308	SEQ ID NO: 1308	PEgRNA (TGG;TG; TGGG PAM)
1316	SEQ ID NO: 1316	PEgRNA (TGG;TG; TGGG PAM)
1302	SEQ ID NO: 1302	PEgRNA (TGG;TG; TGGG PAM)
1319	SEQ ID NO: 1319	PEgRNA (TGG;TG; TGGG PAM)
1336	SEQ ID NO: 1336	PEgRNA (TGG;TG; TGGG PAM)
1331	SEQ ID NO: 1331	PEgRNA (TGG;TG; TGGG PAM)
1317	SEQ ID NO: 1317	PEgRNA (TGG;TG; TGGG PAM)
1318	SEQ ID NO: 1318	PEgRNA (TGG;TG; TGGG PAM)
1330	SEQ ID NO: 1330	PEgRNA (TGG;TG; TGGG PAM)
1332	SEQ ID NO: 1332	PEgRNA (TGG;TG; TGGG PAM)
1329	SEQ ID NO: 1329	PEgRNA (TGG;TG; TGGG PAM)
1328	SEQ ID NO: 1328	PEgRNA (TGG;TG; TGGG PAM)
1323	SEQ ID NO: 1323	PEgRNA (TGG;TG; TGGG PAM)
1324	SEQ ID NO: 1324	PEgRNA (TGG;TG; TGGG PAM)
1325	SEQ ID NO: 1325	PEgRNA (TGG;TG; TGGG PAM)

Sequence Number	Sequence	Description
1333	SEQ ID NO: 1333	PEgRNA (TGG;TG; TGGG PAM)
1327	SEQ ID NO: 1327	PEgRNA (TGG;TG; TGGG PAM)
1335	SEQ ID NO: 1335	PEgRNA (TGG;TG; TGGG PAM)
1326	SEQ ID NO: 1326	PEgRNA (TGG;TG; TGGG PAM)
1321	SEQ ID NO: 1321	PEgRNA (TGG;TG; TGGG PAM)
1334	SEQ ID NO: 1334	PEgRNA (TGG;TG; TGGG PAM)
1322	SEQ ID NO: 1322	PEgRNA (TGG;TG; TGGG PAM)
1320	SEQ ID NO: 1320	PEgRNA (TGG;TG; TGGG PAM)
1352	SEQ ID NO: 1352	PEgRNA (TGG;TG; TGGG PAM)
1350	SEQ ID NO: 1350	PEgRNA (TGG;TG; TGGG PAM)
1353	SEQ ID NO: 1353	PEgRNA (TGG;TG; TGGG PAM)
1343	SEQ ID NO: 1343	PEgRNA (TGG;TG; TGGG PAM)
1339	SEQ ID NO: 1339	PEgRNA (TGG;TG; TGGG PAM)
1349	SEQ ID NO: 1349	PEgRNA (TGG;TG; TGGG PAM)
1355	SEQ ID NO: 1355	PEgRNA (TGG;TG; TGGG PAM)
1342	SEQ ID NO: 1342	PEgRNA (TGG;TG; TGGG PAM)
1338	SEQ ID NO: 1338	PEgRNA (TGG;TG; TGGG PAM)
1356	SEQ ID NO: 1356	PEgRNA (TGG;TG; TGGG PAM)
1341	SEQ ID NO: 1341	PEgRNA (TGG;TG; TGGG PAM)
1351	SEQ ID NO: 1351	PEgRNA (TGG;TG; TGGG PAM)
1345	SEQ ID NO: 1345	PEgRNA (TGG;TG; TGGG PAM)
1344	SEQ ID NO: 1344	PEgRNA (TGG;TG; TGGG PAM)
1347	SEQ ID NO: 1347	PEgRNA (TGG;TG; TGGG PAM)
1337	SEQ ID NO: 1337	PEgRNA (TGG;TG; TGGG PAM)
1340	SEQ ID NO: 1340	PEgRNA (TGG;TG; TGGG PAM)
1348	SEQ ID NO: 1348	PEgRNA (TGG;TG; TGGG PAM)
1354	SEQ ID NO: 1354	PEgRNA (TGG;TG; TGGG PAM)
1346	SEQ ID NO: 1346	PEgRNA (TGG;TG; TGGG PAM)
1365	SEQ ID NO: 1365	PEgRNA (TGG;TG; TGGG PAM)
1367	SEQ ID NO: 1367	PEgRNA (TGG;TG; TGGG PAM)
1366	SEQ ID NO: 1366	PEgRNA (TGG;TG; TGGG PAM)
1363	SEQ ID NO: 1363	PEgRNA (TGG;TG; TGGG PAM)
1358	SEQ ID NO: 1358	PEgRNA (TGG;TG; TGGG PAM)
1376	SEQ ID NO: 1376	PEgRNA (TGG;TG; TGGG PAM)
1362	SEQ ID NO: 1362	PEgRNA (TGG;TG; TGGG PAM)
1364	SEQ ID NO: 1364	PEgRNA (TGG;TG; TGGG PAM)
1357	SEQ ID NO: 1357	PEgRNA (TGG;TG; TGGG PAM)
1360	SEQ ID NO: 1360	PEgRNA (TGG;TG; TGGG PAM)
1359	SEQ ID NO: 1359	PEgRNA (TGG;TG; TGGG PAM)
1368	SEQ ID NO: 1368	PEgRNA (TGG;TG; TGGG PAM)
1370	SEQ ID NO: 1370	PEgRNA (TGG;TG; TGGG PAM)
1371	SEQ ID NO: 1371	PEgRNA (TGG;TG; TGGG PAM)
1372	SEQ ID NO: 1372	PEgRNA (TGG;TG; TGGG PAM)
1373	SEQ ID NO: 1373	PEgRNA (TGG;TG; TGGG PAM)
1374	SEQ ID NO: 1374	PEgRNA (TGG;TG; TGGG PAM)
1375	SEQ ID NO: 1375	PEgRNA (TGG;TG; TGGG PAM)
1369	SEQ ID NO: 1369	PEgRNA (TGG;TG; TGGG PAM)
1361	SEQ ID NO: 1361	PEgRNA (TGG;TG; TGGG PAM)
1394	SEQ ID NO: 1394	PEgRNA (TGG;TG; TGGG PAM)
1378	SEQ ID NO: 1378	PEgRNA (TGG;TG;

Sequence Number	Sequence	Description
		TGGG PAM)
1391	SEQ ID NO: 1391	PEgRNA (TGG;TG; TGGG PAM)
1384	SEQ ID NO: 1384	PEgRNA (TGG;TG; TGGG PAM)
1389	SEQ ID NO: 1389	PEgRNA (TGG;TG; TGGG PAM)
1395	SEQ ID NO: 1395	PEgRNA (TGG;TG; TGGG PAM)
1386	SEQ ID NO: 1386	PEgRNA (TGG;TG; TGGG PAM)
1380	SEQ ID NO: 1380	PEgRNA (TGG;TG; TGGG PAM)
1390	SEQ ID NO: 1390	PEgRNA (TGG;TG; TGGG PAM)
1393	SEQ ID NO: 1393	PEgRNA (TGG;TG; TGGG PAM)
1383	SEQ ID NO: 1383	PEgRNA (TGG;TG; TGGG PAM)
1392	SEQ ID NO: 1392	PEgRNA (TGG;TG; TGGG PAM)
1396	SEQ ID NO: 1396	PEgRNA (TGG;TG; TGGG PAM)
1388	SEQ ID NO: 1388	PEgRNA (TGG;TG; TGGG PAM)
1387	SEQ ID NO: 1387	PEgRNA (TGG;TG; TGGG PAM)
1379	SEQ ID NO: 1379	PEgRNA (TGG;TG; TGGG PAM)
1382	SEQ ID NO: 1382	PEgRNA (TGG;TG; TGGG PAM)
1381	SEQ ID NO: 1381	PEgRNA (TGG;TG; TGGG PAM)
1385	SEQ ID NO: 1385	PEgRNA (TGG;TG; TGGG PAM)
1377	SEQ ID NO: 1377	PEgRNA (TGG;TG; TGGG PAM)
1400	SEQ ID NO: 1400	PEgRNA (TGG;TG; TGGG PAM)
1397	SEQ ID NO: 1397	PEgRNA (TGG;TG; TGGG PAM)
1403	SEQ ID NO: 1403	PEgRNA (TGG;TG; TGGG PAM)
1412	SEQ ID NO: 1412	PEgRNA (TGG;TG; TGGG PAM)
1414	SEQ ID NO: 1414	PEgRNA (TGG;TG; TGGG PAM)
1411	SEQ ID NO: 1411	PEgRNA (TGG;TG; TGGG PAM)
1406	SEQ ID NO: 1406	PEgRNA (TGG;TG; TGGG PAM)
1404	SEQ ID NO: 1404	PEgRNA (TGG;TG; TGGG PAM)
1401	SEQ ID NO: 1401	PEgRNA (TGG;TG; TGGG PAM)
1407	SEQ ID NO: 1407	PEgRNA (TGG;TG; TGGG PAM)
1398	SEQ ID NO: 1398	PEgRNA (TGG;TG; TGGG PAM)
1416	SEQ ID NO: 1416	PEgRNA (TGG;TG; TGGG PAM)
1402	SEQ ID NO: 1402	PEgRNA (TGG;TG; TGGG PAM)
1408	SEQ ID NO: 1408	PEgRNA (TGG;TG; TGGG PAM)
1405	SEQ ID NO: 1405	PEgRNA (TGG;TG;
		TGGG PAM)
1410	SEQ ID NO: 1410	PEgRNA (TGG;TG; TGGG PAM)
1409	SEQ ID NO: 1409	PEgRNA (TGG;TG; TGGG PAM)
1413	SEQ ID NO: 1413	PEgRNA (TGG;TG; TGGG PAM)
1399	SEQ ID NO: 1399	PEgRNA (TGG;TG; TGGG PAM)
1415	SEQ ID NO: 1415	PEgRNA (TGG;TG; TGGG PAM)
1424	SEQ ID NO: 1424	PEgRNA (TGG;TG; TGGG PAM)
1432	SEQ ID NO: 1432	PEgRNA (TGG;TG; TGGG PAM)
1427	SEQ ID NO: 1427	PEgRNA (TGG;TG; TGGG PAM)
1425	SEQ ID NO: 1425	PEgRNA (TGG;TG; TGGG PAM)
1426	SEQ ID NO: 1426	PEgRNA (TGG;TG; TGGG PAM)
1417	SEQ ID NO: 1417	PEgRNA (TGG;TG; TGGG PAM)
1418	SEQ ID NO: 1418	PEgRNA (TGG;TG; TGGG PAM)
1422	SEQ ID NO: 1422	PEgRNA (TGG;TG; TGGG PAM)
1421	SEQ ID NO: 1421	PEgRNA (TGG;TG; TGGG PAM)
1420	SEQ ID NO: 1420	PEgRNA (TGG;TG; TGGG PAM)
1428	SEQ ID NO: 1428	PEgRNA (TGG;TG; TGGG PAM)

Sequence Number	Sequence	Description
1423	SEQ ID NO: 1423	PEgRNA (TGG;TG; TGGG PAM)
1434	SEQ ID NO: 1434	PEgRNA (TGG;TG; TGGG PAM)
1436	SEQ ID NO: 1436	PEgRNA (TGG;TG; TGGG PAM)
1431	SEQ ID NO: 1431	PEgRNA (TGG;TG; TGGG PAM)
1430	SEQ ID NO: 1430	PEgRNA (TGG;TG; TGGG PAM)
1419	SEQ ID NO: 1419	PEgRNA (TGG;TG; TGGG PAM)
1435	SEQ ID NO: 1435	PEgRNA (TGG;TG; TGGG PAM)
1433	SEQ ID NO: 1433	PEgRNA (TGG;TG; TGGG PAM)
1429	SEQ ID NO: 1429	PEgRNA (TGG;TG; TGGG PAM)
1441	SEQ ID NO: 1441	PEgRNA (TGG;TG; TGGG PAM)
1444	SEQ ID NO: 1444	PEgRNA (TGG;TG; TGGG PAM)
1447	SEQ ID NO: 1447	PEgRNA (TGG;TG; TGGG PAM)
1452	SEQ ID NO: 1452	PEgRNA (TGG;TG; TGGG PAM)
1442	SEQ ID NO: 1442	PEgRNA (TGG;TG; TGGG PAM)
1439	SEQ ID NO: 1439	PEgRNA (TGG;TG; TGGG PAM)
1443	SEQ ID NO: 1443	PEgRNA (TGG;TG; TGGG PAM)
1448	SEQ ID NO: 1448	PEgRNA (TGG;TG; TGGG PAM)
1451	SEQ ID NO: 1451	PEgRNA (TGG;TG; TGGG PAM)
1446	SEQ ID NO: 1446	PEgRNA (TGG;TG; TGGG PAM)
1450	SEQ ID NO: 1450	PEgRNA (TGG;TG; TGGG PAM)
1438	SEQ ID NO: 1438	PEgRNA (TGG;TG; TGGG PAM)
1449	SEQ ID NO: 1449	PEgRNA (TGG;TG; TGGG PAM)
1445	SEQ ID NO: 1445	PEgRNA (TGG;TG; TGGG PAM)
1440	SEQ ID NO: 1440	PEgRNA (TGG;TG; TGGG PAM)
1437	SEQ ID NO: 1437	PEgRNA (TGG;TG; TGGG PAM)
1459	SEQ ID NO: 1459	PEgRNA (TGG;TG; TGGG PAM)
1466	SEQ ID NO: 1466	PEgRNA (TGG;TG; TGGG PAM)
1455	SEQ ID NO: 1455	PEgRNA (TGG;TG; TGGG PAM)
1456	SEQ ID NO: 1456	PEgRNA (TGG;TG; TGGG PAM)
1457	SEQ ID NO: 1457	PEgRNA (TGG;TG; TGGG PAM)
1458	SEQ ID NO: 1458	PEgRNA (TGG;TG; TGGG PAM)
1462	SEQ ID NO: 1462	PEgRNA (TGG;TG; TGGG PAM)
1467	SEQ ID NO: 1467	PEgRNA (TGG;TG; TGGG PAM)
1460	SEQ ID NO: 1460	PEgRNA (TGG;TG; TGGG PAM)
1468	SEQ ID NO: 1468	PEgRNA (TGG;TG; TGGG PAM)
1463	SEQ ID NO: 1463	PEgRNA (TGG;TG; TGGG PAM)
1464	SEQ ID NO: 1464	PEgRNA (TGG;TG; TGGG PAM)
1453	SEQ ID NO: 1453	PEgRNA (TGG;TG; TGGG PAM)
1465	SEQ ID NO: 1465	PEgRNA (TGG;TG; TGGG PAM)
1454	SEQ ID NO: 1454	PEgRNA (TGG;TG; TGGG PAM)
1461	SEQ ID NO: 1461	PEgRNA (TGG;TG; TGGG PAM)
1469	SEQ ID NO: 1469	PEgRNA (TGG;TG; TGGG PAM)
1470	SEQ ID NO: 1470	PEgRNA (TGG;TG; TGGG PAM)
1471	SEQ ID NO: 1471	PEgRNA (TGG;TG; TGGG PAM)
1479	SEQ ID NO: 1479	PEgRNA (TGG;TG; TGGG PAM)
1476	SEQ ID NO: 1476	PEgRNA (TGG;TG; TGGG PAM)
1478	SEQ ID NO: 1478	PEgRNA (TGG;TG; TGGG PAM)
1473	SEQ ID NO: 1473	PEgRNA (TGG;TG; TGGG PAM)
1475	SEQ ID NO: 1475	PEgRNA (TGG;TG; TGGG PAM)
1474	SEQ ID NO: 1474	PEgRNA (TGG;TG;

Sequence Number	Sequence	Description
		TGGG PAM)
1472	SEQ ID NO: 1472	PEgRNA (TGG;TG; TGGG PAM)
1480	SEQ ID NO: 1480	PEgRNA (TGG;TG; TGGG PAM)
1477	SEQ ID NO: 1477	PEgRNA (TGG;TG; TGGG PAM)
1482	SEQ ID NO: 1482	PEgRNA (TGG;TG; TGGG PAM)
1483	SEQ ID NO: 1483	PEgRNA (TGG;TG; TGGG PAM)
1481	SEQ ID NO: 1481	PEgRNA (TGG;TG; TGGG PAM)
1484	SEQ ID NO: 1484	PEgRNA (TGG;TG; TGGG PAM)
1493	SEQ ID NO: 1493	PEgRNA (TGG;TG; TGGG PAM)
1494	SEQ ID NO: 1494	PEgRNA (TGG;TG; TGGG PAM)
1495	SEQ ID NO: 1495	PEgRNA (TGG;TG; TGGG PAM)
1485	SEQ ID NO: 1485	PEgRNA (TGG;TG; TGGG PAM)
1490	SEQ ID NO: 1490	PEgRNA (TGG;TG; TGGG PAM)
1486	SEQ ID NO: 1486	PEgRNA (TGG;TG; TGGG PAM)
1491	SEQ ID NO: 1491	PEgRNA (TGG;TG; TGGG PAM)
1487	SEQ ID NO: 1487	PEgRNA (TGG;TG; TGGG PAM)
1488	SEQ ID NO: 1488	PEgRNA (TGG;TG; TGGG PAM)
1492	SEQ ID NO: 1492	PEgRNA (TGG;TG; TGGG PAM)
1489	SEQ ID NO: 1489	PEgRNA (TGG;TG; TGGG PAM)
1496	SEQ ID NO: 1496	PEgRNA (TGG;TG; TGGG PAM)
1498	SEQ ID NO: 1498	PEgRNA (TGG;TG; TGGG PAM)
1504	SEQ ID NO: 1504	PEgRNA (TGG;TG; TGGG PAM)
1503	SEQ ID NO: 1503	PEgRNA (TGG;TG; TGGG PAM)
1502	SEQ ID NO: 1502	PEgRNA (TGG;TG; TGGG PAM)
1501	SEQ ID NO: 1501	PEgRNA (TGG;TG; TGGG PAM)
1500	SEQ ID NO: 1500	PEgRNA (TGG;TG; TGGG PAM)
1499	SEQ ID NO: 1499	PEgRNA (TGG;TG; TGGG PAM)
1497	SEQ ID NO: 1497	PEgRNA (TGG;TG; TGGG PAM)
1505	SEQ ID NO: 1505	PEgRNA (TGG;TG; TGGG PAM)
1506	SEQ ID NO: 1506	PEgRNA (TGG;TG; TGGG PAM)
1507	SEQ ID NO: 1507	PEgRNA (TGG;TG; TGGG PAM)
1508	SEQ ID NO: 1508	PEgRNA (TGG;TG; TGGG PAM)
1509	SEQ ID NO: 1509	PEgRNA (TGG;TG; TGGG PAM)
1510	SEQ ID NO: 1510	PEgRNA (TGG;TG;
		TGGG PAM)
1511	SEQ ID NO: 1511	PEgRNA (TGG;TG; TGGG PAM)
1512	SEQ ID NO: 1512	PEgRNA (TGG;TG; TGGG PAM)
1513	SEQ ID NO: 1513	PEgRNA (TGG;TG; TGGG PAM)
1514	SEQ ID NO: 1514	PEgRNA (TGG;TG; TGGG PAM)
1515	SEQ ID NO: 1515	PEgRNA (TGG;TG; TGGG PAM)
1516	SEQ ID NO: 1516	PEgRNA (TGG;TG; TGGG PAM)
1517	SEQ ID NO: 1517	PEgRNA (TGG;TG; TGGG PAM)
1518	SEQ ID NO: 1518	PEgRNA (TGG;TG; TGGG PAM)
1519	SEQ ID NO: 1519	PEgRNA (TGG;TG; TGGG PAM)
1520	SEQ ID NO: 1520	PEgRNA (TGG;TG; TGGG PAM)
1521	SEQ ID NO: 1521	PEgRNA (TGG;TG; TGGG PAM)
1522	SEQ ID NO: 1522	PEgRNA (TGG;TG; TGGG PAM)
1523	SEQ ID NO: 1523	PEgRNA (TGG;TG; TGGG PAM)
1524	SEQ ID NO: 1524	PEgRNA (TGG;TG; TGGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG; AGGG PAM)
1525	SEQ ID NO: 1525	ngRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
1526	SEQ ID NO: 1526	ngRNA (AG;AGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG;AGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG; AGGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
1528	SEQ ID NO: 1528	ngRNA (AG;AGG PAM)

Table 8

Sequence Number	Sequence	Description
1529	SEQ ID NO: 1529	PEgRNA spacer (GGG;GG PAM)
1530	SEQ ID NO: 1530	PEgRNA spacer (GGG;GG PAM)
1531	SEQ ID NO: 1531	PEgRNA spacer (GGG;GG PAM)
1532	SEQ ID NO: 1532	PEgRNA spacer (GGG;GG PAM)
1533	SEQ ID NO: 1533	PEgRNA spacer (GGG;GG PAM)
1534	SEQ ID NO: 1534	PEgRNA spacer (GGG;GG PAM)
1535	SEQ ID NO: 1535	PEgRNA spacer (GGG;GG PAM)
1536	GCA	PBS
1537	GCAA	PBS
1538	GCAAT	PBS
1539	GCAATG	PBS
1540	GCAATGA	PBS
1541	GCAATGAA	PBS
1542	GCAATGAAC	PBS
1543	SEQ ID NO: 1543	PBS
1544	SEQ ID NO: 1544	PBS
1545	SEQ ID NO: 1545	PBS
1546	SEQ ID NO: 1546	PBS
1547	SEQ ID NO: 1547	PBS
1548	SEQ ID NO: 1548	PBS
1549	SEQ ID NO: 1549	PBS
1550	SEQ ID NO: 1550	PBS
1551	SEQ ID NO: 1551	PBS
1552	SEQ ID NO: 1552	PBS
1553	SEQ ID NO: 1553	RTT
1554	SEQ ID NO: 1554	RTT
1555	SEQ ID NO: 1555	RTT
1556	SEQ ID NO: 1556	RTT
1557	SEQ ID NO: 1557	RTT
1558	SEQ ID NO: 1558	RTT
1559	SEQ ID NO: 1559	RTT
1560	SEQ ID NO: 1560	RTT
1561	SEQ ID NO: 1561	RTT
1562	SEQ ID NO: 1562	RTT
1563	SEQ ID NO: 1563	RTT
1564	SEQ ID NO: 1564	RTT
1565	SEQ ID NO: 1565	RTT
1566	SEQ ID NO: 1566	RTT
1567	SEQ ID NO: 1567	RTT
1568	SEQ ID NO: 1568	RTT
1569	SEQ ID NO: 1569	RTT
1570	SEQ ID NO: 1570	RTT
1571	SEQ ID NO: 1571	RTT
1572	SEQ ID NO: 1572	RTT
1573	SEQ ID NO: 1573	RTT
1574	SEQ ID NO: 1574	RTT
1575	SEQ ID NO: 1575	RTT
1576	SEQ ID NO: 1576	RTT
1577	SEQ ID NO: 1577	RTT
1578	SEQ ID NO: 1578	RTT
1579	SEQ ID NO: 1579	RTT
1580	SEQ ID NO: 1580	RTT
1581	SEQ ID NO: 1581	RTT
1582	SEQ ID NO: 1582	RTT
1583	SEQ ID NO: 1583	RTT
1584	SEQ ID NO: 1584	RTT
1585	SEQ ID NO: 1585	RTT
1586	SEQ ID NO: 1586	RTT
1587	SEQ ID NO: 1587	RTT
1588	SEQ ID NO: 1588	RTT
1589	SEQ ID NO: 1589	RTT
1590	SEQ ID NO: 1590	RTT
1591	SEQ ID NO: 1591	RTT
1592	SEQ ID NO: 1592	RTT
1593	SEQ ID NO: 1593	RTT
1594	SEQ ID NO: 1594	RTT
1595	SEQ ID NO: 1595	RTT
1596	SEQ ID NO: 1596	RTT
1597	SEQ ID NO: 1597	RTT
1598	SEQ ID NO: 1598	RTT
1599	SEQ ID NO: 1599	RTT
1600	SEQ ID NO: 1600	RTT
1601	SEQ ID NO: 1601	RTT
1602	SEQ ID NO: 1602	RTT
1603	SEQ ID NO: 1603	RTT
1604	SEQ ID NO: 1604	RTT
1605	SEQ ID NO: 1605	RTT
1606	SEQ ID NO: 1606	RTT

Sequence Number	Sequence	Description
1607	SEQ ID NO: 1607	RTT
1608	SEQ ID NO: 1608	RTT
1609	SEQ ID NO: 1609	RTT
1610	SEQ ID NO: 1610	RTT
1611	SEQ ID NO: 1611	RTT
1612	SEQ ID NO: 1612	RTT
1613	SEQ ID NO: 1613	RTT
1614	SEQ ID NO: 1614	RTT
1615	SEQ ID NO: 1615	RTT
1616	SEQ ID NO: 1616	RTT
1617	SEQ ID NO: 1617	RTT
1618	SEQ ID NO: 1618	RTT
1619	SEQ ID NO: 1619	RTT
1620	SEQ ID NO: 1620	RTT
1621	SEQ ID NO: 1621	RTT
1622	SEQ ID NO: 1622	RTT
1623	SEQ ID NO: 1623	RTT
1624	SEQ ID NO: 1624	RTT
1625	SEQ ID NO: 1625	RTT
1626	SEQ ID NO: 1626	RTT
1627	SEQ ID NO: 1627	RTT
1628	SEQ ID NO: 1628	RTT
1629	SEQ ID NO: 1629	RTT
1630	SEQ ID NO: 1630	RTT
1631	SEQ ID NO: 1631	RTT
1632	SEQ ID NO: 1632	RTT
1633	SEQ ID NO: 1633	RTT
1634	SEQ ID NO: 1634	RTT
1635	SEQ ID NO: 1635	RTT
1636	SEQ ID NO: 1636	RTT
1637	SEQ ID NO: 1637	RTT
1638	SEQ ID NO: 1638	RTT
1639	SEQ ID NO: 1639	RTT
1640	SEQ ID NO: 1640	RTT
1641	SEQ ID NO: 1641	RTT
1642	SEQ ID NO: 1642	RTT
1643	SEQ ID NO: 1643	RTT
1217	SEQ ID NO: 1217	PE3 ngRNA spacer (TG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
1238	SEQ ID NO: 1238	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
1220	SEQ ID NO: 1220	PE3 ngRNA spacer (TG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
1243	SEQ ID NO: 1243	PE3 ngRNA spacer (AG PAM)
1240	SEQ ID NO: 1240	PE3 ngRNA spacer (AG PAM)
1222	SEQ ID NO: 1222	PE3 ngRNA spacer (GG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG;AGG PAM)

Sequence Number	Sequence	Description
1239	SEQ ID NO: 1239	PE3 ngRNA spacer (AG;AGG PAM)
1644	SEQ ID NO: 1644	PEgRNA (GGG;GG PAM)
1645	SEQ ID NO: 1645	PEgRNA (GGG;GG PAM)
1646	SEQ ID NO: 1646	PEgRNA (GGG;GG PAM)
1647	SEQ ID NO: 1647	PEgRNA (GGG;GG PAM)
1648	SEQ ID NO: 1648	PEgRNA (GGG;GG PAM)
1650	SEQ ID NO: 1650	PEgRNA (GGG;GG PAM)
1649	SEQ ID NO: 1649	PEgRNA (GGG;GG PAM)
1651	SEQ ID NO: 1651	PEgRNA (GGG;GG PAM)
1652	SEQ ID NO: 1652	PEgRNA (GGG;GG PAM)
1654	SEQ ID NO: 1654	PEgRNA (GGG;GG PAM)
1653	SEQ ID NO: 1653	PEgRNA (GGG;GG PAM)
1657	SEQ ID NO: 1657	PEgRNA (GGG;GG PAM)
1655	SEQ ID NO: 1655	PEgRNA (GGG;GG PAM)
1656	SEQ ID NO: 1656	PEgRNA (GGG;GG PAM)
1659	SEQ ID NO: 1659	PEgRNA (GGG;GG PAM)
1660	SEQ ID NO: 1660	PEgRNA (GGG;GG PAM)
1658	SEQ ID NO: 1658	PEgRNA (GGG;GG PAM)
1662	SEQ ID NO: 1662	PEgRNA (GGG;GG PAM)
1661	SEQ ID NO: 1661	PEgRNA (GGG;GG PAM)
1665	SEQ ID NO: 1665	PEgRNA (GGG;GG PAM)
1663	SEQ ID NO: 1663	PEgRNA (GGG;GG PAM)
1664	SEQ ID NO: 1664	PEgRNA (GGG;GG PAM)
1669	SEQ ID NO: 1669	PEgRNA (GGG;GG PAM)
1671	SEQ ID NO: 1671	PEgRNA (GGG;GG PAM)
1666	SEQ ID NO: 1666	PEgRNA (GGG;GG PAM)
1668	SEQ ID NO: 1668	PEgRNA (GGG;GG PAM)
1667	SEQ ID NO: 1667	PEgRNA (GGG;GG PAM)
1670	SEQ ID NO: 1670	PEgRNA (GGG;GG PAM)
1672	SEQ ID NO: 1672	PEgRNA (GGG;GG PAM)
1674	SEQ ID NO: 1674	PEgRNA (GGG;GG PAM)
1675	SEQ ID NO: 1675	PEgRNA (GGG;GG PAM)
1676	SEQ ID NO: 1676	PEgRNA (GGG;GG PAM)
1673	SEQ ID NO: 1673	PEgRNA (GGG;GG PAM)
1679	SEQ ID NO: 1679	PEgRNA (GGG;GG PAM)
1677	SEQ ID NO: 1677	PEgRNA (GGG;GG PAM)
1678	SEQ ID NO: 1678	PEgRNA (GGG;GG PAM)
1681	SEQ ID NO: 1681	PEgRNA (GGG;GG PAM)
1680	SEQ ID NO: 1680	PEgRNA (GGG;GG PAM)
1687	SEQ ID NO: 1687	PEgRNA (GGG;GG PAM)
1682	SEQ ID NO: 1682	PEgRNA (GGG;GG PAM)
1686	SEQ ID NO: 1686	PEgRNA (GGG;GG PAM)
1685	SEQ ID NO: 1685	PEgRNA (GGG;GG PAM)
1684	SEQ ID NO: 1684	PEgRNA (GGG;GG PAM)
1683	SEQ ID NO: 1683	PEgRNA (GGG;GG PAM)
1688	SEQ ID NO: 1688	PEgRNA (GGG;GG PAM)
1689	SEQ ID NO: 1689	PEgRNA (GGG;GG PAM)
1691	SEQ ID NO: 1691	PEgRNA (GGG;GG PAM)
1692	SEQ ID NO: 1692	PEgRNA (GGG;GG PAM)
1693	SEQ ID NO: 1693	PEgRNA (GGG;GG PAM)
1690	SEQ ID NO: 1690	PEgRNA (GGG;GG PAM)
1697	SEQ ID NO: 1697	PEgRNA (GGG;GG PAM)
1694	SEQ ID NO: 1694	PEgRNA (GGG;GG PAM)
1698	SEQ ID NO: 1698	PEgRNA (GGG;GG PAM)
1696	SEQ ID NO: 1696	PEgRNA (GGG;GG PAM)
1695	SEQ ID NO: 1695	PEgRNA (GGG;GG PAM)
1701	SEQ ID NO: 1701	PEgRNA (GGG;GG PAM)
1702	SEQ ID NO: 1702	PEgRNA (GGG;GG PAM)
1700	SEQ ID NO: 1700	PEgRNA (GGG;GG PAM)
1699	SEQ ID NO: 1699	PEgRNA (GGG;GG PAM)
1705	SEQ ID NO: 1705	PEgRNA (GGG;GG PAM)
1706	SEQ ID NO: 1706	PEgRNA (GGG;GG PAM)
1704	SEQ ID NO: 1704	PEgRNA (GGG;GG PAM)
1703	SEQ ID NO: 1703	PEgRNA (GGG;GG PAM)
1708	SEQ ID NO: 1708	PEgRNA (GGG;GG PAM)

Sequence Number	Sequence	Description
1709	SEQ ID NO: 1709	PEgRNA (GGG;GG PAM)
1710	SEQ ID NO: 1710	PEgRNA (GGG;GG PAM)
1711	SEQ ID NO: 1711	PEgRNA (GGG;GG PAM)
1707	SEQ ID NO: 1707	PEgRNA (GGG;GG PAM)
1712	SEQ ID NO: 1712	PEgRNA (GGG;GG PAM)
1715	SEQ ID NO: 1715	PEgRNA (GGG;GG PAM)
1713	SEQ ID NO: 1713	PEgRNA (GGG;GG PAM)
1714	SEQ ID NO: 1714	PEgRNA (GGG;GG PAM)
1716	SEQ ID NO: 1716	PEgRNA (GGG;GG PAM)
1717	SEQ ID NO: 1717	PEgRNA (GGG;GG PAM)
1718	SEQ ID NO: 1718	PEgRNA (GGG;GG PAM)
1720	SEQ ID NO: 1720	PEgRNA (GGG;GG PAM)
1719	SEQ ID NO: 1719	PEgRNA (GGG;GG PAM)
1721	SEQ ID NO: 1721	PEgRNA (GGG;GG PAM)
1722	SEQ ID NO: 1722	PEgRNA (GGG;GG PAM)
1723	SEQ ID NO: 1723	PEgRNA (GGG;GG PAM)
1724	SEQ ID NO: 1724	PEgRNA (GGG;GG PAM)
1725	SEQ ID NO: 1725	PEgRNA (GGG;GG PAM)
1726	SEQ ID NO: 1726	PEgRNA (GGG;GG PAM)
1727	SEQ ID NO: 1727	PEgRNA (GGG;GG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
1525	SEQ ID NO: 1525	ngRNA (AG;AGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG;AGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG;AGG PAM)
1528	SEQ ID NO: 1528	ngRNA (AG;AGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)

Table 9

Sequence Number	Sequence	Description
1728	SEQ ID NO: 1728	PEgRNA spacer (TGG;TG PAM)
1729	SEQ ID NO: 1729	PEgRNA spacer (TGG;TG PAM)
1730	SEQ ID NO: 1730	PEgRNA spacer (TGG;TG PAM)
1731	SEQ ID NO: 1731	PEgRNA spacer (TGG;TG PAM)
1732	SEQ ID NO: 1732	PEgRNA spacer (TGG;TG PAM)
1733	SEQ ID NO: 1733	PEgRNA spacer (TGG;TG PAM)
1734	SEQ ID NO: 1734	PEgRNA spacer (TGG;TG PAM)
1735	GCC	PBS
1736	GCCC	PBS
1737	GCCCA	PBS
1738	GCCCAG	PBS
1739	GCCCAG G	PBS
1740	GCCCAG GG	PBS
1741	GCCCAG GGC	PBS
1742	SEQ ID NO: 1742	PBS
1743	SEQ ID NO: 1743	PBS
1744	SEQ ID NO: 1744	PBS
1745	SEQ ID NO: 1745	PBS
1746	SEQ ID NO: 1746	PBS
1747	SEQ ID NO: 1747	PBS
1748	SEQ ID NO: 1748	PBS
1749	SEQ ID NO: 1749	PBS
1750	SEQ ID NO: 1750	PBS
1751	SEQ ID NO: 1751	PBS
1752	SEQ ID NO: 1752	RTT
1753	SEQ ID NO: 1753	RTT
1754	SEQ ID NO: 1754	RTT
1755	SEQ ID NO: 1755	RTT
1756	SEQ ID NO: 1756	RTT
1757	SEQ ID NO: 1757	RTT
1758	SEQ ID NO: 1758	RTT
1759	SEQ ID NO: 1759	RTT
1760	SEQ ID NO: 1760	RTT
1761	SEQ ID NO: 1761	RTT
1762	SEQ ID NO: 1762	RTT
1763	SEQ ID NO: 1763	RTT
1764	SEQ ID NO: 1764	RTT
1765	SEQ ID NO: 1765	RTT
1766	SEQ ID NO: 1766	RTT
1767	SEQ ID NO: 1767	RTT
1768	SEQ ID NO: 1768	RTT
1769	SEQ ID NO: 1769	RTT
1770	SEQ ID NO: 1770	RTT
1771	SEQ ID NO: 1771	RTT
1772	SEQ ID NO: 1772	RTT

Sequence Number	Sequence	Description
1773	SEQ ID NO: 1773	RTT
1774	SEQ ID NO: 1774	RTT
1775	SEQ ID NO: 1775	RTT
1776	SEQ ID NO: 1776	RTT
1777	SEQ ID NO: 1777	RTT
1778	SEQ ID NO: 1778	RTT
1779	SEQ ID NO: 1779	RTT
1780	SEQ ID NO: 1780	RTT
1781	SEQ ID NO: 1781	RTT
1782	SEQ ID NO: 1782	RTT
1783	SEQ ID NO: 1783	RTT
1784	SEQ ID NO: 1784	RTT
1785	SEQ ID NO: 1785	RTT
1786	SEQ ID NO: 1786	RTT
1787	SEQ ID NO: 1787	RTT
1788	SEQ ID NO: 1788	RTT
1789	SEQ ID NO: 1789	RTT
1790	SEQ ID NO: 1790	RTT
1791	SEQ ID NO: 1791	RTT
1792	SEQ ID NO: 1792	RTT
1793	SEQ ID NO: 1793	RTT
1794	SEQ ID NO: 1794	RTT
1795	SEQ ID NO: 1795	RTT
1796	SEQ ID NO: 1796	RTT
1797	SEQ ID NO: 1797	RTT
1798	SEQ ID NO: 1798	RTT
1799	SEQ ID NO: 1799	RTT
1800	SEQ ID NO: 1800	RTT
1801	SEQ ID NO: 1801	RTT
1802	SEQ ID NO: 1802	RTT
1803	SEQ ID NO: 1803	RTT
1804	SEQ ID NO: 1804	RTT
1805	SEQ ID NO: 1805	RTT

Sequence Number	Sequence	Description
1806	SEQ ID NO: 1806	RTT
1807	SEQ ID NO: 1807	RTT
1808	SEQ ID NO: 1808	RTT
1809	SEQ ID NO: 1809	RTT
1810	SEQ ID NO: 1810	RTT
1811	SEQ ID NO: 1811	RTT
1812	SEQ ID NO: 1812	RTT
1813	SEQ ID NO: 1813	RTT
1814	SEQ ID NO: 1814	RTT
1815	SEQ ID NO: 1815	RTT
1816	SEQ ID NO: 1816	RTT
1817	SEQ ID NO: 1817	RTT
1818	SEQ ID NO: 1818	RTT
1819	SEQ ID NO: 1819	RTT
1820	SEQ ID NO: 1820	RTT
1821	SEQ ID NO: 1821	RTT
1822	SEQ ID NO: 1822	RTT
1823	SEQ ID NO: 1823	RTT
1824	SEQ ID NO: 1824	RTT
1825	SEQ ID NO: 1825	RTT
1826	SEQ ID NO: 1826	RTT
1827	SEQ ID NO: 1827	RTT
1828	SEQ ID NO: 1828	RTT
1829	SEQ ID NO: 1829	RTT
1830	SEQ ID NO: 1830	RTT
1831	SEQ ID NO: 1831	RTT
1832	SEQ ID NO: 1832	RTT
1833	SEQ ID NO: 1833	RTT
1834	SEQ ID NO: 1834	RTT
1835	SEQ ID NO: 1835	RTT
1836	SEQ ID NO: 1836	RTT
1837	SEQ ID NO: 1837	RTT
1838	SEQ ID NO: 1838	RTT

Sequence Number	Sequence	Description
1839	SEQ ID NO: 1839	RTT
1840	SEQ ID NO: 1840	RTT
1841	SEQ ID NO: 1841	RTT
1842	SEQ ID NO: 1842	RTT
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
1240	SEQ ID NO: 1240	PE3 ngRNA spacer (AG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
1222	SEQ ID NO: 1222	PE3 ngRNA spacer (GG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
1243	SEQ ID NO: 1243	PE3 ngRNA spacer (AG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
1239	SEQ ID NO: 1239	PE3 ngRNA spacer (AG;AGG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
63	SEQ ID NO: 63	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (TG;TGG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
1217	SEQ ID NO: 1217	PE3 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
1220	SEQ ID NO: 1220	PE3 ngRNA spacer (TG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
1843	SEQ ID NO: 1843	PE3 ngRNA spacer (TG PAM)
1844	SEQ ID NO: 1844	PE3 ngRNA spacer (GG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG;AGG PAM)
1238	SEQ ID NO: 1238	PE3 ngRNA spacer (AG PAM)

Sequence Number	Sequence	Description
1845	SEQ ID NO: 1845	PE3 ngRNA spacer (TG;TGG PAM)
1846	SEQ ID NO: 1846	PEgRNA (TGG;TG PAM)
1847	SEQ ID NO: 1847	PEgRNA (TGG;TG PAM)
1848	SEQ ID NO: 1848	PEgRNA (TGG;TG PAM)
1851	SEQ ID NO: 1851	PEgRNA (TGG;TG PAM)
1849	SEQ ID NO: 1849	PEgRNA (TGG;TG PAM)
1850	SEQ ID NO: 1850	PEgRNA (TGG;TG PAM)
1855	SEQ ID NO: 1855	PEgRNA (TGG;TG PAM)
1852	SEQ ID NO: 1852	PEgRNA (TGG;TG PAM)
1854	SEQ ID NO: 1854	PEgRNA (TGG;TG PAM)
1853	SEQ ID NO: 1853	PEgRNA (TGG;TG PAM)
1858	SEQ ID NO: 1858	PEgRNA (TGG;TG PAM)
1859	SEQ ID NO: 1859	PEgRNA (TGG;TG PAM)
1856	SEQ ID NO: 1856	PEgRNA (TGG;TG PAM)
1857	SEQ ID NO: 1857	PEgRNA (TGG;TG PAM)
1860	SEQ ID NO: 1860	PEgRNA (TGG;TG PAM)
1861	SEQ ID NO: 1861	PEgRNA (TGG;TG PAM)
1866	SEQ ID NO: 1866	PEgRNA (TGG;TG PAM)
1864	SEQ ID NO: 1864	PEgRNA (TGG;TG PAM)
1862	SEQ ID NO: 1862	PEgRNA (TGG;TG PAM)
1865	SEQ ID NO: 1865	PEgRNA (TGG;TG PAM)

Sequence Number	Sequence	Description
1863	SEQ ID NO: 1863	PEgRNA (TGG;TG PAM)
1870	SEQ ID NO: 1870	PEgRNA (TGG;TG PAM)
1872	SEQ ID NO: 1872	PEgRNA (TGG;TG PAM)
1867	SEQ ID NO: 1867	PEgRNA (TGG;TG PAM)
1873	SEQ ID NO: 1873	PEgRNA (TGG;TG PAM)
1868	SEQ ID NO: 1868	PEgRNA (TGG;TG PAM)
1871	SEQ ID NO: 1871	PEgRNA (TGG;TG PAM)
1869	SEQ ID NO: 1869	PEgRNA (TGG;TG PAM)
1879	SEQ ID NO: 1879	PEgRNA (TGG;TG PAM)
1876	SEQ ID NO: 1876	PEgRNA (TGG;TG PAM)
1877	SEQ ID NO: 1877	PEgRNA (TGG;TG PAM)
1878	SEQ ID NO: 1878	PEgRNA (TGG;TG PAM)
1874	SEQ ID NO: 1874	PEgRNA (TGG;TG PAM)
1875	SEQ ID NO: 1875	PEgRNA (TGG;TG PAM)
1881	SEQ ID NO: 1881	PEgRNA (TGG;TG PAM)
1882	SEQ ID NO: 1882	PEgRNA (TGG;TG PAM)
1884	SEQ ID NO: 1884	PEgRNA (TGG;TG PAM)
1880	SEQ ID NO: 1880	PEgRNA (TGG;TG PAM)
1883	SEQ ID NO: 1883	PEgRNA (TGG;TG PAM)
1885	SEQ ID NO: 1885	PEgRNA (TGG;TG PAM)
1886	SEQ ID NO: 1886	PEgRNA (TGG;TG PAM)
1887	SEQ ID NO: 1887	PEgRNA (TGG;TG PAM)

Sequence Number	Sequence	Description
1888	SEQ ID NO: 1888	PEgRNA (TGG;TG PAM)
1891	SEQ ID NO: 1891	PEgRNA (TGG;TG PAM)
1890	SEQ ID NO: 1890	PEgRNA (TGG;TG PAM)
1889	SEQ ID NO: 1889	PEgRNA (TGG;TG PAM)
1892	SEQ ID NO: 1892	PEgRNA (TGG;TG PAM)
1897	SEQ ID NO: 1897	PEgRNA (TGG;TG PAM)
1898	SEQ ID NO: 1898	PEgRNA (TGG;TG PAM)
1899	SEQ ID NO: 1899	PEgRNA (TGG;TG PAM)
1896	SEQ ID NO: 1896	PEgRNA (TGG;TG PAM)
1893	SEQ ID NO: 1893	PEgRNA (TGG;TG PAM)
1895	SEQ ID NO: 1895	PEgRNA (TGG;TG PAM)
1894	SEQ ID NO: 1894	PEgRNA (TGG;TG PAM)
1900	SEQ ID NO: 1900	PEgRNA (TGG;TG PAM)
1905	SEQ ID NO: 1905	PEgRNA (TGG;TG PAM)
1906	SEQ ID NO: 1906	PEgRNA (TGG;TG PAM)
1902	SEQ ID NO: 1902	PEgRNA (TGG;TG PAM)
1901	SEQ ID NO: 1901	PEgRNA (TGG;TG PAM)
1903	SEQ ID NO: 1903	PEgRNA (TGG;TG PAM)
1904	SEQ ID NO: 1904	PEgRNA (TGG;TG PAM)
1913	SEQ ID NO: 1913	PEgRNA (TGG;TG PAM)
1910	SEQ ID NO: 1910	PEgRNA (TGG;TG PAM)
1907	SEQ ID NO: 1907	PEgRNA (TGG;TG PAM)

Sequence Number	Sequence	Description
1909	SEQ ID NO: 1909	PEgRNA (TGG;TG PAM)
1908	SEQ ID NO: 1908	PEgRNA (TGG;TG PAM)
1911	SEQ ID NO: 1911	PEgRNA (TGG;TG PAM)
1912	SEQ ID NO: 1912	PEgRNA (TGG;TG PAM)
1920	SEQ ID NO: 1920	PEgRNA (TGG;TG PAM)
1919	SEQ ID NO: 1919	PEgRNA (TGG;TG PAM)
1918	SEQ ID NO: 1918	PEgRNA (TGG;TG PAM)
1916	SEQ ID NO: 1916	PEgRNA (TGG;TG PAM)
1915	SEQ ID NO: 1915	PEgRNA (TGG;TG PAM)
1914	SEQ ID NO: 1914	PEgRNA (TGG;TG PAM)
1917	SEQ ID NO: 1917	PEgRNA (TGG;TG PAM)
1921	SEQ ID NO: 1921	PEgRNA (TGG;TG PAM)
1922	SEQ ID NO: 1922	PEgRNA (TGG;TG PAM)
1924	SEQ ID NO: 1924	PEgRNA (TGG;TG PAM)
1923	SEQ ID NO: 1923	PEgRNA (TGG;TG PAM)
1925	SEQ ID NO: 1925	PEgRNA (TGG;TG PAM)
1926	SEQ ID NO: 1926	PEgRNA (TGG;TG PAM)
1927	SEQ ID NO: 1927	PEgRNA (TGG;TG PAM)
1928	SEQ ID NO: 1928	PEgRNA (TGG;TG PAM)
1935	SEQ ID NO: 1935	PEgRNA (TGG;TG PAM)
1934	SEQ ID NO: 1934	PEgRNA (TGG;TG PAM)
1933	SEQ ID NO: 1933	PEgRNA (TGG;TG PAM)

Sequence Number	Sequence	Description
1930	SEQ ID NO: 1930	PEgRNA (TGG;TG PAM)
1932	SEQ ID NO: 1932	PEgRNA (TGG;TG PAM)
1929	SEQ ID NO: 1929	PEgRNA (TGG;TG PAM)
1931	SEQ ID NO: 1931	PEgRNA (TGG;TG PAM)
1937	SEQ ID NO: 1937	PEgRNA (TGG;TG PAM)
1939	SEQ ID NO: 1939	PEgRNA (TGG;TG PAM)
1936	SEQ ID NO: 1936	PEgRNA (TGG;TG PAM)
1940	SEQ ID NO: 1940	PEgRNA (TGG;TG PAM)
1938	SEQ ID NO: 1938	PEgRNA (TGG;TG PAM)
1941	SEQ ID NO: 1941	PEgRNA (TGG;TG PAM)
1942	SEQ ID NO: 1942	PEgRNA (TGG;TG PAM)
1945	SEQ ID NO: 1945	PEgRNA (TGG;TG PAM)
1944	SEQ ID NO: 1944	PEgRNA (TGG;TG PAM)
1943	SEQ ID NO: 1943	PEgRNA (TGG;TG PAM)
1946	SEQ ID NO: 1946	PEgRNA (TGG;TG PAM)
1947	SEQ ID NO: 1947	PEgRNA (TGG;TG PAM)
1948	SEQ ID NO: 1948	PEgRNA (TGG;TG PAM)
1949	SEQ ID NO: 1949	PEgRNA (TGG;TG PAM)
1951	SEQ ID NO: 1951	PEgRNA (TGG;TG PAM)
1950	SEQ ID NO: 1950	PEgRNA (TGG;TG PAM)
1952	SEQ ID NO: 1952	PEgRNA (TGG;TG PAM)
1953	SEQ ID NO: 1953	PEgRNA (TGG;TG PAM)

Sequence Number	Sequence	Description
1954	SEQ ID NO: 1954	PEgRNA (TGG;TG PAM)
1955	SEQ ID NO: 1955	PEgRNA (TGG;TG PAM)
1956	SEQ ID NO: 1956	PEgRNA (TGG;TG PAM)
1957	SEQ ID NO: 1957	PEgRNA (TGG;TG PAM)
1958	SEQ ID NO: 1958	ngRNA (TG;TGG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG;AGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
1525	SEQ ID NO: 1525	ngRNA (AG;AGG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG;AGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
1959	SEQ ID NO: 1959	ngRNA (TG;TGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
1528	SEQ ID NO: 1528	ngRNA (AG;AGG PAM)

Table 10

Sequence Number	Sequence	Description
1960	SEQ ID NO: 1960	PEgRNA spacer (TGG;TG PAM)
1961	SEQ ID NO: 1961	PEgRNA spacer (TGG;TG PAM)
1962	SEQ ID NO: 1962	PEgRNA spacer (TGG;TG PAM)
1963	SEQ ID NO: 1963	PEgRNA spacer (TGG;TG PAM)
1964	SEQ ID NO: 1964	PEgRNA spacer (TGG;TG PAM)
1965	SEQ ID NO: 1965	PEgRNA spacer (TGG;TG PAM)
1966	SEQ ID NO: 1966	PEgRNA spacer (TGG;TG PAM)
1967	TTA	PBS
1968	TTAG	PBS
1969	TTAGA	PBS
1970	TTAGAA	PBS
1971	TTAGAA T	PBS
1972	TTAGAA TT	PBS
1973	TTAGAA TTA	PBS
1974	SEQ ID NO: 1974	PBS
1975	SEQ ID NO: 1975	PBS
1976	SEQ ID NO: 1976	PBS
1977	SEQ ID NO: 1977	PBS
1978	SEQ ID NO: 1978	PBS
1979	SEQ ID NO: 1979	PBS
1980	SEQ ID NO: 1980	PBS
1981	SEQ ID NO: 1981	PBS
1982	SEQ ID NO: 1982	PBS
1983	SEQ ID NO: 1983	PBS
1984	SEQ ID NO: 1984	RTT
1985	SEQ ID NO: 1985	RTT
1986	SEQ ID NO: 1986	RTT
1987	SEQ ID NO: 1987	RTT
1988	SEQ ID NO: 1988	RTT
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
1991	SEQ ID NO: 1991	PE3 ngRNA spacer (TG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)

Sequence Number	Sequence	Description
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
2007	SEQ ID NO: 2007	PE3 ngRNA spacer (TG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
2009	SEQ ID NO: 2009	PE3 ngRNA spacer (AG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)

Table 11

Sequence Number	Sequence	Description
2017	SEQ ID NO: 2017	PEgRNA spacer (AGG;AG PAM)
2018	SEQ ID NO: 2018	PEgRNA spacer
		(AGG;AG PAM)
2019	SEQ ID NO: 2019	PEgRNA spacer (AGG;AG PAM)
2020	SEQ ID NO: 2020	PEgRNA spacer (AGG;AG PAM)
2021	SEQ ID NO: 2021	PEgRNA spacer (AGG;AG PAM)
2022	SEQ ID NO: 2022	PEgRNA spacer (AGG;AG PAM)
2023	SEQ ID NO: 2023	PEgRNA spacer (AGG;AG PAM)
2024	AAC	PBS
2025	AACA	PBS
2026	AACAC	PBS
2027	AACACC	PBS
2028	AACACC A	PBS
2029	AACACC AT	PBS
2030	AACACC ATG	PBS
2031	SEQ ID NO: 2031	PBS
2032	SEQ ID NO: 2032	PBS
2033	SEQ ID NO: 2033	PBS
2034	SEQ ID NO: 2034	PBS
2035	SEQ ID NO: 2035	PBS
2036	SEQ ID NO: 2036	PBS
2037	SEQ ID NO: 2037	PBS
2038	SEQ ID NO: 2038	PBS
2039	SEQ ID NO: 2039	PBS
2040	SEQ ID NO: 2040	PBS
2041	SEQ ID NO: 2041	RTT
2042	SEQ ID NO: 2042	RTT
2043	SEQ ID NO: 2043	RTT
2044	SEQ ID NO: 2044	RTT
2045	SEQ ID NO: 2045	RTT
2046	SEQ ID NO: 2046	RTT
2047	SEQ ID NO: 2047	RTT
2048	SEQ ID NO: 2048	RTT
2049	SEQ ID NO: 2049	RTT
2050	SEQ ID NO: 2050	RTT
2051	SEQ ID NO: 2051	RTT
2052	SEQ ID NO: 2052	RTT
2053	SEQ ID NO: 2053	RTT
2054	SEQ ID NO: 2054	RTT
2055	SEQ ID NO: 2055	RTT
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
1991	SEQ ID NO: 1991	PE3 ngRNA spacer (TG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(AG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)

Table 12

Sequence Number	Sequence	Description
2063	SEQ ID NO: 2063	PEgRNA spacer (AGG;AG PAM)
2064	SEQ ID NO: 2064	PEgRNA spacer (AGG;AG PAM)
2065	SEQ ID NO: 2065	PEgRNA spacer (AGG;AG PAM)
2066	SEQ ID NO: 2066	PEgRNA spacer (AGG;AG PAM)
2067	SEQ ID NO: 2067	PEgRNA spacer (AGG;AG PAM)
2068	SEQ ID NO: 2068	PEgRNA spacer (AGG;AG PAM)
2069	SEQ ID NO: 2069	PEgRNA spacer (AGG;AG PAM)
2070	GTA	PBS
2071	GTAA	PBS
2072	GTAAA	PBS
2073	GTAAAC	PBS
2074	GTAAACA	PBS
2075	GTAAACAA	PBS
2076	GTAAACAAA	PBS
2077	SEQ ID NO: 2077	PBS
2078	SEQ ID NO: 2078	PBS
2079	SEQ ID NO: 2079	PBS
2080	SEQ ID NO: 2080	PBS
2081	SEQ ID NO: 2081	PBS
2082	SEQ ID NO: 2082	PBS
2083	SEQ ID NO: 2083	PBS
2084	SEQ ID NO: 2084	PBS
2085	SEQ ID NO: 2085	PBS
2086	SEQ ID NO: 2086	PBS
2087	SEQ ID NO: 2087	RTT
2088	SEQ ID NO: 2088	RTT
2089	SEQ ID NO: 2089	RTT
2090	SEQ ID NO: 2090	RTT
2091	SEQ ID NO: 2091	RTT
2092	SEQ ID NO: 2092	RTT
2093	SEQ ID NO: 2093	RTT
2094	SEQ ID NO: 2094	RTT
2095	SEQ ID NO: 2095	RTT
2096	SEQ ID NO: 2096	RTT
2097	SEQ ID NO: 2097	RTT
2098	SEQ ID NO: 2098	RTT
2099	SEQ ID NO: 2099	RTT
2100	SEQ ID NO: 2100	RTT
2101	SEQ ID NO: 2101	RTT

Sequence Number	Sequence	Description
2102	SEQ ID NO: 2102	RTT
2103	SEQ ID NO: 2103	RTT
2104	SEQ ID NO: 2104	RTT
2105	SEQ ID NO: 2105	RTT
2106	SEQ ID NO: 2106	RTT
2107	SEQ ID NO: 2107	RTT
2108	SEQ ID NO: 2108	RTT
2109	SEQ ID NO: 2109	RTT
2110	SEQ ID NO: 2110	RTT
2111	SEQ ID NO: 2111	RTT
2112	SEQ ID NO: 2112	RTT
2113	SEQ ID NO: 2113	RTT
2114	SEQ ID NO: 2114	RTT
2115	SEQ ID NO: 2115	RTT
2116	SEQ ID NO: 2116	RTT
2117	SEQ ID NO: 2117	RTT
2118	SEQ ID NO: 2118	RTT
2119	SEQ ID NO: 2119	RTT
2120	SEQ ID NO: 2120	RTT
2121	SEQ ID NO: 2121	RTT
2122	SEQ ID NO: 2122	RTT
2123	SEQ ID NO: 2123	RTT
2124	SEQ ID NO: 2124	RTT
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer
		(AG;AGG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)

Sequence Number	Sequence	Description
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)

Table 13

Sequence Number	Sequence	Description
2128	SEQ ID NO: 2128	PEgRNA spacer (AG;AGG PAM)
2129	SEQ ID NO: 2129	PEgRNA spacer (AG;AGG PAM)
2130	SEQ ID NO: 2130	PEgRNA spacer (AG;AGG PAM)
2131	SEQ ID NO: 2131	PEgRNA spacer (AG;AGG PAM)
2132	SEQ ID NO: 2132	PEgRNA spacer (AG;AGG PAM)
2133	SEQ ID NO: 2133	PEgRNA spacer (AG;AGG PAM)
2134	SEQ ID NO: 2134	PEgRNA spacer (AG;AGG PAM)
2135	GCT	PBS
2136	GCTG	PBS
2137	GCTGG	PBS
2138	GCTGGA	PBS
2139	GCTGGAA	PBS
2140	GCTGGAAC	PBS
2141	GCTGGAACA	PBS
2142	SEQ ID NO: 2142	PBS
2143	SEQ ID NO: 2143	PBS
2144	SEQ ID NO: 2144	PBS
2145	SEQ ID NO: 2145	PBS
2146	SEQ ID NO: 2146	PBS
2147	SEQ ID NO: 2147	PBS
2148	SEQ ID NO: 2148	PBS
2149	SEQ ID NO: 2149	PBS
2150	SEQ ID NO: 2150	PBS
2151	SEQ ID NO: 2151	PBS
2152	SEQ ID NO: 2152	RTT*62 (PAM silencing)
2153	SEQ ID NO: 2153	RTT*61 (PAM silencing)
2154	SEQ ID NO: 2154	RTT*59 (PAM silencing)
2155	SEQ ID NO: 2155	RTT*57 (PAM silencing)
2156	SEQ ID NO: 2156	RTT*64 (PAM silencing)
2157	SEQ ID NO: 2157	RTT*63 (PAM silencing)
2158	SEQ ID NO: 2158	RTT*66 (PAM silencing)
2159	SEQ ID NO: 2159	RTT*58 (PAM silencing)
2160	SEQ ID NO: 2160	RTT*60 (PAM silencing)
2161	SEQ ID NO: 2161	RTT*65 (PAM silencing)
2162	SEQ ID NO: 2162	RTT
2163	SEQ ID NO: 2163	RTT*67 (PAM silencing)
2164	SEQ ID NO: 2164	RTT*64 (PAM silencing)
2165	SEQ ID NO: 2165	RTT*58 (PAM silencing)
2166	SEQ ID NO: 2166	RTT*59 (PAM silencing)
2167	SEQ ID NO: 2167	RTT*57 (PAM silencing)
2168	SEQ ID NO: 2168	RTT*62 (PAM silencing)
2169	SEQ ID NO: 2169	RTT*67 (PAM silencing)
2170	SEQ ID NO: 2170	RTT*66 (PAM silencing)
2171	SEQ ID NO: 2171	RTT*60 (PAM silencing)
2172	SEQ ID NO: 2172	RTT*65 (PAM silencing)
2173	SEQ ID NO: 2173	RTT*61 (PAM silencing)
2174	SEQ ID NO: 2174	RTT*63 (PAM silencing)
2175	SEQ ID NO: 2175	RTT
2176	SEQ ID NO: 2176	RTT*62 (PAM silencing)
2177	SEQ ID NO: 2177	RTT*59 (PAM silencing)
2178	SEQ ID NO: 2178	RTT*66 (PAM silencing)
2179	SEQ ID NO: 2179	RTT*61 (PAM silencing)
2180	SEQ ID NO: 2180	RTT
2181	SEQ ID NO: 2181	RTT*65 (PAM silencing)
2182	SEQ ID NO: 2182	RTT*57 (PAM silencing)
2183	SEQ ID NO: 2183	RTT*58 (PAM silencing)
2184	SEQ ID NO: 2184	RTT*67 (PAM silencing)
2185	SEQ ID NO: 2185	RTT*63 (PAM silencing)
2186	SEQ ID NO: 2186	RTT*60 (PAM silencing)
2187	SEQ ID NO: 2187	RTT*64 (PAM silencing)
2188	SEQ ID NO: 2188	RTT*63 (PAM silencing)
2189	SEQ ID NO: 2189	RTT*59 (PAM silencing)
2190	SEQ ID NO: 2190	RTT*62 (PAM silencing)
2191	SEQ ID NO: 2191	RTT
2192	SEQ ID NO: 2192	RTT*67 (PAM silencing)
2193	SEQ ID NO: 2193	RTT*64 (PAM silencing)
2194	SEQ ID NO: 2194	RTT*58 (PAM silencing)

Sequence Number	Sequence	Description
2195	SEQ ID NO: 2195	RTT*57 (PAM silencing)
2196	SEQ ID NO: 2196	RTT*60 (PAM silencing)
2197	SEQ ID NO: 2197	RTT*65 (PAM silencing)
2198	SEQ ID NO: 2198	RTT*61 (PAM silencing)
2199	SEQ ID NO: 2199	RTT*66 (PAM silencing)
2200	SEQ ID NO: 2200	RTT*62 (PAM silencing)
2201	SEQ ID NO: 2201	RTT*58 (PAM silencing)
2202	SEQ ID NO: 2202	RTT*61 (PAM silencing)
2203	SEQ ID NO: 2203	RTT*65 (PAM silencing)
2204	SEQ ID NO: 2204	RTT*59 (PAM silencing)
2205	SEQ ID NO: 2205	RTT*63 (PAM silencing)
2206	SEQ ID NO: 2206	RTT*60 (PAM silencing)
2207	SEQ ID NO: 2207	RTT*66 (PAM silencing)
2208	SEQ ID NO: 2208	RTT*67 (PAM silencing)
2209	SEQ ID NO: 2209	RTT
2210	SEQ ID NO: 2210	RTT*64 (PAM silencing)
2211	SEQ ID NO: 2211	RTT*57 (PAM silencing)
2212	SEQ ID NO: 2212	RTT*63 (PAM silencing)
2213	SEQ ID NO: 2213	RTT*65 (PAM silencing)
2214	SEQ ID NO: 2214	RTT*60 (PAM silencing)
2215	SEQ ID NO: 2215	RTT*58 (PAM silencing)
2216	SEQ ID NO: 2216	RTT*57 (PAM silencing)
2217	SEQ ID NO: 2217	RTT*64 (PAM silencing)
2218	SEQ ID NO: 2218	RTT*59 (PAM silencing)
2219	SEQ ID NO: 2219	RTT*66 (PAM silencing)
2220	SEQ ID NO: 2220	RTT*67 (PAM silencing)
2221	SEQ ID NO: 2221	RTT*62 (PAM silencing)
2222	SEQ ID NO: 2222	RTT*61 (PAM silencing)
2223	SEQ ID NO: 2223	RTT
2224	SEQ ID NO: 2224	RTT*60 (PAM silencing)
2225	SEQ ID NO: 2225	RTT*62 (PAM silencing)
2226	SEQ ID NO: 2226	RTT
2227	SEQ ID NO: 2227	RTT*57 (PAM silencing)
2228	SEQ ID NO: 2228	RTT*64 (PAM silencing)
2229	SEQ ID NO: 2229	RTT*61 (PAM silencing)
2230	SEQ ID NO: 2230	RTT*66 (PAM silencing)
2231	SEQ ID NO: 2231	RTT*65 (PAM silencing)
2232	SEQ ID NO: 2232	RTT*59 (PAM silencing)
2233	SEQ ID NO: 2233	RTT*63 (PAM silencing)
2234	SEQ ID NO: 2234	RTT*67 (PAM silencing)
2235	SEQ ID NO: 2235	RTT*58 (PAM silencing)
2236	SEQ ID NO: 2236	RTT*61 (PAM silencing)
2237	SEQ ID NO: 2237	RTT*63 (PAM silencing)
2238	SEQ ID NO: 2238	RTT
2239	SEQ ID NO: 2239	RTT*66 (PAM silencing)
2240	SEQ ID NO: 2240	RTT*58 (PAM silencing)
2241	SEQ ID NO: 2241	RTT*64 (PAM silencing)
2242	SEQ ID NO: 2242	RTT*59 (PAM silencing)
2243	SEQ ID NO: 2243	RTT*60 (PAM silencing)
2244	SEQ ID NO: 2244	RTT*62 (PAM silencing)
2245	SEQ ID NO: 2245	RTT*57 (PAM silencing)
2246	SEQ ID NO: 2246	RTT*65 (PAM silencing)
2247	SEQ ID NO: 2247	RTT*67 (PAM silencing)
2248	SEQ ID NO: 2248	RTT*66 (PAM silencing)
2249	SEQ ID NO: 2249	RTT*58 (PAM silencing)
2250	SEQ ID NO: 2250	RTT*59 (PAM silencing)
2251	SEQ ID NO: 2251	RTT*64 (PAM silencing)
2252	SEQ ID NO: 2252	RTT*60 (PAM silencing)
2253	SEQ ID NO: 2253	RTT*65 (PAM silencing)
2254	SEQ ID NO: 2254	RTT*57 (PAM silencing)
2255	SEQ ID NO: 2255	RTT*62 (PAM silencing)
2256	SEQ ID NO: 2256	RTT
2257	SEQ ID NO: 2257	RTT*67 (PAM silencing)
2258	SEQ ID NO: 2258	RTT*63 (PAM silencing)
2259	SEQ ID NO: 2259	RTT*61 (PAM silencing)
2260	SEQ ID NO: 2260	RTT*57 (PAM silencing)
2261	SEQ ID NO: 2261	RTT*66 (PAM silencing)

Sequence Number	Sequence	Description
2262	SEQ ID NO: 2262	RTT*62 (PAM silencing)
2263	SEQ ID NO: 2263	RTT
2264	SEQ ID NO: 2264	RTT*61 (PAM silencing)
2265	SEQ ID NO: 2265	RTT*63 (PAM silencing)
2266	SEQ ID NO: 2266	RTT*64 (PAM silencing)
2267	SEQ ID NO: 2267	RTT*65 (PAM silencing)
2268	SEQ ID NO: 2268	RTT*60 (PAM silencing)
2269	SEQ ID NO: 2269	RTT*58 (PAM silencing)
2270	SEQ ID NO: 2270	RTT*67 (PAM silencing)
2271	SEQ ID NO: 2271	RTT*59 (PAM silencing)
2272	SEQ ID NO: 2272	RTT*62 (PAM silencing)
2273	SEQ ID NO: 2273	RTT*65 (PAM silencing)
2274	SEQ ID NO: 2274	RTT*63 (PAM silencing)
2275	SEQ ID NO: 2275	RTT*66 (PAM silencing)
2276	SEQ ID NO: 2276	RTT*61 (PAM silencing)
2277	SEQ ID NO: 2277	RTT*58 (PAM silencing)
2278	SEQ ID NO: 2278	RTT*67 (PAM silencing)
2279	SEQ ID NO: 2279	RTT
2280	SEQ ID NO: 2280	RTT*59 (PAM silencing)
2281	SEQ ID NO: 2281	RTT*60 (PAM silencing)
2282	SEQ ID NO: 2282	RTT*57 (PAM silencing)
2283	SEQ ID NO: 2283	RTT*64 (PAM silencing)
2284	SEQ ID NO: 2284	RTT*61 (PAM silencing)
2285	SEQ ID NO: 2285	RTT*58 (PAM silencing)
2286	SEQ ID NO: 2286	RTT*67 (PAM silencing)
2287	SEQ ID NO: 2287	RTT*64 (PAM silencing)
2288	SEQ ID NO: 2288	RTT*59 (PAM silencing)
2289	SEQ ID NO: 2289	RTT*65 (PAM silencing)
2290	SEQ ID NO: 2290	RTT*57 (PAM silencing)
2291	SEQ ID NO: 2291	RTT*63 (PAM silencing)
2292	SEQ ID NO: 2292	RTT*62 (PAM silencing)
2293	SEQ ID NO: 2293	RTT*60 (PAM silencing)
2294	SEQ ID NO: 2294	RTT*66 (PAM silencing)
2295	SEQ ID NO: 2295	RTT
2296	SEQ ID NO: 2296	RTT*64 (PAM silencing)
2297	SEQ ID NO: 2297	RTT*67 (PAM silencing)
2298	SEQ ID NO: 2298	RTT*57 (PAM silencing)
2299	SEQ ID NO: 2299	RTT*60 (PAM silencing)
2300	SEQ ID NO: 2300	RTT*63 (PAM silencing)
2301	SEQ ID NO: 2301	RTT*66 (PAM silencing)
2302	SEQ ID NO: 2302	RTT*58 (PAM silencing)
2303	SEQ ID NO: 2303	RTT*59 (PAM silencing)
2304	SEQ ID NO: 2304	RTT*65 (PAM silencing)
2305	SEQ ID NO: 2305	RTT*62 (PAM silencing)
2306	SEQ ID NO: 2306	RTT*61 (PAM silencing)
2307	SEQ ID NO: 2307	RTT
2308	SEQ ID NO: 2308	RTT*64 (PAM silencing)
2309	SEQ ID NO: 2309	RTT*62 (PAM silencing)
2310	SEQ ID NO: 2310	RTT*63 (PAM silencing)
2311	SEQ ID NO: 2311	RTT*59 (PAM silencing)
2312	SEQ ID NO: 2312	RTT*66 (PAM silencing)
2313	SEQ ID NO: 2313	RTT
2314	SEQ ID NO: 2314	RTT*60 (PAM silencing)
2315	SEQ ID NO: 2315	RTT*67 (PAM silencing)
2316	SEQ ID NO: 2316	RTT*61 (PAM silencing)
2317	SEQ ID NO: 2317	RTT*65 (PAM silencing)
2318	SEQ ID NO: 2318	RTT*58 (PAM silencing)
2319	SEQ ID NO: 2319	RTT*57 (PAM silencing)
2320	SEQ ID NO: 2320	RTT*67 (PAM silencing)
2321	SEQ ID NO: 2321	RTT*62 (PAM silencing)
2322	SEQ ID NO: 2322	RTT*61 (PAM silencing)
2323	SEQ ID NO: 2323	RTT*66 (PAM silencing)
2324	SEQ ID NO: 2324	RTT
2325	SEQ ID NO: 2325	RTT*59 (PAM silencing)
2326	SEQ ID NO: 2326	RTT*58 (PAM silencing)
2327	SEQ ID NO: 2327	RTT*64 (PAM silencing)
2328	SEQ ID NO: 2328	RTT*65 (PAM silencing)
2329	SEQ ID NO: 2329	RTT*60 (PAM silencing)
2330	SEQ ID NO: 2330	RTT*57 (PAM silencing)

Sequence Number	Sequence	Description
2331	SEQ ID NO: 2331	RTT*63 (PAM silencing)
2332	SEQ ID NO: 2332	RTT*63 (PAM silencing)
2333	SEQ ID NO: 2333	RTT*58 (PAM silencing)
2334	SEQ ID NO: 2334	RTT*66 (PAM silencing)
2335	SEQ ID NO: 2335	RTT*60 (PAM silencing)
2336	SEQ ID NO: 2336	RTT*59 (PAM silencing)
2337	SEQ ID NO: 2337	RTT*57 (PAM silencing)
2338	SEQ ID NO: 2338	RTT
2339	SEQ ID NO: 2339	RTT*61 (PAM silencing)
2340	SEQ ID NO: 2340	RTT*62 (PAM silencing)
2341	SEQ ID NO: 2341	RTT*65 (PAM silencing)
2342	SEQ ID NO: 2342	RTT*64 (PAM silencing)
2343	SEQ ID NO: 2343	RTT*67 (PAM silencing)
2344	SEQ ID NO: 2344	RTT*58 (PAM silencing)
2345	SEQ ID NO: 2345	RTT*65 (PAM silencing)
2346	SEQ ID NO: 2346	RTT*62 (PAM silencing)
2347	SEQ ID NO: 2347	RTT*63 (PAM silencing)
2348	SEQ ID NO: 2348	RTT
2349	SEQ ID NO: 2349	RTT*59 (PAM silencing)
2350	SEQ ID NO: 2350	RTT*67 (PAM silencing)
2351	SEQ ID NO: 2351	RTT*64 (PAM silencing)
2352	SEQ ID NO: 2352	RTT*66 (PAM silencing)
2353	SEQ ID NO: 2353	RTT*61 (PAM silencing)
2354	SEQ ID NO: 2354	RTT*57 (PAM silencing)
2355	SEQ ID NO: 2355	RTT*60 (PAM silencing)
2356	SEQ ID NO: 2356	RTT*64 (PAM silencing)
2357	SEQ ID NO: 2357	RTT*63 (PAM silencing)
2358	SEQ ID NO: 2358	RTT*62 (PAM silencing)
2359	SEQ ID NO: 2359	RTT*59 (PAM silencing)
2360	SEQ ID NO: 2360	RTT
2361	SEQ ID NO: 2361	RTT*67 (PAM silencing)
2362	SEQ ID NO: 2362	RTT*60 (PAM silencing)
2363	SEQ ID NO: 2363	RTT*61 (PAM silencing)
2364	SEQ ID NO: 2364	RTT*58 (PAM silencing)
2365	SEQ ID NO: 2365	RTT*66 (PAM silencing)
2366	SEQ ID NO: 2366	RTT*57 (PAM silencing)
2367	SEQ ID NO: 2367	RTT*65 (PAM silencing)
2368	SEQ ID NO: 2368	RTT*67 (PAM silencing)
2369	SEQ ID NO: 2369	RTT*62 (PAM silencing)
2370	SEQ ID NO: 2370	RTT*57 (PAM silencing)
2371	SEQ ID NO: 2371	RTT*58 (PAM silencing)
2372	SEQ ID NO: 2372	RTT
2373	SEQ ID NO: 2373	RTT*66 (PAM silencing)
2374	SEQ ID NO: 2374	RTT*59 (PAM silencing)
2375	SEQ ID NO: 2375	RTT*63 (PAM silencing)
2376	SEQ ID NO: 2376	RTT*61 (PAM silencing)
2377	SEQ ID NO: 2377	RTT*60 (PAM silencing)
2378	SEQ ID NO: 2378	RTT*65 (PAM silencing)
2379	SEQ ID NO: 2379	RTT*64 (PAM silencing)
2380	SEQ ID NO: 2380	RTT
2381	SEQ ID NO: 2381	RTT*63 (PAM silencing)
2382	SEQ ID NO: 2382	RTT*64 (PAM silencing)
2383	SEQ ID NO: 2383	RTT*58 (PAM silencing)
2384	SEQ ID NO: 2384	RTT*61 (PAM silencing)
2385	SEQ ID NO: 2385	RTT*66 (PAM silencing)
2386	SEQ ID NO: 2386	RTT*65 (PAM silencing)
2387	SEQ ID NO: 2387	RTT*57 (PAM silencing)
2388	SEQ ID NO: 2388	RTT*62 (PAM silencing)
2389	SEQ ID NO: 2389	RTT*67 (PAM silencing)
2390	SEQ ID NO: 2390	RTT*60 (PAM silencing)
2391	SEQ ID NO: 2391	RTT*59 (PAM silencing)
2392	SEQ ID NO: 2392	RTT*62 (PAM silencing)
2393	SEQ ID NO: 2393	RTT*64 (PAM silencing)
2394	SEQ ID NO: 2394	RTT
2395	SEQ ID NO: 2395	RTT*61 (PAM silencing)
2396	SEQ ID NO: 2396	RTT*65 (PAM silencing)
2397	SEQ ID NO: 2397	RTT*60 (PAM silencing)
2398	SEQ ID NO: 2398	RTT*67 (PAM silencing)
2399	SEQ ID NO: 2399	RTT*57 (PAM silencing)

Sequence Number	Sequence	Description
2400	SEQ ID NO: 2400	RTT*58 (PAM silencing)
2401	SEQ ID NO: 2401	RTT*59 (PAM silencing)
2402	SEQ ID NO: 2402	RTT*63 (PAM silencing)
2403	SEQ ID NO: 2403	RTT*66 (PAM silencing)
2404	SEQ ID NO: 2404	RTT*64 (PAM silencing)
2405	SEQ ID NO: 2405	RTT*67 (PAM silencing)
2406	SEQ ID NO: 2406	RTT
2407	SEQ ID NO: 2407	RTT*63 (PAM silencing)
2408	SEQ ID NO: 2408	RTT*58 (PAM silencing)
2409	SEQ ID NO: 2409	RTT*65 (PAM silencing)
2410	SEQ ID NO: 2410	RTT*59 (PAM silencing)
2411	SEQ ID NO: 2411	RTT*61 (PAM silencing)
2412	SEQ ID NO: 2412	RTT*66 (PAM silencing)
2413	SEQ ID NO: 2413	RTT*62 (PAM silencing)
2414	SEQ ID NO: 2414	RTT*57 (PAM silencing)
2415	SEQ ID NO: 2415	RTT*60 (PAM silencing)
2416	SEQ ID NO: 2416	RTT*64 (PAM silencing)
2417	SEQ ID NO: 2417	RTT*61 (PAM silencing)
2418	SEQ ID NO: 2418	RTT*58 (PAM silencing)
2419	SEQ ID NO: 2419	RTT*63 (PAM silencing)
2420	SEQ ID NO: 2420	RTT*66 (PAM silencing)
2421	SEQ ID NO: 2421	RTT*57 (PAM silencing)
2422	SEQ ID NO: 2422	RTT*59 (PAM silencing)
2423	SEQ ID NO: 2423	RTT
2424	SEQ ID NO: 2424	RTT*62 (PAM silencing)
2425	SEQ ID NO: 2425	RTT*65 (PAM silencing)
2426	SEQ ID NO: 2426	RTT*67 (PAM silencing)
2427	SEQ ID NO: 2427	RTT*60 (PAM silencing)
2428	SEQ ID NO: 2428	RTT*66 (PAM silencing)
2429	SEQ ID NO: 2429	RTT*63 (PAM silencing)
2430	SEQ ID NO: 2430	RTT*57 (PAM silencing)
2431	SEQ ID NO: 2431	RTT*64 (PAM silencing)
2432	SEQ ID NO: 2432	RTT*60 (PAM silencing)
2433	SEQ ID NO: 2433	RTT*61 (PAM silencing)
2434	SEQ ID NO: 2434	RTT*58 (PAM silencing)
2435	SEQ ID NO: 2435	RTT*67 (PAM silencing)
2436	SEQ ID NO: 2436	RTT
2437	SEQ ID NO: 2437	RTT*62 (PAM silencing)
2438	SEQ ID NO: 2438	RTT*59 (PAM silencing)
2439	SEQ ID NO: 2439	RTT*65 (PAM silencing)
2440	SEQ ID NO: 2440	RTT*59 (PAM silencing)
2441	SEQ ID NO: 2441	RTT*60 (PAM silencing)
2442	SEQ ID NO: 2442	RTT*67 (PAM silencing)
2443	SEQ ID NO: 2443	RTT*62 (PAM silencing)
2444	SEQ ID NO: 2444	RTT*64 (PAM silencing)
2445	SEQ ID NO: 2445	RTT*61 (PAM silencing)
2446	SEQ ID NO: 2446	RTT*66 (PAM silencing)
2447	SEQ ID NO: 2447	RTT
2448	SEQ ID NO: 2448	RTT*63 (PAM silencing)
2449	SEQ ID NO: 2449	RTT*58 (PAM silencing)
2450	SEQ ID NO: 2450	RTT*57 (PAM silencing)
2451	SEQ ID NO: 2451	RTT*65 (PAM silencing)
2452	SEQ ID NO: 2452	RTT*60 (PAM silencing)
2453	SEQ ID NO: 2453	RTT*66 (PAM silencing)
2454	SEQ ID NO: 2454	RTT
2455	SEQ ID NO: 2455	RTT*63 (PAM silencing)
2456	SEQ ID NO: 2456	RTT*65 (PAM silencing)
2457	SEQ ID NO: 2457	RTT*67 (PAM silencing)
2458	SEQ ID NO: 2458	RTT*64 (PAM silencing)
2459	SEQ ID NO: 2459	RTT*62 (PAM silencing)
2460	SEQ ID NO: 2460	RTT*59 (PAM silencing)
2461	SEQ ID NO: 2461	RTT*57 (PAM silencing)
2462	SEQ ID NO: 2462	RTT*61 (PAM silencing)
2463	SEQ ID NO: 2463	RTT*58 (PAM silencing)
2464	SEQ ID NO: 2464	RTT*60 (PAM silencing)
2465	SEQ ID NO: 2465	RTT*67 (PAM silencing)
2466	SEQ ID NO: 2466	RTT*58 (PAM silencing)
2467	SEQ ID NO: 2467	RTT*59 (PAM silencing)

Sequence Number	Sequence	Description
2468	SEQ ID NO: 2468	RTT*57 (PAM silencing)
2469	SEQ ID NO: 2469	RTT
2470	SEQ ID NO: 2470	RTT*61 (PAM silencing)
2471	SEQ ID NO: 2471	RTT*63 (PAM silencing)
2472	SEQ ID NO: 2472	RTT*62 (PAM silencing)
2473	SEQ ID NO: 2473	RTT*66 (PAM silencing)
2474	SEQ ID NO: 2474	RTT*64 (PAM silencing)
2475	SEQ ID NO: 2475	RTT*65 (PAM silencing)
2476	SEQ ID NO: 2476	RTT*60 (PAM silencing)
2477	SEQ ID NO: 2477	RTT*57 (PAM silencing)
2478	SEQ ID NO: 2478	RTT*66 (PAM silencing)
2479	SEQ ID NO: 2479	RTT*61 (PAM silencing)
2480	SEQ ID NO: 2480	RTT*62 (PAM silencing)
2481	SEQ ID NO: 2481	RTT*64 (PAM silencing)
2482	SEQ ID NO: 2482	RTT*59 (PAM silencing)
2483	SEQ ID NO: 2483	RTT*58 (PAM silencing)
2484	SEQ ID NO: 2484	RTT*65 (PAM silencing)
2485	SEQ ID NO: 2485	RTT*67 (PAM silencing)
2486	SEQ ID NO: 2486	RTT*63 (PAM silencing)
2487	SEQ ID NO: 2487	RTT
2488	SEQ ID NO: 2488	RTT*67 (PAM silencing)
2489	SEQ ID NO: 2489	RTT*64 (PAM silencing)
2490	SEQ ID NO: 2490	RTT*60 (PAM silencing)

Sequence Number	Sequence	Description
2491	SEQ ID NO: 2491	RTT*59 (PAM silencing)
2492	SEQ ID NO: 2492	RTT*61 (PAM silencing)
2493	SEQ ID NO: 2493	RTT*58 (PAM silencing)
2494	SEQ ID NO: 2494	RTT
2495	SEQ ID NO: 2495	RTT*66 (PAM silencing)
2496	SEQ ID NO: 2496	RTT*57 (PAM silencing)
2497	SEQ ID NO: 2497	RTT*63 (PAM silencing)
2498	SEQ ID NO: 2498	RTT*65 (PAM silencing)
2499	SEQ ID NO: 2499	RTT*62 (PAM silencing)
2500	SEQ ID NO: 2500	RTT*58 (PAM silencing)
2501	SEQ ID NO: 2501	RTT*65 (PAM silencing)
2502	SEQ ID NO: 2502	RTT*63 (PAM silencing)
2503	SEQ ID NO: 2503	RTT
2504	SEQ ID NO: 2504	RTT*59 (PAM silencing)
2505	SEQ ID NO: 2505	RTT*62 (PAM silencing)
2506	SEQ ID NO: 2506	RTT*67 (PAM silencing)
2511	SEQ ID NO: 2511	RTT*60 (PAM silencing)
2509	SEQ ID NO: 2509	RTT*57 (PAM silencing)
2508	SEQ ID NO: 2508	RTT*61 (PAM silencing)
2507	SEQ ID NO: 2507	RTT*64 (PAM silencing)
2510	SEQ ID NO: 2510	RTT*66 (PAM silencing)
2512	SEQ ID NO: 2512	RTT*65 (PAM silencing)
2513	SEQ ID NO: 2513	RTT*63 (PAM silencing)

Sequence Number	Sequence	Description
2514	SEQ ID NO: 2514	RTT*57 (PAM silencing)
2515	SEQ ID NO: 2515	RTT*58 (PAM silencing)
2516	SEQ ID NO: 2516	RTT*66 (PAM silencing)
2523	SEQ ID NO: 2523	RTT*62 (PAM silencing)
2519	SEQ ID NO: 2519	RTT*64 (PAM silencing)
2520	SEQ ID NO: 2520	RTT*67 (PAM silencing)
2518	SEQ ID NO: 2518	RTT*59 (PAM silencing)
2517	SEQ ID NO: 2517	RTT*61 (PAM silencing)
2521	SEQ ID NO: 2521	RTT*60 (PAM silencing)
2522	SEQ ID NO: 2522	RTT
2524	SEQ ID NO: 2524	RTT*62 (PAM silencing)
2525	SEQ ID NO: 2525	RTT*61 (PAM silencing)
2526	SEQ ID NO: 2526	RTT*64 (PAM silencing)
2527	SEQ ID NO: 2527	RTT*66 (PAM silencing)
2528	SEQ ID NO: 2528	RTT*59 (PAM silencing)
2529	SEQ ID NO: 2529	RTT*65 (PAM silencing)
2530	SEQ ID NO: 2530	RTT*57 (PAM silencing)
2531	SEQ ID NO: 2531	RTT*58 (PAM silencing)
2532	SEQ ID NO: 2532	RTT*63 (PAM silencing)
2533	SEQ ID NO: 2533	RTT
2534	SEQ ID NO: 2534	RTT*60 (PAM silencing)
2535	SEQ ID NO: 2535	RTT*67 (PAM silencing)
2536	SEQ ID NO: 2536	RTT*66 (PAM silencing)

Sequence Number	Sequence	Description
2537	SEQ ID NO: 2537	RTT*59 (PAM silencing)
2538	SEQ ID NO: 2538	RTT*62 (PAM silencing)
2539	SEQ ID NO: 2539	RTT*60 (PAM silencing)
2540	SEQ ID NO: 2540	RTT*65 (PAM silencing)
2541	SEQ ID NO: 2541	RTT*57 (PAM silencing)
2542	SEQ ID NO: 2542	RTT*61 (PAM silencing)
2543	SEQ ID NO: 2543	RTT*64 (PAM silencing)
2544	SEQ ID NO: 2544	RTT*67 (PAM silencing)
2545	SEQ ID NO: 2545	RTT*58 (PAM silencing)
2546	SEQ ID NO: 2546	RTT
2547	SEQ ID NO: 2547	RTT*63 (PAM silencing)
2548	SEQ ID NO: 2548	RTT*58 (PAM silencing)
2549	SEQ ID NO: 2549	RTT*61 (PAM silencing)
2550	SEQ ID NO: 2550	RTT*64 (PAM silencing)
2551	SEQ ID NO: 2551	RTT*63 (PAM silencing)
2552	SEQ ID NO: 2552	RTT*66 (PAM silencing)
2553	SEQ ID NO: 2553	RTT*59 (PAM silencing)
2554	SEQ ID NO: 2554	RTT*62 (PAM silencing)
2555	SEQ ID NO: 2555	RTT*60 (PAM silencing)
2556	SEQ ID NO: 2556	RTT*67 (PAM silencing)
2557	SEQ ID NO: 2557	RTT*65 (PAM silencing)
2558	SEQ ID NO: 2558	RTT*57 (PAM silencing)
2559	SEQ ID NO: 2559	RTT
2560	SEQ ID NO: 2560	RTT*59 (PAM silencing)
2561	SEQ ID NO: 2561	RTT*61 (PAM silencing)
2562	SEQ ID NO: 2562	RTT*66 (PAM silencing)
2563	SEQ ID NO: 2563	RTT*67 (PAM silencing)
2564	SEQ ID NO: 2564	RTT*63 (PAM silencing)
2565	SEQ ID NO: 2565	RTT*58 (PAM silencing)
2566	SEQ ID NO: 2566	RTT*57 (PAM silencing)
2567	SEQ ID NO: 2567	RTT
2568	SEQ ID NO: 2568	RTT*65 (PAM silencing)
2569	SEQ ID NO: 2569	RTT*60 (PAM silencing)
2570	SEQ ID NO: 2570	RTT*62 (PAM silencing)
2571	SEQ ID NO: 2571	RTT*64 (PAM silencing)
2572	SEQ ID NO: 2572	RTT*57 (PAM silencing)
2573	SEQ ID NO: 2573	RTT*60 (PAM silencing)
2574	SEQ ID NO: 2574	RTT*65 (PAM silencing)
2575	SEQ ID NO: 2575	RTT*59 (PAM silencing)
2576	SEQ ID NO: 2576	RTT
2577	SEQ ID NO: 2577	RTT*63 (PAM silencing)
2578	SEQ ID NO: 2578	RTT*67 (PAM silencing)
2579	SEQ ID NO: 2579	RTT*64 (PAM silencing)
2580	SEQ ID NO: 2580	RTT*66 (PAM silencing)
2581	SEQ ID NO: 2581	RTT*61 (PAM silencing)
2582	SEQ ID NO: 2582	RTT*58 (PAM silencing)
2583	SEQ ID NO: 2583	RTT*62 (PAM silencing)
2584	SEQ ID NO: 2584	RTT*63 (PAM silencing)
2585	SEQ ID NO: 2585	RTT*64 (PAM silencing)
2586	SEQ ID NO: 2586	RTT*67 (PAM silencing)
2587	SEQ ID NO: 2587	RTT
2588	SEQ ID NO: 2588	RTT*59 (PAM silencing)
2589	SEQ ID NO: 2589	RTT*62 (PAM silencing)
2590	SEQ ID NO: 2590	RTT*66 (PAM silencing)
2591	SEQ ID NO: 2591	RTT*58 (PAM silencing)
2592	SEQ ID NO: 2592	RTT*61 (PAM silencing)
2593	SEQ ID NO: 2593	RTT*60 (PAM silencing)
2594	SEQ ID NO: 2594	RTT*57 (PAM silencing)
2595	SEQ ID NO: 2595	RTT*65 (PAM silencing)
2596	SEQ ID NO: 2596	RTT*61 (PAM silencing)
2597	SEQ ID NO: 2597	RTT*67 (PAM silencing)
2598	SEQ ID NO: 2598	RTT*65 (PAM silencing)
2599	SEQ ID NO: 2599	RTT*57 (PAM silencing)
2600	SEQ ID NO: 2600	RTT*66 (PAM silencing)
2601	SEQ ID NO: 2601	RTT
2602	SEQ ID NO: 2602	RTT*60 (PAM silencing)
2603	SEQ ID NO: 2603	RTT*59 (PAM silencing)
2604	SEQ ID NO: 2604	RTT*64 (PAM silencing)
2605	SEQ ID NO: 2605	RTT*62 (PAM silencing)

Sequence Number	Sequence	Description
2606	SEQ ID NO: 2606	RTT*58 (PAM silencing)
2607	SEQ ID NO: 2607	RTT*63 (PAM silencing)
2608	SEQ ID NO: 2608	RTT*67 (PAM silencing)
2609	SEQ ID NO: 2609	RTT*66 (PAM silencing)
2610	SEQ ID NO: 2610	RTT*62 (PAM silencing)
2611	SEQ ID NO: 2611	RTT*57 (PAM silencing)
2612	SEQ ID NO: 2612	RTT*59 (PAM silencing)
2613	SEQ ID NO: 2613	RTT*65 (PAM silencing)
2614	SEQ ID NO: 2614	RTT*61 (PAM silencing)
2615	SEQ ID NO: 2615	RTT*58 (PAM silencing)
2616	SEQ ID NO: 2616	RTT*63 (PAM silencing)
2617	SEQ ID NO: 2617	RTT*60 (PAM silencing)
2618	SEQ ID NO: 2618	RTT*64 (PAM silencing)
2619	SEQ ID NO: 2619	RTT
2620	SEQ ID NO: 2620	RTT
2621	SEQ ID NO: 2621	RTT*66 (PAM silencing)
2622	SEQ ID NO: 2622	RTT*58 (PAM silencing)
2623	SEQ ID NO: 2623	RTT*57 (PAM silencing)
2624	SEQ ID NO: 2624	RTT*60 (PAM silencing)
2625	SEQ ID NO: 2625	RTT*61 (PAM silencing)
2626	SEQ ID NO: 2626	RTT*62 (PAM silencing)
2627	SEQ ID NO: 2627	RTT*59 (PAM silencing)
2628	SEQ ID NO: 2628	RTT*65 (PAM silencing)

Sequence Number	Sequence	Description
2629	SEQ ID NO: 2629	RTT*67 (PAM silencing)
2630	SEQ ID NO: 2630	RTT*63 (PAM silencing)
2631	SEQ ID NO: 2631	RTT*64 (PAM silencing)
2632	SEQ ID NO: 2632	RTT*64 (PAM silencing)
2633	SEQ ID NO: 2633	RTT*67 (PAM silencing)
2634	SEQ ID NO: 2634	RTT*62 (PAM silencing)
2635	SEQ ID NO: 2635	RTT*61 (PAM silencing)
2636	SEQ ID NO: 2636	RTT*60 (PAM silencing)
2637	SEQ ID NO: 2637	RTT*66 (PAM silencing)
2638	SEQ ID NO: 2638	RTT
2639	SEQ ID NO: 2639	RTT*58 (PAM silencing)
2640	SEQ ID NO: 2640	RTT*65 (PAM silencing)
2641	SEQ ID NO: 2641	RTT*63 (PAM silencing)
2642	SEQ ID NO: 2642	RTT*59 (PAM silencing)
2643	SEQ ID NO: 2643	RTT*57 (PAM silencing)
2644	SEQ ID NO: 2644	RTT*66 (PAM silencing)
2645	SEQ ID NO: 2645	RTT*67 (PAM silencing)
2646	SEQ ID NO: 2646	RTT*58 (PAM silencing)
2647	SEQ ID NO: 2647	RTT*59 (PAM silencing)
2648	SEQ ID NO: 2648	RTT*61 (PAM silencing)
2649	SEQ ID NO: 2649	RTT*64 (PAM silencing)
2650	SEQ ID NO: 2650	RTT*63 (PAM silencing)

Sequence Number	Sequence	Description
2651	SEQ ID NO: 2651	RTT*57 (PAM silencing)
2652	SEQ ID NO: 2652	RTT
2653	SEQ ID NO: 2653	RTT*65 (PAM silencing)
2654	SEQ ID NO: 2654	RTT*62 (PAM silencing)
2655	SEQ ID NO: 2655	RTT*60 (PAM silencing)
2656	SEQ ID NO: 2656	RTT*60 (PAM silencing)
2657	SEQ ID NO: 2657	RTT*58 (PAM silencing)
2658	SEQ ID NO: 2658	RTT*59 (PAM silencing)
2659	SEQ ID NO: 2659	RTT*61 (PAM silencing)
2660	SEQ ID NO: 2660	RTT*57 (PAM silencing)
2661	SEQ ID NO: 2661	RTT*64 (PAM silencing)
2662	SEQ ID NO: 2662	RTT*66 (PAM silencing)
2663	SEQ ID NO: 2663	RTT*67 (PAM silencing)
2664	SEQ ID NO: 2664	RTT*63 (PAM silencing)
2665	SEQ ID NO: 2665	RTT
2666	SEQ ID NO: 2666	RTT*62 (PAM silencing)
2667	SEQ ID NO: 2667	RTT*65 (PAM silencing)
2668	SEQ ID NO: 2668	RTT*61 (PAM silencing)
2669	SEQ ID NO: 2669	RTT*58 (PAM silencing)
2670	SEQ ID NO: 2670	RTT*63 (PAM silencing)
2671	SEQ ID NO: 2671	RTT
2672	SEQ ID NO: 2672	RTT*67 (PAM silencing)
2673	SEQ ID NO: 2673	RTT*57 (PAM silencing)

Sequence Number	Sequence	Description
2674	SEQ ID NO: 2674	RTT*65 (PAM silencing)
2675	SEQ ID NO: 2675	RTT*62 (PAM silencing)
2676	SEQ ID NO: 2676	RTT*60 (PAM silencing)
2677	SEQ ID NO: 2677	RTT*64 (PAM silencing)
2678	SEQ ID NO: 2678	RTT*59 (PAM silencing)
2679	SEQ ID NO: 2679	RTT*66 (PAM silencing)
2680	SEQ ID NO: 2680	RTT*59 (PAM silencing)
2681	SEQ ID NO: 2681	RTT*58 (PAM silencing)
2682	SEQ ID NO: 2682	RTT
2683	SEQ ID NO: 2683	RTT*62 (PAM silencing)
2684	SEQ ID NO: 2684	RTT*66 (PAM silencing)
2685	SEQ ID NO: 2685	RTT*64 (PAM silencing)
2686	SEQ ID NO: 2686	RTT*63 (PAM silencing)
2687	SEQ ID NO: 2687	RTT*67 (PAM silencing)
2688	SEQ ID NO: 2688	RTT*60 (PAM silencing)
2689	SEQ ID NO: 2689	RTT*61 (PAM silencing)
2690	SEQ ID NO: 2690	RTT*65 (PAM silencing)
2691	SEQ ID NO: 2691	RTT*57 (PAM silencing)
2692	SEQ ID NO: 2692	RTT*60 (PAM silencing)
2693	SEQ ID NO: 2693	RTT*57 (PAM silencing)
2694	SEQ ID NO: 2694	RTT*62 (PAM silencing)
2695	SEQ ID NO: 2695	RTT*67 (PAM silencing)
2696	SEQ ID NO: 2696	RTT*59 (PAM silencing)
2697	SEQ ID NO: 2697	RTT*61 (PAM silencing)
2698	SEQ ID NO: 2698	RTT*58 (PAM silencing)
2699	SEQ ID NO: 2699	RTT*64 (PAM silencing)
2700	SEQ ID NO: 2700	RTT*63 (PAM silencing)
2701	SEQ ID NO: 2701	RTT
2702	SEQ ID NO: 2702	RTT*65 (PAM silencing)
2703	SEQ ID NO: 2703	RTT*66 (PAM silencing)
2704	SEQ ID NO: 2704	RTT*67 (PAM silencing)
2705	SEQ ID NO: 2705	RTT*65 (PAM silencing)
2706	SEQ ID NO: 2706	RTT*62 (PAM silencing)
2707	SEQ ID NO: 2707	RTT*58 (PAM silencing)
2708	SEQ ID NO: 2708	RTT*57 (PAM silencing)
2709	SEQ ID NO: 2709	RTT*59 (PAM silencing)
2710	SEQ ID NO: 2710	RTT*63 (PAM silencing)
2711	SEQ ID NO: 2711	RTT*61 (PAM silencing)
2712	SEQ ID NO: 2712	RTT
2713	SEQ ID NO: 2713	RTT*60 (PAM silencing)
2714	SEQ ID NO: 2714	RTT*64 (PAM silencing)
2715	SEQ ID NO: 2715	RTT*66 (PAM silencing)
2716	SEQ ID NO: 2716	RTT*63 (PAM silencing)
2717	SEQ ID NO: 2717	RTT*62 (PAM silencing)
2718	SEQ ID NO: 2718	RTT*59 (PAM silencing)
2719	SEQ ID NO: 2719	RTT*57 (PAM silencing)
2720	SEQ ID NO: 2720	RTT*66 (PAM silencing)
2721	SEQ ID NO: 2721	RTT*67 (PAM silencing)
2722	SEQ ID NO: 2722	RTT*60 (PAM silencing)
2723	SEQ ID NO: 2723	RTT*64 (PAM silencing)
2724	SEQ ID NO: 2724	RTT
2725	SEQ ID NO: 2725	RTT*58 (PAM silencing)
2726	SEQ ID NO: 2726	RTT*65 (PAM silencing)
2727	SEQ ID NO: 2727	RTT*61 (PAM silencing)
2728	SEQ ID NO: 2728	RTT*57 (PAM silencing)
2729	SEQ ID NO: 2729	RTT*59 (PAM silencing)
2730	SEQ ID NO: 2730	RTT*64 (PAM silencing)
2731	SEQ ID NO: 2731	RTT*65 (PAM silencing)
2732	SEQ ID NO: 2732	RTT
2733	SEQ ID NO: 2733	RTT*66 (PAM silencing)
2734	SEQ ID NO: 2734	RTT*63 (PAM silencing)
2735	SEQ ID NO: 2735	RTT*58 (PAM silencing)
2736	SEQ ID NO: 2736	RTT*61 (PAM silencing)
2737	SEQ ID NO: 2737	RTT*60 (PAM silencing)
2738	SEQ ID NO: 2738	RTT*62 (PAM silencing)
2739	SEQ ID NO: 2739	RTT*67 (PAM silencing)
2740	SEQ ID NO: 2740	RTT*58 (PAM silencing)
2741	SEQ ID NO: 2741	RTT*61 (PAM silencing)

Sequence Number	Sequence	Description
2742	SEQ ID NO: 2742	RTT*67 (PAM silencing)
2743	SEQ ID NO: 2743	RTT*59 (PAM silencing)
2744	SEQ ID NO: 2744	RTT*66 (PAM silencing)
2745	SEQ ID NO: 2745	RTT*64 (PAM silencing)
2746	SEQ ID NO: 2746	RTT*63 (PAM silencing)
2747	SEQ ID NO: 2747	RTT
2748	SEQ ID NO: 2748	RTT*60 (PAM silencing)
2749	SEQ ID NO: 2749	RTT*57 (PAM silencing)
2750	SEQ ID NO: 2750	RTT*62 (PAM silencing)
2751	SEQ ID NO: 2751	RTT*65 (PAM silencing)
2752	SEQ ID NO: 2752	RTT*63 (PAM silencing)
2753	SEQ ID NO: 2753	RTT*64 (PAM silencing)
2754	SEQ ID NO: 2754	RTT*61 (PAM silencing)
2755	SEQ ID NO: 2755	RTT*60 (PAM silencing)
2756	SEQ ID NO: 2756	RTT*65 (PAM silencing)
2757	SEQ ID NO: 2757	RTT*57 (PAM silencing)
2758	SEQ ID NO: 2758	RTT
2759	SEQ ID NO: 2759	RTT*67 (PAM silencing)
2760	SEQ ID NO: 2760	RTT*59 (PAM silencing)
2761	SEQ ID NO: 2761	RTT*66 (PAM silencing)
2762	SEQ ID NO: 2762	RTT*58 (PAM silencing)
2763	SEQ ID NO: 2763	RTT*62 (PAM silencing)
2764	SEQ ID NO: 2764	RTT*64 (PAM silencing)
2765	SEQ ID NO: 2765	RTT
2766	SEQ ID NO: 2766	RTT*58 (PAM silencing)
2767	SEQ ID NO: 2767	RTT*61 (PAM silencing)
2768	SEQ ID NO: 2768	RTT*59 (PAM silencing)
2769	SEQ ID NO: 2769	RTT*65 (PAM silencing)
2770	SEQ ID NO: 2770	RTT*62 (PAM silencing)
2771	SEQ ID NO: 2771	RTT*63 (PAM silencing)
2772	SEQ ID NO: 2772	RTT*57 (PAM silencing)
2773	SEQ ID NO: 2773	RTT*67 (PAM silencing)
2774	SEQ ID NO: 2774	RTT*66 (PAM silencing)
2775	SEQ ID NO: 2775	RTT*60 (PAM silencing)
2776	SEQ ID NO: 2776	RTT*62 (PAM silencing)
2777	SEQ ID NO: 2777	RTT*66 (PAM silencing)
2778	SEQ ID NO: 2778	RTT*65 (PAM silencing)
2779	SEQ ID NO: 2779	RTT*59 (PAM silencing)
2780	SEQ ID NO: 2780	RTT*63 (PAM silencing)
2781	SEQ ID NO: 2781	RTT*61 (PAM silencing)
2782	SEQ ID NO: 2782	RTT*60 (PAM silencing)
2783	SEQ ID NO: 2783	RTT*64 (PAM silencing)
2784	SEQ ID NO: 2784	RTT*58 (PAM silencing)
2785	SEQ ID NO: 2785	RTT
2786	SEQ ID NO: 2786	RTT*67 (PAM silencing)
2787	SEQ ID NO: 2787	RTT*57 (PAM silencing)
2788	SEQ ID NO: 2788	RTT*67 (PAM silencing)
2789	SEQ ID NO: 2789	RTT*58 (PAM silencing)
2790	SEQ ID NO: 2790	RTT*61 (PAM silencing)
2791	SEQ ID NO: 2791	RTT*57 (PAM silencing)
2792	SEQ ID NO: 2792	RTT*66 (PAM silencing)
2793	SEQ ID NO: 2793	RTT*60 (PAM silencing)
2794	SEQ ID NO: 2794	RTT*65 (PAM silencing)
2795	SEQ ID NO: 2795	RTT*59 (PAM silencing)
2796	SEQ ID NO: 2796	RTT*63 (PAM silencing)
2797	SEQ ID NO: 2797	RTT*62 (PAM silencing)
2798	SEQ ID NO: 2798	RTT
2799	SEQ ID NO: 2799	RTT*64 (PAM silencing)
2800	SEQ ID NO: 2800	RTT*60 (PAM silencing)
2801	SEQ ID NO: 2801	RTT*58 (PAM silencing)
2802	SEQ ID NO: 2802	RTT*65 (PAM silencing)
2803	SEQ ID NO: 2803	RTT*61 (PAM silencing)
2804	SEQ ID NO: 2804	RTT
2805	SEQ ID NO: 2805	RTT*66 (PAM silencing)
2806	SEQ ID NO: 2806	RTT*62 (PAM silencing)
2807	SEQ ID NO: 2807	RTT*63 (PAM silencing)
2808	SEQ ID NO: 2808	RTT*57 (PAM silencing)
2809	SEQ ID NO: 2809	RTT*64 (PAM silencing)
2810	SEQ ID NO: 2810	RTT*59 (PAM silencing)

Sequence Number	Sequence	Description
2811	SEQ ID NO: 2811	RTT*67 (PAM silencing)
2812	SEQ ID NO: 2812	RTT*65 (PAM silencing)
2813	SEQ ID NO: 2813	RTT*61 (PAM silencing)
2814	SEQ ID NO: 2814	RTT
2815	SEQ ID NO: 2815	RTT*63 (PAM silencing)
2816	SEQ ID NO: 2816	RTT*62 (PAM silencing)
2817	SEQ ID NO: 2817	RTT*58 (PAM silencing)
2818	SEQ ID NO: 2818	RTT*60 (PAM silencing)
2819	SEQ ID NO: 2819	RTT*67 (PAM silencing)
2820	SEQ ID NO: 2820	RTT*64 (PAM silencing)
2821	SEQ ID NO: 2821	RTT*59 (PAM silencing)
2822	SEQ ID NO: 2822	RTT*57 (PAM silencing)
2823	SEQ ID NO: 2823	RTT*66 (PAM silencing)
2824	SEQ ID NO: 2824	RTT*65 (PAM silencing)
2825	SEQ ID NO: 2825	RTT
2826	SEQ ID NO: 2826	RTT*67 (PAM silencing)
2827	SEQ ID NO: 2827	RTT*57 (PAM silencing)
2828	SEQ ID NO: 2828	RTT*59 (PAM silencing)
2829	SEQ ID NO: 2829	RTT*58 (PAM silencing)
2830	SEQ ID NO: 2830	RTT*66 (PAM silencing)
2831	SEQ ID NO: 2831	RTT*62 (PAM silencing)
2832	SEQ ID NO: 2832	RTT*60 (PAM silencing)
2833	SEQ ID NO: 2833	RTT*63 (PAM silencing)
2834	SEQ ID NO: 2834	RTT*61 (PAM silencing)
2835	SEQ ID NO: 2835	RTT*64 (PAM silencing)
2836	SEQ ID NO: 2836	RTT*57 (PAM silencing)
2837	SEQ ID NO: 2837	RTT*64 (PAM silencing)
2838	SEQ ID NO: 2838	RTT*58 (PAM silencing)
2839	SEQ ID NO: 2839	RTT
2840	SEQ ID NO: 2840	RTT*61 (PAM silencing)
2841	SEQ ID NO: 2841	RTT*59 (PAM silencing)
2842	SEQ ID NO: 2842	RTT*63 (PAM silencing)
2843	SEQ ID NO: 2843	RTT*67 (PAM silencing)
2844	SEQ ID NO: 2844	RTT*62 (PAM silencing)
2845	SEQ ID NO: 2845	RTT*66 (PAM silencing)
2846	SEQ ID NO: 2846	RTT*65 (PAM silencing)
2847	SEQ ID NO: 2847	RTT*60 (PAM silencing)
2848	SEQ ID NO: 2848	RTT*66 (PAM silencing)
2849	SEQ ID NO: 2849	RTT*60 (PAM silencing)
2850	SEQ ID NO: 2850	RTT*63 (PAM silencing)
2851	SEQ ID NO: 2851	RTT*57 (PAM silencing)
2852	SEQ ID NO: 2852	RTT*58 (PAM silencing)
2853	SEQ ID NO: 2853	RTT*67 (PAM silencing)
2854	SEQ ID NO: 2854	RTT*59 (PAM silencing)
2855	SEQ ID NO: 2855	RTT*64 (PAM silencing)
2856	SEQ ID NO: 2856	RTT*65 (PAM silencing)
2857	SEQ ID NO: 2857	RTT*61 (PAM silencing)
2858	SEQ ID NO: 2858	RTT
2859	SEQ ID NO: 2859	RTT*62 (PAM silencing)
2860	SEQ ID NO: 2860	RTT*57 (PAM silencing)
2861	SEQ ID NO: 2861	RTT*67 (PAM silencing)
2862	SEQ ID NO: 2862	RTT*64 (PAM silencing)
2863	SEQ ID NO: 2863	RTT*60 (PAM silencing)
2864	SEQ ID NO: 2864	RTT*58 (PAM silencing)
2865	SEQ ID NO: 2865	RTT
2866	SEQ ID NO: 2866	RTT*66 (PAM silencing)
2867	SEQ ID NO: 2867	RTT*63 (PAM silencing)
2868	SEQ ID NO: 2868	RTT*65 (PAM silencing)
2869	SEQ ID NO: 2869	RTT*61 (PAM silencing)
2870	SEQ ID NO: 2870	RTT*62 (PAM silencing)
2871	SEQ ID NO: 2871	RTT*59 (PAM silencing)
2872	SEQ ID NO: 2872	RTT*62 (PAM silencing)
2873	SEQ ID NO: 2873	RTT*63 (PAM silencing)
2874	SEQ ID NO: 2874	RTT*59 (PAM silencing)
2875	SEQ ID NO: 2875	RTT
2876	SEQ ID NO: 2876	RTT*65 (PAM silencing)
2877	SEQ ID NO: 2877	RTT*60 (PAM silencing)
2878	SEQ ID NO: 2878	RTT*57 (PAM silencing)

Sequence Number	Sequence	Description
2879	SEQ ID NO: 2879	RTT*58 (PAM silencing)
2880	SEQ ID NO: 2880	RTT*64 (PAM silencing)
2881	SEQ ID NO: 2881	RTT*66 (PAM silencing)
2882	SEQ ID NO: 2882	RTT*67 (PAM silencing)
2883	SEQ ID NO: 2883	RTT*61 (PAM silencing)
2884	SEQ ID NO: 2884	RTT*67 (PAM silencing)
2885	SEQ ID NO: 2885	RTT*61 (PAM silencing)
2886	SEQ ID NO: 2886	RTT*64 (PAM silencing)
2887	SEQ ID NO: 2887	RTT
2888	SEQ ID NO: 2888	RTT*59 (PAM silencing)
2889	SEQ ID NO: 2889	RTT*66 (PAM silencing)
2890	SEQ ID NO: 2890	RTT*60 (PAM silencing)
2891	SEQ ID NO: 2891	RTT*62 (PAM silencing)
2892	SEQ ID NO: 2892	RTT*63 (PAM silencing)
2893	SEQ ID NO: 2893	RTT*65 (PAM silencing)
2894	SEQ ID NO: 2894	RTT*58 (PAM silencing)
2895	SEQ ID NO: 2895	RTT*57 (PAM silencing)
2896	SEQ ID NO: 2896	RTT*64 (PAM silencing)
2897	SEQ ID NO: 2897	RTT*59 (PAM silencing)
2898	SEQ ID NO: 2898	RTT*57 (PAM silencing)
2899	SEQ ID NO: 2899	RTT*65 (PAM silencing)
2900	SEQ ID NO: 2900	RTT*61 (PAM silencing)

Sequence Number	Sequence	Description
2901	SEQ ID NO: 2901	RTT*66 (PAM silencing)
2902	SEQ ID NO: 2902	RTT*58 (PAM silencing)
2903	SEQ ID NO: 2903	RTT*62 (PAM silencing)
2904	SEQ ID NO: 2904	RTT*67 (PAM silencing)
2905	SEQ ID NO: 2905	RTT*63 (PAM silencing)
2906	SEQ ID NO: 2906	RTT
2907	SEQ ID NO: 2907	RTT*60 (PAM silencing)
2908	SEQ ID NO: 2908	RTT*65 (PAM silencing)
2909	SEQ ID NO: 2909	RTT*58 (PAM silencing)
2910	SEQ ID NO: 2910	RTT*59 (PAM silencing)
2911	SEQ ID NO: 2911	RTT*62 (PAM silencing)
2912	SEQ ID NO: 2912	RTT*67 (PAM silencing)
2913	SEQ ID NO: 2913	RTT
2914	SEQ ID NO: 2914	RTT*63 (PAM silencing)
2915	SEQ ID NO: 2915	RTT*66 (PAM silencing)
2916	SEQ ID NO: 2916	RTT*64 (PAM silencing)
2917	SEQ ID NO: 2917	RTT*57 (PAM silencing)
2918	SEQ ID NO: 2918	RTT*61 (PAM silencing)
2919	SEQ ID NO: 2919	RTT*60 (PAM silencing)
2920	SEQ ID NO: 2920	RTT*66 (PAM silencing)
2921	SEQ ID NO: 2921	RTT*61 (PAM silencing)
2922	SEQ ID NO: 2922	RTT*57 (PAM silencing)
2923	SEQ ID NO: 2923	RTT*59 (PAM silencing)

Sequence Number	Sequence	Description
2924	SEQ ID NO: 2924	RTT*63 (PAM silencing)
2925	SEQ ID NO: 2925	RTT*67 (PAM silencing)
2926	SEQ ID NO: 2926	RTT*65 (PAM silencing)
2927	SEQ ID NO: 2927	RTT
2928	SEQ ID NO: 2928	RTT*62 (PAM silencing)
2929	SEQ ID NO: 2929	RTT*60 (PAM silencing)
2930	SEQ ID NO: 2930	RTT*64 (PAM silencing)
2931	SEQ ID NO: 2931	RTT*58 (PAM silencing)
2932	SEQ ID NO: 2932	RTT*61 (PAM silencing)
2933	SEQ ID NO: 2933	RTT*64 (PAM silencing)
2934	SEQ ID NO: 2934	RTT*57 (PAM silencing)
2935	SEQ ID NO: 2935	RTT*60 (PAM silencing)
2936	SEQ ID NO: 2936	RTT*66 (PAM silencing)
2937	SEQ ID NO: 2937	RTT*58 (PAM silencing)
2938	SEQ ID NO: 2938	RTT*62 (PAM silencing)
2939	SEQ ID NO: 2939	RTT*59 (PAM silencing)
2940	SEQ ID NO: 2940	RTT*65 (PAM silencing)
2941	SEQ ID NO: 2941	RTT
2942	SEQ ID NO: 2942	RTT*63 (PAM silencing)
2943	SEQ ID NO: 2943	RTT*67 (PAM silencing)
2944	SEQ ID NO: 2944	RTT
2945	SEQ ID NO: 2945	RTT*57 (PAM silencing)
2946	SEQ ID NO: 2946	RTT*64 (PAM silencing)

Sequence Number	Sequence	Description
2947	SEQ ID NO: 2947	RTT*66 (PAM silencing)
2948	SEQ ID NO: 2948	RTT*60 (PAM silencing)
2949	SEQ ID NO: 2949	RTT*58 (PAM silencing)
2950	SEQ ID NO: 2950	RTT*63 (PAM silencing)
2951	SEQ ID NO: 2951	RTT*62 (PAM silencing)
2952	SEQ ID NO: 2952	RTT*61 (PAM silencing)
2953	SEQ ID NO: 2953	RTT*67 (PAM silencing)
2954	SEQ ID NO: 2954	RTT*59 (PAM silencing)
2955	SEQ ID NO: 2955	RTT*65 (PAM silencing)
2956	SEQ ID NO: 2956	RTT
2957	SEQ ID NO: 2957	RTT*64 (PAM silencing)
2958	SEQ ID NO: 2958	RTT*60 (PAM silencing)
2959	SEQ ID NO: 2959	RTT*65 (PAM silencing)
2960	SEQ ID NO: 2960	RTT*57 (PAM silencing)
2961	SEQ ID NO: 2961	RTT*62 (PAM silencing)
2962	SEQ ID NO: 2962	RTT*63 (PAM silencing)
2963	SEQ ID NO: 2963	RTT*61 (PAM silencing)
2964	SEQ ID NO: 2964	RTT*58 (PAM silencing)
2965	SEQ ID NO: 2965	RTT*67 (PAM silencing)
2966	SEQ ID NO: 2966	RTT*66 (PAM silencing)
2967	SEQ ID NO: 2967	RTT*59 (PAM silencing)
2968	SEQ ID NO: 2968	RTT
2969	SEQ ID NO: 2969	RTT*63 (PAM silencing)
2970	SEQ ID NO: 2970	RTT*64 (PAM silencing)
2971	SEQ ID NO: 2971	RTT*57 (PAM silencing)
2972	SEQ ID NO: 2972	RTT*62 (PAM silencing)
2973	SEQ ID NO: 2973	RTT*59 (PAM silencing)
2974	SEQ ID NO: 2974	RTT*60 (PAM silencing)
2975	SEQ ID NO: 2975	RTT*65 (PAM silencing)
2976	SEQ ID NO: 2976	RTT*67 (PAM silencing)
2977	SEQ ID NO: 2977	RTT*58 (PAM silencing)
2978	SEQ ID NO: 2978	RTT*66 (PAM silencing)
2979	SEQ ID NO: 2979	RTT*61 (PAM silencing)
2980	SEQ ID NO: 2980	RTT*63 (PAM silencing)
2981	SEQ ID NO: 2981	RTT*61 (PAM silencing)
2982	SEQ ID NO: 2982	RTT
2983	SEQ ID NO: 2983	RTT*67 (PAM silencing)
2984	SEQ ID NO: 2984	RTT*59 (PAM silencing)
2985	SEQ ID NO: 2985	RTT*62 (PAM silencing)
2986	SEQ ID NO: 2986	RTT*60 (PAM silencing)
2987	SEQ ID NO: 2987	RTT*64 (PAM silencing)
2988	SEQ ID NO: 2988	RTT*58 (PAM silencing)
2989	SEQ ID NO: 2989	RTT*65 (PAM silencing)
2990	SEQ ID NO: 2990	RTT*66 (PAM silencing)
2991	SEQ ID NO: 2991	RTT*57 (PAM silencing)
2992	SEQ ID NO: 2992	RTT*65 (PAM silencing)
2993	SEQ ID NO: 2993	RTT*63 (PAM silencing)
2994	SEQ ID NO: 2994	RTT*67 (PAM silencing)
2995	SEQ ID NO: 2995	RTT*62 (PAM silencing)
2996	SEQ ID NO: 2996	RTT
2997	SEQ ID NO: 2997	RTT*59 (PAM silencing)
2998	SEQ ID NO: 2998	RTT*64 (PAM silencing)
2999	SEQ ID NO: 2999	RTT*58 (PAM silencing)
3000	SEQ ID NO: 3000	RTT*66 (PAM silencing)
3001	SEQ ID NO: 3001	RTT*60 (PAM silencing)
3002	SEQ ID NO: 3002	RTT*61 (PAM silencing)
3003	SEQ ID NO: 3003	RTT*57 (PAM silencing)
3004	SEQ ID NO: 3004	RTT*67 (PAM silencing)
3005	SEQ ID NO: 3005	RTT*63 (PAM silencing)
3006	SEQ ID NO: 3006	RTT*60 (PAM silencing)
3007	SEQ ID NO: 3007	RTT*58 (PAM silencing)
3008	SEQ ID NO: 3008	RTT*64 (PAM silencing)
3009	SEQ ID NO: 3009	RTT*57 (PAM silencing)
3010	SEQ ID NO: 3010	RTT*59 (PAM silencing)
3011	SEQ ID NO: 3011	RTT*66 (PAM silencing)
3012	SEQ ID NO: 3012	RTT
3013	SEQ ID NO: 3013	RTT*65 (PAM silencing)
3014	SEQ ID NO: 3014	RTT*62 (PAM silencing)

Sequence Number	Sequence	Description
3015	SEQ ID NO: 3015	RTT*61 (PAM silencing)
3016	SEQ ID NO: 3016	RTT*58 (PAM silencing)
3017	SEQ ID NO: 3017	RTT*67 (PAM silencing)
3018	SEQ ID NO: 3018	RTT*66 (PAM silencing)
3019	SEQ ID NO: 3019	RTT
3020	SEQ ID NO: 3020	RTT*60 (PAM silencing)
3021	SEQ ID NO: 3021	RTT*65 (PAM silencing)
3022	SEQ ID NO: 3022	RTT*63 (PAM silencing)
3023	SEQ ID NO: 3023	RTT*62 (PAM silencing)
3024	SEQ ID NO: 3024	RTT*61 (PAM silencing)
3025	SEQ ID NO: 3025	RTT*57 (PAM silencing)
3026	SEQ ID NO: 3026	RTT*64 (PAM silencing)
3027	SEQ ID NO: 3027	RTT*59 (PAM silencing)
3028	SEQ ID NO: 3028	RTT*65 (PAM silencing)
3029	SEQ ID NO: 3029	RTT*66 (PAM silencing)
3030	SEQ ID NO: 3030	RTT*64 (PAM silencing)
3031	SEQ ID NO: 3031	RTT*59 (PAM silencing)
3032	SEQ ID NO: 3032	RTT*57 (PAM silencing)
3033	SEQ ID NO: 3033	RTT*67 (PAM silencing)
3034	SEQ ID NO: 3034	RTT*62 (PAM silencing)
3035	SEQ ID NO: 3035	RTT*61 (PAM silencing)
3036	SEQ ID NO: 3036	RTT*60 (PAM silencing)
3037	SEQ ID NO: 3037	RTT*63 (PAM silencing)
3038	SEQ ID NO: 3038	RTT
3039	SEQ ID NO: 3039	RTT*58 (PAM silencing)
3040	SEQ ID NO: 3040	RTT*66 (PAM silencing)
3041	SEQ ID NO: 3041	RTT*61 (PAM silencing)
3042	SEQ ID NO: 3042	RTT*60 (PAM silencing)
3043	SEQ ID NO: 3043	RTT*59 (PAM silencing)
3044	SEQ ID NO: 3044	RTT*64 (PAM silencing)
3045	SEQ ID NO: 3045	RTT*58 (PAM silencing)
3046	SEQ ID NO: 3046	RTT*67 (PAM silencing)
3047	SEQ ID NO: 3047	RTT
3048	SEQ ID NO: 3048	RTT*62 (PAM silencing)
3049	SEQ ID NO: 3049	RTT*63 (PAM silencing)
3050	SEQ ID NO: 3050	RTT*65 (PAM silencing)
3051	SEQ ID NO: 3051	RTT*57 (PAM silencing)
3052	SEQ ID NO: 3052	RTT*59 (PAM silencing)
3053	SEQ ID NO: 3053	RTT*66 (PAM silencing)
3054	SEQ ID NO: 3054	RTT*67 (PAM silencing)
3055	SEQ ID NO: 3055	RTT*60 (PAM silencing)
3056	SEQ ID NO: 3056	RTT*57 (PAM silencing)
3057	SEQ ID NO: 3057	RTT*65 (PAM silencing)
3058	SEQ ID NO: 3058	RTT*58 (PAM silencing)
3059	SEQ ID NO: 3059	RTT*63 (PAM silencing)
3060	SEQ ID NO: 3060	RTT*62 (PAM silencing)
3061	SEQ ID NO: 3061	RTT
3062	SEQ ID NO: 3062	RTT*61 (PAM silencing)
3063	SEQ ID NO: 3063	RTT*64 (PAM silencing)
3064	SEQ ID NO: 3064	RTT*64 (PAM silencing)
3065	SEQ ID NO: 3065	RTT*62 (PAM silencing)
3066	SEQ ID NO: 3066	RTT*65 (PAM silencing)
3067	SEQ ID NO: 3067	RTT*57 (PAM silencing)
3068	SEQ ID NO: 3068	RTT*61 (PAM silencing)
3069	SEQ ID NO: 3069	RTT*59 (PAM silencing)
3070	SEQ ID NO: 3070	RTT*58 (PAM silencing)
3071	SEQ ID NO: 3071	RTT*66 (PAM silencing)
3072	SEQ ID NO: 3072	RTT*60 (PAM silencing)
3073	SEQ ID NO: 3073	RTT
3074	SEQ ID NO: 3074	RTT*63 (PAM silencing)
3075	SEQ ID NO: 3075	RTT*67 (PAM silencing)
3076	SEQ ID NO: 3076	RTT*61 (PAM silencing)
3077	SEQ ID NO: 3077	RTT*58 (PAM silencing)
3078	SEQ ID NO: 3078	RTT*62 (PAM silencing)
3079	SEQ ID NO: 3079	RTT*67 (PAM silencing)
3080	SEQ ID NO: 3080	RTT*59 (PAM silencing)
3081	SEQ ID NO: 3081	RTT*66 (PAM silencing)
3082	SEQ ID NO: 3082	RTT*64 (PAM silencing)

Sequence Number	Sequence	Description
3083	SEQ ID NO: 3083	RTT*65 (PAM silencing)
3084	SEQ ID NO: 3084	RTT
3085	SEQ ID NO: 3085	RTT*60 (PAM silencing)
3086	SEQ ID NO: 3086	RTT*63 (PAM silencing)
3087	SEQ ID NO: 3087	RTT*57 (PAM silencing)
3088	SEQ ID NO: 3088	RTT*60 (PAM silencing)
3089	SEQ ID NO: 3089	RTT*57 (PAM silencing)
3090	SEQ ID NO: 3090	RTT*62 (PAM silencing)
3091	SEQ ID NO: 3091	RTT*67 (PAM silencing)
3092	SEQ ID NO: 3092	RTT
3093	SEQ ID NO: 3093	RTT*65 (PAM silencing)
3094	SEQ ID NO: 3094	RTT*58 (PAM silencing)
3095	SEQ ID NO: 3095	RTT*61 (PAM silencing)
3096	SEQ ID NO: 3096	RTT*64 (PAM silencing)
3097	SEQ ID NO: 3097	RTT*63 (PAM silencing)
3098	SEQ ID NO: 3098	RTT*59 (PAM silencing)
3099	SEQ ID NO: 3099	RTT*66 (PAM silencing)
3100	SEQ ID NO: 3100	RTT*62 (PAM silencing)
3101	SEQ ID NO: 3101	RTT*63 (PAM silencing)
3102	SEQ ID NO: 3102	RTT
3103	SEQ ID NO: 3103	RTT*66 (PAM silencing)
3104	SEQ ID NO: 3104	RTT*59 (PAM silencing)
3105	SEQ ID NO: 3105	RTT*65 (PAM silencing)
3106	SEQ ID NO: 3106	RTT*61 (PAM silencing)
3107	SEQ ID NO: 3107	RTT*57 (PAM silencing)
3108	SEQ ID NO: 3108	RTT*64 (PAM silencing)
3109	SEQ ID NO: 3109	RTT*58 (PAM silencing)
3110	SEQ ID NO: 3110	RTT*67 (PAM silencing)
3111	SEQ ID NO: 3111	RTT*60 (PAM silencing)
3112	SEQ ID NO: 3112	RTT*57 (PAM silencing)
3113	SEQ ID NO: 3113	RTT*66 (PAM silencing)
3114	SEQ ID NO: 3114	RTT
3115	SEQ ID NO: 3115	RTT*60 (PAM silencing)
3116	SEQ ID NO: 3116	RTT*61 (PAM silencing)
3117	SEQ ID NO: 3117	RTT*59 (PAM silencing)
3118	SEQ ID NO: 3118	RTT*64 (PAM silencing)
3119	SEQ ID NO: 3119	RTT*67 (PAM silencing)
3120	SEQ ID NO: 3120	RTT*62 (PAM silencing)
3121	SEQ ID NO: 3121	RTT*58 (PAM silencing)
3122	SEQ ID NO: 3122	RTT*63 (PAM silencing)
3123	SEQ ID NO: 3123	RTT*65 (PAM silencing)
3124	SEQ ID NO: 3124	RTT*64 (PAM silencing)
3125	SEQ ID NO: 3125	RTT
3126	SEQ ID NO: 3126	RTT*65 (PAM silencing)
3127	SEQ ID NO: 3127	RTT*58 (PAM silencing)
3128	SEQ ID NO: 3128	RTT*57 (PAM silencing)
3129	SEQ ID NO: 3129	RTT*63 (PAM silencing)
3130	SEQ ID NO: 3130	RTT*67 (PAM silencing)
3131	SEQ ID NO: 3131	RTT*60 (PAM silencing)
3132	SEQ ID NO: 3132	RTT*66 (PAM silencing)
3133	SEQ ID NO: 3133	RTT*61 (PAM silencing)
3134	SEQ ID NO: 3134	RTT*62 (PAM silencing)
3135	SEQ ID NO: 3135	RTT*59 (PAM silencing)
3136	SEQ ID NO: 3136	RTT*67 (PAM silencing)
3137	SEQ ID NO: 3137	RTT*57 (PAM silencing)
3138	SEQ ID NO: 3138	RTT*61 (PAM silencing)
3139	SEQ ID NO: 3139	RTT*64 (PAM silencing)
3140	SEQ ID NO: 3140	RTT*65 (PAM silencing)
3141	SEQ ID NO: 3141	RTT*58 (PAM silencing)
3142	SEQ ID NO: 3142	RTT*60 (PAM silencing)
3143	SEQ ID NO: 3143	RTT*59 (PAM silencing)
3144	SEQ ID NO: 3144	RTT*66 (PAM silencing)
3145	SEQ ID NO: 3145	RTT
3146	SEQ ID NO: 3146	RTT*63 (PAM silencing)
3147	SEQ ID NO: 3147	RTT*62 (PAM silencing)
3159	SEQ ID NO: 3159	RTT
3149	SEQ ID NO: 3149	RTT*62 (PAM silencing)
3157	SEQ ID NO: 3157	RTT*66 (PAM silencing)
3151	SEQ ID NO: 3151	RTT*63 (PAM silencing)

Sequence Number	Sequence	Description
3152	SEQ ID NO: 3152	RTT*64 (PAM silencing)
3153	SEQ ID NO: 3153	RTT*67 (PAM silencing)
3148	SEQ ID NO: 3148	RTT*61 (PAM silencing)
3155	SEQ ID NO: 3155	RTT*60 (PAM silencing)
3156	SEQ ID NO: 3156	RTT*59 (PAM silencing)
3154	SEQ ID NO: 3154	RTT*58 (PAM silencing)
3158	SEQ ID NO: 3158	RTT*65 (PAM silencing)
3150	SEQ ID NO: 3150	RTT*57 (PAM silencing)
3167	SEQ ID NO: 3167	RTT*62 (PAM silencing)
3160	SEQ ID NO: 3160	RTT*67 (PAM silencing)
3171	SEQ ID NO: 3171	RTT*60 (PAM silencing)
3164	SEQ ID NO: 3164	RTT*64 (PAM silencing)
3165	SEQ ID NO: 3165	RTT
3166	SEQ ID NO: 3166	RTT*63 (PAM silencing)
3168	SEQ ID NO: 3168	RTT*61 (PAM silencing)
3163	SEQ ID NO: 3163	RTT*59 (PAM silencing)
3162	SEQ ID NO: 3162	RTT*66 (PAM silencing)
3170	SEQ ID NO: 3170	RTT*65 (PAM silencing)
3161	SEQ ID NO: 3161	RTT*57 (PAM silencing)
3169	SEQ ID NO: 3169	RTT*58 (PAM silencing)
3183	SEQ ID NO: 3183	RTT*64 (PAM silencing)
3173	SEQ ID NO: 3173	RTT*63 (PAM silencing)
3174	SEQ ID NO: 3174	RTT*57 (PAM silencing)
3176	SEQ ID NO: 3176	RTT*66 (PAM silencing)
3177	SEQ ID NO: 3177	RTT*65 (PAM silencing)
3178	SEQ ID NO: 3178	RTT*60 (PAM silencing)
3179	SEQ ID NO: 3179	RTT*59 (PAM silencing)
3180	SEQ ID NO: 3180	RTT
3181	SEQ ID NO: 3181	RTT*61 (PAM silencing)
3182	SEQ ID NO: 3182	RTT*67 (PAM silencing)
3172	SEQ ID NO: 3172	RTT*62 (PAM silencing)
3175	SEQ ID NO: 3175	RTT*58 (PAM silencing)
3184	SEQ ID NO: 3184	RTT
3185	SEQ ID NO: 3185	RTT*57 (PAM silencing)
3195	SEQ ID NO: 3195	RTT*60 (PAM silencing)
3187	SEQ ID NO: 3187	RTT*58 (PAM silencing)
3188	SEQ ID NO: 3188	RTT*65 (PAM silencing)
3189	SEQ ID NO: 3189	RTT*64 (PAM silencing)
3190	SEQ ID NO: 3190	RTT*66 (PAM silencing)
3191	SEQ ID NO: 3191	RTT*63 (PAM silencing)
3192	SEQ ID NO: 3192	RTT*61 (PAM silencing)
3193	SEQ ID NO: 3193	RTT*62 (PAM silencing)
3194	SEQ ID NO: 3194	RTT*59 (PAM silencing)
3186	SEQ ID NO: 3186	RTT*67 (PAM silencing)
3202	SEQ ID NO: 3202	RTT*63 (PAM silencing)
3204	SEQ ID NO: 3204	RTT*61 (PAM silencing)
3203	SEQ ID NO: 3203	RTT*60 (PAM silencing)
3200	SEQ ID NO: 3200	RTT*57 (PAM silencing)
3199	SEQ ID NO: 3199	RTT*65 (PAM silencing)
3205	SEQ ID NO: 3205	RTT*59 (PAM silencing)
3201	SEQ ID NO: 3201	RTT*62 (PAM silencing)
3206	SEQ ID NO: 3206	RTT
3207	SEQ ID NO: 3207	RTT*66 (PAM silencing)
3197	SEQ ID NO: 3197	RTT*58 (PAM silencing)
3196	SEQ ID NO: 3196	RTT*64 (PAM silencing)
3198	SEQ ID NO: 3198	RTT*67 (PAM silencing)
3210	SEQ ID NO: 3210	RTT*60 (PAM silencing)
3218	SEQ ID NO: 3218	RTT*57 (PAM silencing)
3215	SEQ ID NO: 3215	RTT*67 (PAM silencing)
3208	SEQ ID NO: 3208	RTT*64 (PAM silencing)
3211	SEQ ID NO: 3211	RTT*65 (PAM silencing)
3213	SEQ ID NO: 3213	RTT*61 (PAM silencing)
3219	SEQ ID NO: 3219	RTT*62 (PAM silencing)
3209	SEQ ID NO: 3209	RTT*63 (PAM silencing)
3217	SEQ ID NO: 3217	RTT*59 (PAM silencing)
3216	SEQ ID NO: 3216	RTT*58 (PAM silencing)
3212	SEQ ID NO: 3212	RTT*66 (PAM silencing)
3214	SEQ ID NO: 3214	RTT

Sequence Number	Sequence	Description
3223	SEQ ID NO: 3223	RTT*57 (PAM silencing)
3221	SEQ ID NO: 3221	RTT*64 (PAM silencing)
3220	SEQ ID NO: 3220	RTT*60 (PAM silencing)
3225	SEQ ID NO: 3225	RTT*62 (PAM silencing)
3222	SEQ ID NO: 3222	RTT*61 (PAM silencing)
3226	SEQ ID NO: 3226	RTT*66 (PAM silencing)
3227	SEQ ID NO: 3227	RTT
3230	SEQ ID NO: 3230	RTT*65 (PAM silencing)
3229	SEQ ID NO: 3229	RTT*67 (PAM silencing)
3228	SEQ ID NO: 3228	RTT*59 (PAM silencing)
3224	SEQ ID NO: 3224	RTT*63 (PAM silencing)
3231	SEQ ID NO: 3231	RTT*58 (PAM silencing)
3239	SEQ ID NO: 3239	RTT*62 (PAM silencing)
3238	SEQ ID NO: 3238	RTT*61 (PAM silencing)
3233	SEQ ID NO: 3233	RTT*59 (PAM silencing)
3236	SEQ ID NO: 3236	RTT*58 (PAM silencing)
3237	SEQ ID NO: 3237	RTT*60 (PAM silencing)
3240	SEQ ID NO: 3240	RTT*57 (PAM silencing)
3234	SEQ ID NO: 3234	RTT*67 (PAM silencing)
3235	SEQ ID NO: 3235	RTT*65 (PAM silencing)
3241	SEQ ID NO: 3241	RTT*64 (PAM silencing)
3242	SEQ ID NO: 3242	RTT
3232	SEQ ID NO: 3232	RTT*66 (PAM silencing)

Sequence Number	Sequence	Description
3243	SEQ ID NO: 3243	RTT*63 (PAM silencing)
3288	SEQ ID NO: 3288	PE3b*62 ngRNA spacer (TG;TGG PAM)
3259	SEQ ID NO: 3259	PE3b*66 ngRNA spacer (GG PAM)
3260	SEQ ID NO: 3260	PE3 ngRNA spacer (AG;AGG PAM)
3261	SEQ ID NO: 3261	PE3b*64 ngRNA spacer (TG;TGG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
3263	SEQ ID NO: 3263	PE3 ngRNA spacer (AG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
3269	SEQ ID NO: 3269	PE3 ngRNA spacer (CG;CGG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
3244	SEQ ID NO: 3244	PE3 ngRNA spacer (TG;TGG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
3245	SEQ ID NO: 3245	PE3b*66 ngRNA spacer (TG;TGG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)

Sequence Number	Sequence	Description
3246	SEQ ID NO: 3246	PE3b*67 ngRNA spacer (TG;TGG PAM)
3247	SEQ ID NO: 3247	PE3b*59 ngRNA spacer (TG;TGG PAM)
3270	SEQ ID NO: 3270	PE3 ngRNA spacer (GG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)
3250	SEQ ID NO: 3250	PE3b*62 ngRNA spacer (GG PAM)
3257	SEQ ID NO: 3257	PE3b*67 ngRNA spacer (TG;TGG PAM)
3266	SEQ ID NO: 3266	PE3 ngRNA spacer (TG PAM)
3267	SEQ ID NO: 3267	PE3b*63 ngRNA spacer (TG;TGG PAM)
3268	SEQ ID NO: 3268	PE3 ngRNA spacer (AG;AGG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
3249	SEQ ID NO: 3249	PE3b*61 ngRNA spacer (TG;TGG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
3256	SEQ ID NO: 3256	PE3b*63 ngRNA spacer (TG;TGG PAM)
3264	SEQ ID NO: 3264	PE3b*58 ngRNA spacer (TG;TGG PAM)

Sequence Number	Sequence	Description
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
3274	SEQ ID NO: 3274	PE3b*61 ngRNA spacer (TG;TGG PAM)
3275	SEQ ID NO: 3275	PE3 ngRNA spacer (TG;TGG PAM)
3286	SEQ ID NO: 3286	PE3b*62 ngRNA spacer (TG;TGG PAM)
3276	SEQ ID NO: 3276	PE3b*62 ngRNA spacer (GG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
3278	SEQ ID NO: 3278	PE3 ngRNA spacer (GG PAM)
3279	SEQ ID NO: 3279	PE3 ngRNA spacer (TG;TGG PAM)
3280	SEQ ID NO: 3280	PE3 ngRNA spacer (TG PAM)
3281	SEQ ID NO: 3281	PE3b*63 ngRNA spacer (TG;TGG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
3282	SEQ ID NO: 3282	PE3 ngRNA spacer (AG PAM)
3283	SEQ ID NO: 3283	PE3 ngRNA spacer (GG PAM)
3284	SEQ ID NO: 3284	PE3b*64 ngRNA spacer (TG;TGG PAM)
3285	SEQ ID NO: 3285	PE3 ngRNA spacer (GG PAM)
3265	SEQ ID NO: 3265	PE3b*58 ngRNA spacer (TG;TGG PAM)
88	SEQ ID NO: 88	PE3 ngRNA spacer (TG;TGG PAM)
63	SEQ ID NO: 63	PE3 ngRNA spacer (TG;TGG PAM)
3271	SEQ ID NO: 3271	PE3b*57 ngRNA spacer (TG;TGG PAM)
3252	SEQ ID NO: 3252	PE3b*62 ngRNA spacer (TG;TGG PAM)
3253	SEQ ID NO: 3253	PE3b*59 ngRNA spacer (TG;TGG PAM)
3254	SEQ ID NO: 3254	PE3b*60 ngRNA spacer (TG;TGG PAM)
3251	SEQ ID NO: 3251	PE3b*61 ngRNA spacer (TG;TGG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)
3255	SEQ ID NO: 3255	PE3b*57 ngRNA spacer (TG;TGG PAM)
3258	SEQ ID NO: 3258	PE3b*60 ngRNA spacer (TG;TGG PAM)
3273	SEQ ID NO: 3273	PE3 ngRNA spacer (TG PAM)
3272	SEQ ID NO: 3272	PE3b*57 ngRNA spacer (TG;TGG PAM)
3299	SEQ ID NO: 3299	PE3b*58 ngRNA spacer (TG;TGG PAM)
3289	SEQ ID NO: 3289	PE3b*66 ngRNA spacer (GG PAM)
3290	SEQ ID NO: 3290	PE3b*65 ngRNA spacer (TG;TGG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
3292	SEQ ID NO: 3292	PE3b*62 ngRNA spacer (GG PAM)
3293	SEQ ID NO: 3293	PE3 ngRNA spacer (GG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
3295	SEQ ID NO: 3295	PE3 ngRNA spacer (GG PAM)
3296	SEQ ID NO: 3296	PE3b*65 ngRNA spacer (TG;TGG PAM)
3297	SEQ ID NO: 3297	PE3b*59 ngRNA spacer (TG;TGG PAM)
3294	SEQ ID NO: 3294	PE3b*60 ngRNA spacer (TG;TGG PAM)
3298	SEQ ID NO: 3298	PE3b*66 ngRNA

Sequence Number	Sequence	Description
		spacer (TG;TGG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
3302	SEQ ID NO: 3302	PEgRNA (AG;AGG PAM)
3307	SEQ ID NO: 3307	PEgRNA (AG;AGG PAM)
3300	SEQ ID NO: 3300	PEgRNA (AG;AGG PAM)
3303	SEQ ID NO: 3303	PEgRNA (AG;AGG PAM)
3304	SEQ ID NO: 3304	PEgRNA (AG;AGG PAM)
3301	SEQ ID NO: 3301	PEgRNA (AG;AGG PAM)
3306	SEQ ID NO: 3306	PEgRNA (AG;AGG PAM)
3305	SEQ ID NO: 3305	PEgRNA (AG;AGG PAM)
3308	SEQ ID NO: 3308	PEgRNA (AG;AGG PAM)
3313	SEQ ID NO: 3313	PEgRNA (AG;AGG PAM)
3309	SEQ ID NO: 3309	PEgRNA (AG;AGG PAM)
3314	SEQ ID NO: 3314	PEgRNA (AG;AGG PAM)
3312	SEQ ID NO: 3312	PEgRNA (AG;AGG PAM)
3315	SEQ ID NO: 3315	PEgRNA (AG;AGG PAM)
3310	SEQ ID NO: 3310	PEgRNA (AG;AGG PAM)
3311	SEQ ID NO: 3311	PEgRNA (AG;AGG PAM)
3318	SEQ ID NO: 3318	PEgRNA (AG;AGG PAM)
3322	SEQ ID NO: 3322	PEgRNA (AG;AGG PAM)
3316	SEQ ID NO: 3316	PEgRNA (AG;AGG PAM)
3320	SEQ ID NO: 3320	PEgRNA (AG;AGG PAM)
3317	SEQ ID NO: 3317	PEgRNA (AG;AGG PAM)
3321	SEQ ID NO: 3321	PEgRNA (AG;AGG PAM)
3323	SEQ ID NO: 3323	PEgRNA (AG;AGG PAM)
3319	SEQ ID NO: 3319	PEgRNA (AG;AGG PAM)
3324	SEQ ID NO: 3324	PEgRNA (AG;AGG PAM)
3325	SEQ ID NO: 3325	PEgRNA (AG;AGG PAM)
3330	SEQ ID NO: 3330	PEgRNA (AG;AGG PAM)
3327	SEQ ID NO: 3327	PEgRNA (AG;AGG PAM)
3331	SEQ ID NO: 3331	PEgRNA (AG;AGG PAM)
3326	SEQ ID NO: 3326	PEgRNA (AG;AGG PAM)
3329	SEQ ID NO: 3329	PEgRNA (AG;AGG PAM)
3328	SEQ ID NO: 3328	PEgRNA (AG;AGG PAM)
3335	SEQ ID NO: 3335	PEgRNA (AG;AGG PAM)
3333	SEQ ID NO: 3333	PEgRNA (AG;AGG PAM)
3332	SEQ ID NO: 3332	PEgRNA (AG;AGG PAM)
3337	SEQ ID NO: 3337	PEgRNA (AG;AGG PAM)
3347	SEQ ID NO: 3347	PEgRNA (AG;AGG PAM)
3345	SEQ ID NO: 3345	PEgRNA (AG;AGG PAM)
3338	SEQ ID NO: 3338	PEgRNA (AG;AGG PAM)
3340	SEQ ID NO: 3340	PEgRNA (AG;AGG PAM)
3346	SEQ ID NO: 3346	PEgRNA (AG;AGG PAM)
3334	SEQ ID NO: 3334	PEgRNA (AG;AGG PAM)
3341	SEQ ID NO: 3341	PEgRNA (AG;AGG PAM)
3342	SEQ ID NO: 3342	PEgRNA (AG;AGG PAM)
3336	SEQ ID NO: 3336	PEgRNA (AG;AGG PAM)
3339	SEQ ID NO: 3339	PEgRNA (AG;AGG PAM)
3344	SEQ ID NO: 3344	PEgRNA (AG;AGG PAM)
3343	SEQ ID NO: 3343	PEgRNA (AG;AGG PAM)
3371	SEQ ID NO: 3371	PEgRNA (AG;AGG PAM)
3349	SEQ ID NO: 3349	PEgRNA (AG;AGG PAM)
3350	SEQ ID NO: 3350	PEgRNA (AG;AGG PAM)
3370	SEQ ID NO: 3370	PEgRNA (AG;AGG PAM)
3367	SEQ ID NO: 3367	PEgRNA (AG;AGG PAM)
3358	SEQ ID NO: 3358	PEgRNA (AG;AGG PAM)
3369	SEQ ID NO: 3369	PEgRNA (AG;AGG PAM)
3363	SEQ ID NO: 3363	PEgRNA (AG;AGG PAM)
3360	SEQ ID NO: 3360	PEgRNA (AG;AGG PAM)
3352	SEQ ID NO: 3352	PEgRNA (AG;AGG PAM)
3348	SEQ ID NO: 3348	PEgRNA (AG;AGG PAM)
3365	SEQ ID NO: 3365	PEgRNA (AG;AGG PAM)
3353	SEQ ID NO: 3353	PEgRNA (AG;AGG PAM)
3362	SEQ ID NO: 3362	PEgRNA (AG;AGG PAM)
3364	SEQ ID NO: 3364	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3368	SEQ ID NO: 3368	PEgRNA (AG;AGG PAM)
3356	SEQ ID NO: 3356	PEgRNA (AG;AGG PAM)
3359	SEQ ID NO: 3359	PEgRNA (AG;AGG PAM)
3357	SEQ ID NO: 3357	PEgRNA (AG;AGG PAM)
3366	SEQ ID NO: 3366	PEgRNA (AG;AGG PAM)
3351	SEQ ID NO: 3351	PEgRNA (AG;AGG PAM)
3355	SEQ ID NO: 3355	PEgRNA (AG;AGG PAM)
3361	SEQ ID NO: 3361	PEgRNA (AG;AGG PAM)
3354	SEQ ID NO: 3354	PEgRNA (AG;AGG PAM)
3398	SEQ ID NO: 3398	PEgRNA (AG;AGG PAM)
3386	SEQ ID NO: 3386	PEgRNA (AG;AGG PAM)
3402	SEQ ID NO: 3402	PEgRNA (AG;AGG PAM)
3373	SEQ ID NO: 3373	PEgRNA (AG;AGG PAM)
3401	SEQ ID NO: 3401	PEgRNA (AG;AGG PAM)
3392	SEQ ID NO: 3392	PEgRNA (AG;AGG PAM)
3396	SEQ ID NO: 3396	PEgRNA (AG;AGG PAM)
3375	SEQ ID NO: 3375	PEgRNA (AG;AGG PAM)
3403	SEQ ID NO: 3403	PEgRNA (AG;AGG PAM)
3385	SEQ ID NO: 3385	PEgRNA (AG;AGG PAM)
3397	SEQ ID NO: 3397	PEgRNA (AG;AGG PAM)
3378	SEQ ID NO: 3378	PEgRNA (AG;AGG PAM)
3394	SEQ ID NO: 3394	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3393	SEQ ID NO: 3393	PEgRNA (AG;AGG PAM)
3383	SEQ ID NO: 3383	PEgRNA (AG;AGG PAM)
3400	SEQ ID NO: 3400	PEgRNA (AG;AGG PAM)
3384	SEQ ID NO: 3384	PEgRNA (AG;AGG PAM)
3381	SEQ ID NO: 3381	PEgRNA (AG;AGG PAM)
3395	SEQ ID NO: 3395	PEgRNA (AG;AGG PAM)
3389	SEQ ID NO: 3389	PEgRNA (AG;AGG PAM)
3390	SEQ ID NO: 3390	PEgRNA (AG;AGG PAM)
3380	SEQ ID NO: 3380	PEgRNA (AG;AGG PAM)
3391	SEQ ID NO: 3391	PEgRNA (AG;AGG PAM)
3382	SEQ ID NO: 3382	PEgRNA (AG;AGG PAM)
3379	SEQ ID NO: 3379	PEgRNA (AG;AGG PAM)
3376	SEQ ID NO: 3376	PEgRNA (AG;AGG PAM)
3387	SEQ ID NO: 3387	PEgRNA (AG;AGG PAM)
3399	SEQ ID NO: 3399	PEgRNA (AG;AGG PAM)
3377	SEQ ID NO: 3377	PEgRNA (AG;AGG PAM)
3388	SEQ ID NO: 3388	PEgRNA (AG;AGG PAM)
3374	SEQ ID NO: 3374	PEgRNA (AG;AGG PAM)
3372	SEQ ID NO: 3372	PEgRNA (AG;AGG PAM)
3421	SEQ ID NO: 3421	PEgRNA (AG;AGG PAM)
3431	SEQ ID NO: 3431	PEgRNA (AG;AGG PAM)
3417	SEQ ID NO: 3417	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3414	SEQ ID NO: 3414	PEgRNA (AG;AGG PAM)
3426	SEQ ID NO: 3426	PEgRNA (AG;AGG PAM)
3423	SEQ ID NO: 3423	PEgRNA (AG;AGG PAM)
3413	SEQ ID NO: 3413	PEgRNA (AG;AGG PAM)
3428	SEQ ID NO: 3428	PEgRNA (AG;AGG PAM)
3425	SEQ ID NO: 3425	PEgRNA (AG;AGG PAM)
3422	SEQ ID NO: 3422	PEgRNA (AG;AGG PAM)
3435	SEQ ID NO: 3435	PEgRNA (AG;AGG PAM)
3408	SEQ ID NO: 3408	PEgRNA (AG;AGG PAM)
3411	SEQ ID NO: 3411	PEgRNA (AG;AGG PAM)
3412	SEQ ID NO: 3412	PEgRNA (AG;AGG PAM)
3433	SEQ ID NO: 3433	PEgRNA (AG;AGG PAM)
3429	SEQ ID NO: 3429	PEgRNA (AG;AGG PAM)
3434	SEQ ID NO: 3434	PEgRNA (AG;AGG PAM)
3432	SEQ ID NO: 3432	PEgRNA (AG;AGG PAM)
3420	SEQ ID NO: 3420	PEgRNA (AG;AGG PAM)
3418	SEQ ID NO: 3418	PEgRNA (AG;AGG PAM)
3424	SEQ ID NO: 3424	PEgRNA (AG;AGG PAM)
3410	SEQ ID NO: 3410	PEgRNA (AG;AGG PAM)
3404	SEQ ID NO: 3404	PEgRNA (AG;AGG PAM)
3430	SEQ ID NO: 3430	PEgRNA (AG;AGG PAM)
3427	SEQ ID NO: 3427	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3409	SEQ ID NO: 3409	PEgRNA (AG;AGG PAM)
3416	SEQ ID NO: 3416	PEgRNA (AG;AGG PAM)
3415	SEQ ID NO: 3415	PEgRNA (AG;AGG PAM)
3419	SEQ ID NO: 3419	PEgRNA (AG;AGG PAM)
3407	SEQ ID NO: 3407	PEgRNA (AG;AGG PAM)
3405	SEQ ID NO: 3405	PEgRNA (AG;AGG PAM)
3406	SEQ ID NO: 3406	PEgRNA (AG;AGG PAM)
3464	SEQ ID NO: 3464	PEgRNA (AG;AGG PAM)
3447	SEQ ID NO: 3447	PEgRNA (AG;AGG PAM)
3460	SEQ ID NO: 3460	PEgRNA (AG;AGG PAM)
3471	SEQ ID NO: 3471	PEgRNA (AG;AGG PAM)
3448	SEQ ID NO: 3448	PEgRNA (AG;AGG PAM)
3454	SEQ ID NO: 3454	PEgRNA (AG;AGG PAM)
3452	SEQ ID NO: 3452	PEgRNA (AG;AGG PAM)
3468	SEQ ID NO: 3468	PEgRNA (AG;AGG PAM)
3443	SEQ ID NO: 3443	PEgRNA (AG;AGG PAM)
3453	SEQ ID NO: 3453	PEgRNA (AG;AGG PAM)
3449	SEQ ID NO: 3449	PEgRNA (AG;AGG PAM)
3466	SEQ ID NO: 3466	PEgRNA (AG;AGG PAM)
3436	SEQ ID NO: 3436	PEgRNA (AG;AGG PAM)
3465	SEQ ID NO: 3465	PEgRNA (AG;AGG PAM)
3451	SEQ ID NO: 3451	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3459	SEQ ID NO: 3459	PEgRNA (AG;AGG PAM)
3463	SEQ ID NO: 3463	PEgRNA (AG;AGG PAM)
3469	SEQ ID NO: 3469	PEgRNA (AG;AGG PAM)
3467	SEQ ID NO: 3467	PEgRNA (AG;AGG PAM)
3461	SEQ ID NO: 3461	PEgRNA (AG;AGG PAM)
3456	SEQ ID NO: 3456	PEgRNA (AG;AGG PAM)
3442	SEQ ID NO: 3442	PEgRNA (AG;AGG PAM)
3439	SEQ ID NO: 3439	PEgRNA (AG;AGG PAM)
3441	SEQ ID NO: 3441	PEgRNA (AG;AGG PAM)
3455	SEQ ID NO: 3455	PEgRNA (AG;AGG PAM)
3473	SEQ ID NO: 3473	PEgRNA (AG;AGG PAM)
3445	SEQ ID NO: 3445	PEgRNA (AG;AGG PAM)
3458	SEQ ID NO: 3458	PEgRNA (AG;AGG PAM)
3446	SEQ ID NO: 3446	PEgRNA (AG;AGG PAM)
3462	SEQ ID NO: 3462	PEgRNA (AG;AGG PAM)
3440	SEQ ID NO: 3440	PEgRNA (AG;AGG PAM)
3474	SEQ ID NO: 3474	PEgRNA (AG;AGG PAM)
3450	SEQ ID NO: 3450	PEgRNA (AG;AGG PAM)
3438	SEQ ID NO: 3438	PEgRNA (AG;AGG PAM)
3437	SEQ ID NO: 3437	PEgRNA (AG;AGG PAM)
3457	SEQ ID NO: 3457	PEgRNA (AG;AGG PAM)
3475	SEQ ID NO: 3475	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3472	SEQ ID NO: 3472	PEgRNA (AG;AGG PAM)
3470	SEQ ID NO: 3470	PEgRNA (AG;AGG PAM)
3444	SEQ ID NO: 3444	PEgRNA (AG;AGG PAM)
3501	SEQ ID NO: 3501	PEgRNA (AG;AGG PAM)
3510	SEQ ID NO: 3510	PEgRNA (AG;AGG PAM)
3497	SEQ ID NO: 3497	PEgRNA (AG;AGG PAM)
3487	SEQ ID NO: 3487	PEgRNA (AG;AGG PAM)
3508	SEQ ID NO: 3508	PEgRNA (AG;AGG PAM)
3488	SEQ ID NO: 3488	PEgRNA (AG;AGG PAM)
3506	SEQ ID NO: 3506	PEgRNA (AG;AGG PAM)
3494	SEQ ID NO: 3494	PEgRNA (AG;AGG PAM)
3500	SEQ ID NO: 3500	PEgRNA (AG;AGG PAM)
3479	SEQ ID NO: 3479	PEgRNA (AG;AGG PAM)
3523	SEQ ID NO: 3523	PEgRNA (AG;AGG PAM)
3492	SEQ ID NO: 3492	PEgRNA (AG;AGG PAM)
3476	SEQ ID NO: 3476	PEgRNA (AG;AGG PAM)
3519	SEQ ID NO: 3519	PEgRNA (AG;AGG PAM)
3516	SEQ ID NO: 3516	PEgRNA (AG;AGG PAM)
3478	SEQ ID NO: 3478	PEgRNA (AG;AGG PAM)
3509	SEQ ID NO: 3509	PEgRNA (AG;AGG PAM)
3514	SEQ ID NO: 3514	PEgRNA (AG;AGG PAM)
3485	SEQ ID NO: 3485	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3515	SEQ ID NO: 3515	PEgRNA (AG;AGG PAM)
3495	SEQ ID NO: 3495	PEgRNA (AG;AGG PAM)
3481	SEQ ID NO: 3481	PEgRNA (AG;AGG PAM)
3486	SEQ ID NO: 3486	PEgRNA (AG;AGG PAM)
3498	SEQ ID NO: 3498	PEgRNA (AG;AGG PAM)
3477	SEQ ID NO: 3477	PEgRNA (AG;AGG PAM)
3490	SEQ ID NO: 3490	PEgRNA (AG;AGG PAM)
3504	SEQ ID NO: 3504	PEgRNA (AG;AGG PAM)
3499	SEQ ID NO: 3499	PEgRNA (AG;AGG PAM)
3517	SEQ ID NO: 3517	PEgRNA (AG;AGG PAM)
3505	SEQ ID NO: 3505	PEgRNA (AG;AGG PAM)
3503	SEQ ID NO: 3503	PEgRNA (AG;AGG PAM)
3484	SEQ ID NO: 3484	PEgRNA (AG;AGG PAM)
3496	SEQ ID NO: 3496	PEgRNA (AG;AGG PAM)
3522	SEQ ID NO: 3522	PEgRNA (AG;AGG PAM)
3512	SEQ ID NO: 3512	PEgRNA (AG;AGG PAM)
3489	SEQ ID NO: 3489	PEgRNA (AG;AGG PAM)
3521	SEQ ID NO: 3521	PEgRNA (AG;AGG PAM)
3502	SEQ ID NO: 3502	PEgRNA (AG;AGG PAM)
3507	SEQ ID NO: 3507	PEgRNA (AG;AGG PAM)
3518	SEQ ID NO: 3518	PEgRNA (AG;AGG PAM)
3491	SEQ ID NO: 3491	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3520	SEQ ID NO: 3520	PEgRNA (AG;AGG PAM)
3480	SEQ ID NO: 3480	PEgRNA (AG;AGG PAM)
3513	SEQ ID NO: 3513	PEgRNA (AG;AGG PAM)
3493	SEQ ID NO: 3493	PEgRNA (AG;AGG PAM)
3482	SEQ ID NO: 3482	PEgRNA (AG;AGG PAM)
3483	SEQ ID NO: 3483	PEgRNA (AG;AGG PAM)
3511	SEQ ID NO: 3511	PEgRNA (AG;AGG PAM)
3539	SEQ ID NO: 3539	PEgRNA (AG;AGG PAM)
3553	SEQ ID NO: 3553	PEgRNA (AG;AGG PAM)
3558	SEQ ID NO: 3558	PEgRNA (AG;AGG PAM)
3561	SEQ ID NO: 3561	PEgRNA (AG;AGG PAM)
3577	SEQ ID NO: 3577	PEgRNA (AG;AGG PAM)
3537	SEQ ID NO: 3537	PEgRNA (AG;AGG PAM)
3545	SEQ ID NO: 3545	PEgRNA (AG;AGG PAM)
3560	SEQ ID NO: 3560	PEgRNA (AG;AGG PAM)
3557	SEQ ID NO: 3557	PEgRNA (AG;AGG PAM)
3572	SEQ ID NO: 3572	PEgRNA (AG;AGG PAM)
3578	SEQ ID NO: 3578	PEgRNA (AG;AGG PAM)
3550	SEQ ID NO: 3550	PEgRNA (AG;AGG PAM)
3575	SEQ ID NO: 3575	PEgRNA (AG;AGG PAM)
3569	SEQ ID NO: 3569	PEgRNA (AG;AGG PAM)
3563	SEQ ID NO: 3563	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3531	SEQ ID NO: 3531	PEgRNA (AG;AGG PAM)
3546	SEQ ID NO: 3546	PEgRNA (AG;AGG PAM)
3570	SEQ ID NO: 3570	PEgRNA (AG;AGG PAM)
3524	SEQ ID NO: 3524	PEgRNA (AG;AGG PAM)
3562	SEQ ID NO: 3562	PEgRNA (AG;AGG PAM)
3542	SEQ ID NO: 3542	PEgRNA (AG;AGG PAM)
3529	SEQ ID NO: 3529	PEgRNA (AG;AGG PAM)
3541	SEQ ID NO: 3541	PEgRNA (AG;AGG PAM)
3525	SEQ ID NO: 3525	PEgRNA (AG;AGG PAM)
3555	SEQ ID NO: 3555	PEgRNA (AG;AGG PAM)
3543	SEQ ID NO: 3543	PEgRNA (AG;AGG PAM)
3544	SEQ ID NO: 3544	PEgRNA (AG;AGG PAM)
3530	SEQ ID NO: 3530	PEgRNA (AG;AGG PAM)
3571	SEQ ID NO: 3571	PEgRNA (AG;AGG PAM)
3535	SEQ ID NO: 3535	PEgRNA (AG;AGG PAM)
3568	SEQ ID NO: 3568	PEgRNA (AG;AGG PAM)
3540	SEQ ID NO: 3540	PEgRNA (AG;AGG PAM)
3564	SEQ ID NO: 3564	PEgRNA (AG;AGG PAM)
3527	SEQ ID NO: 3527	PEgRNA (AG;AGG PAM)
3536	SEQ ID NO: 3536	PEgRNA (AG;AGG PAM)
3526	SEQ ID NO: 3526	PEgRNA (AG;AGG PAM)
3559	SEQ ID NO: 3559	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3554	SEQ ID NO: 3554	PEgRNA (AG;AGG PAM)
3556	SEQ ID NO: 3556	PEgRNA (AG;AGG PAM)
3573	SEQ ID NO: 3573	PEgRNA (AG;AGG PAM)
3533	SEQ ID NO: 3533	PEgRNA (AG;AGG PAM)
3534	SEQ ID NO: 3534	PEgRNA (AG;AGG PAM)
3548	SEQ ID NO: 3548	PEgRNA (AG;AGG PAM)
3549	SEQ ID NO: 3549	PEgRNA (AG;AGG PAM)
3567	SEQ ID NO: 3567	PEgRNA (AG;AGG PAM)
3547	SEQ ID NO: 3547	PEgRNA (AG;AGG PAM)
3565	SEQ ID NO: 3565	PEgRNA (AG;AGG PAM)
3538	SEQ ID NO: 3538	PEgRNA (AG;AGG PAM)
3551	SEQ ID NO: 3551	PEgRNA (AG;AGG PAM)
3574	SEQ ID NO: 3574	PEgRNA (AG;AGG PAM)
3579	SEQ ID NO: 3579	PEgRNA (AG;AGG PAM)
3528	SEQ ID NO: 3528	PEgRNA (AG;AGG PAM)
3552	SEQ ID NO: 3552	PEgRNA (AG;AGG PAM)
3576	SEQ ID NO: 3576	PEgRNA (AG;AGG PAM)
3532	SEQ ID NO: 3532	PEgRNA (AG;AGG PAM)
3566	SEQ ID NO: 3566	PEgRNA (AG;AGG PAM)
3582	SEQ ID NO: 3582	PEgRNA (AG;AGG PAM)
3624	SEQ ID NO: 3624	PEgRNA (AG;AGG PAM)
3622	SEQ ID NO: 3622	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3621	SEQ ID NO: 3621	PEgRNA (AG;AGG PAM)
3617	SEQ ID NO: 3617	PEgRNA (AG;AGG PAM)
3587	SEQ ID NO: 3587	PEgRNA (AG;AGG PAM)
3603	SEQ ID NO: 3603	PEgRNA (AG;AGG PAM)
3609	SEQ ID NO: 3609	PEgRNA (AG;AGG PAM)
3604	SEQ ID NO: 3604	PEgRNA (AG;AGG PAM)
3586	SEQ ID NO: 3586	PEgRNA (AG;AGG PAM)
3602	SEQ ID NO: 3602	PEgRNA (AG;AGG PAM)
3593	SEQ ID NO: 3593	PEgRNA (AG;AGG PAM)
3625	SEQ ID NO: 3625	PEgRNA (AG;AGG PAM)
3627	SEQ ID NO: 3627	PEgRNA (AG;AGG PAM)
3580	SEQ ID NO: 3580	PEgRNA (AG;AGG PAM)
3590	SEQ ID NO: 3590	PEgRNA (AG;AGG PAM)
3616	SEQ ID NO: 3616	PEgRNA (AG;AGG PAM)
3618	SEQ ID NO: 3618	PEgRNA (AG;AGG PAM)
3611	SEQ ID NO: 3611	PEgRNA (AG;AGG PAM)
3584	SEQ ID NO: 3584	PEgRNA (AG;AGG PAM)
3588	SEQ ID NO: 3588	PEgRNA (AG;AGG PAM)
3626	SEQ ID NO: 3626	PEgRNA (AG;AGG PAM)
3600	SEQ ID NO: 3600	PEgRNA (AG;AGG PAM)
3589	SEQ ID NO: 3589	PEgRNA (AG;AGG PAM)
3606	SEQ ID NO: 3606	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3592	SEQ ID NO: 3592	PEgRNA (AG;AGG PAM)
3599	SEQ ID NO: 3599	PEgRNA (AG;AGG PAM)
3607	SEQ ID NO: 3607	PEgRNA (AG;AGG PAM)
3583	SEQ ID NO: 3583	PEgRNA (AG;AGG PAM)
3613	SEQ ID NO: 3613	PEgRNA (AG;AGG PAM)
3597	SEQ ID NO: 3597	PEgRNA (AG;AGG PAM)
3581	SEQ ID NO: 3581	PEgRNA (AG;AGG PAM)
3596	SEQ ID NO: 3596	PEgRNA (AG;AGG PAM)
3620	SEQ ID NO: 3620	PEgRNA (AG;AGG PAM)
3605	SEQ ID NO: 3605	PEgRNA (AG;AGG PAM)
3598	SEQ ID NO: 3598	PEgRNA (AG;AGG PAM)
3614	SEQ ID NO: 3614	PEgRNA (AG;AGG PAM)
3619	SEQ ID NO: 3619	PEgRNA (AG;AGG PAM)
3610	SEQ ID NO: 3610	PEgRNA (AG;AGG PAM)
3608	SEQ ID NO: 3608	PEgRNA (AG;AGG PAM)
3612	SEQ ID NO: 3612	PEgRNA (AG;AGG PAM)
3594	SEQ ID NO: 3594	PEgRNA (AG;AGG PAM)
3615	SEQ ID NO: 3615	PEgRNA (AG;AGG PAM)
3623	SEQ ID NO: 3623	PEgRNA (AG;AGG PAM)
3591	SEQ ID NO: 3591	PEgRNA (AG;AGG PAM)
3585	SEQ ID NO: 3585	PEgRNA (AG;AGG PAM)
3601	SEQ ID NO: 3601	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3595	SEQ ID NO: 3595	PEgRNA (AG;AGG PAM)
3644	SEQ ID NO: 3644	PEgRNA (AG;AGG PAM)
3673	SEQ ID NO: 3673	PEgRNA (AG;AGG PAM)
3672	SEQ ID NO: 3672	PEgRNA (AG;AGG PAM)
3671	SEQ ID NO: 3671	PEgRNA (AG;AGG PAM)
3654	SEQ ID NO: 3654	PEgRNA (AG;AGG PAM)
3668	SEQ ID NO: 3668	PEgRNA (AG;AGG PAM)
3656	SEQ ID NO: 3656	PEgRNA (AG;AGG PAM)
3662	SEQ ID NO: 3662	PEgRNA (AG;AGG PAM)
3650	SEQ ID NO: 3650	PEgRNA (AG;AGG PAM)
3669	SEQ ID NO: 3669	PEgRNA (AG;AGG PAM)
3666	SEQ ID NO: 3666	PEgRNA (AG;AGG PAM)
3631	SEQ ID NO: 3631	PEgRNA (AG;AGG PAM)
3667	SEQ ID NO: 3667	PEgRNA (AG;AGG PAM)
3634	SEQ ID NO: 3634	PEgRNA (AG;AGG PAM)
3648	SEQ ID NO: 3648	PEgRNA (AG;AGG PAM)
3628	SEQ ID NO: 3628	PEgRNA (AG;AGG PAM)
3632	SEQ ID NO: 3632	PEgRNA (AG;AGG PAM)
3642	SEQ ID NO: 3642	PEgRNA (AG;AGG PAM)
3674	SEQ ID NO: 3674	PEgRNA (AG;AGG PAM)
3658	SEQ ID NO: 3658	PEgRNA (AG;AGG PAM)
3640	SEQ ID NO: 3640	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3657	SEQ ID NO: 3657	PEgRNA (AG;AGG PAM)
3645	SEQ ID NO: 3645	PEgRNA (AG;AGG PAM)
3660	SEQ ID NO: 3660	PEgRNA (AG;AGG PAM)
3670	SEQ ID NO: 3670	PEgRNA (AG;AGG PAM)
3647	SEQ ID NO: 3647	PEgRNA (AG;AGG PAM)
3664	SEQ ID NO: 3664	PEgRNA (AG;AGG PAM)
3649	SEQ ID NO: 3649	PEgRNA (AG;AGG PAM)
3641	SEQ ID NO: 3641	PEgRNA (AG;AGG PAM)
3639	SEQ ID NO: 3639	PEgRNA (AG;AGG PAM)
3630	SEQ ID NO: 3630	PEgRNA (AG;AGG PAM)
3635	SEQ ID NO: 3635	PEgRNA (AG;AGG PAM)
3643	SEQ ID NO: 3643	PEgRNA (AG;AGG PAM)
3638	SEQ ID NO: 3638	PEgRNA (AG;AGG PAM)
3665	SEQ ID NO: 3665	PEgRNA (AG;AGG PAM)
3653	SEQ ID NO: 3653	PEgRNA (AG;AGG PAM)
3659	SEQ ID NO: 3659	PEgRNA (AG;AGG PAM)
3646	SEQ ID NO: 3646	PEgRNA (AG;AGG PAM)
3629	SEQ ID NO: 3629	PEgRNA (AG;AGG PAM)
3637	SEQ ID NO: 3637	PEgRNA (AG;AGG PAM)
3663	SEQ ID NO: 3663	PEgRNA (AG;AGG PAM)
3633	SEQ ID NO: 3633	PEgRNA (AG;AGG PAM)
3651	SEQ ID NO: 3651	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3661	SEQ ID NO: 3661	PEgRNA (AG;AGG PAM)
3655	SEQ ID NO: 3655	PEgRNA (AG;AGG PAM)
3636	SEQ ID NO: 3636	PEgRNA (AG;AGG PAM)
3675	SEQ ID NO: 3675	PEgRNA (AG;AGG PAM)
3652	SEQ ID NO: 3652	PEgRNA (AG;AGG PAM)
3689	SEQ ID NO: 3689	PEgRNA (AG;AGG PAM)
3687	SEQ ID NO: 3687	PEgRNA (AG;AGG PAM)
3713	SEQ ID NO: 3713	PEgRNA (AG;AGG PAM)
3714	SEQ ID NO: 3714	PEgRNA (AG;AGG PAM)
3682	SEQ ID NO: 3682	PEgRNA (AG;AGG PAM)
3701	SEQ ID NO: 3701	PEgRNA (AG;AGG PAM)
3683	SEQ ID NO: 3683	PEgRNA (AG;AGG PAM)
3708	SEQ ID NO: 3708	PEgRNA (AG;AGG PAM)
3720	SEQ ID NO: 3720	PEgRNA (AG;AGG PAM)
3695	SEQ ID NO: 3695	PEgRNA (AG;AGG PAM)
3685	SEQ ID NO: 3685	PEgRNA (AG;AGG PAM)
3709	SEQ ID NO: 3709	PEgRNA (AG;AGG PAM)
3686	SEQ ID NO: 3686	PEgRNA (AG;AGG PAM)
3698	SEQ ID NO: 3698	PEgRNA (AG;AGG PAM)
3676	SEQ ID NO: 3676	PEgRNA (AG;AGG PAM)
3690	SEQ ID NO: 3690	PEgRNA (AG;AGG PAM)
3691	SEQ ID NO: 3691	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3692	SEQ ID NO: 3692	PEgRNA (AG;AGG PAM)
3693	SEQ ID NO: 3693	PEgRNA (AG;AGG PAM)
3694	SEQ ID NO: 3694	PEgRNA (AG;AGG PAM)
3699	SEQ ID NO: 3699	PEgRNA (AG;AGG PAM)
3696	SEQ ID NO: 3696	PEgRNA (AG;AGG PAM)
3688	SEQ ID NO: 3688	PEgRNA (AG;AGG PAM)
3684	SEQ ID NO: 3684	PEgRNA (AG;AGG PAM)
3680	SEQ ID NO: 3680	PEgRNA (AG;AGG PAM)
3678	SEQ ID NO: 3678	PEgRNA (AG;AGG PAM)
3705	SEQ ID NO: 3705	PEgRNA (AG;AGG PAM)
3712	SEQ ID NO: 3712	PEgRNA (AG;AGG PAM)
3715	SEQ ID NO: 3715	PEgRNA (AG;AGG PAM)
3704	SEQ ID NO: 3704	PEgRNA (AG;AGG PAM)
3706	SEQ ID NO: 3706	PEgRNA (AG;AGG PAM)
3679	SEQ ID NO: 3679	PEgRNA (AG;AGG PAM)
3707	SEQ ID NO: 3707	PEgRNA (AG;AGG PAM)
3711	SEQ ID NO: 3711	PEgRNA (AG;AGG PAM)
3717	SEQ ID NO: 3717	PEgRNA (AG;AGG PAM)
3710	SEQ ID NO: 3710	PEgRNA (AG;AGG PAM)
3681	SEQ ID NO: 3681	PEgRNA (AG;AGG PAM)
3677	SEQ ID NO: 3677	PEgRNA (AG;AGG PAM)
3702	SEQ ID NO: 3702	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3703	SEQ ID NO: 3703	PEgRNA (AG;AGG PAM)
3718	SEQ ID NO: 3718	PEgRNA (AG;AGG PAM)
3697	SEQ ID NO: 3697	PEgRNA (AG;AGG PAM)
3719	SEQ ID NO: 3719	PEgRNA (AG;AGG PAM)
3723	SEQ ID NO: 3723	PEgRNA (AG;AGG PAM)
3700	SEQ ID NO: 3700	PEgRNA (AG;AGG PAM)
3722	SEQ ID NO: 3722	PEgRNA (AG;AGG PAM)
3716	SEQ ID NO: 3716	PEgRNA (AG;AGG PAM)
3721	SEQ ID NO: 3721	PEgRNA (AG;AGG PAM)
3725	SEQ ID NO: 3725	PEgRNA (AG;AGG PAM)
3749	SEQ ID NO: 3749	PEgRNA (AG;AGG PAM)
3724	SEQ ID NO: 3724	PEgRNA (AG;AGG PAM)
3769	SEQ ID NO: 3769	PEgRNA (AG;AGG PAM)
3767	SEQ ID NO: 3767	PEgRNA (AG;AGG PAM)
3729	SEQ ID NO: 3729	PEgRNA (AG;AGG PAM)
3762	SEQ ID NO: 3762	PEgRNA (AG;AGG PAM)
3771	SEQ ID NO: 3771	PEgRNA (AG;AGG PAM)
3731	SEQ ID NO: 3731	PEgRNA (AG;AGG PAM)
3730	SEQ ID NO: 3730	PEgRNA (AG;AGG PAM)
3742	SEQ ID NO: 3742	PEgRNA (AG;AGG PAM)
3743	SEQ ID NO: 3743	PEgRNA (AG;AGG PAM)
3732	SEQ ID NO: 3732	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3740	SEQ ID NO: 3740	PEgRNA (AG;AGG PAM)
3734	SEQ ID NO: 3734	PEgRNA (AG;AGG PAM)
3741	SEQ ID NO: 3741	PEgRNA (AG;AGG PAM)
3751	SEQ ID NO: 3751	PEgRNA (AG;AGG PAM)
3739	SEQ ID NO: 3739	PEgRNA (AG;AGG PAM)
3748	SEQ ID NO: 3748	PEgRNA (AG;AGG PAM)
3736	SEQ ID NO: 3736	PEgRNA (AG;AGG PAM)
3744	SEQ ID NO: 3744	PEgRNA (AG;AGG PAM)
3746	SEQ ID NO: 3746	PEgRNA (AG;AGG PAM)
3747	SEQ ID NO: 3747	PEgRNA (AG;AGG PAM)
3765	SEQ ID NO: 3765	PEgRNA (AG;AGG PAM)
3726	SEQ ID NO: 3726	PEgRNA (AG;AGG PAM)
3738	SEQ ID NO: 3738	PEgRNA (AG;AGG PAM)
3770	SEQ ID NO: 3770	PEgRNA (AG;AGG PAM)
3752	SEQ ID NO: 3752	PEgRNA (AG;AGG PAM)
3750	SEQ ID NO: 3750	PEgRNA (AG;AGG PAM)
3759	SEQ ID NO: 3759	PEgRNA (AG;AGG PAM)
3758	SEQ ID NO: 3758	PEgRNA (AG;AGG PAM)
3757	SEQ ID NO: 3757	PEgRNA (AG;AGG PAM)
3761	SEQ ID NO: 3761	PEgRNA (AG;AGG PAM)
3764	SEQ ID NO: 3764	PEgRNA (AG;AGG PAM)
3754	SEQ ID NO: 3754	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3753	SEQ ID NO: 3753	PEgRNA (AG;AGG PAM)
3733	SEQ ID NO: 3733	PEgRNA (AG;AGG PAM)
3755	SEQ ID NO: 3755	PEgRNA (AG;AGG PAM)
3756	SEQ ID NO: 3756	PEgRNA (AG;AGG PAM)
3760	SEQ ID NO: 3760	PEgRNA (AG;AGG PAM)
3763	SEQ ID NO: 3763	PEgRNA (AG;AGG PAM)
3735	SEQ ID NO: 3735	PEgRNA (AG;AGG PAM)
3745	SEQ ID NO: 3745	PEgRNA (AG;AGG PAM)
3766	SEQ ID NO: 3766	PEgRNA (AG;AGG PAM)
3728	SEQ ID NO: 3728	PEgRNA (AG;AGG PAM)
3727	SEQ ID NO: 3727	PEgRNA (AG;AGG PAM)
3737	SEQ ID NO: 3737	PEgRNA (AG;AGG PAM)
3768	SEQ ID NO: 3768	PEgRNA (AG;AGG PAM)
3791	SEQ ID NO: 3791	PEgRNA (AG;AGG PAM)
3782	SEQ ID NO: 3782	PEgRNA (AG;AGG PAM)
3776	SEQ ID NO: 3776	PEgRNA (AG;AGG PAM)
3798	SEQ ID NO: 3798	PEgRNA (AG;AGG PAM)
3785	SEQ ID NO: 3785	PEgRNA (AG;AGG PAM)
3805	SEQ ID NO: 3805	PEgRNA (AG;AGG PAM)
3784	SEQ ID NO: 3784	PEgRNA (AG;AGG PAM)
3777	SEQ ID NO: 3777	PEgRNA (AG;AGG PAM)
3772	SEQ ID NO: 3772	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3815	SEQ ID NO: 3815	PEgRNA (AG;AGG PAM)
3780	SEQ ID NO: 3780	PEgRNA (AG;AGG PAM)
3789	SEQ ID NO: 3789	PEgRNA (AG;AGG PAM)
3775	SEQ ID NO: 3775	PEgRNA (AG;AGG PAM)
3808	SEQ ID NO: 3808	PEgRNA (AG;AGG PAM)
3790	SEQ ID NO: 3790	PEgRNA (AG;AGG PAM)
3813	SEQ ID NO: 3813	PEgRNA (AG;AGG PAM)
3792	SEQ ID NO: 3792	PEgRNA (AG;AGG PAM)
3801	SEQ ID NO: 3801	PEgRNA (AG;AGG PAM)
3781	SEQ ID NO: 3781	PEgRNA (AG;AGG PAM)
3783	SEQ ID NO: 3783	PEgRNA (AG;AGG PAM)
3812	SEQ ID NO: 3812	PEgRNA (AG;AGG PAM)
3799	SEQ ID NO: 3799	PEgRNA (AG;AGG PAM)
3787	SEQ ID NO: 3787	PEgRNA (AG;AGG PAM)
3788	SEQ ID NO: 3788	PEgRNA (AG;AGG PAM)
3778	SEQ ID NO: 3778	PEgRNA (AG;AGG PAM)
3817	SEQ ID NO: 3817	PEgRNA (AG;AGG PAM)
3819	SEQ ID NO: 3819	PEgRNA (AG;AGG PAM)
3794	SEQ ID NO: 3794	PEgRNA (AG;AGG PAM)
3818	SEQ ID NO: 3818	PEgRNA (AG;AGG PAM)
3802	SEQ ID NO: 3802	PEgRNA (AG;AGG PAM)
3816	SEQ ID NO: 3816	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3814	SEQ ID NO: 3814	PEgRNA (AG;AGG PAM)
3773	SEQ ID NO: 3773	PEgRNA (AG;AGG PAM)
3810	SEQ ID NO: 3810	PEgRNA (AG;AGG PAM)
3797	SEQ ID NO: 3797	PEgRNA (AG;AGG PAM)
3807	SEQ ID NO: 3807	PEgRNA (AG;AGG PAM)
3803	SEQ ID NO: 3803	PEgRNA (AG;AGG PAM)
3804	SEQ ID NO: 3804	PEgRNA (AG;AGG PAM)
3793	SEQ ID NO: 3793	PEgRNA (AG;AGG PAM)
3809	SEQ ID NO: 3809	PEgRNA (AG;AGG PAM)
3811	SEQ ID NO: 3811	PEgRNA (AG;AGG PAM)
3796	SEQ ID NO: 3796	PEgRNA (AG;AGG PAM)
3786	SEQ ID NO: 3786	PEgRNA (AG;AGG PAM)
3774	SEQ ID NO: 3774	PEgRNA (AG;AGG PAM)
3806	SEQ ID NO: 3806	PEgRNA (AG;AGG PAM)
3800	SEQ ID NO: 3800	PEgRNA (AG;AGG PAM)
3795	SEQ ID NO: 3795	PEgRNA (AG;AGG PAM)
3779	SEQ ID NO: 3779	PEgRNA (AG;AGG PAM)
3851	SEQ ID NO: 3851	PEgRNA (AG;AGG PAM)
3830	SEQ ID NO: 3830	PEgRNA (AG;AGG PAM)
3824	SEQ ID NO: 3824	PEgRNA (AG;AGG PAM)
3836	SEQ ID NO: 3836	PEgRNA (AG;AGG PAM)
3823	SEQ ID NO: 3823	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3821	SEQ ID NO: 3821	PEgRNA (AG;AGG PAM)
3822	SEQ ID NO: 3822	PEgRNA (AG;AGG PAM)
3826	SEQ ID NO: 3826	PEgRNA (AG;AGG PAM)
3820	SEQ ID NO: 3820	PEgRNA (AG;AGG PAM)
3841	SEQ ID NO: 3841	PEgRNA (AG;AGG PAM)
3838	SEQ ID NO: 3838	PEgRNA (AG;AGG PAM)
3840	SEQ ID NO: 3840	PEgRNA (AG;AGG PAM)
3833	SEQ ID NO: 3833	PEgRNA (AG;AGG PAM)
3837	SEQ ID NO: 3837	PEgRNA (AG;AGG PAM)
3831	SEQ ID NO: 3831	PEgRNA (AG;AGG PAM)
3854	SEQ ID NO: 3854	PEgRNA (AG;AGG PAM)
3835	SEQ ID NO: 3835	PEgRNA (AG;AGG PAM)
3857	SEQ ID NO: 3857	PEgRNA (AG;AGG PAM)
3855	SEQ ID NO: 3855	PEgRNA (AG;AGG PAM)
3843	SEQ ID NO: 3843	PEgRNA (AG;AGG PAM)
3844	SEQ ID NO: 3844	PEgRNA (AG;AGG PAM)
3845	SEQ ID NO: 3845	PEgRNA (AG;AGG PAM)
3856	SEQ ID NO: 3856	PEgRNA (AG;AGG PAM)
3834	SEQ ID NO: 3834	PEgRNA (AG;AGG PAM)
3847	SEQ ID NO: 3847	PEgRNA (AG;AGG PAM)
3850	SEQ ID NO: 3850	PEgRNA (AG;AGG PAM)
3859	SEQ ID NO: 3859	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3853	SEQ ID NO: 3853	PEgRNA (AG;AGG PAM)
3858	SEQ ID NO: 3858	PEgRNA (AG;AGG PAM)
3852	SEQ ID NO: 3852	PEgRNA (AG;AGG PAM)
3846	SEQ ID NO: 3846	PEgRNA (AG;AGG PAM)
3829	SEQ ID NO: 3829	PEgRNA (AG;AGG PAM)
3848	SEQ ID NO: 3848	PEgRNA (AG;AGG PAM)
3825	SEQ ID NO: 3825	PEgRNA (AG;AGG PAM)
3839	SEQ ID NO: 3839	PEgRNA (AG;AGG PAM)
3832	SEQ ID NO: 3832	PEgRNA (AG;AGG PAM)
3849	SEQ ID NO: 3849	PEgRNA (AG;AGG PAM)
3842	SEQ ID NO: 3842	PEgRNA (AG;AGG PAM)
3827	SEQ ID NO: 3827	PEgRNA (AG;AGG PAM)
3828	SEQ ID NO: 3828	PEgRNA (AG;AGG PAM)
3867	SEQ ID NO: 3867	PEgRNA (AG;AGG PAM)
3863	SEQ ID NO: 3863	PEgRNA (AG;AGG PAM)
3864	SEQ ID NO: 3864	PEgRNA (AG;AGG PAM)
3871	SEQ ID NO: 3871	PEgRNA (AG;AGG PAM)
3870	SEQ ID NO: 3870	PEgRNA (AG;AGG PAM)
3869	SEQ ID NO: 3869	PEgRNA (AG;AGG PAM)
3860	SEQ ID NO: 3860	PEgRNA (AG;AGG PAM)
3877	SEQ ID NO: 3877	PEgRNA (AG;AGG PAM)
3872	SEQ ID NO: 3872	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3875	SEQ ID NO: 3875	PEgRNA (AG;AGG PAM)
3874	SEQ ID NO: 3874	PEgRNA (AG;AGG PAM)
3866	SEQ ID NO: 3866	PEgRNA (AG;AGG PAM)
3865	SEQ ID NO: 3865	PEgRNA (AG;AGG PAM)
3873	SEQ ID NO: 3873	PEgRNA (AG;AGG PAM)
3862	SEQ ID NO: 3862	PEgRNA (AG;AGG PAM)
3861	SEQ ID NO: 3861	PEgRNA (AG;AGG PAM)
3876	SEQ ID NO: 3876	PEgRNA (AG;AGG PAM)
3868	SEQ ID NO: 3868	PEgRNA (AG;AGG PAM)
3888	SEQ ID NO: 3888	PEgRNA (AG;AGG PAM)
3894	SEQ ID NO: 3894	PEgRNA (AG;AGG PAM)
3879	SEQ ID NO: 3879	PEgRNA (AG;AGG PAM)
3880	SEQ ID NO: 3880	PEgRNA (AG;AGG PAM)
3881	SEQ ID NO: 3881	PEgRNA (AG;AGG PAM)
3882	SEQ ID NO: 3882	PEgRNA (AG;AGG PAM)
3883	SEQ ID NO: 3883	PEgRNA (AG;AGG PAM)
3884	SEQ ID NO: 3884	PEgRNA (AG;AGG PAM)
3885	SEQ ID NO: 3885	PEgRNA (AG;AGG PAM)
3889	SEQ ID NO: 3889	PEgRNA (AG;AGG PAM)
3886	SEQ ID NO: 3886	PEgRNA (AG;AGG PAM)
3899	SEQ ID NO: 3899	PEgRNA (AG;AGG PAM)
3890	SEQ ID NO: 3890	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3887	SEQ ID NO: 3887	PEgRNA (AG;AGG PAM)
3891	SEQ ID NO: 3891	PEgRNA (AG;AGG PAM)
3892	SEQ ID NO: 3892	PEgRNA (AG;AGG PAM)
3893	SEQ ID NO: 3893	PEgRNA (AG;AGG PAM)
3895	SEQ ID NO: 3895	PEgRNA (AG;AGG PAM)
3896	SEQ ID NO: 3896	PEgRNA (AG;AGG PAM)
3897	SEQ ID NO: 3897	PEgRNA (AG;AGG PAM)
3898	SEQ ID NO: 3898	PEgRNA (AG;AGG PAM)
3878	SEQ ID NO: 3878	PEgRNA (AG;AGG PAM)
3900	SEQ ID NO: 3900	PEgRNA (AG;AGG PAM)
3924	SEQ ID NO: 3924	PEgRNA (AG;AGG PAM)
3940	SEQ ID NO: 3940	PEgRNA (AG;AGG PAM)
3923	SEQ ID NO: 3923	PEgRNA (AG;AGG PAM)
3905	SEQ ID NO: 3905	PEgRNA (AG;AGG PAM)
3906	SEQ ID NO: 3906	PEgRNA (AG;AGG PAM)
3907	SEQ ID NO: 3907	PEgRNA (AG;AGG PAM)
3908	SEQ ID NO: 3908	PEgRNA (AG;AGG PAM)
3909	SEQ ID NO: 3909	PEgRNA (AG;AGG PAM)
3911	SEQ ID NO: 3911	PEgRNA (AG;AGG PAM)
3910	SEQ ID NO: 3910	PEgRNA (AG;AGG PAM)
3927	SEQ ID NO: 3927	PEgRNA (AG;AGG PAM)
3913	SEQ ID NO: 3913	PEgRNA (AG;AGG PAM)
3914	SEQ ID NO: 3914	PEgRNA (AG;AGG PAM)
3915	SEQ ID NO: 3915	PEgRNA (AG;AGG PAM)
3916	SEQ ID NO: 3916	PEgRNA (AG;AGG PAM)
3917	SEQ ID NO: 3917	PEgRNA (AG;AGG PAM)
3918	SEQ ID NO: 3918	PEgRNA (AG;AGG PAM)
3919	SEQ ID NO: 3919	PEgRNA (AG;AGG PAM)
3920	SEQ ID NO: 3920	PEgRNA (AG;AGG PAM)
3921	SEQ ID NO: 3921	PEgRNA (AG;AGG PAM)
3902	SEQ ID NO: 3902	PEgRNA (AG;AGG PAM)
3912	SEQ ID NO: 3912	PEgRNA (AG;AGG PAM)
3925	SEQ ID NO: 3925	PEgRNA (AG;AGG PAM)
3901	SEQ ID NO: 3901	PEgRNA (AG;AGG PAM)
3926	SEQ ID NO: 3926	PEgRNA (AG;AGG PAM)
3922	SEQ ID NO: 3922	PEgRNA (AG;AGG PAM)
3928	SEQ ID NO: 3928	PEgRNA (AG;AGG PAM)
3904	SEQ ID NO: 3904	PEgRNA (AG;AGG PAM)
3929	SEQ ID NO: 3929	PEgRNA (AG;AGG PAM)
3930	SEQ ID NO: 3930	PEgRNA (AG;AGG PAM)
3931	SEQ ID NO: 3931	PEgRNA (AG;AGG PAM)
3932	SEQ ID NO: 3932	PEgRNA (AG;AGG PAM)
3933	SEQ ID NO: 3933	PEgRNA (AG;AGG PAM)
3934	SEQ ID NO: 3934	PEgRNA (AG;AGG PAM)
3935	SEQ ID NO: 3935	PEgRNA (AG;AGG PAM)
3936	SEQ ID NO: 3936	PEgRNA (AG;AGG PAM)
3937	SEQ ID NO: 3937	PEgRNA (AG;AGG PAM)
3938	SEQ ID NO: 3938	PEgRNA (AG;AGG PAM)
3939	SEQ ID NO: 3939	PEgRNA (AG;AGG PAM)
3903	SEQ ID NO: 3903	PEgRNA (AG;AGG PAM)
3941	SEQ ID NO: 3941	PEgRNA (AG;AGG PAM)
3942	SEQ ID NO: 3942	PEgRNA (AG;AGG PAM)
3943	SEQ ID NO: 3943	PEgRNA (AG;AGG PAM)
3944	SEQ ID NO: 3944	PEgRNA (AG;AGG PAM)
3945	SEQ ID NO: 3945	PEgRNA (AG;AGG PAM)
3946	SEQ ID NO: 3946	PEgRNA (AG;AGG PAM)
3947	SEQ ID NO: 3947	PEgRNA (AG;AGG PAM)
3948	SEQ ID NO: 3948	PEgRNA (AG;AGG PAM)
3949	SEQ ID NO: 3949	PEgRNA (AG;AGG PAM)
3950	SEQ ID NO: 3950	PEgRNA (AG;AGG PAM)
3951	SEQ ID NO: 3951	PEgRNA (AG;AGG PAM)
3952	SEQ ID NO: 3952	PEgRNA (AG;AGG PAM)
3953	SEQ ID NO: 3953	PEgRNA (AG;AGG PAM)
3954	SEQ ID NO: 3954	PEgRNA (AG;AGG PAM)
3955	SEQ ID NO: 3955	PEgRNA (AG;AGG PAM)
3956	SEQ ID NO: 3956	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3957	SEQ ID NO: 3957	PEgRNA (AG;AGG PAM)
3958	SEQ ID NO: 3958	PEgRNA (AG;AGG PAM)
3959	SEQ ID NO: 3959	PEgRNA (AG;AGG PAM)
3960	SEQ ID NO: 3960	PEgRNA (AG;AGG PAM)
3961	SEQ ID NO: 3961	PEgRNA (AG;AGG PAM)
3962	SEQ ID NO: 3962	PEgRNA (AG;AGG PAM)
3963	SEQ ID NO: 3963	PEgRNA (AG;AGG PAM)
3964	SEQ ID NO: 3964	PEgRNA (AG;AGG PAM)
3965	SEQ ID NO: 3965	PEgRNA (AG;AGG PAM)
3966	SEQ ID NO: 3966	PEgRNA (AG;AGG PAM)
3967	SEQ ID NO: 3967	PEgRNA (AG;AGG PAM)
3968	SEQ ID NO: 3968	PEgRNA (AG;AGG PAM)
3969	SEQ ID NO: 3969	PEgRNA (AG;AGG PAM)
3978	SEQ ID NO: 3978	PEgRNA (AG;AGG PAM)
3971	SEQ ID NO: 3971	PEgRNA (AG;AGG PAM)
3972	SEQ ID NO: 3972	PEgRNA (AG;AGG PAM)
3973	SEQ ID NO: 3973	PEgRNA (AG;AGG PAM)
3974	SEQ ID NO: 3974	PEgRNA (AG;AGG PAM)
3975	SEQ ID NO: 3975	PEgRNA (AG;AGG PAM)
3976	SEQ ID NO: 3976	PEgRNA (AG;AGG PAM)
3977	SEQ ID NO: 3977	PEgRNA (AG;AGG PAM)
3970	SEQ ID NO: 3970	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
3979	SEQ ID NO: 3979	PEgRNA (AG;AGG PAM)
3980	SEQ ID NO: 3980	PEgRNA (AG;AGG PAM)
3981	SEQ ID NO: 3981	PEgRNA (AG;AGG PAM)
3982	SEQ ID NO: 3982	PEgRNA (AG;AGG PAM)
3983	SEQ ID NO: 3983	PEgRNA (AG;AGG PAM)
3984	SEQ ID NO: 3984	PEgRNA (AG;AGG PAM)
3985	SEQ ID NO: 3985	PEgRNA (AG;AGG PAM)
3986	SEQ ID NO: 3986	PEgRNA (AG;AGG PAM)
3987	SEQ ID NO: 3987	PEgRNA (AG;AGG PAM)
3988	SEQ ID NO: 3988	PEgRNA (AG;AGG PAM)
3989	SEQ ID NO: 3989	PEgRNA (AG;AGG PAM)
3990	SEQ ID NO: 3990	PEgRNA (AG;AGG PAM)
3991	SEQ ID NO: 3991	PEgRNA (AG;AGG PAM)
3992	SEQ ID NO: 3992	PEgRNA (AG;AGG PAM)
3993	SEQ ID NO: 3993	PEgRNA (AG;AGG PAM)
3994	SEQ ID NO: 3994	PEgRNA (AG;AGG PAM)
3995	SEQ ID NO: 3995	PEgRNA (AG;AGG PAM)
3996	SEQ ID NO: 3996	PEgRNA (AG;AGG PAM)
3997	SEQ ID NO: 3997	PEgRNA (AG;AGG PAM)
3998	SEQ ID NO: 3998	PEgRNA (AG;AGG PAM)
3999	SEQ ID NO: 3999	PEgRNA (AG;AGG PAM)
4000	SEQ ID NO: 4000	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
4001	SEQ ID NO: 4001	PEgRNA (AG;AGG PAM)
4002	SEQ ID NO: 4002	PEgRNA (AG;AGG PAM)
4003	SEQ ID NO: 4003	PEgRNA (AG;AGG PAM)
4004	SEQ ID NO: 4004	PEgRNA (AG;AGG PAM)
4005	SEQ ID NO: 4005	PEgRNA (AG;AGG PAM)
4006	SEQ ID NO: 4006	PEgRNA (AG;AGG PAM)
4007	SEQ ID NO: 4007	PEgRNA (AG;AGG PAM)
4008	SEQ ID NO: 4008	PEgRNA (AG;AGG PAM)
4009	SEQ ID NO: 4009	PEgRNA (AG;AGG PAM)
4010	SEQ ID NO: 4010	PEgRNA (AG;AGG PAM)
4011	SEQ ID NO: 4011	PEgRNA (AG;AGG PAM)
4012	SEQ ID NO: 4012	PEgRNA (AG;AGG PAM)
4013	SEQ ID NO: 4013	PEgRNA (AG;AGG PAM)
4014	SEQ ID NO: 4014	PEgRNA (AG;AGG PAM)
4015	SEQ ID NO: 4015	PEgRNA (AG;AGG PAM)
4016	SEQ ID NO: 4016	PEgRNA (AG;AGG PAM)
4017	SEQ ID NO: 4017	PEgRNA (AG;AGG PAM)
4018	SEQ ID NO: 4018	PEgRNA (AG;AGG PAM)
4019	SEQ ID NO: 4019	PEgRNA (AG;AGG PAM)
4020	SEQ ID NO: 4020	PEgRNA (AG;AGG PAM)
4021	SEQ ID NO: 4021	PEgRNA (AG;AGG PAM)
4022	SEQ ID NO: 4022	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
4023	SEQ ID NO: 4023	PEgRNA (AG;AGG PAM)
4024	SEQ ID NO: 4024	PEgRNA (AG;AGG PAM)
4025	SEQ ID NO: 4025	PEgRNA (AG;AGG PAM)
4026	SEQ ID NO: 4026	PEgRNA (AG;AGG PAM)
4027	SEQ ID NO: 4027	PEgRNA (AG;AGG PAM)
4028	SEQ ID NO: 4028	PEgRNA (AG;AGG PAM)
4029	SEQ ID NO: 4029	PEgRNA (AG;AGG PAM)
4030	SEQ ID NO: 4030	PEgRNA (AG;AGG PAM)
4031	SEQ ID NO: 4031	PEgRNA (AG;AGG PAM)
4032	SEQ ID NO: 4032	PEgRNA (AG;AGG PAM)
4033	SEQ ID NO: 4033	PEgRNA (AG;AGG PAM)
4034	SEQ ID NO: 4034	PEgRNA (AG;AGG PAM)
4035	SEQ ID NO: 4035	PEgRNA (AG;AGG PAM)
4036	SEQ ID NO: 4036	PEgRNA (AG;AGG PAM)
4037	SEQ ID NO: 4037	PEgRNA (AG;AGG PAM)
4038	SEQ ID NO: 4038	PEgRNA (AG;AGG PAM)
4039	SEQ ID NO: 4039	PEgRNA (AG;AGG PAM)
4040	SEQ ID NO: 4040	PEgRNA (AG;AGG PAM)
4041	SEQ ID NO: 4041	PEgRNA (AG;AGG PAM)
4042	SEQ ID NO: 4042	PEgRNA (AG;AGG PAM)
4043	SEQ ID NO: 4043	PEgRNA (AG;AGG PAM)
4044	SEQ ID NO: 4044	PEgRNA (AG;AGG PAM)
4045	SEQ ID NO: 4045	PEgRNA (AG;AGG PAM)
4046	SEQ ID NO: 4046	PEgRNA (AG;AGG PAM)
4047	SEQ ID NO: 4047	PEgRNA (AG;AGG PAM)
4048	SEQ ID NO: 4048	PEgRNA (AG;AGG PAM)
4049	SEQ ID NO: 4049	PEgRNA (AG;AGG PAM)
4050	SEQ ID NO: 4050	PEgRNA (AG;AGG PAM)
4051	SEQ ID NO: 4051	PEgRNA (AG;AGG PAM)
4052	SEQ ID NO: 4052	PEgRNA (AG;AGG PAM)
4053	SEQ ID NO: 4053	PEgRNA (AG;AGG PAM)
4054	SEQ ID NO: 4054	PEgRNA (AG;AGG PAM)
4055	SEQ ID NO: 4055	PEgRNA (AG;AGG PAM)
4056	SEQ ID NO: 4056	PEgRNA (AG;AGG PAM)
4057	SEQ ID NO: 4057	PEgRNA (AG;AGG PAM)
4058	SEQ ID NO: 4058	PEgRNA (AG;AGG PAM)
4059	SEQ ID NO: 4059	PEgRNA (AG;AGG PAM)
4060	SEQ ID NO: 4060	PEgRNA (AG;AGG PAM)
4061	SEQ ID NO: 4061	PEgRNA (AG;AGG PAM)
4062	SEQ ID NO: 4062	PEgRNA (AG;AGG PAM)
4063	SEQ ID NO: 4063	PEgRNA (AG;AGG PAM)
4064	SEQ ID NO: 4064	PEgRNA (AG;AGG PAM)
4065	SEQ ID NO: 4065	PEgRNA (AG;AGG PAM)
4066	SEQ ID NO: 4066	PEgRNA (AG;AGG PAM)
4067	SEQ ID NO: 4067	PEgRNA (AG;AGG PAM)
4068	SEQ ID NO: 4068	PEgRNA (AG;AGG PAM)
4069	SEQ ID NO: 4069	PEgRNA (AG;AGG PAM)
4070	SEQ ID NO: 4070	PEgRNA (AG;AGG PAM)
4071	SEQ ID NO: 4071	PEgRNA (AG;AGG PAM)
4072	SEQ ID NO: 4072	PEgRNA (AG;AGG PAM)
4073	SEQ ID NO: 4073	PEgRNA (AG;AGG PAM)
4074	SEQ ID NO: 4074	PEgRNA (AG;AGG PAM)
4075	SEQ ID NO: 4075	PEgRNA (AG;AGG PAM)
4076	SEQ ID NO: 4076	PEgRNA (AG;AGG PAM)
4077	SEQ ID NO: 4077	PEgRNA (AG;AGG PAM)
4078	SEQ ID NO: 4078	PEgRNA (AG;AGG PAM)
4079	SEQ ID NO: 4079	PEgRNA (AG;AGG PAM)
4080	SEQ ID NO: 4080	PEgRNA (AG;AGG PAM)
4081	SEQ ID NO: 4081	PEgRNA (AG;AGG PAM)
4082	SEQ ID NO: 4082	PEgRNA (AG;AGG PAM)
4083	SEQ ID NO: 4083	PEgRNA (AG;AGG PAM)
14769	SEQ ID NO: 14769	PEgRNA (AG;AGG PAM)
14770	SEQ ID NO: 14770	PEgRNA (AG;AGG PAM)
14771	SEQ ID NO: 14771	PEgRNA (AG;AGG PAM)
14772	SEQ ID NO: 14772	PEgRNA (AG;AGG PAM)
14773	SEQ ID NO: 14773	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
14774	SEQ ID NO: 14774	PEgRNA (AG;AGG PAM)
14775	SEQ ID NO: 14775	PEgRNA (AG;AGG PAM)
14776	SEQ ID NO: 14776	PEgRNA (AG;AGG PAM)
14777	SEQ ID NO: 14777	PEgRNA (AG;AGG PAM)
14778	SEQ ID NO: 14778	PEgRNA (AG;AGG PAM)
14779	SEQ ID NO: 14779	PEgRNA (AG;AGG PAM)
14780	SEQ ID NO: 14780	PEgRNA (AG;AGG PAM)
14781	SEQ ID NO: 14781	PEgRNA (AG;AGG PAM)
14782	SEQ ID NO: 14782	PEgRNA (AG;AGG PAM)
14783	SEQ ID NO: 14783	PEgRNA (AG;AGG PAM)
14784	SEQ ID NO: 14784	PEgRNA (AG;AGG PAM)
14785	SEQ ID NO: 14785	PEgRNA (AG;AGG PAM)
14786	SEQ ID NO: 14786	PEgRNA (AG;AGG PAM)
14787	SEQ ID NO: 14787	PEgRNA (AG;AGG PAM)
14788	SEQ ID NO: 14788	PEgRNA (AG;AGG PAM)
14789	SEQ ID NO: 14789	PEgRNA (AG;AGG PAM)
14790	SEQ ID NO: 14790	PEgRNA (AG;AGG PAM)
14791	SEQ ID NO: 14791	PEgRNA (AG;AGG PAM)
14792	SEQ ID NO: 14792	PEgRNA (AG;AGG PAM)
14793	SEQ ID NO: 14793	PEgRNA (AG;AGG PAM)
14794	SEQ ID NO: 14794	PEgRNA (AG;AGG PAM)
14795	SEQ ID NO: 14795	PEgRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
14796	SEQ ID NO: 14796	PEgRNA (AG;AGG PAM)
14797	SEQ ID NO: 14797	PEgRNA (AG;AGG PAM)
14798	SEQ ID NO: 14798	PEgRNA (AG;AGG PAM)
14799	SEQ ID NO: 14799	PEgRNA (AG;AGG PAM)
4105	SEQ ID NO: 4105	ngRNA (AG;AGG PAM)
4106	SEQ ID NO: 4106	ngRNA (CG;CGG PAM)
4091	SEQ ID NO: 4091	ngRNA (AG;AGG PAM)
4109	SEQ ID NO: 4109	ngRNA (TG;TGG PAM)
4086	SEQ ID NO: 4086	ngRNA (TG;TGG PAM)
4088	SEQ ID NO: 4088	ngRNA (TG;TGG PAM)
4101	SEQ ID NO: 4101	ngRNA (TG;TGG PAM)
4102	SEQ ID NO: 4102	ngRNA (TG;TGG PAM)
4110	SEQ ID NO: 4110	ngRNA (TG;TGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
4096	SEQ ID NO: 4096	ngRNA (TG;TGG PAM)
4104	SEQ ID NO: 4104	ngRNA (TG;TGG PAM)
4090	SEQ ID NO: 4090	ngRNA (TG;TGG PAM)
4084	SEQ ID NO: 4084	ngRNA (TG;TGG PAM)
4103	SEQ ID NO: 4103	ngRNA (TG;TGG PAM)
4093	SEQ ID NO: 4093	ngRNA (TG;TGG PAM)
4094	SEQ ID NO: 4094	ngRNA (TG;TGG PAM)

Sequence Number	Sequence	Description
4095	SEQ ID NO: 4095	ngRNA (TG;TGG PAM)
4085	SEQ ID NO: 4085	ngRNA (TG;TGG PAM)
4097	SEQ ID NO: 4097	ngRNA (TG;TGG PAM)
4098	SEQ ID NO: 4098	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
4087	SEQ ID NO: 4087	ngRNA (TG;TGG PAM)
4100	SEQ ID NO: 4100	ngRNA (TG;TGG PAM)
4092	SEQ ID NO: 4092	ngRNA (TG;TGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)
4099	SEQ ID NO: 4099	ngRNA (TG;TGG PAM)
4107	SEQ ID NO: 4107	ngRNA (TG;TGG PAM)
4089	SEQ ID NO: 4089	ngRNA (TG;TGG PAM)
4108	SEQ ID NO: 4108	ngRNA (TG;TGG PAM)
4113	SEQ ID NO: 4113	ngRNA (TG;TGG PAM)
4127	SEQ ID NO: 4127	ngRNA (TG;TGG PAM)
4115	SEQ ID NO: 4115	ngRNA (TG;TGG PAM)
4123	SEQ ID NO: 4123	ngRNA (TG;TGG PAM)
116	SEQ ID NO: 116	ngRNA (TG;TGG PAM)
115	SEQ ID NO: 115	ngRNA (TG;TGG PAM)
4120	SEQ ID NO: 4120	ngRNA (TG;TGG PAM)
4119	SEQ ID NO: 4119	ngRNA (TG;TGG PAM)
4114	SEQ ID NO: 4114	ngRNA (TG;TGG PAM)

Sequence Number	Sequence	Description
4121	SEQ ID NO: 4121	ngRNA (TG;TGG PAM)
4122	SEQ ID NO: 4122	ngRNA (TG;TGG PAM)
4111	SEQ ID NO: 4111	ngRNA (TG;TGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)
4126	SEQ ID NO: 4126	ngRNA (TG;TGG PAM)
4118	SEQ ID NO: 4118	ngRNA (TG;TGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
4116	SEQ ID NO: 4116	ngRNA (TG;TGG PAM)
4112	SEQ ID NO: 4112	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)
4125	SEQ ID NO: 4125	ngRNA (TG;TGG PAM)
4124	SEQ ID NO: 4124	ngRNA (AG;AGG PAM)
4117	SEQ ID NO: 4117	ngRNA (TG;TGG PAM)
14800	SEQ ID NO: 14800	ngRNA (CG;CGG PAM)
14801	SEQ ID NO: 14801	ngRNA (TG;TGG PAM)
14802	SEQ ID NO: 14802	ngRNA (TG;TGG PAM)
14803	SEQ ID NO: 14803	ngRNA (TG;TGG PAM)
14804	SEQ ID NO: 14804	ngRNA (TG;TGG PAM)
14805	SEQ ID NO: 14805	ngRNA (TG;TGG PAM)
14806	SEQ ID NO: 14806	ngRNA (TG;TGG PAM)
14807	SEQ ID NO: 14807	ngRNA (TG;TGG PAM)
14808	SEQ ID NO: 14808	ngRNA (TG;TGG PAM)
14809	SEQ ID NO: 14809	ngRNA (TG;TGG PAM)
14811	SEQ ID NO: 14811	ngRNA (TG;TGG PAM)
14812	SEQ ID NO: 14812	ngRNA (TG;TGG PAM)
14813	SEQ ID NO: 14813	ngRNA (TG;TGG PAM)
14814	SEQ ID NO: 14814	ngRNA (TG;TGG PAM)
14815	SEQ ID NO: 14815	ngRNA (TG;TGG PAM)
14816	SEQ ID NO: 14816	ngRNA (TG;TGG PAM)
14817	SEQ ID NO: 14817	ngRNA (TG;TGG PAM)
14818	SEQ ID NO: 14818	ngRNA (TG;TGG PAM)
14819	SEQ ID NO: 14819	ngRNA (TG;TGG PAM)
14820	SEQ ID NO: 14820	ngRNA (TG;TGG PAM)
14821	SEQ ID NO: 14821	ngRNA (TG;TGG PAM)
14822	SEQ ID NO: 14822	ngRNA (TG;TGG PAM)
14823	SEQ ID NO: 14823	ngRNA (TG;TGG PAM)
14824	SEQ ID NO: 14824	ngRNA (TG;TGG PAM)
14825	SEQ ID NO: 14825	ngRNA (TG;TGG PAM)

Table 14

Sequence Number	Sequence	Description
4128	SEQ ID NO: 4128	PEgRNA spacer (TGA;TG PAM)
4129	SEQ ID NO: 4129	PEgRNA spacer (TGA;TG PAM)
4130	SEQ ID NO: 4130	PEgRNA spacer (TGA;TG PAM)
4131	SEQ ID NO: 4131	PEgRNA spacer (TGA;TG PAM)
4132	SEQ ID NO: 4132	PEgRNA spacer (TGA;TG PAM)
4133	SEQ ID NO: 4133	PEgRNA spacer (TGA;TG PAM)
4134	SEQ ID NO: 4134	PEgRNA spacer (TGA;TG PAM)
4135	ACA	PBS
4136	ACAG	PBS
4137	ACAGC	PBS
4138	ACAGCA	PBS
4139	ACAGCAA	PBS
4140	ACAGCAAC	PBS
4141	ACAGCAACC	PBS
4142	SEQ ID NO: 4142	PBS
4143	SEQ ID NO: 4143	PBS
4144	SEQ ID NO: 4144	PBS
4145	SEQ ID NO: 4145	PBS
4146	SEQ ID NO: 4146	PBS
4147	SEQ ID NO: 4147	PBS
4148	SEQ ID NO: 4148	PBS
4149	SEQ ID NO: 4149	PBS
4150	SEQ ID NO: 4150	PBS
4151	SEQ ID NO: 4151	PBS
4152	SEQ ID NO: 4152	RTT
4153	SEQ ID NO: 4153	RTT
4154	SEQ ID NO: 4154	RTT
4155	SEQ ID NO: 4155	RTT
4156	SEQ ID NO: 4156	RTT
4157	SEQ ID NO: 4157	RTT
4158	SEQ ID NO: 4158	RTT
4159	SEQ ID NO: 4159	RTT
4160	SEQ ID NO: 4160	RTT
4161	SEQ ID NO: 4161	RTT
4162	SEQ ID NO: 4162	RTT

Sequence Number	Sequence	Description
4163	SEQ ID NO: 4163	RTT
4164	SEQ ID NO: 4164	RTT
4165	SEQ ID NO: 4165	RTT
4166	SEQ ID NO: 4166	RTT
4167	SEQ ID NO: 4167	RTT
4168	SEQ ID NO: 4168	RTT
4169	SEQ ID NO: 4169	RTT
4170	SEQ ID NO: 4170	RTT
4171	SEQ ID NO: 4171	RTT
4172	SEQ ID NO: 4172	RTT
4173	SEQ ID NO: 4173	RTT
4174	SEQ ID NO: 4174	RTT
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG;AGA PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG;AGA PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG;TGA PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG;CGA PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)

Table 15

Sequence Number	Sequence	Description
4176	SEQ ID NO: 4176	PEgRNA spacer (AGA;AG PAM)
4177	SEQ ID NO: 4177	PEgRNA spacer (AGA;AG PAM)
4178	SEQ ID NO: 4178	PEgRNA spacer (AGA;AG PAM)
4179	SEQ ID NO: 4179	PEgRNA spacer (AGA;AG PAM)
4180	SEQ ID NO: 4180	PEgRNA spacer (AGA;AG PAM)
4181	SEQ ID NO: 4181	PEgRNA spacer (AGA;AG PAM)
4182	SEQ ID NO: 4182	PEgRNA spacer (AGA;AG PAM)
4183	CCA	PBS
4184	CCAC	PBS
4185	CCACA	PBS
4186	CCACAG	PBS
4187	CCACAG C	PBS
4188	CCACAG CA	PBS
4189	CCACAG CAA	PBS
4190	SEQ ID NO: 4190	PBS
4191	SEQ ID NO: 4191	PBS
4192	SEQ ID NO: 4192	PBS
4193	SEQ ID NO: 4193	PBS
4194	SEQ ID NO: 4194	PBS
4195	SEQ ID NO: 4195	PBS
4196	SEQ ID NO: 4196	PBS
4197	SEQ ID NO: 4197	PBS
4198	SEQ ID NO: 4198	PBS
4199	SEQ ID NO: 4199	PBS
4200	SEQ ID NO: 4200	RTT
4201	SEQ ID NO: 4201	RTT*11 (PAM silencing)
4202	SEQ ID NO: 4202	RTT*11 (PAM silencing)
4203	SEQ ID NO: 4203	RTT
4204	SEQ ID NO: 4204	RTT
4205	SEQ ID NO: 4205	RTT*11 (PAM silencing)
4206	SEQ ID NO: 4206	RTT*11 (PAM silencing)
4207	SEQ ID NO: 4207	RTT
4208	SEQ ID NO: 4208	RTT*11 (PAM silencing)
4209	SEQ ID NO: 4209	RTT
4210	SEQ ID NO: 4210	RTT
4211	SEQ ID NO: 4211	RTT*11 (PAM silencing)
4212	SEQ ID NO: 4212	RTT*11 (PAM silencing)
4213	SEQ ID NO: 4213	RTT
4214	SEQ ID NO: 4214	RTT*11 (PAM silencing)
4215	SEQ ID NO: 4215	RTT
4216	SEQ ID NO: 4216	RTT
4217	SEQ ID NO: 4217	RTT*11 (PAM silencing)
4218	SEQ ID NO: 4218	RTT
4219	SEQ ID NO: 4219	RTT*11 (PAM silencing)
4220	SEQ ID NO: 4220	RTT*11 (PAM silencing)
4221	SEQ ID NO: 4221	RTT
4222	SEQ ID NO: 4222	RTT*11 (PAM silencing)
4223	SEQ ID NO: 4223	RTT
4224	SEQ ID NO: 4224	RTT*11 (PAM silencing)
4225	SEQ ID NO: 4225	RTT
4226	SEQ ID NO: 4226	RTT
4227	SEQ ID NO: 4227	RTT*11 (PAM silencing)
4228	SEQ ID NO: 4228	RTT
4229	SEQ ID NO: 4229	RTT*11 (PAM silencing)
4230	SEQ ID NO: 4230	RTT*11 (PAM silencing)
4231	SEQ ID NO: 4231	RTT
4232	SEQ ID NO: 4232	RTT
4233	SEQ ID NO: 4233	RTT*11 (PAM silencing)
4234	SEQ ID NO: 4234	RTT*11 (PAM silencing)
4235	SEQ ID NO: 4235	RTT
4236	SEQ ID NO: 4236	RTT
4237	SEQ ID NO: 4237	RTT*11 (PAM silencing)
4238	SEQ ID NO: 4238	RTT*11 (PAM silencing)
4239	SEQ ID NO: 4239	RTT
4240	SEQ ID NO: 4240	RTT*11 (PAM silencing)
4241	SEQ ID NO: 4241	RTT
4242	SEQ ID NO: 4242	RTT*11 (PAM silencing)
4243	SEQ ID NO: 4243	RTT
4244	SEQ ID NO: 4244	RTT
4245	SEQ ID NO: 4245	RTT*11 (PAM silencing)
4246	SEQ ID NO: 4246	RTT*11 (PAM silencing)
4247	SEQ ID NO: 4247	RTT

Sequence Number	Sequence	Description
4248	SEQ ID NO: 4248	RTT
4249	SEQ ID NO: 4249	RTT*11 (PAM silencing)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG;AGA PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG;CGA PAM)
4250	SEQ ID NO: 4250	PE3b*11 ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG;AGA PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG;TGA PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)

Table 16

Sequence Number	Sequence	Description
4251	SEQ ID NO: 4251	PEgRNA spacer

Sequence Number	Sequence	Description
		(GGA;GG PAM)
4252	SEQ ID NO: 4252	PEgRNA spacer (GGA;GG PAM)
4253	SEQ ID NO: 4253	PEgRNA spacer (GGA;GG PAM)
4254	SEQ ID NO: 4254	PEgRNA spacer (GGA;GG PAM)
4255	SEQ ID NO: 4255	PEgRNA spacer (GGA;GG PAM)
4256	SEQ ID NO: 4256	PEgRNA spacer (GGA;GG PAM)
4257	SEQ ID NO: 4257	PEgRNA spacer (GGA;GG PAM)
4258	TTC	PBS
4259	TTCT	PBS
4260	TTCTC	PBS
4261	TTCTCA	PBS
4262	TTCTCA G	PBS
4263	TTCTCA GC	PBS
4264	TTCTCA GCC	PBS
4265	SEQ ID NO: 4265	PBS
4266	SEQ ID NO: 4266	PBS
4267	SEQ ID NO: 4267	PBS
4268	SEQ ID NO: 4268	PBS
4269	SEQ ID NO: 4269	PBS
4270	SEQ ID NO: 4270	PBS
4271	SEQ ID NO: 4271	PBS
4272	SEQ ID NO: 4272	PBS
4273	SEQ ID NO: 4273	PBS
4274	SEQ ID NO: 4274	PBS
4275	SEQ ID NO: 4275	RTT
4276	SEQ ID NO: 4276	RTT
4277	SEQ ID NO: 4277	RTT
4278	SEQ ID NO: 4278	RTT
4279	SEQ ID NO: 4279	RTT

Sequence Number	Sequence	Description
4280	SEQ ID NO: 4280	RTT
4281	SEQ ID NO: 4281	RTT
4282	SEQ ID NO: 4282	RTT
4283	SEQ ID NO: 4283	RTT
4284	SEQ ID NO: 4284	RTT
4285	SEQ ID NO: 4285	RTT
4286	SEQ ID NO: 4286	RTT
4287	SEQ ID NO: 4287	RTT
4288	SEQ ID NO: 4288	RTT
4289	SEQ ID NO: 4289	RTT
4290	SEQ ID NO: 4290	RTT
4291	SEQ ID NO: 4291	RTT
4292	SEQ ID NO: 4292	RTT
4293	SEQ ID NO: 4293	RTT
4294	SEQ ID NO: 4294	RTT
4295	SEQ ID NO: 4295	RTT
4296	SEQ ID NO: 4296	RTT
4297	SEQ ID NO: 4297	RTT
4298	SEQ ID NO: 4298	RTT
4299	SEQ ID NO: 4299	RTT
4300	SEQ ID NO: 4300	RTT
4301	SEQ ID NO: 4301	RTT
4302	SEQ ID NO: 4302	RTT
4303	SEQ ID NO: 4303	RTT
4304	SEQ ID NO: 4304	RTT
4305	SEQ ID NO: 4305	RTT
4306	SEQ ID NO: 4306	RTT
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
733	SEQ ID NO: 733	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (TG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG;AGA PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG;CGA PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG;TGA PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG;AGA PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)

Sequence Number	Sequence	Description
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)

Table 17

Sequence Number	Sequence	Description
4307	SEQ ID NO: 4307	PEgRNA spacer (AGA;AG PAM)
4308	SEQ ID NO: 4308	PEgRNA spacer (AGA;AG PAM)
4309	SEQ ID NO: 4309	PEgRNA spacer (AGA;AG PAM)
4310	SEQ ID NO: 4310	PEgRNA spacer (AGA;AG PAM)
4311	SEQ ID NO: 4311	PEgRNA spacer (AGA;AG PAM)
4312	SEQ ID NO: 4312	PEgRNA spacer (AGA;AG PAM)
4313	SEQ ID NO: 4313	PEgRNA spacer (AGA;AG PAM)
4314	CCT	PBS
4315	CCTT	PBS
4316	CCTTC	PBS
4317	CCTTCT	PBS
4318	CCTTCTC	PBS
4319	CCTTCTCA	PBS
4320	CCTTCTCAG	PBS
4321	SEQ ID NO: 4321	PBS
4322	SEQ ID NO: 4322	PBS
4323	SEQ ID NO: 4323	PBS
4324	SEQ ID NO: 4324	PBS
4325	SEQ ID NO: 4325	PBS
4326	SEQ ID NO: 4326	PBS
4327	SEQ ID NO: 4327	PBS
4328	SEQ ID NO: 4328	PBS
4329	SEQ ID NO: 4329	PBS
4330	SEQ ID NO: 4330	PBS
4331	SEQ ID NO: 4331	RTT*8 (PAM silencing)
4332	SEQ ID NO: 4332	RTT*6 (PAM silencing)
4333	SEQ ID NO: 4333	RTT*9 (PAM silencing)
4334	SEQ ID NO: 4334	RTT*2 (PAM silencing)
4335	SEQ ID NO: 4335	RTT*7 (PAM silencing)
4336	SEQ ID NO: 4336	RTT
4337	SEQ ID NO: 4337	RTT*10 (PAM silencing)
4338	SEQ ID NO: 4338	RTT*5 (PAM silencing)
4339	SEQ ID NO: 4339	RTT*4 (PAM silencing)
4340	SEQ ID NO: 4340	RTT*3 (PAM silencing)

Sequence Number	Sequence	Description
4341	SEQ ID NO: 4341	RTT*8 (PAM silencing)
4342	SEQ ID NO: 4342	RTT*2 (PAM silencing)
4343	SEQ ID NO: 4343	RTT*9 (PAM silencing)
4344	SEQ ID NO: 4344	RTT*10 (PAM silencing)
4345	SEQ ID NO: 4345	RTT*5 (PAM silencing)
4346	SEQ ID NO: 4346	RTT*3 (PAM silencing)
4347	SEQ ID NO: 4347	RTT*4 (PAM silencing)
4348	SEQ ID NO: 4348	RTT
4349	SEQ ID NO: 4349	RTT*6 (PAM silencing)
4350	SEQ ID NO: 4350	RTT*7 (PAM silencing)
4351	SEQ ID NO: 4351	RTT*9 (PAM silencing)
4352	SEQ ID NO: 4352	RTT*2 (PAM silencing)
4353	SEQ ID NO: 4353	RTT*3 (PAM silencing)
4354	SEQ ID NO: 4354	RTT*6 (PAM silencing)
4355	SEQ ID NO: 4355	RTT*8 (PAM silencing)
4356	SEQ ID NO: 4356	RTT
4357	SEQ ID NO: 4357	RTT*7 (PAM silencing)
4358	SEQ ID NO: 4358	RTT*4 (PAM silencing)
4359	SEQ ID NO: 4359	RTT*10 (PAM silencing)
4360	SEQ ID NO: 4360	RTT*5 (PAM silencing)
4361	SEQ ID NO: 4361	RTT*6 (PAM silencing)
4362	SEQ ID NO: 4362	RTT*5 (PAM silencing)
4363	SEQ ID NO: 4363	RTT*7 (PAM silencing)
4364	SEQ ID NO: 4364	RTT*9 (PAM silencing)
4365	SEQ ID NO: 4365	RTT*4 (PAM silencing)
4366	SEQ ID NO: 4366	RTT*3 (PAM silencing)
4367	SEQ ID NO: 4367	RTT*2 (PAM silencing)
4368	SEQ ID NO: 4368	RTT
4369	SEQ ID NO: 4369	RTT*8 (PAM silencing)
4370	SEQ ID NO: 4370	RTT*10 (PAM silencing)
4371	SEQ ID NO: 4371	RTT*9 (PAM silencing)
4372	SEQ ID NO: 4372	RTT*5 (PAM silencing)
4373	SEQ ID NO: 4373	RTT
4374	SEQ ID NO: 4374	RTT*3 (PAM silencing)
4375	SEQ ID NO: 4375	RTT*6 (PAM silencing)
4376	SEQ ID NO: 4376	RTT*10 (PAM silencing)
4377	SEQ ID NO: 4377	RTT*8 (PAM silencing)
4378	SEQ ID NO: 4378	RTT*7 (PAM silencing)
4379	SEQ ID NO: 4379	RTT*4 (PAM silencing)
4380	SEQ ID NO: 4380	RTT*2 (PAM silencing)
4381	SEQ ID NO: 4381	RTT*8 (PAM silencing)
4382	SEQ ID NO: 4382	RTT*3 (PAM silencing)
4383	SEQ ID NO: 4383	RTT
4384	SEQ ID NO: 4384	RTT*9 (PAM silencing)
4385	SEQ ID NO: 4385	RTT*2 (PAM silencing)
4386	SEQ ID NO: 4386	RTT*4 (PAM silencing)
4387	SEQ ID NO: 4387	RTT*7 (PAM silencing)
4388	SEQ ID NO: 4388	RTT*10 (PAM silencing)
4389	SEQ ID NO: 4389	RTT*5 (PAM silencing)
4390	SEQ ID NO: 4390	RTT*6 (PAM silencing)
4391	SEQ ID NO: 4391	RTT*4 (PAM silencing)
4392	SEQ ID NO: 4392	RTT*7 (PAM silencing)
4393	SEQ ID NO: 4393	RTT*8 (PAM silencing)
4394	SEQ ID NO: 4394	RTT*2 (PAM silencing)
4395	SEQ ID NO: 4395	RTT*5 (PAM silencing)
4396	SEQ ID NO: 4396	RTT*10 (PAM silencing)
4397	SEQ ID NO: 4397	RTT*6 (PAM silencing)
4398	SEQ ID NO: 4398	RTT
4399	SEQ ID NO: 4399	RTT*3 (PAM silencing)
4400	SEQ ID NO: 4400	RTT*9 (PAM silencing)
4401	SEQ ID NO: 4401	RTT*10 (PAM silencing)
4402	SEQ ID NO: 4402	RTT*7 (PAM silencing)
4403	SEQ ID NO: 4403	RTT*8 (PAM silencing)
4404	SEQ ID NO: 4404	RTT*2 (PAM silencing)
4405	SEQ ID NO: 4405	RTT
4406	SEQ ID NO: 4406	RTT*4 (PAM silencing)
4407	SEQ ID NO: 4407	RTT*6 (PAM silencing)
4408	SEQ ID NO: 4408	RTT*3 (PAM silencing)
4409	SEQ ID NO: 4409	RTT*5 (PAM silencing)

Sequence Number	Sequence	Description
4410	SEQ ID NO: 4410	RTT*9 (PAM silencing)
4411	SEQ ID NO: 4411	RTT
4412	SEQ ID NO: 4412	RTT*2 (PAM silencing)
4413	SEQ ID NO: 4413	RTT*5 (PAM silencing)
4414	SEQ ID NO: 4414	RTT*8 (PAM silencing)
4415	SEQ ID NO: 4415	RTT*3 (PAM silencing)
4416	SEQ ID NO: 4416	RTT*4 (PAM silencing)
4417	SEQ ID NO: 4417	RTT*6 (PAM silencing)
4418	SEQ ID NO: 4418	RTT*10 (PAM silencing)
4419	SEQ ID NO: 4419	RTT*7 (PAM silencing)
4420	SEQ ID NO: 4420	RTT*9 (PAM silencing)
4421	SEQ ID NO: 4421	RTT*3 (PAM silencing)
4422	SEQ ID NO: 4422	RTT*2 (PAM silencing)
4423	SEQ ID NO: 4423	RTT*9 (PAM silencing)
4424	SEQ ID NO: 4424	RTT*10 (PAM silencing)
4425	SEQ ID NO: 4425	RTT*5 (PAM silencing)
4426	SEQ ID NO: 4426	RTT*4 (PAM silencing)
4427	SEQ ID NO: 4427	RTT*6 (PAM silencing)
4428	SEQ ID NO: 4428	RTT
4429	SEQ ID NO: 4429	RTT*7 (PAM silencing)
4430	SEQ ID NO: 4430	RTT*8 (PAM silencing)
4431	SEQ ID NO: 4431	RTT*9 (PAM silencing)
4432	SEQ ID NO: 4432	RTT*6 (PAM silencing)
4433	SEQ ID NO: 4433	RTT*8 (PAM silencing)
4434	SEQ ID NO: 4434	RTT*4 (PAM silencing)
4435	SEQ ID NO: 4435	RTT*5 (PAM silencing)
4436	SEQ ID NO: 4436	RTT*7 (PAM silencing)
4437	SEQ ID NO: 4437	RTT
4438	SEQ ID NO: 4438	RTT*2 (PAM silencing)
4439	SEQ ID NO: 4439	RTT*3 (PAM silencing)
4440	SEQ ID NO: 4440	RTT*10 (PAM silencing)
4441	SEQ ID NO: 4441	RTT*3 (PAM silencing)
4442	SEQ ID NO: 4442	RTT
4443	SEQ ID NO: 4443	RTT*2 (PAM silencing)
4444	SEQ ID NO: 4444	RTT*8 (PAM silencing)
4445	SEQ ID NO: 4445	RTT*5 (PAM silencing)
4446	SEQ ID NO: 4446	RTT*9 (PAM silencing)
4447	SEQ ID NO: 4447	RTT*6 (PAM silencing)
4448	SEQ ID NO: 4448	RTT*4 (PAM silencing)
4449	SEQ ID NO: 4449	RTT*7 (PAM silencing)
4450	SEQ ID NO: 4450	RTT*10 (PAM silencing)
4451	SEQ ID NO: 4451	RTT*4 (PAM silencing)
4452	SEQ ID NO: 4452	RTT*3 (PAM silencing)
4453	SEQ ID NO: 4453	RTT*2 (PAM silencing)
4454	SEQ ID NO: 4454	RTT*6 (PAM silencing)
4455	SEQ ID NO: 4455	RTT*10 (PAM silencing)
4456	SEQ ID NO: 4456	RTT
4457	SEQ ID NO: 4457	RTT*5 (PAM silencing)
4458	SEQ ID NO: 4458	RTT*9 (PAM silencing)
4459	SEQ ID NO: 4459	RTT*8 (PAM silencing)
4460	SEQ ID NO: 4460	RTT*7 (PAM silencing)
4461	SEQ ID NO: 4461	RTT
4462	SEQ ID NO: 4462	RTT*9 (PAM silencing)
4463	SEQ ID NO: 4463	RTT*3 (PAM silencing)
4464	SEQ ID NO: 4464	RTT*4 (PAM silencing)
4465	SEQ ID NO: 4465	RTT*2 (PAM silencing)
4466	SEQ ID NO: 4466	RTT*5 (PAM silencing)
4467	SEQ ID NO: 4467	RTT*7 (PAM silencing)
4468	SEQ ID NO: 4468	RTT*8 (PAM silencing)
4469	SEQ ID NO: 4469	RTT*10 (PAM silencing)
4470	SEQ ID NO: 4470	RTT*6 (PAM silencing)
4471	SEQ ID NO: 4471	RTT*8 (PAM silencing)
4472	SEQ ID NO: 4472	RTT*10 (PAM silencing)
4473	SEQ ID NO: 4473	RTT*7 (PAM silencing)
4474	SEQ ID NO: 4474	RTT*9 (PAM silencing)
4475	SEQ ID NO: 4475	RTT*3 (PAM silencing)
4476	SEQ ID NO: 4476	RTT*5 (PAM silencing)
4477	SEQ ID NO: 4477	RTT*6 (PAM silencing)
4478	SEQ ID NO: 4478	RTT*4 (PAM silencing)

Sequence Number	Sequence	Description
4479	SEQ ID NO: 4479	RTT
4480	SEQ ID NO: 4480	RTT*2 (PAM silencing)
4481	SEQ ID NO: 4481	RTT*4 (PAM silencing)
4482	SEQ ID NO: 4482	RTT*8 (PAM silencing)
4483	SEQ ID NO: 4483	RTT*5 (PAM silencing)
4484	SEQ ID NO: 4484	RTT*2 (PAM silencing)
4485	SEQ ID NO: 4485	RTT*10 (PAM silencing)
4486	SEQ ID NO: 4486	RTT*9 (PAM silencing)
4487	SEQ ID NO: 4487	RTT*3 (PAM silencing)
4488	SEQ ID NO: 4488	RTT*6 (PAM silencing)
4489	SEQ ID NO: 4489	RTT*7 (PAM silencing)
4490	SEQ ID NO: 4490	RTT
4491	SEQ ID NO: 4491	RTT*9 (PAM silencing)
4492	SEQ ID NO: 4492	RTT*7 (PAM silencing)
4493	SEQ ID NO: 4493	RTT*2 (PAM silencing)
4494	SEQ ID NO: 4494	RTT*4 (PAM silencing)
4495	SEQ ID NO: 4495	RTT*3 (PAM silencing)
4496	SEQ ID NO: 4496	RTT
4497	SEQ ID NO: 4497	RTT*8 (PAM silencing)
4498	SEQ ID NO: 4498	RTT*6 (PAM silencing)
4499	SEQ ID NO: 4499	RTT*5 (PAM silencing)
4500	SEQ ID NO: 4500	RTT*10 (PAM silencing)
4501	SEQ ID NO: 4501	RTT*6 (PAM silencing)
4502	SEQ ID NO: 4502	RTT
4503	SEQ ID NO: 4503	RTT*9 (PAM silencing)
4504	SEQ ID NO: 4504	RTT*5 (PAM silencing)
4505	SEQ ID NO: 4505	RTT*3 (PAM silencing)
4506	SEQ ID NO: 4506	RTT*8 (PAM silencing)
4507	SEQ ID NO: 4507	RTT*2 (PAM silencing)
4508	SEQ ID NO: 4508	RTT*4 (PAM silencing)
4509	SEQ ID NO: 4509	RTT*10 (PAM silencing)
4510	SEQ ID NO: 4510	RTT*7 (PAM silencing)
4511	SEQ ID NO: 4511	RTT*10 (PAM silencing)
4512	SEQ ID NO: 4512	RTT*7 (PAM silencing)
4513	SEQ ID NO: 4513	RTT*5 (PAM silencing)
4514	SEQ ID NO: 4514	RTT
4515	SEQ ID NO: 4515	RTT*3 (PAM silencing)
4516	SEQ ID NO: 4516	RTT*4 (PAM silencing)
4517	SEQ ID NO: 4517	RTT*2 (PAM silencing)
4518	SEQ ID NO: 4518	RTT*6 (PAM silencing)
4519	SEQ ID NO: 4519	RTT*8 (PAM silencing)
4520	SEQ ID NO: 4520	RTT*9 (PAM silencing)
4521	SEQ ID NO: 4521	RTT*3 (PAM silencing)
4522	SEQ ID NO: 4522	RTT*6 (PAM silencing)
4523	SEQ ID NO: 4523	RTT*2 (PAM silencing)
4524	SEQ ID NO: 4524	RTT*9 (PAM silencing)
4525	SEQ ID NO: 4525	RTT*10 (PAM silencing)
4526	SEQ ID NO: 4526	RTT*8 (PAM silencing)
4527	SEQ ID NO: 4527	RTT
4528	SEQ ID NO: 4528	RTT*7 (PAM silencing)
4529	SEQ ID NO: 4529	RTT*5 (PAM silencing)
4530	SEQ ID NO: 4530	RTT*4 (PAM silencing)
4531	SEQ ID NO: 4531	RTT
4532	SEQ ID NO: 4532	RTT*2 (PAM silencing)
4533	SEQ ID NO: 4533	RTT*10 (PAM silencing)
4534	SEQ ID NO: 4534	RTT*7 (PAM silencing)
4535	SEQ ID NO: 4535	RTT*6 (PAM silencing)
4536	SEQ ID NO: 4536	RTT*4 (PAM silencing)
4537	SEQ ID NO: 4537	RTT*5 (PAM silencing)
4538	SEQ ID NO: 4538	RTT*3 (PAM silencing)
4539	SEQ ID NO: 4539	RTT*9 (PAM silencing)
4540	SEQ ID NO: 4540	RTT*8 (PAM silencing)
4541	SEQ ID NO: 4541	RTT*4 (PAM silencing)
4542	SEQ ID NO: 4542	RTT*3 (PAM silencing)
4543	SEQ ID NO: 4543	RTT*6 (PAM silencing)
4544	SEQ ID NO: 4544	RTT
4545	SEQ ID NO: 4545	RTT*10 (PAM silencing)
4546	SEQ ID NO: 4546	RTT*2 (PAM silencing)
4547	SEQ ID NO: 4547	RTT*5 (PAM silencing)

Sequence Number	Sequence	Description
4548	SEQ ID NO: 4548	RTT*8 (PAM silencing)
4549	SEQ ID NO: 4549	RTT*9 (PAM silencing)
4550	SEQ ID NO: 4550	RTT*7 (PAM silencing)
4551	SEQ ID NO: 4551	RTT
4552	SEQ ID NO: 4552	RTT*7 (PAM silencing)
4553	SEQ ID NO: 4553	RTT*10 (PAM silencing)
4554	SEQ ID NO: 4554	RTT*6 (PAM silencing)
4555	SEQ ID NO: 4555	RTT*8 (PAM silencing)
4556	SEQ ID NO: 4556	RTT*3 (PAM silencing)
4557	SEQ ID NO: 4557	RTT*4 (PAM silencing)
4558	SEQ ID NO: 4558	RTT*9 (PAM silencing)
4559	SEQ ID NO: 4559	RTT*5 (PAM silencing)
4560	SEQ ID NO: 4560	RTT*2 (PAM silencing)
4561	SEQ ID NO: 4561	RTT*10 (PAM silencing)
4562	SEQ ID NO: 4562	RTT*3 (PAM silencing)
4563	SEQ ID NO: 4563	RTT*2 (PAM silencing)
4564	SEQ ID NO: 4564	RTT*9 (PAM silencing)
4565	SEQ ID NO: 4565	RTT*5 (PAM silencing)
4566	SEQ ID NO: 4566	RTT*4 (PAM silencing)
4567	SEQ ID NO: 4567	RTT*7 (PAM silencing)
4568	SEQ ID NO: 4568	RTT*8 (PAM silencing)
4569	SEQ ID NO: 4569	RTT
4570	SEQ ID NO: 4570	RTT*6 (PAM silencing)

Sequence Number	Sequence	Description
4571	SEQ ID NO: 4571	RTT*8 (PAM silencing)
4572	SEQ ID NO: 4572	RTT
4573	SEQ ID NO: 4573	RTT*10 (PAM silencing)
4574	SEQ ID NO: 4574	RTT*2 (PAM silencing)
4575	SEQ ID NO: 4575	RTT*3 (PAM silencing)
4576	SEQ ID NO: 4576	RTT*6 (PAM silencing)
4577	SEQ ID NO: 4577	RTT*5 (PAM silencing)
4578	SEQ ID NO: 4578	RTT*4 (PAM silencing)
4579	SEQ ID NO: 4579	RTT*7 (PAM silencing)
4580	SEQ ID NO: 4580	RTT*9 (PAM silencing)
4581	SEQ ID NO: 4581	RTT*5 (PAM silencing)
4582	SEQ ID NO: 4582	RTT*4 (PAM silencing)
4583	SEQ ID NO: 4583	RTT*9 (PAM silencing)
4584	SEQ ID NO: 4584	RTT*10 (PAM silencing)
4585	SEQ ID NO: 4585	RTT
4586	SEQ ID NO: 4586	RTT*7 (PAM silencing)
4587	SEQ ID NO: 4587	RTT*8 (PAM silencing)
4588	SEQ ID NO: 4588	RTT*6 (PAM silencing)
4589	SEQ ID NO: 4589	RTT*3 (PAM silencing)
4590	SEQ ID NO: 4590	RTT*2 (PAM silencing)
4591	SEQ ID NO: 4591	RTT*8 (PAM silencing)
4592	SEQ ID NO: 4592	RTT*4 (PAM silencing)
4593	SEQ ID NO: 4593	RTT*6 (PAM silencing)

Sequence Number	Sequence	Description
4594	SEQ ID NO: 4594	RTT*3 (PAM silencing)
4595	SEQ ID NO: 4595	RTT*5 (PAM silencing)
4596	SEQ ID NO: 4596	RTT*7 (PAM silencing)
4597	SEQ ID NO: 4597	RTT*9 (PAM silencing)
4598	SEQ ID NO: 4598	RTT*10 (PAM silencing)
4599	SEQ ID NO: 4599	RTT
4600	SEQ ID NO: 4600	RTT*2 (PAM silencing)
4601	SEQ ID NO: 4601	RTT*2 (PAM silencing)
4602	SEQ ID NO: 4602	RTT*3 (PAM silencing)
4603	SEQ ID NO: 4603	RTT*7 (PAM silencing)
4604	SEQ ID NO: 4604	RTT
4605	SEQ ID NO: 4605	RTT*9 (PAM silencing)
4606	SEQ ID NO: 4606	RTT*10 (PAM silencing)
4607	SEQ ID NO: 4607	RTT*4 (PAM silencing)
4608	SEQ ID NO: 4608	RTT*5 (PAM silencing)
4609	SEQ ID NO: 4609	RTT*6 (PAM silencing)
4610	SEQ ID NO: 4610	RTT*8 (PAM silencing)
4611	SEQ ID NO: 4611	RTT
4612	SEQ ID NO: 4612	RTT*10 (PAM silencing)
4613	SEQ ID NO: 4613	RTT*8 (PAM silencing)
4614	SEQ ID NO: 4614	RTT*7 (PAM silencing)
4615	SEQ ID NO: 4615	RTT*5 (PAM silencing)
4616	SEQ ID NO: 4616	RTT*4 (PAM silencing)

Sequence Number	Sequence	Description
4617	SEQ ID NO: 4617	RTT*3 (PAM silencing)
4618	SEQ ID NO: 4618	RTT*9 (PAM silencing)
4619	SEQ ID NO: 4619	RTT*2 (PAM silencing)
4620	SEQ ID NO: 4620	RTT*6 (PAM silencing)
4621	SEQ ID NO: 4621	RTT*9 (PAM silencing)
4622	SEQ ID NO: 4622	RTT
4623	SEQ ID NO: 4623	RTT*5 (PAM silencing)
4624	SEQ ID NO: 4624	RTT*8 (PAM silencing)
4625	SEQ ID NO: 4625	RTT*2 (PAM silencing)
4626	SEQ ID NO: 4626	RTT*7 (PAM silencing)
4627	SEQ ID NO: 4627	RTT*10 (PAM silencing)
4628	SEQ ID NO: 4628	RTT*4 (PAM silencing)
4629	SEQ ID NO: 4629	RTT*3 (PAM silencing)
4630	SEQ ID NO: 4630	RTT*6 (PAM silencing)
4631	SEQ ID NO: 4631	RTT*7 (PAM silencing)
4632	SEQ ID NO: 4632	RTT*4 (PAM silencing)
4633	SEQ ID NO: 4633	RTT*3 (PAM silencing)
4634	SEQ ID NO: 4634	RTT*8 (PAM silencing)
4635	SEQ ID NO: 4635	RTT*9 (PAM silencing)
4636	SEQ ID NO: 4636	RTT
4637	SEQ ID NO: 4637	RTT*5 (PAM silencing)
4638	SEQ ID NO: 4638	RTT*6 (PAM silencing)
4639	SEQ ID NO: 4639	RTT*10 (PAM silencing)
4640	SEQ ID NO: 4640	RTT*2 (PAM silencing)
4641	SEQ ID NO: 4641	RTT*2 (PAM silencing)
4642	SEQ ID NO: 4642	RTT
4643	SEQ ID NO: 4643	RTT*9 (PAM silencing)
4644	SEQ ID NO: 4644	RTT*5 (PAM silencing)
4645	SEQ ID NO: 4645	RTT*7 (PAM silencing)
4646	SEQ ID NO: 4646	RTT*6 (PAM silencing)
4647	SEQ ID NO: 4647	RTT*3 (PAM silencing)
4648	SEQ ID NO: 4648	RTT*4 (PAM silencing)
4649	SEQ ID NO: 4649	RTT*8 (PAM silencing)
4650	SEQ ID NO: 4650	RTT*10 (PAM silencing)
4651	SEQ ID NO: 4651	RTT*2 (PAM silencing)
4652	SEQ ID NO: 4652	RTT*7 (PAM silencing)
4653	SEQ ID NO: 4653	RTT*9 (PAM silencing)
4654	SEQ ID NO: 4654	RTT*8 (PAM silencing)
4655	SEQ ID NO: 4655	RTT*5 (PAM silencing)
4656	SEQ ID NO: 4656	RTT*10 (PAM silencing)
4657	SEQ ID NO: 4657	RTT
4658	SEQ ID NO: 4658	RTT*3 (PAM silencing)
4659	SEQ ID NO: 4659	RTT*6 (PAM silencing)
4660	SEQ ID NO: 4660	RTT*4 (PAM silencing)
4661	SEQ ID NO: 4661	RTT*4 (PAM silencing)
4662	SEQ ID NO: 4662	RTT
4663	SEQ ID NO: 4663	RTT*10 (PAM silencing)
4664	SEQ ID NO: 4664	RTT*9 (PAM silencing)
4665	SEQ ID NO: 4665	RTT*3 (PAM silencing)
4666	SEQ ID NO: 4666	RTT*7 (PAM silencing)
4667	SEQ ID NO: 4667	RTT*2 (PAM silencing)
4668	SEQ ID NO: 4668	RTT*8 (PAM silencing)
4669	SEQ ID NO: 4669	RTT*6 (PAM silencing)
4670	SEQ ID NO: 4670	RTT*5 (PAM silencing)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG;CGA PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG;AGA PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)

Sequence Number	Sequence	Description
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG;AGA PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG;TGA PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
4671	SEQ ID NO: 4671	PE3b*2 ngRNA spacer (CG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)

Sequence Number	Sequence	Description
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)

Table 18

Sequence Number	Sequence	Description
4672	SEQ ID NO: 4672	PEgRNA spacer (GGA;GG PAM)
4673	SEQ ID NO: 4673	PEgRNA spacer (GGA;GG PAM)
4674	SEQ ID NO: 4674	PEgRNA spacer (GGA;GG PAM)
4675	SEQ ID NO: 4675	PEgRNA spacer (GGA;GG PAM)
4676	SEQ ID NO: 4676	PEgRNA spacer (GGA;GG PAM)
4677	SEQ ID NO: 4677	PEgRNA spacer (GGA;GG PAM)
4678	SEQ ID NO: 4678	PEgRNA spacer (GGA;GG PAM)
4679	CCG	PBS
4680	CCGC	PBS
4681	CCGCC	PBS
4682	CCGCCT	PBS
4683	CCGCCT T	PBS
4684	CCGCCT TC	PBS
4685	CCGCCT TCT	PBS
4686	SEQ ID NO: 4686	PBS
4687	SEQ ID NO: 4687	PBS
4688	SEQ ID NO: 4688	PBS
4689	SEQ ID NO: 4689	PBS
4690	SEQ ID NO: 4690	PBS
4691	SEQ ID NO: 4691	PBS

Sequence Number	Sequence	Description
4692	SEQ ID NO: 4692	PBS
4693	SEQ ID NO: 4693	PBS
4694	SEQ ID NO: 4694	PBS
4695	SEQ ID NO: 4695	PBS
4696	SEQ ID NO: 4696	RTT*27 (PAM silencing)
4697	SEQ ID NO: 4697	RTT*33 (PAM silencing)
4698	SEQ ID NO: 4698	RTT
4699	SEQ ID NO: 4699	RTT*35 (PAM silencing)
4700	SEQ ID NO: 4700	RTT*28 (PAM silencing)
4701	SEQ ID NO: 4701	RTT*20 (PAM silencing)
4702	SEQ ID NO: 4702	RTT*31 (PAM silencing)
4703	SEQ ID NO: 4703	RTT*17 (PAM silencing)
4704	SEQ ID NO: 4704	RTT*38 (PAM silencing)
4705	SEQ ID NO: 4705	RTT*22 (PAM silencing)
4706	SEQ ID NO: 4706	RTT*23 (PAM silencing)
4707	SEQ ID NO: 4707	RTT*26 (PAM silencing)
4708	SEQ ID NO: 4708	RTT*34 (PAM silencing)
4709	SEQ ID NO: 4709	RTT*39 (PAM silencing)
4710	SEQ ID NO: 4710	RTT*32 (PAM silencing)
4711	SEQ ID NO: 4711	RTT*24 (PAM silencing)
4712	SEQ ID NO: 4712	RTT*30 (PAM silencing)
4713	SEQ ID NO: 4713	RTT*19 (PAM silencing)
4714	SEQ ID NO: 4714	RTT*37 (PAM silencing)
4715	SEQ ID NO: 4715	RTT*16 (PAM silencing)
4716	SEQ ID NO: 4716	RTT*21 (PAM silencing)
4717	SEQ ID NO: 4717	RTT*18 (PAM silencing)
4718	SEQ ID NO: 4718	RTT*29 (PAM silencing)
4719	SEQ ID NO: 4719	RTT*25 (PAM silencing)
4720	SEQ ID NO: 4720	RTT*36 (PAM silencing)
4721	SEQ ID NO: 4721	RTT*18 (PAM silencing)
4722	SEQ ID NO: 4722	RTT*23 (PAM silencing)
4723	SEQ ID NO: 4723	RTT*31 (PAM silencing)
4724	SEQ ID NO: 4724	RTT*37 (PAM silencing)
4725	SEQ ID NO: 4725	RTT*29 (PAM silencing)
4726	SEQ ID NO: 4726	RTT*17 (PAM silencing)
4727	SEQ ID NO: 4727	RTT*35 (PAM silencing)
4728	SEQ ID NO: 4728	RTT
4729	SEQ ID NO: 4729	RTT*21 (PAM silencing)
4730	SEQ ID NO: 4730	RTT*32 (PAM silencing)
4731	SEQ ID NO: 4731	RTT*28 (PAM silencing)
4732	SEQ ID NO: 4732	RTT*26 (PAM silencing)
4733	SEQ ID NO: 4733	RTT*22 (PAM silencing)
4734	SEQ ID NO: 4734	RTT*24 (PAM silencing)
4735	SEQ ID NO: 4735	RTT*16 (PAM silencing)
4736	SEQ ID NO: 4736	RTT*33 (PAM silencing)
4737	SEQ ID NO: 4737	RTT*38 (PAM silencing)
4738	SEQ ID NO: 4738	RTT*19 (PAM silencing)
4739	SEQ ID NO: 4739	RTT*39 (PAM silencing)
4740	SEQ ID NO: 4740	RTT*20 (PAM silencing)
4741	SEQ ID NO: 4741	RTT*36 (PAM silencing)
4742	SEQ ID NO: 4742	RTT*30 (PAM silencing)
4743	SEQ ID NO: 4743	RTT*27 (PAM silencing)
4744	SEQ ID NO: 4744	RTT*34 (PAM silencing)
4745	SEQ ID NO: 4745	RTT*25 (PAM silencing)
4746	SEQ ID NO: 4746	RTT*31 (PAM silencing)
4747	SEQ ID NO: 4747	RTT*24 (PAM silencing)
4748	SEQ ID NO: 4748	RTT*21 (PAM silencing)
4749	SEQ ID NO: 4749	RTT*28 (PAM silencing)
4750	SEQ ID NO: 4750	RTT*29 (PAM silencing)
4751	SEQ ID NO: 4751	RTT*38 (PAM silencing)
4752	SEQ ID NO: 4752	RTT*23 (PAM silencing)
4753	SEQ ID NO: 4753	RTT*37 (PAM silencing)
4754	SEQ ID NO: 4754	RTT*16 (PAM silencing)
4755	SEQ ID NO: 4755	RTT*35 (PAM silencing)
4756	SEQ ID NO: 4756	RTT*32 (PAM silencing)
4757	SEQ ID NO: 4757	RTT*33 (PAM silencing)
4758	SEQ ID NO: 4758	RTT*36 (PAM silencing)
4759	SEQ ID NO: 4759	RTT*19 (PAM silencing)

Sequence Number	Sequence	Description
4760	SEQ ID NO: 4760	RTT*17 (PAM silencing)
4761	SEQ ID NO: 4761	RTT*26 (PAM silencing)
4762	SEQ ID NO: 4762	RTT
4763	SEQ ID NO: 4763	RTT*39 (PAM silencing)
4764	SEQ ID NO: 4764	RTT*34 (PAM silencing)
4765	SEQ ID NO: 4765	RTT*25 (PAM silencing)
4766	SEQ ID NO: 4766	RTT*30 (PAM silencing)
4767	SEQ ID NO: 4767	RTT*27 (PAM silencing)
4768	SEQ ID NO: 4768	RTT*18 (PAM silencing)
4769	SEQ ID NO: 4769	RTT*22 (PAM silencing)
4770	SEQ ID NO: 4770	RTT*20 (PAM silencing)
4771	SEQ ID NO: 4771	RTT*37 (PAM silencing)
4772	SEQ ID NO: 4772	RTT*22 (PAM silencing)
4773	SEQ ID NO: 4773	RTT*31 (PAM silencing)
4774	SEQ ID NO: 4774	RTT*28 (PAM silencing)
4775	SEQ ID NO: 4775	RTT
4776	SEQ ID NO: 4776	RTT*35 (PAM silencing)
4777	SEQ ID NO: 4777	RTT*26 (PAM silencing)
4778	SEQ ID NO: 4778	RTT*20 (PAM silencing)
4779	SEQ ID NO: 4779	RTT*19 (PAM silencing)
4780	SEQ ID NO: 4780	RTT*36 (PAM silencing)
4781	SEQ ID NO: 4781	RTT*38 (PAM silencing)
4782	SEQ ID NO: 4782	RTT*16 (PAM silencing)
4783	SEQ ID NO: 4783	RTT*25 (PAM silencing)
4784	SEQ ID NO: 4784	RTT*29 (PAM silencing)
4785	SEQ ID NO: 4785	RTT*17 (PAM silencing)
4786	SEQ ID NO: 4786	RTT*34 (PAM silencing)
4787	SEQ ID NO: 4787	RTT*39 (PAM silencing)
4788	SEQ ID NO: 4788	RTT*30 (PAM silencing)
4789	SEQ ID NO: 4789	RTT*33 (PAM silencing)
4790	SEQ ID NO: 4790	RTT*27 (PAM silencing)
4791	SEQ ID NO: 4791	RTT*21 (PAM silencing)
4792	SEQ ID NO: 4792	RTT*23 (PAM silencing)
4793	SEQ ID NO: 4793	RTT*18 (PAM silencing)
4794	SEQ ID NO: 4794	RTT*24 (PAM silencing)
4795	SEQ ID NO: 4795	RTT*32 (PAM silencing)
4796	SEQ ID NO: 4796	RTT*26 (PAM silencing)
4797	SEQ ID NO: 4797	RTT*16 (PAM silencing)
4798	SEQ ID NO: 4798	RTT*33 (PAM silencing)
4799	SEQ ID NO: 4799	RTT
4800	SEQ ID NO: 4800	RTT*19 (PAM silencing)
4801	SEQ ID NO: 4801	RTT*20 (PAM silencing)
4802	SEQ ID NO: 4802	RTT*28 (PAM silencing)
4803	SEQ ID NO: 4803	RTT*21 (PAM silencing)
4804	SEQ ID NO: 4804	RTT*17 (PAM silencing)
4805	SEQ ID NO: 4805	RTT*38 (PAM silencing)
4806	SEQ ID NO: 4806	RTT*36 (PAM silencing)
4807	SEQ ID NO: 4807	RTT*22 (PAM silencing)
4808	SEQ ID NO: 4808	RTT*31 (PAM silencing)
4809	SEQ ID NO: 4809	RTT*34 (PAM silencing)
4810	SEQ ID NO: 4810	RTT*27 (PAM silencing)
4811	SEQ ID NO: 4811	RTT*29 (PAM silencing)
4812	SEQ ID NO: 4812	RTT*30 (PAM silencing)
4813	SEQ ID NO: 4813	RTT*32 (PAM silencing)
4814	SEQ ID NO: 4814	RTT*18 (PAM silencing)
4815	SEQ ID NO: 4815	RTT*39 (PAM silencing)
4816	SEQ ID NO: 4816	RTT*35 (PAM silencing)
4817	SEQ ID NO: 4817	RTT*25 (PAM silencing)
4818	SEQ ID NO: 4818	RTT*37 (PAM silencing)
4819	SEQ ID NO: 4819	RTT*23 (PAM silencing)
4820	SEQ ID NO: 4820	RTT*24 (PAM silencing)
4821	SEQ ID NO: 4821	RTT*17 (PAM silencing)
4822	SEQ ID NO: 4822	RTT*36 (PAM silencing)
4823	SEQ ID NO: 4823	RTT*37 (PAM silencing)
4824	SEQ ID NO: 4824	RTT*30 (PAM silencing)
4825	SEQ ID NO: 4825	RTT*18 (PAM silencing)
4826	SEQ ID NO: 4826	RTT*26 (PAM silencing)

Sequence Number	Sequence	Description
4827	SEQ ID NO: 4827	RTT
4828	SEQ ID NO: 4828	RTT*34 (PAM silencing)
4829	SEQ ID NO: 4829	RTT*28 (PAM silencing)
4830	SEQ ID NO: 4830	RTT*38 (PAM silencing)
4831	SEQ ID NO: 4831	RTT*25 (PAM silencing)
4832	SEQ ID NO: 4832	RTT*31 (PAM silencing)
4833	SEQ ID NO: 4833	RTT*19 (PAM silencing)
4834	SEQ ID NO: 4834	RTT*20 (PAM silencing)
4835	SEQ ID NO: 4835	RTT*16 (PAM silencing)
4836	SEQ ID NO: 4836	RTT*32 (PAM silencing)
4837	SEQ ID NO: 4837	RTT*39 (PAM silencing)
4838	SEQ ID NO: 4838	RTT*22 (PAM silencing)
4839	SEQ ID NO: 4839	RTT*21 (PAM silencing)
4840	SEQ ID NO: 4840	RTT*33 (PAM silencing)
4841	SEQ ID NO: 4841	RTT*23 (PAM silencing)
4842	SEQ ID NO: 4842	RTT*35 (PAM silencing)
4843	SEQ ID NO: 4843	RTT*24 (PAM silencing)
4844	SEQ ID NO: 4844	RTT*27 (PAM silencing)
4845	SEQ ID NO: 4845	RTT*29 (PAM silencing)
4846	SEQ ID NO: 4846	RTT*29 (PAM silencing)
4847	SEQ ID NO: 4847	RTT*35 (PAM silencing)
4848	SEQ ID NO: 4848	RTT*26 (PAM silencing)
4849	SEQ ID NO: 4849	RTT*32 (PAM silencing)
4850	SEQ ID NO: 4850	RTT*17 (PAM silencing)
4851	SEQ ID NO: 4851	RTT
4852	SEQ ID NO: 4852	RTT*23 (PAM silencing)
4853	SEQ ID NO: 4853	RTT*20 (PAM silencing)
4854	SEQ ID NO: 4854	RTT*33 (PAM silencing)
4855	SEQ ID NO: 4855	RTT*37 (PAM silencing)
4856	SEQ ID NO: 4856	RTT*34 (PAM silencing)
4857	SEQ ID NO: 4857	RTT*36 (PAM silencing)
4858	SEQ ID NO: 4858	RTT*39 (PAM silencing)
4859	SEQ ID NO: 4859	RTT*16 (PAM silencing)
4860	SEQ ID NO: 4860	RTT*25 (PAM silencing)
4861	SEQ ID NO: 4861	RTT*22 (PAM silencing)
4862	SEQ ID NO: 4862	RTT*21 (PAM silencing)
4863	SEQ ID NO: 4863	RTT*19 (PAM silencing)
4864	SEQ ID NO: 4864	RTT*28 (PAM silencing)
4865	SEQ ID NO: 4865	RTT*18 (PAM silencing)
4866	SEQ ID NO: 4866	RTT*30 (PAM silencing)
4867	SEQ ID NO: 4867	RTT*31 (PAM silencing)
4868	SEQ ID NO: 4868	RTT*24 (PAM silencing)
4869	SEQ ID NO: 4869	RTT*38 (PAM silencing)
4870	SEQ ID NO: 4870	RTT*27 (PAM silencing)
4871	SEQ ID NO: 4871	RTT*22 (PAM silencing)
4872	SEQ ID NO: 4872	RTT*33 (PAM silencing)
4873	SEQ ID NO: 4873	RTT*30 (PAM silencing)
4874	SEQ ID NO: 4874	RTT*19 (PAM silencing)
4875	SEQ ID NO: 4875	RTT*16 (PAM silencing)
4876	SEQ ID NO: 4876	RTT*38 (PAM silencing)
4877	SEQ ID NO: 4877	RTT*17 (PAM silencing)
4878	SEQ ID NO: 4878	RTT*34 (PAM silencing)
4879	SEQ ID NO: 4879	RTT
4880	SEQ ID NO: 4880	RTT*26 (PAM silencing)
4881	SEQ ID NO: 4881	RTT*31 (PAM silencing)
4882	SEQ ID NO: 4882	RTT*27 (PAM silencing)
4883	SEQ ID NO: 4883	RTT*18 (PAM silencing)
4884	SEQ ID NO: 4884	RTT*32 (PAM silencing)
4885	SEQ ID NO: 4885	RTT*21 (PAM silencing)
4886	SEQ ID NO: 4886	RTT*37 (PAM silencing)
4887	SEQ ID NO: 4887	RTT*36 (PAM silencing)
4888	SEQ ID NO: 4888	RTT*28 (PAM silencing)
4889	SEQ ID NO: 4889	RTT*25 (PAM silencing)
4890	SEQ ID NO: 4890	RTT*20 (PAM silencing)
4891	SEQ ID NO: 4891	RTT*29 (PAM silencing)
4892	SEQ ID NO: 4892	RTT*39 (PAM silencing)

Sequence Number	Sequence	Description
4893	SEQ ID NO: 4893	RTT*24 (PAM silencing)
4894	SEQ ID NO: 4894	RTT*35 (PAM silencing)
4895	SEQ ID NO: 4895	RTT*23 (PAM silencing)
4896	SEQ ID NO: 4896	RTT*30 (PAM silencing)
4897	SEQ ID NO: 4897	RTT*33 (PAM silencing)
4898	SEQ ID NO: 4898	RTT*39 (PAM silencing)
4899	SEQ ID NO: 4899	RTT*28 (PAM silencing)
4900	SEQ ID NO: 4900	RTT*26 (PAM silencing)
4901	SEQ ID NO: 4901	RTT
4902	SEQ ID NO: 4902	RTT*29 (PAM silencing)
4903	SEQ ID NO: 4903	RTT*22 (PAM silencing)
4904	SEQ ID NO: 4904	RTT*35 (PAM silencing)
4905	SEQ ID NO: 4905	RTT*23 (PAM silencing)
4906	SEQ ID NO: 4906	RTT*32 (PAM silencing)
4907	SEQ ID NO: 4907	RTT*38 (PAM silencing)
4908	SEQ ID NO: 4908	RTT*24 (PAM silencing)
4909	SEQ ID NO: 4909	RTT*20 (PAM silencing)
4910	SEQ ID NO: 4910	RTT*17 (PAM silencing)
4911	SEQ ID NO: 4911	RTT*19 (PAM silencing)
4912	SEQ ID NO: 4912	RTT*16 (PAM silencing)
4913	SEQ ID NO: 4913	RTT*27 (PAM silencing)
4914	SEQ ID NO: 4914	RTT*34 (PAM silencing)
4915	SEQ ID NO: 4915	RTT*36 (PAM silencing)
4916	SEQ ID NO: 4916	RTT*37 (PAM silencing)
4917	SEQ ID NO: 4917	RTT*25 (PAM silencing)
4918	SEQ ID NO: 4918	RTT*31 (PAM silencing)
4919	SEQ ID NO: 4919	RTT*21 (PAM silencing)
4920	SEQ ID NO: 4920	RTT*18 (PAM silencing)
4921	SEQ ID NO: 4921	RTT*20 (PAM silencing)
4922	SEQ ID NO: 4922	RTT*25 (PAM silencing)
4923	SEQ ID NO: 4923	RTT*36 (PAM silencing)
4924	SEQ ID NO: 4924	RTT*28 (PAM silencing)
4925	SEQ ID NO: 4925	RTT*35 (PAM silencing)
4926	SEQ ID NO: 4926	RTT*38 (PAM silencing)
4927	SEQ ID NO: 4927	RTT*30 (PAM silencing)
4928	SEQ ID NO: 4928	RTT*22 (PAM silencing)
4929	SEQ ID NO: 4929	RTT*17 (PAM silencing)
4930	SEQ ID NO: 4930	RTT*31 (PAM silencing)
4931	SEQ ID NO: 4931	RTT*34 (PAM silencing)
4932	SEQ ID NO: 4932	RTT*21 (PAM silencing)
4933	SEQ ID NO: 4933	RTT
4934	SEQ ID NO: 4934	RTT*39 (PAM silencing)
4935	SEQ ID NO: 4935	RTT*32 (PAM silencing)
4936	SEQ ID NO: 4936	RTT*19 (PAM silencing)
4937	SEQ ID NO: 4937	RTT*37 (PAM silencing)
4938	SEQ ID NO: 4938	RTT*18 (PAM silencing)
4939	SEQ ID NO: 4939	RTT*16 (PAM silencing)
4940	SEQ ID NO: 4940	RTT*26 (PAM silencing)
4941	SEQ ID NO: 4941	RTT*33 (PAM silencing)
4942	SEQ ID NO: 4942	RTT*23 (PAM silencing)
4943	SEQ ID NO: 4943	RTT*27 (PAM silencing)
4944	SEQ ID NO: 4944	RTT*24 (PAM silencing)
4945	SEQ ID NO: 4945	RTT*29 (PAM silencing)
4946	SEQ ID NO: 4946	RTT*23 (PAM silencing)
4947	SEQ ID NO: 4947	RTT*30 (PAM silencing)
4948	SEQ ID NO: 4948	RTT*20 (PAM silencing)
4949	SEQ ID NO: 4949	RTT
4950	SEQ ID NO: 4950	RTT*16 (PAM silencing)
4951	SEQ ID NO: 4951	RTT*21 (PAM silencing)
4952	SEQ ID NO: 4952	RTT*17 (PAM silencing)
4953	SEQ ID NO: 4953	RTT*32 (PAM silencing)
4954	SEQ ID NO: 4954	RTT*22 (PAM silencing)
4955	SEQ ID NO: 4955	RTT*24 (PAM silencing)
4956	SEQ ID NO: 4956	RTT*18 (PAM silencing)
4957	SEQ ID NO: 4957	RTT*39 (PAM silencing)
4958	SEQ ID NO: 4958	RTT*25 (PAM silencing)

Sequence Number	Sequence	Description
4959	SEQ ID NO: 4959	RTT*35 (PAM silencing)
4960	SEQ ID NO: 4960	RTT*33 (PAM silencing)
4961	SEQ ID NO: 4961	RTT*29 (PAM silencing)
4962	SEQ ID NO: 4962	RTT*28 (PAM silencing)
4963	SEQ ID NO: 4963	RTT*19 (PAM silencing)
4964	SEQ ID NO: 4964	RTT*38 (PAM silencing)
4965	SEQ ID NO: 4965	RTT*37 (PAM silencing)
4966	SEQ ID NO: 4966	RTT*36 (PAM silencing)
4967	SEQ ID NO: 4967	RTT*31 (PAM silencing)
4968	SEQ ID NO: 4968	RTT*26 (PAM silencing)
4969	SEQ ID NO: 4969	RTT*27 (PAM silencing)
4970	SEQ ID NO: 4970	RTT*34 (PAM silencing)
4971	SEQ ID NO: 4971	RTT*20 (PAM silencing)
4972	SEQ ID NO: 4972	RTT*25 (PAM silencing)
4973	SEQ ID NO: 4973	RTT*37 (PAM silencing)
4974	SEQ ID NO: 4974	RTT*27 (PAM silencing)
4975	SEQ ID NO: 4975	RTT*24 (PAM silencing)
4976	SEQ ID NO: 4976	RTT*16 (PAM silencing)
4977	SEQ ID NO: 4977	RTT*21 (PAM silencing)
4978	SEQ ID NO: 4978	RTT*34 (PAM silencing)
4979	SEQ ID NO: 4979	RTT*33 (PAM silencing)
4980	SEQ ID NO: 4980	RTT*30 (PAM silencing)
4981	SEQ ID NO: 4981	RTT*35 (PAM silencing)
4982	SEQ ID NO: 4982	RTT
4983	SEQ ID NO: 4983	RTT*23 (PAM silencing)
4984	SEQ ID NO: 4984	RTT*28 (PAM silencing)
4985	SEQ ID NO: 4985	RTT*38 (PAM silencing)
4986	SEQ ID NO: 4986	RTT*31 (PAM silencing)
4987	SEQ ID NO: 4987	RTT*29 (PAM silencing)
4988	SEQ ID NO: 4988	RTT*17 (PAM silencing)
4989	SEQ ID NO: 4989	RTT*26 (PAM silencing)
4990	SEQ ID NO: 4990	RTT*18 (PAM silencing)
4991	SEQ ID NO: 4991	RTT*19 (PAM silencing)
4992	SEQ ID NO: 4992	RTT*39 (PAM silencing)
4993	SEQ ID NO: 4993	RTT*32 (PAM silencing)
4994	SEQ ID NO: 4994	RTT*22 (PAM silencing)
4995	SEQ ID NO: 4995	RTT*36 (PAM silencing)
4996	SEQ ID NO: 4996	RTT*18 (PAM silencing)
4997	SEQ ID NO: 4997	RTT*20 (PAM silencing)
4998	SEQ ID NO: 4998	RTT*32 (PAM silencing)
4999	SEQ ID NO: 4999	RTT*39 (PAM silencing)
5000	SEQ ID NO: 5000	RTT*37 (PAM silencing)
5001	SEQ ID NO: 5001	RTT*26 (PAM silencing)
5002	SEQ ID NO: 5002	RTT*35 (PAM silencing)
5003	SEQ ID NO: 5003	RTT*28 (PAM silencing)
5004	SEQ ID NO: 5004	RTT
5005	SEQ ID NO: 5005	RTT*17 (PAM silencing)
5006	SEQ ID NO: 5006	RTT*25 (PAM silencing)
5007	SEQ ID NO: 5007	RTT*30 (PAM silencing)
5008	SEQ ID NO: 5008	RTT*27 (PAM silencing)
5009	SEQ ID NO: 5009	RTT*29 (PAM silencing)
5010	SEQ ID NO: 5010	RTT*19 (PAM silencing)
5011	SEQ ID NO: 5011	RTT*31 (PAM silencing)
5012	SEQ ID NO: 5012	RTT*21 (PAM silencing)
5013	SEQ ID NO: 5013	RTT*24 (PAM silencing)
5014	SEQ ID NO: 5014	RTT*34 (PAM silencing)
5015	SEQ ID NO: 5015	RTT*16 (PAM silencing)
5016	SEQ ID NO: 5016	RTT*38 (PAM silencing)
5017	SEQ ID NO: 5017	RTT*22 (PAM silencing)
5018	SEQ ID NO: 5018	RTT*23 (PAM silencing)
5019	SEQ ID NO: 5019	RTT*36 (PAM silencing)
5020	SEQ ID NO: 5020	RTT*33 (PAM silencing)
5021	SEQ ID NO: 5021	RTT*20 (PAM silencing)
5022	SEQ ID NO: 5022	RTT*31 (PAM silencing)
5023	SEQ ID NO: 5023	RTT*21 (PAM silencing)
5024	SEQ ID NO: 5024	RTT*30 (PAM silencing)

Sequence Number	Sequence	Description
5025	SEQ ID NO: 5025	RTT*32 (PAM silencing)
5026	SEQ ID NO: 5026	RTT*17 (PAM silencing)
5027	SEQ ID NO: 5027	RTT*22 (PAM silencing)
5028	SEQ ID NO: 5028	RTT*25 (PAM silencing)
5029	SEQ ID NO: 5029	RTT*36 (PAM silencing)
5030	SEQ ID NO: 5030	RTT*19 (PAM silencing)
5031	SEQ ID NO: 5031	RTT*35 (PAM silencing)
5032	SEQ ID NO: 5032	RTT*33 (PAM silencing)
5033	SEQ ID NO: 5033	RTT*37 (PAM silencing)
5034	SEQ ID NO: 5034	RTT*16 (PAM silencing)
5035	SEQ ID NO: 5035	RTT*38 (PAM silencing)
5036	SEQ ID NO: 5036	RTT*28 (PAM silencing)
5037	SEQ ID NO: 5037	RTT*29 (PAM silencing)
5038	SEQ ID NO: 5038	RTT*39 (PAM silencing)
5039	SEQ ID NO: 5039	RTT*18 (PAM silencing)
5040	SEQ ID NO: 5040	RTT*34 (PAM silencing)
5041	SEQ ID NO: 5041	RTT*27 (PAM silencing)
5042	SEQ ID NO: 5042	RTT
5043	SEQ ID NO: 5043	RTT*23 (PAM silencing)
5044	SEQ ID NO: 5044	RTT*24 (PAM silencing)
5045	SEQ ID NO: 5045	RTT*26 (PAM silencing)
5046	SEQ ID NO: 5046	RTT*27 (PAM silencing)
5047	SEQ ID NO: 5047	RTT*39 (PAM silencing)
5048	SEQ ID NO: 5048	RTT*36 (PAM silencing)
5049	SEQ ID NO: 5049	RTT*18 (PAM silencing)
5050	SEQ ID NO: 5050	RTT*35 (PAM silencing)
5051	SEQ ID NO: 5051	RTT*20 (PAM silencing)
5052	SEQ ID NO: 5052	RTT*16 (PAM silencing)
5053	SEQ ID NO: 5053	RTT*23 (PAM silencing)
5054	SEQ ID NO: 5054	RTT*31 (PAM silencing)
5055	SEQ ID NO: 5055	RTT*19 (PAM silencing)
5056	SEQ ID NO: 5056	RTT
5057	SEQ ID NO: 5057	RTT*25 (PAM silencing)
5058	SEQ ID NO: 5058	RTT*34 (PAM silencing)
5059	SEQ ID NO: 5059	RTT*24 (PAM silencing)
5060	SEQ ID NO: 5060	RTT*37 (PAM silencing)
5061	SEQ ID NO: 5061	RTT*29 (PAM silencing)
5062	SEQ ID NO: 5062	RTT*21 (PAM silencing)
5063	SEQ ID NO: 5063	RTT*22 (PAM silencing)
5064	SEQ ID NO: 5064	RTT*26 (PAM silencing)
5065	SEQ ID NO: 5065	RTT*32 (PAM silencing)
5066	SEQ ID NO: 5066	RTT*38 (PAM silencing)
5067	SEQ ID NO: 5067	RTT*17 (PAM silencing)
5068	SEQ ID NO: 5068	RTT*33 (PAM silencing)
5069	SEQ ID NO: 5069	RTT*30 (PAM silencing)
5070	SEQ ID NO: 5070	RTT*28 (PAM silencing)
5071	SEQ ID NO: 5071	RTT*37 (PAM silencing)
5072	SEQ ID NO: 5072	RTT*38 (PAM silencing)
5073	SEQ ID NO: 5073	RTT*39 (PAM silencing)
5074	SEQ ID NO: 5074	RTT*21 (PAM silencing)
5075	SEQ ID NO: 5075	RTT*34 (PAM silencing)
5076	SEQ ID NO: 5076	RTT*20 (PAM silencing)
5077	SEQ ID NO: 5077	RTT
5078	SEQ ID NO: 5078	RTT*27 (PAM silencing)
5079	SEQ ID NO: 5079	RTT*28 (PAM silencing)
5080	SEQ ID NO: 5080	RTT*18 (PAM silencing)
5081	SEQ ID NO: 5081	RTT*16 (PAM silencing)
5082	SEQ ID NO: 5082	RTT*35 (PAM silencing)
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5086	SEQ ID NO: 5086	RTT*24 (PAM silencing)
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5088	SEQ ID NO: 5088	RTT*36 (PAM silencing)
5089	SEQ ID NO: 5089	RTT*31 (PAM silencing)
5090	SEQ ID NO: 5090	RTT*17 (PAM silencing)

Sequence Number	Sequence	Description
5091	SEQ ID NO: 5091	RTT*19 (PAM silencing)
5092	SEQ ID NO: 5092	RTT*23 (PAM silencing)
5093	SEQ ID NO: 5093	RTT*33 (PAM silencing)
5094	SEQ ID NO: 5094	RTT*32 (PAM silencing)
5095	SEQ ID NO: 5095	RTT*30 (PAM silencing)
5096	SEQ ID NO: 5096	RTT*38 (PAM silencing)
5097	SEQ ID NO: 5097	RTT*33 (PAM silencing)
5098	SEQ ID NO: 5098	RTT*32 (PAM silencing)
5099	SEQ ID NO: 5099	RTT*39 (PAM silencing)
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5108	SEQ ID NO: 5108	RTT*28 (PAM silencing)
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5110	SEQ ID NO: 5110	RTT*37 (PAM silencing)
5111	SEQ ID NO: 5111	RTT*23 (PAM silencing)
5112	SEQ ID NO: 5112	RTT*17 (PAM silencing)
5113	SEQ ID NO: 5113	RTT*24 (PAM silencing)
5114	SEQ ID NO: 5114	RTT*34 (PAM silencing)
5115	SEQ ID NO: 5115	RTT*36 (PAM silencing)
5116	SEQ ID NO: 5116	RTT*25 (PAM silencing)
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5119	SEQ ID NO: 5119	RTT*20 (PAM silencing)
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5133	SEQ ID NO: 5133	RTT*23 (PAM silencing)
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5154	SEQ ID NO: 5154	RTT*33 (PAM silencing)
5155	SEQ ID NO: 5155	RTT
5156	SEQ ID NO: 5156	RTT*20 (PAM silencing)

Sequence Number	Sequence	Description
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5222	SEQ ID NO: 5222	RTT*21 (PAM silencing)
5223	SEQ ID NO: 5223	RTT*19 (PAM silencing)

Sequence Number	Sequence	Description
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5229	SEQ ID NO: 5229	RTT*32 (PAM silencing)
5230	SEQ ID NO: 5230	RTT*26 (PAM silencing)
5231	SEQ ID NO: 5231	RTT*18 (PAM silencing)
5232	SEQ ID NO: 5232	RTT*37 (PAM silencing)
5233	SEQ ID NO: 5233	RTT*23 (PAM silencing)
5234	SEQ ID NO: 5234	RTT*34 (PAM silencing)
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5289	SEQ ID NO: 5289	RTT*23 (PAM silencing)

Sequence Number	Sequence	Description
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5297	SEQ ID NO: 5297	RTT*34 (PAM silencing)
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5301	SEQ ID NO: 5301	RTT*32 (PAM silencing)
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5322	SEQ ID NO: 5322	RTT*35 (PAM silencing)
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Sequence Number	Sequence	Description
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5363	SEQ ID NO: 5363	RTT*20 (PAM silencing)
5364	SEQ ID NO: 5364	RTT*27 (PAM silencing)
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5366	SEQ ID NO: 5366	RTT*23 (PAM silencing)
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5419	SEQ ID NO: 5419	RTT*25 (PAM silencing)
5420	SEQ ID NO: 5420	RTT*26 (PAM silencing)
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Sequence Number	Sequence	Description
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5428	SEQ ID NO: 5428	RTT*33 (PAM silencing)
5429	SEQ ID NO: 5429	RTT*22 (PAM silencing)
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5431	SEQ ID NO: 5431	RTT*16 (PAM silencing)
5432	SEQ ID NO: 5432	RTT*26 (PAM silencing)
5433	SEQ ID NO: 5433	RTT*30 (PAM silencing)
5434	SEQ ID NO: 5434	RTT*38 (PAM silencing)
5435	SEQ ID NO: 5435	RTT*31 (PAM silencing)
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5438	SEQ ID NO: 5438	RTT*34 (PAM silencing)
5439	SEQ ID NO: 5439	RTT*35 (PAM silencing)
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5471	SEQ ID NO: 5471	RTT*21 (PAM silencing)
5472	SEQ ID NO: 5472	RTT*26 (PAM silencing)
5473	SEQ ID NO: 5473	RTT*29 (PAM silencing)
5474	SEQ ID NO: 5474	RTT*17 (PAM silencing)
5475	SEQ ID NO: 5475	RTT*39 (PAM silencing)
5476	SEQ ID NO: 5476	RTT*23 (PAM silencing)
5477	SEQ ID NO: 5477	RTT*22 (PAM silencing)
5478	SEQ ID NO: 5478	RTT*27 (PAM silencing)
5479	SEQ ID NO: 5479	RTT*31 (PAM silencing)
5480	SEQ ID NO: 5480	RTT*32 (PAM silencing)
5481	SEQ ID NO: 5481	RTT*30 (PAM silencing)
5482	SEQ ID NO: 5482	RTT*24 (PAM silencing)
5483	SEQ ID NO: 5483	RTT*20 (PAM silencing)
5484	SEQ ID NO: 5484	RTT*25 (PAM silencing)
5485	SEQ ID NO: 5485	RTT*34 (PAM silencing)
5486	SEQ ID NO: 5486	RTT
5487	SEQ ID NO: 5487	RTT*37 (PAM silencing)

Sequence Number	Sequence	Description
5488	SEQ ID NO: 5488	RTT*18 (PAM silencing)
5489	SEQ ID NO: 5489	RTT*16 (PAM silencing)
5490	SEQ ID NO: 5490	RTT*19 (PAM silencing)
5491	SEQ ID NO: 5491	RTT*35 (PAM silencing)
5492	SEQ ID NO: 5492	RTT*38 (PAM silencing)
5493	SEQ ID NO: 5493	RTT*36 (PAM silencing)
5494	SEQ ID NO: 5494	RTT*33 (PAM silencing)
5495	SEQ ID NO: 5495	RTT*28 (PAM silencing)
5496	SEQ ID NO: 5496	RTT*16 (PAM silencing)
5497	SEQ ID NO: 5497	RTT*30 (PAM silencing)
5498	SEQ ID NO: 5498	RTT*25 (PAM silencing)
5499	SEQ ID NO: 5499	RTT*22 (PAM silencing)
5500	SEQ ID NO: 5500	RTT
5501	SEQ ID NO: 5501	RTT*21 (PAM silencing)
5502	SEQ ID NO: 5502	RTT*24 (PAM silencing)
5503	SEQ ID NO: 5503	RTT*38 (PAM silencing)
5504	SEQ ID NO: 5504	RTT*17 (PAM silencing)
5505	SEQ ID NO: 5505	RTT*39 (PAM silencing)
5506	SEQ ID NO: 5506	RTT*33 (PAM silencing)
5507	SEQ ID NO: 5507	RTT*36 (PAM silencing)
5508	SEQ ID NO: 5508	RTT*20 (PAM silencing)
5509	SEQ ID NO: 5509	RTT*31 (PAM silencing)
5510	SEQ ID NO: 5510	RTT*18 (PAM silencing)
5511	SEQ ID NO: 5511	RTT*23 (PAM silencing)
5512	SEQ ID NO: 5512	RTT*28 (PAM silencing)
5513	SEQ ID NO: 5513	RTT*19 (PAM silencing)
5514	SEQ ID NO: 5514	RTT*35 (PAM silencing)
5515	SEQ ID NO: 5515	RTT*32 (PAM silencing)
5516	SEQ ID NO: 5516	RTT*26 (PAM silencing)
5517	SEQ ID NO: 5517	RTT*27 (PAM silencing)
5518	SEQ ID NO: 5518	RTT*29 (PAM silencing)
5519	SEQ ID NO: 5519	RTT*34 (PAM silencing)
5520	SEQ ID NO: 5520	RTT*37 (PAM silencing)
5521	SEQ ID NO: 5521	RTT*29 (PAM silencing)
5522	SEQ ID NO: 5522	RTT*37 (PAM silencing)
5523	SEQ ID NO: 5523	RTT*16 (PAM silencing)
5524	SEQ ID NO: 5524	RTT*24 (PAM silencing)
5525	SEQ ID NO: 5525	RTT*26 (PAM silencing)
5526	SEQ ID NO: 5526	RTT*38 (PAM silencing)
5527	SEQ ID NO: 5527	RTT*25 (PAM silencing)
5528	SEQ ID NO: 5528	RTT*39 (PAM silencing)
5529	SEQ ID NO: 5529	RTT
5530	SEQ ID NO: 5530	RTT*22 (PAM silencing)
5531	SEQ ID NO: 5531	RTT*36 (PAM silencing)
5532	SEQ ID NO: 5532	RTT*27 (PAM silencing)
5533	SEQ ID NO: 5533	RTT*23 (PAM silencing)
5534	SEQ ID NO: 5534	RTT*19 (PAM silencing)
5535	SEQ ID NO: 5535	RTT*20 (PAM silencing)
5536	SEQ ID NO: 5536	RTT*32 (PAM silencing)
5537	SEQ ID NO: 5537	RTT*33 (PAM silencing)
5538	SEQ ID NO: 5538	RTT*28 (PAM silencing)
5539	SEQ ID NO: 5539	RTT*30 (PAM silencing)
5540	SEQ ID NO: 5540	RTT*21 (PAM silencing)
5541	SEQ ID NO: 5541	RTT*34 (PAM silencing)
5542	SEQ ID NO: 5542	RTT*17 (PAM silencing)
5543	SEQ ID NO: 5543	RTT*35 (PAM silencing)
5544	SEQ ID NO: 5544	RTT*31 (PAM silencing)
5545	SEQ ID NO: 5545	RTT*18 (PAM silencing)
5546	SEQ ID NO: 5546	RTT*29 (PAM silencing)
5547	SEQ ID NO: 5547	RTT*24 (PAM silencing)
5548	SEQ ID NO: 5548	RTT*37 (PAM silencing)
5549	SEQ ID NO: 5549	RTT*20 (PAM silencing)
5550	SEQ ID NO: 5550	RTT*19 (PAM silencing)
5551	SEQ ID NO: 5551	RTT*21 (PAM silencing)
5552	SEQ ID NO: 5552	RTT*23 (PAM silencing)
5553	SEQ ID NO: 5553	RTT*31 (PAM silencing)

Sequence Number	Sequence	Description
5554	SEQ ID NO: 5554	RTT*22 (PAM silencing)
5555	SEQ ID NO: 5555	RTT*17 (PAM silencing)
5556	SEQ ID NO: 5556	RTT*30 (PAM silencing)
5557	SEQ ID NO: 5557	RTT
5558	SEQ ID NO: 5558	RTT*16 (PAM silencing)
5559	SEQ ID NO: 5559	RTT*39 (PAM silencing)
5560	SEQ ID NO: 5560	RTT*26 (PAM silencing)
5561	SEQ ID NO: 5561	RTT*33 (PAM silencing)
5562	SEQ ID NO: 5562	RTT*18 (PAM silencing)
5563	SEQ ID NO: 5563	RTT*28 (PAM silencing)
5564	SEQ ID NO: 5564	RTT*36 (PAM silencing)
5565	SEQ ID NO: 5565	RTT*32 (PAM silencing)
5566	SEQ ID NO: 5566	RTT*25 (PAM silencing)
5567	SEQ ID NO: 5567	RTT*35 (PAM silencing)
5568	SEQ ID NO: 5568	RTT*34 (PAM silencing)
5569	SEQ ID NO: 5569	RTT*27 (PAM silencing)
5570	SEQ ID NO: 5570	RTT*38 (PAM silencing)
5571	SEQ ID NO: 5571	RTT*18 (PAM silencing)
5572	SEQ ID NO: 5572	RTT*28 (PAM silencing)
5573	SEQ ID NO: 5573	RTT*20 (PAM silencing)
5574	SEQ ID NO: 5574	RTT*25 (PAM silencing)
5575	SEQ ID NO: 5575	RTT*39 (PAM silencing)
5576	SEQ ID NO: 5576	RTT*26 (PAM silencing)
5577	SEQ ID NO: 5577	RTT*33 (PAM silencing)
5578	SEQ ID NO: 5578	RTT*17 (PAM silencing)
5579	SEQ ID NO: 5579	RTT*34 (PAM silencing)
5580	SEQ ID NO: 5580	RTT*30 (PAM silencing)
5581	SEQ ID NO: 5581	RTT*22 (PAM silencing)
5582	SEQ ID NO: 5582	RTT*38 (PAM silencing)
5583	SEQ ID NO: 5583	RTT*31 (PAM silencing)
5584	SEQ ID NO: 5584	RTT*19 (PAM silencing)
5585	SEQ ID NO: 5585	RTT*16 (PAM silencing)
5586	SEQ ID NO: 5586	RTT
5587	SEQ ID NO: 5587	RTT*29 (PAM silencing)
5588	SEQ ID NO: 5588	RTT*24 (PAM silencing)
5589	SEQ ID NO: 5589	RTT*21 (PAM silencing)
5590	SEQ ID NO: 5590	RTT*27 (PAM silencing)
5591	SEQ ID NO: 5591	RTT*35 (PAM silencing)
5592	SEQ ID NO: 5592	RTT*32 (PAM silencing)
5593	SEQ ID NO: 5593	RTT*37 (PAM silencing)
5594	SEQ ID NO: 5594	RTT*36 (PAM silencing)
5595	SEQ ID NO: 5595	RTT*23 (PAM silencing)
5596	SEQ ID NO: 5596	RTT*18 (PAM silencing)
5597	SEQ ID NO: 5597	RTT*16 (PAM silencing)
5598	SEQ ID NO: 5598	RTT*33 (PAM silencing)
5599	SEQ ID NO: 5599	RTT*28 (PAM silencing)
5600	SEQ ID NO: 5600	RTT*26 (PAM silencing)
5601	SEQ ID NO: 5601	RTT*22 (PAM silencing)
5602	SEQ ID NO: 5602	RTT*25 (PAM silencing)
5603	SEQ ID NO: 5603	RTT*27 (PAM silencing)
5604	SEQ ID NO: 5604	RTT*34 (PAM silencing)
5605	SEQ ID NO: 5605	RTT*39 (PAM silencing)
5606	SEQ ID NO: 5606	RTT*30 (PAM silencing)
5607	SEQ ID NO: 5607	RTT*20 (PAM silencing)
5608	SEQ ID NO: 5608	RTT*38 (PAM silencing)
5609	SEQ ID NO: 5609	RTT
5610	SEQ ID NO: 5610	RTT*35 (PAM silencing)
5611	SEQ ID NO: 5611	RTT*29 (PAM silencing)
5612	SEQ ID NO: 5612	RTT*36 (PAM silencing)
5613	SEQ ID NO: 5613	RTT*37 (PAM silencing)
5614	SEQ ID NO: 5614	RTT*32 (PAM silencing)
5615	SEQ ID NO: 5615	RTT*21 (PAM silencing)
5616	SEQ ID NO: 5616	RTT*23 (PAM silencing)
5617	SEQ ID NO: 5617	RTT*19 (PAM silencing)
5618	SEQ ID NO: 5618	RTT*17 (PAM silencing)
5619	SEQ ID NO: 5619	RTT*31 (PAM silencing)

Sequence Number	Sequence	Description
5620	SEQ ID NO: 5620	RTT*24 (PAM silencing)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
5621	SEQ ID NO: 5621	PE3b*30 ngRNA spacer (CG PAM)
5622	SEQ ID NO: 5622	PE3b*25 ngRNA spacer (CG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
5623	SEQ ID NO: 5623	PE3b*35 ngRNA spacer (CG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG;AGA PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG;CGA PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG;TGA PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
5624	SEQ ID NO: 5624	PE3b*16 ngRNA spacer (CG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG;AGA PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)

Sequence Number	Sequence	Description
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)

Table 19

Sequence Number	Sequence	Description
5625	SEQ ID NO: 5625	PEgRNA spacer (TGA;TG PAM)
5626	SEQ ID NO: 5626	PEgRNA spacer (TGA;TG PAM)
5627	SEQ ID NO: 5627	PEgRNA spacer (TGA;TG PAM)
5628	SEQ ID NO: 5628	PEgRNA spacer (TGA;TG PAM)
5629	SEQ ID NO: 5629	PEgRNA spacer (TGA;TG PAM)
5630	SEQ ID NO: 5630	PEgRNA spacer (TGA;TG PAM)
5631	SEQ ID NO: 5631	PEgRNA spacer (TGA;TG PAM)
5632	GGC	PBS
5633	GGCT	PBS
5634	GGCTC	PBS
5635	GGCTCC	PBS
5636	GGCTCC T	PBS
5637	GGCTCC TC	PBS
5638	GGCTCC TCT	PBS
5639	SEQ ID NO: 5639	PBS
5640	SEQ ID NO: 5640	PBS
5641	SEQ ID NO: 5641	PBS
5642	SEQ ID NO: 5642	PBS
5643	SEQ ID NO: 5643	PBS
5644	SEQ ID NO: 5644	PBS
5645	SEQ ID NO: 5645	PBS
5646	SEQ ID NO: 5646	PBS
5647	SEQ ID NO: 5647	PBS
5648	SEQ ID NO: 5648	PBS
5649	SEQ ID NO: 5649	RTT*105 (PAM silencing)
5650	SEQ ID NO: 5650	RTT
5651	SEQ ID NO: 5651	RTT*106 (PAM silencing)
5652	SEQ ID NO: 5652	RTT*107 (PAM silencing)
5653	SEQ ID NO: 5653	RTT*105 (PAM silencing)
5654	SEQ ID NO: 5654	RTT*106 (PAM silencing)
5655	SEQ ID NO: 5655	RTT
5656	SEQ ID NO: 5656	RTT*107 (PAM silencing)
5657	SEQ ID NO: 5657	RTT
5658	SEQ ID NO: 5658	RTT*107 (PAM silencing)
5659	SEQ ID NO: 5659	RTT*105 (PAM silencing)
5660	SEQ ID NO: 5660	RTT*106 (PAM silencing)
5661	SEQ ID NO: 5661	RTT*107 (PAM silencing)
5662	SEQ ID NO: 5662	RTT*105 (PAM silencing)
5663	SEQ ID NO: 5663	RTT*106 (PAM silencing)
5664	SEQ ID NO: 5664	RTT
5665	SEQ ID NO: 5665	RTT*105 (PAM silencing)
5666	SEQ ID NO: 5666	RTT*106 (PAM silencing)
5667	SEQ ID NO: 5667	RTT
5668	SEQ ID NO: 5668	RTT*107 (PAM silencing)
5669	SEQ ID NO: 5669	RTT
5670	SEQ ID NO: 5670	RTT*105 (PAM silencing)
5671	SEQ ID NO: 5671	RTT*106 (PAM silencing)
5672	SEQ ID NO: 5672	RTT*107 (PAM silencing)
5673	SEQ ID NO: 5673	RTT*107 (PAM silencing)
5674	SEQ ID NO: 5674	RTT*105 (PAM silencing)
5675	SEQ ID NO: 5675	RTT*106 (PAM silencing)
5676	SEQ ID NO: 5676	RTT
5677	SEQ ID NO: 5677	RTT*107 (PAM silencing)
5678	SEQ ID NO: 5678	RTT*105 (PAM silencing)
5679	SEQ ID NO: 5679	RTT
5680	SEQ ID NO: 5680	RTT*106 (PAM silencing)
5681	SEQ ID NO: 5681	RTT*106 (PAM silencing)
5682	SEQ ID NO: 5682	RTT
5683	SEQ ID NO: 5683	RTT*105 (PAM silencing)
5684	SEQ ID NO: 5684	RTT*107 (PAM silencing)
5685	SEQ ID NO: 5685	RTT*105 (PAM silencing)
5686	SEQ ID NO: 5686	RTT*107 (PAM silencing)
5687	SEQ ID NO: 5687	RTT
5688	SEQ ID NO: 5688	RTT*106 (PAM silencing)
5689	SEQ ID NO: 5689	RTT*105 (PAM silencing)
5690	SEQ ID NO: 5690	RTT*106 (PAM silencing)
5691	SEQ ID NO: 5691	RTT*107 (PAM silencing)
5692	SEQ ID NO: 5692	RTT
5693	SEQ ID NO: 5693	RTT*106 (PAM silencing)
5694	SEQ ID NO: 5694	RTT*105 (PAM silencing)
5695	SEQ ID NO: 5695	RTT

Sequence Number	Sequence	Description
5696	SEQ ID NO: 5696	RTT*107 (PAM silencing)
5697	SEQ ID NO: 5697	RTT*105 (PAM silencing)
5698	SEQ ID NO: 5698	RTT*106 (PAM silencing)
5699	SEQ ID NO: 5699	RTT*107 (PAM silencing)
5700	SEQ ID NO: 5700	RTT
5701	SEQ ID NO: 5701	RTT*107 (PAM silencing)
5702	SEQ ID NO: 5702	RTT*106 (PAM silencing)
5703	SEQ ID NO: 5703	RTT
5704	SEQ ID NO: 5704	RTT*105 (PAM silencing)
5705	SEQ ID NO: 5705	RTT*107 (PAM silencing)
5706	SEQ ID NO: 5706	RTT*106 (PAM silencing)
5707	SEQ ID NO: 5707	RTT
5708	SEQ ID NO: 5708	RTT*105 (PAM silencing)
5709	SEQ ID NO: 5709	RTT*106 (PAM silencing)
5710	SEQ ID NO: 5710	RTT*107 (PAM silencing)
5711	SEQ ID NO: 5711	RTT
5712	SEQ ID NO: 5712	RTT*105 (PAM silencing)
5713	SEQ ID NO: 5713	RTT*105 (PAM silencing)
5714	SEQ ID NO: 5714	RTT*107 (PAM silencing)
5715	SEQ ID NO: 5715	RTT*106 (PAM silencing)
5716	SEQ ID NO: 5716	RTT
5717	SEQ ID NO: 5717	RTT
5718	SEQ ID NO: 5718	RTT*106 (PAM silencing)
5719	SEQ ID NO: 5719	RTT*107 (PAM silencing)
5720	SEQ ID NO: 5720	RTT*105 (PAM silencing)
5721	SEQ ID NO: 5721	RTT
5722	SEQ ID NO: 5722	RTT*106 (PAM silencing)
5723	SEQ ID NO: 5723	RTT*105 (PAM silencing)
5724	SEQ ID NO: 5724	RTT*107 (PAM silencing)
5725	SEQ ID NO: 5725	RTT*105 (PAM silencing)
5726	SEQ ID NO: 5726	RTT*107 (PAM silencing)
5727	SEQ ID NO: 5727	RTT*106 (PAM silencing)
5728	SEQ ID NO: 5728	RTT
5729	SEQ ID NO: 5729	RTT*105 (PAM silencing)
5730	SEQ ID NO: 5730	RTT
5731	SEQ ID NO: 5731	RTT*107 (PAM silencing)
5732	SEQ ID NO: 5732	RTT*106 (PAM silencing)
5733	SEQ ID NO: 5733	RTT*105 (PAM silencing)
5734	SEQ ID NO: 5734	RTT
5735	SEQ ID NO: 5735	RTT*107 (PAM silencing)
5736	SEQ ID NO: 5736	RTT*106 (PAM silencing)
5737	SEQ ID NO: 5737	RTT
5738	SEQ ID NO: 5738	RTT*107 (PAM silencing)
5739	SEQ ID NO: 5739	RTT*105 (PAM silencing)
5740	SEQ ID NO: 5740	RTT*106 (PAM silencing)
5741	SEQ ID NO: 5741	RTT
5742	SEQ ID NO: 5742	RTT*107 (PAM silencing)
5743	SEQ ID NO: 5743	RTT*105 (PAM silencing)
5744	SEQ ID NO: 5744	RTT*106 (PAM silencing)
5745	SEQ ID NO: 5745	RTT*107 (PAM silencing)
5746	SEQ ID NO: 5746	RTT*106 (PAM silencing)
5747	SEQ ID NO: 5747	RTT
5748	SEQ ID NO: 5748	RTT*105 (PAM silencing)
5749	SEQ ID NO: 5749	RTT*106 (PAM silencing)
5750	SEQ ID NO: 5750	RTT*105 (PAM silencing)
5751	SEQ ID NO: 5751	RTT
5752	SEQ ID NO: 5752	RTT*107 (PAM silencing)
5753	SEQ ID NO: 5753	RTT*105 (PAM silencing)
5754	SEQ ID NO: 5754	RTT*107 (PAM silencing)
5755	SEQ ID NO: 5755	RTT*106 (PAM silencing)
5756	SEQ ID NO: 5756	RTT
5757	SEQ ID NO: 5757	RTT
5758	SEQ ID NO: 5758	RTT*105 (PAM silencing)
5759	SEQ ID NO: 5759	RTT*107 (PAM silencing)
5760	SEQ ID NO: 5760	RTT*106 (PAM silencing)
5761	SEQ ID NO: 5761	RTT*105 (PAM silencing)
5762	SEQ ID NO: 5762	RTT*107 (PAM silencing)
5763	SEQ ID NO: 5763	RTT
5764	SEQ ID NO: 5764	RTT*106 (PAM silencing)
5765	SEQ ID NO: 5765	RTT*105 (PAM silencing)
5766	SEQ ID NO: 5766	RTT*107 (PAM silencing)
5767	SEQ ID NO: 5767	RTT*106 (PAM silencing)

Sequence Number	Sequence	Description
5768	SEQ ID NO: 5768	RTT
5769	SEQ ID NO: 5769	RTT*105 (PAM silencing)
5770	SEQ ID NO: 5770	RTT*106 (PAM silencing)
5771	SEQ ID NO: 5771	RTT
5772	SEQ ID NO: 5772	RTT*107 (PAM silencing)
5773	SEQ ID NO: 5773	RTT*106 (PAM silencing)
5774	SEQ ID NO: 5774	RTT*105 (PAM silencing)
5775	SEQ ID NO: 5775	RTT*107 (PAM silencing)
5776	SEQ ID NO: 5776	RTT
5777	SEQ ID NO: 5777	RTT
5778	SEQ ID NO: 5778	RTT*105 (PAM silencing)
5779	SEQ ID NO: 5779	RTT*106 (PAM silencing)
5780	SEQ ID NO: 5780	RTT*107 (PAM silencing)
5781	SEQ ID NO: 5781	RTT*106 (PAM silencing)
5782	SEQ ID NO: 5782	RTT*107 (PAM silencing)
5783	SEQ ID NO: 5783	RTT
5784	SEQ ID NO: 5784	RTT*105 (PAM silencing)
5785	SEQ ID NO: 5785	RTT
5786	SEQ ID NO: 5786	RTT*105 (PAM silencing)
5787	SEQ ID NO: 5787	RTT*106 (PAM silencing)
5788	SEQ ID NO: 5788	RTT*107 (PAM silencing)
5789	SEQ ID NO: 5789	RTT*106 (PAM silencing)
5790	SEQ ID NO: 5790	RTT
5791	SEQ ID NO: 5791	RTT*105 (PAM silencing)
5792	SEQ ID NO: 5792	RTT*107 (PAM silencing)
5793	SEQ ID NO: 5793	RTT
5794	SEQ ID NO: 5794	RTT*106 (PAM silencing)
5795	SEQ ID NO: 5795	RTT*105 (PAM silencing)
5796	SEQ ID NO: 5796	RTT*107 (PAM silencing)
5797	SEQ ID NO: 5797	RTT*105 (PAM silencing)
5798	SEQ ID NO: 5798	RTT*107 (PAM silencing)
5799	SEQ ID NO: 5799	RTT*106 (PAM silencing)
5800	SEQ ID NO: 5800	RTT
5801	SEQ ID NO: 5801	RTT*107 (PAM silencing)
5802	SEQ ID NO: 5802	RTT
5803	SEQ ID NO: 5803	RTT*105 (PAM silencing)
5804	SEQ ID NO: 5804	RTT*106 (PAM silencing)
5805	SEQ ID NO: 5805	RTT*105 (PAM silencing)
5806	SEQ ID NO: 5806	RTT*106 (PAM silencing)
5807	SEQ ID NO: 5807	RTT
5808	SEQ ID NO: 5808	RTT*107 (PAM silencing)
5809	SEQ ID NO: 5809	RTT
5810	SEQ ID NO: 5810	RTT*107 (PAM silencing)
5811	SEQ ID NO: 5811	RTT*106 (PAM silencing)
5812	SEQ ID NO: 5812	RTT*105 (PAM silencing)
5813	SEQ ID NO: 5813	RTT*105 (PAM silencing)
5814	SEQ ID NO: 5814	RTT*106 (PAM silencing)
5815	SEQ ID NO: 5815	RTT
5816	SEQ ID NO: 5816	RTT*107 (PAM silencing)
5817	SEQ ID NO: 5817	RTT*107 (PAM silencing)
5818	SEQ ID NO: 5818	RTT
5819	SEQ ID NO: 5819	RTT*106 (PAM silencing)
5820	SEQ ID NO: 5820	RTT*105 (PAM silencing)
5821	SEQ ID NO: 5821	RTT*106 (PAM silencing)
5822	SEQ ID NO: 5822	RTT*105 (PAM silencing)
5823	SEQ ID NO: 5823	RTT
5824	SEQ ID NO: 5824	RTT*107 (PAM silencing)
5825	SEQ ID NO: 5825	RTT*107 (PAM silencing)
5826	SEQ ID NO: 5826	RTT*106 (PAM silencing)
5827	SEQ ID NO: 5827	RTT
5828	SEQ ID NO: 5828	RTT*105 (PAM silencing)
5829	SEQ ID NO: 5829	RTT*107 (PAM silencing)
5830	SEQ ID NO: 5830	RTT
5831	SEQ ID NO: 5831	RTT*105 (PAM silencing)
5832	SEQ ID NO: 5832	RTT*106 (PAM silencing)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
5833	SEQ ID NO: 5833	PE3b*107 ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)

Sequence Number	Sequence	Description
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG;AGG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
5834	SEQ ID NO: 5834	PE3b*106 ngRNA spacer (GG;GGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG;AGA PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG;CGA PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG;TGA PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG;TGA PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG;AGA PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
5835	SEQ ID NO: 5835	PE3b*106 ngRNA spacer (GG PAM)
5836	SEQ ID NO: 5836	PE3b*107 ngRNA spacer (GG;GGG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
5837	SEQ ID NO: 5837	PE3b*106 ngRNA spacer (AG;AGG PAM)
5838	SEQ ID NO: 5838	PE3b*105 ngRNA spacer (GG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG;GGG PAM)
5839	SEQ ID NO: 5839	PE3b*107 ngRNA spacer (AG;AGG PAM)
5840	SEQ ID NO: 5840	PE3b*105 ngRNA spacer (GG;GGG PAM)
5841	SEQ ID NO: 5841	PE3b*105 ngRNA spacer (AG;AGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG;AGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
108	SEQ ID NO: 108	ngRNA (GG;GGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)

Sequence Number	Sequence	Description
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG;AGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)

Table 20

Sequence Number	Sequence	Description
5842	SEQ ID NO: 5842	PEgRNA spacer (CGA;CG PAM)
5843	SEQ ID NO: 5843	PEgRNA spacer (CGA;CG PAM)
5844	SEQ ID NO: 5844	PEgRNA spacer (CGA;CG PAM)
5845	SEQ ID NO: 5845	PEgRNA spacer (CGA;CG PAM)
5846	SEQ ID NO: 5846	PEgRNA spacer (CGA;CG PAM)
5847	SEQ ID NO: 5847	PEgRNA spacer (CGA;CG PAM)
5848	SEQ ID NO: 5848	PEgRNA spacer (CGA;CG PAM)
5849	AAT	PBS
5850	AATG	PBS
5851	AATGT	PBS
5852	AATGTC	PBS
5853	AATGTC A	PBS
5854	AATGTC AC	PBS
5855	AATGTC ACA	PBS
5856	SEQ ID NO: 5856	PBS
5857	SEQ ID NO: 5857	PBS
5858	SEQ ID NO: 5858	PBS
5859	SEQ ID NO: 5859	PBS
5860	SEQ ID NO: 5860	PBS
5861	SEQ ID NO: 5861	PBS
5862	SEQ ID NO: 5862	PBS
5863	SEQ ID NO: 5863	PBS
5864	SEQ ID NO: 5864	PBS
5865	SEQ ID NO: 5865	PBS
5866	SEQ ID NO: 5866	RTT
5867	SEQ ID NO: 5867	RTT
5868	SEQ ID NO: 5868	RTT
5869	SEQ ID NO: 5869	RTT
5870	SEQ ID NO: 5870	RTT
5871	SEQ ID NO: 5871	RTT
5872	SEQ ID NO: 5872	RTT
5873	SEQ ID NO: 5873	RTT
5874	SEQ ID NO: 5874	RTT
5875	SEQ ID NO: 5875	RTT
5876	SEQ ID NO: 5876	RTT
5877	SEQ ID NO: 5877	RTT
5878	SEQ ID NO: 5878	RTT
5879	SEQ ID NO: 5879	RTT
5880	SEQ ID NO: 5880	RTT
5881	SEQ ID NO: 5881	RTT
5882	SEQ ID NO: 5882	RTT
5883	SEQ ID NO: 5883	RTT
5884	SEQ ID NO: 5884	RTT
5885	SEQ ID NO: 5885	RTT
5886	SEQ ID NO: 5886	RTT
5887	SEQ ID NO: 5887	RTT
5888	SEQ ID NO: 5888	RTT
5889	SEQ ID NO: 5889	RTT
5890	SEQ ID NO: 5890	RTT
5891	SEQ ID NO: 5891	RTT
5892	SEQ ID NO: 5892	RTT
5893	SEQ ID NO: 5893	RTT
5894	SEQ ID NO: 5894	RTT
5895	SEQ ID NO: 5895	RTT
5896	SEQ ID NO: 5896	RTT
5897	SEQ ID NO: 5897	RTT
5898	SEQ ID NO: 5898	RTT
5899	SEQ ID NO: 5899	RTT
5900	SEQ ID NO: 5900	RTT
5901	SEQ ID NO: 5901	RTT
5902	SEQ ID NO: 5902	RTT
5903	SEQ ID NO: 5903	RTT
5904	SEQ ID NO: 5904	RTT
5905	SEQ ID NO: 5905	RTT
5906	SEQ ID NO: 5906	RTT
5907	SEQ ID NO: 5907	RTT
5908	SEQ ID NO: 5908	RTT
5909	SEQ ID NO: 5909	RTT
5910	SEQ ID NO: 5910	RTT
5911	SEQ ID NO: 5911	RTT
5912	SEQ ID NO: 5912	RTT
5913	SEQ ID NO: 5913	RTT
5914	SEQ ID NO: 5914	RTT
5915	SEQ ID NO: 5915	RTT
5916	SEQ ID NO: 5916	RTT
5917	SEQ ID NO: 5917	RTT
5918	SEQ ID NO: 5918	RTT
5919	SEQ ID NO: 5919	RTT
5920	SEQ ID NO: 5920	RTT
5921	SEQ ID NO: 5921	RTT
732	SEQ ID NO: 732	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (TG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG;AGA PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG;GGG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG;AGA PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG;CGA PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(TG;TGA PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG;TGA PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG;TGA PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG;GGG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG;GGG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG;AGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA

Sequence Number	Sequence	Description
		spacer (AG;AGG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG PAM)
103	SEQ ID NO: 103	ngRNA (GG;GGG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG;AGG PAM)
110	SEQ ID NO: 110	ngRNA (GG;GGG PAM)
105	SEQ ID NO: 105	ngRNA (GG;GGG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG PAM)
107	SEQ ID NO: 107	ngRNA (AG;AGG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG PAM)
114	SEQ ID NO: 114	ngRNA (AG;AGG PAM)
113	SEQ ID NO: 113	ngRNA (GG;GGG PAM)
118	SEQ ID NO: 118	ngRNA (GG;GGG PAM)
117	SEQ ID NO: 117	ngRNA (AG;AGG PAM)

Table 21

Sequence Number	Sequence	Description
5922	SEQ ID NO: 5922	PEgRNA spacer (AGA;AG PAM)
5923	SEQ ID NO: 5923	PEgRNA spacer (AGA;AG PAM)
5924	SEQ ID NO: 5924	PEgRNA spacer (AGA;AG PAM)
5925	SEQ ID NO: 5925	PEgRNA spacer (AGA;AG PAM)
5926	SEQ ID NO: 5926	PEgRNA spacer (AGA;AG PAM)

Sequence Number	Sequence	Description
5927	SEQ ID NO: 5927	PEgRNA spacer (AGA;AG PAM)
5928	SEQ ID NO: 5928	PEgRNA spacer (AGA;AG PAM)
5929	CAC	PBS
5930	CACC	PBS
5931	CACCA	PBS
5932	CACCAT	PBS
5933	CACCAT G	PBS
5934	CACCAT GT	PBS
5935	CACCAT GTT	PBS
5936	SEQ ID NO: 5936	PBS
5937	SEQ ID NO: 5937	PBS
5938	SEQ ID NO: 5938	PBS
5939	SEQ ID NO: 5939	PBS
5940	SEQ ID NO: 5940	PBS
5941	SEQ ID NO: 5941	PBS
5942	SEQ ID NO: 5942	PBS
5943	SEQ ID NO: 5943	PBS
5944	SEQ ID NO: 5944	PBS
5945	SEQ ID NO: 5945	PBS
5946	SEQ ID NO: 5946	RTT
5947	SEQ ID NO: 5947	RTT
5948	SEQ ID NO: 5948	RTT
5949	SEQ ID NO: 5949	RTT
5950	SEQ ID NO: 5950	RTT
5951	SEQ ID NO: 5951	RTT
5952	SEQ ID NO: 5952	RTT
5953	SEQ ID NO: 5953	RTT
5954	SEQ ID NO: 5954	RTT
5955	SEQ ID NO: 5955	RTT
5956	SEQ ID NO: 5956	RTT
5957	SEQ ID NO: 5957	RTT
5958	SEQ ID NO: 5958	RTT
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG;AGA PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG;GGA PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
1991	SEQ ID NO: 1991	PE3 ngRNA spacer (TG;TGA PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG;AGA PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)

Sequence Number	Sequence	Description
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)
14810	SEQ ID NO: 14810	ngRNA (TG;TGG PAM)

Table 22

Sequence Number	Sequence	Description
5959	SEQ ID NO: 5959	PEgRNA spacer (GGA;GG; GGAAGT PAM)
5960	SEQ ID NO: 5960	PEgRNA spacer (GGA;GG; GGAAGT PAM)
5961	SEQ ID NO: 5961	PEgRNA spacer (GGA;GG; GGAAGT PAM)
5962	SEQ ID NO: 5962	PEgRNA spacer (GGA;GG; GGAAGT PAM)
5963	SEQ ID NO: 5963	PEgRNA spacer (GGA;GG; GGAAGT PAM)
5964	SEQ ID NO: 5964	PEgRNA spacer (GGA;GG; GGAAGT PAM)
5965	SEQ ID NO: 5965	PEgRNA spacer (GGA;GG; GGAAGT PAM)
5966	GAA	PBS
5967	GAAC	PBS
5968	GAACA	PBS
5969	GAACAC	PBS
5970	GAACAC C	PBS
5971	GAACAC CA	PBS
5972	GAACAC CAT	PBS
5973	SEQ ID NO: 5973	PBS
5974	SEQ ID NO: 5974	PBS
5975	SEQ ID NO: 5975	PBS
5976	SEQ ID NO: 5976	PBS
5977	SEQ ID NO: 5977	PBS
5978	SEQ ID NO: 5978	PBS
5979	SEQ ID NO: 5979	PBS
5980	SEQ ID NO: 5980	PBS
5981	SEQ ID NO: 5981	PBS
5982	SEQ ID NO: 5982	PBS
5983	SEQ ID NO: 5983	RTT
5984	SEQ ID NO: 5984	RTT
5985	SEQ ID NO: 5985	RTT
5986	SEQ ID NO: 5986	RTT
5987	SEQ ID NO: 5987	RTT
5988	SEQ ID NO: 5988	RTT
5989	SEQ ID NO: 5989	RTT
5990	SEQ ID NO: 5990	RTT
5991	SEQ ID NO: 5991	RTT
5992	SEQ ID NO: 5992	RTT
5993	SEQ ID NO: 5993	RTT
5994	SEQ ID NO: 5994	RTT
5995	SEQ ID NO: 5995	RTT
5996	SEQ ID NO: 5996	RTT
5997	SEQ ID NO: 5997	RTT
5998	SEQ ID NO: 5998	RTT
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
5999	SEQ ID NO: 5999	PE3b ngRNA spacer
		(AAAGG T PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG; TGGCTG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
6000	SEQ ID NO: 6000	PE3 ngRNA spacer (ACAAAT PAM)
1991	SEQ ID NO: 1991	PE3 ngRNA spacer (TG;TGA PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG;AGA PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
6001	SEQ ID NO: 6001	PE3 ngRNA spacer (TTCAGT PAM)
6002	SEQ ID NO: 6002	PE3 ngRNA spacer (TCAGGT PAM)

Sequence Number	Sequence	Description
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG;GGC TGG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG;AGA PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG;GGC CTG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG;GGA PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG; TGGCTG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG; TGGCTG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)

Table 23

Sequence Number	Sequence	Description
6003	SEQ ID NO: 6003	PEgRNA spacer (TGA;TG; TGAGAT PAM)
6004	SEQ ID NO: 6004	PEgRNA spacer (TGA;TG; TGAGAT PAM)
6005	SEQ ID NO: 6005	PEgRNA spacer (TGA;TG; TGAGAT PAM)
6006	SEQ ID NO: 6006	PEgRNA spacer (TGA;TG; TGAGAT PAM)
6007	SEQ ID NO: 6007	PEgRNA spacer (TGA;TG; TGAGAT PAM)
6008	SEQ ID NO: 6008	PEgRNA spacer (TGA;TG; TGAGAT PAM)
6009	SEQ ID NO: 6009	PEgRNA spacer (TGA;TG; TGAGAT PAM)
4314	CCT	PBS
6010	CCTC	PBS
6011	CCTCT	PBS
6012	CCTCTG	PBS
6013	CCTCTGA	PBS
6014	CCTCTGAA	PBS
6015	CCTCTGAAC	PBS
6016	SEQ ID NO: 6016	PBS
6017	SEQ ID NO: 6017	PBS
6018	SEQ ID NO: 6018	PBS
6019	SEQ ID NO: 6019	PBS
6020	SEQ ID NO: 6020	PBS
6021	SEQ ID NO: 6021	PBS
6022	SEQ ID NO: 6022	PBS
6023	SEQ ID NO: 6023	PBS
6024	SEQ ID NO: 6024	PBS
6025	SEQ ID NO: 6025	PBS
6026	SEQ ID NO: 6026	RTT
6027	SEQ ID NO: 6027	RTT
6028	SEQ ID NO: 6028	RTT
6029	SEQ ID NO: 6029	RTT
6030	SEQ ID NO: 6030	RTT
6031	SEQ ID NO: 6031	RTT
6032	SEQ ID NO: 6032	RTT
6033	SEQ ID NO: 6033	RTT
6034	SEQ ID NO: 6034	RTT
6035	SEQ ID NO: 6035	RTT
6036	SEQ ID NO: 6036	RTT
6037	SEQ ID NO: 6037	RTT
6038	SEQ ID NO: 6038	RTT
6039	SEQ ID NO: 6039	RTT
6040	SEQ ID NO: 6040	RTT
6041	SEQ ID NO: 6041	RTT
6042	SEQ ID NO: 6042	RTT
6043	SEQ ID NO: 6043	RTT
6044	SEQ ID NO: 6044	RTT
6045	SEQ ID NO: 6045	RTT

Sequence Number	Sequence	Description
6046	SEQ ID NO: 6046	RTT
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG; TGGCTG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG;GGC CTG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG;GGC TGG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG;AGA PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
6002	SEQ ID NO: 6002	PE3 ngRNA spacer (TCAGGT PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
6001	SEQ ID NO: 6001	PE3 ngRNA spacer (TTCAGT PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG;AGA PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG;GGA PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
6000	SEQ ID NO: 6000	PE3 ngRNA spacer (ACAAAT PAM)
5999	SEQ ID NO: 5999	PE3b ngRNA spacer (AAAGG T PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG; TGGCTG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG; TGGCTG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)

Table 24

Sequence Number	Sequence	Description
6047	SEQ ID NO: 6047	PEgRNA spacer (AGA;AG PAM)
6048	SEQ ID NO: 6048	PEgRNA spacer (AGA;AG PAM)
6049	SEQ ID NO: 6049	PEgRNA spacer (AGA;AG PAM)
6050	SEQ ID NO: 6050	PEgRNA spacer (AGA;AG PAM)
6051	SEQ ID NO: 6051	PEgRNA spacer (AGA;AG PAM)
6052	SEQ ID NO: 6052	PEgRNA spacer (AGA;AG PAM)
6053	SEQ ID NO: 6053	PEgRNA spacer

Sequence Number	Sequence	Description
		(AGA;AG PAM)
4258	TTC	PBS
6054	TTCC	PBS
6055	TTCCT	PBS
6056	TTCCTC	PBS
6057	TTCCTCT	PBS
6058	TTCCTCT G	PBS
6059	TTCCTCT GA	PBS
6060	SEQ ID NO: 6060	PBS
6061	SEQ ID NO: 6061	PBS
6062	SEQ ID NO: 6062	PBS
6063	SEQ ID NO: 6063	PBS
6064	SEQ ID NO: 6064	PBS
6065	SEQ ID NO: 6065	PBS
6066	SEQ ID NO: 6066	PBS
6067	SEQ ID NO: 6067	PBS
6068	SEQ ID NO: 6068	PBS
6069	SEQ ID NO: 6069	PBS
6070	SEQ ID NO: 6070	RTT
6071	SEQ ID NO: 6071	RTT
6072	SEQ ID NO: 6072	RTT
6073	SEQ ID NO: 6073	RTT
6074	SEQ ID NO: 6074	RTT
6075	SEQ ID NO: 6075	RTT
6076	SEQ ID NO: 6076	RTT
6077	SEQ ID NO: 6077	RTT
6078	SEQ ID NO: 6078	RTT
6079	SEQ ID NO: 6079	RTT
6080	SEQ ID NO: 6080	RTT
6081	SEQ ID NO: 6081	RTT
6082	SEQ ID NO: 6082	RTT
6083	SEQ ID NO: 6083	RTT
6084	SEQ ID NO: 6084	RTT
6085	SEQ ID NO: 6085	RTT
6086	SEQ ID NO: 6086	RTT
6087	SEQ ID NO: 6087	RTT
6088	SEQ ID NO: 6088	RTT
6089	SEQ ID NO: 6089	RTT
6090	SEQ ID NO: 6090	RTT
6091	SEQ ID NO: 6091	RTT
6092	SEQ ID NO: 6092	RTT
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG;GGA PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG;AGA PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG;AGA PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)

Sequence Number	Sequence	Description
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)

Table 25

Sequence Number	Sequence	Description
6093	SEQ ID NO: 6093	PEgRNA spacer (TGA;TG PAM)
6094	SEQ ID NO: 6094	PEgRNA spacer (TGA;TG PAM)
6095	SEQ ID NO: 6095	PEgRNA spacer (TGA;TG PAM)
6096	SEQ ID NO: 6096	PEgRNA spacer (TGA;TG PAM)
6097	SEQ ID NO: 6097	PEgRNA spacer (TGA;TG PAM)
6098	SEQ ID NO: 6098	PEgRNA spacer (TGA;TG PAM)
6099	SEQ ID NO: 6099	PEgRNA spacer (TGA;TG PAM)
2024	AAC	PBS
2025	AACA	PBS
6100	AACAA	PBS
6101	AACAAA	PBS
6102	AACAAAT	PBS
6103	AACAAATC	PBS
6104	AACAAATCT	PBS

Sequence Number	Sequence	Description
6105	SEQ ID NO: 6105	PBS
6106	SEQ ID NO: 6106	PBS
6107	SEQ ID NO: 6107	PBS
6108	SEQ ID NO: 6108	PBS
6109	SEQ ID NO: 6109	PBS
6110	SEQ ID NO: 6110	PBS
6111	SEQ ID NO: 6111	PBS
6112	SEQ ID NO: 6112	PBS
6113	SEQ ID NO: 6113	PBS
6114	SEQ ID NO: 6114	PBS
6115	SEQ ID NO: 6115	RTT
6116	SEQ ID NO: 6116	RTT
6117	SEQ ID NO: 6117	RTT
6118	SEQ ID NO: 6118	RTT
6119	SEQ ID NO: 6119	RTT
6120	SEQ ID NO: 6120	RTT
6121	SEQ ID NO: 6121	RTT
6122	SEQ ID NO: 6122	RTT
6123	SEQ ID NO: 6123	RTT
6124	SEQ ID NO: 6124	RTT
6125	SEQ ID NO: 6125	RTT
6126	SEQ ID NO: 6126	RTT
6127	SEQ ID NO: 6127	RTT
6128	SEQ ID NO: 6128	RTT
6129	SEQ ID NO: 6129	RTT
6130	SEQ ID NO: 6130	RTT
6131	SEQ ID NO: 6131	RTT
6132	SEQ ID NO: 6132	RTT
6133	SEQ ID NO: 6133	RTT
6134	SEQ ID NO: 6134	RTT
6135	SEQ ID NO: 6135	RTT
6136	SEQ ID NO: 6136	RTT
6137	SEQ ID NO: 6137	RTT

Sequence Number	Sequence	Description
6138	SEQ ID NO: 6138	RTT
6139	SEQ ID NO: 6139	RTT
6140	SEQ ID NO: 6140	RTT
6141	SEQ ID NO: 6141	RTT
6142	SEQ ID NO: 6142	RTT
6143	SEQ ID NO: 6143	RTT
6144	SEQ ID NO: 6144	RTT
6145	SEQ ID NO: 6145	RTT
6146	SEQ ID NO: 6146	RTT
6147	SEQ ID NO: 6147	RTT
6148	SEQ ID NO: 6148	RTT
6149	SEQ ID NO: 6149	RTT
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG;GGA PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)

Sequence Number	Sequence	Description
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG;AGA PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG;AGA PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)

Table 26

Sequence Number	Sequence	Description
6150	SEQ ID NO: 6150	PEgRNA spacer (GGA;GG PAM)
6151	SEQ ID NO: 6151	PEgRNA spacer (GGA;GG PAM)
6152	SEQ ID NO: 6152	PEgRNA spacer (GGA;GG PAM)
6153	SEQ ID NO: 6153	PEgRNA spacer (GGA;GG PAM)
6154	SEQ ID NO: 6154	PEgRNA spacer (GGA;GG PAM)
6155	SEQ ID NO: 6155	PEgRNA spacer (GGA;GG PAM)
6156	SEQ ID NO: 6156	PEgRNA spacer (GGA;GG PAM)
6157	AGT	PBS
6158	AGTA	PBS
6159	AGTAA	PBS
6160	AGTAAA	PBS
6161	AGTAAAC	PBS
6162	AGTAAACA	PBS
6163	AGTAAACAA	PBS
6164	SEQ ID NO: 6164	PBS
6165	SEQ ID NO: 6165	PBS
6166	SEQ ID NO: 6166	PBS
6167	SEQ ID NO: 6167	PBS
6168	SEQ ID NO: 6168	PBS
6169	SEQ ID NO: 6169	PBS
6170	SEQ ID NO: 6170	PBS
6171	SEQ ID NO: 6171	PBS
6172	SEQ ID NO: 6172	PBS
6173	SEQ ID NO: 6173	PBS
6174	SEQ ID NO: 6174	RTT
6175	SEQ ID NO: 6175	RTT
6176	SEQ ID NO: 6176	RTT
6177	SEQ ID NO: 6177	RTT
6178	SEQ ID NO: 6178	RTT
6179	SEQ ID NO: 6179	RTT
6180	SEQ ID NO: 6180	RTT
6181	SEQ ID NO: 6181	RTT
6182	SEQ ID NO: 6182	RTT
6183	SEQ ID NO: 6183	RTT
6184	SEQ ID NO: 6184	RTT
6185	SEQ ID NO: 6185	RTT
6186	SEQ ID NO: 6186	RTT

Sequence Number	Sequence	Description
6187	SEQ ID NO: 6187	RTT
6188	SEQ ID NO: 6188	RTT
6189	SEQ ID NO: 6189	RTT
6190	SEQ ID NO: 6190	RTT
6191	SEQ ID NO: 6191	RTT
6192	SEQ ID NO: 6192	RTT
6193	SEQ ID NO: 6193	RTT
6194	SEQ ID NO: 6194	RTT
6195	SEQ ID NO: 6195	RTT
6196	SEQ ID NO: 6196	RTT
6197	SEQ ID NO: 6197	RTT
6198	SEQ ID NO: 6198	RTT
6199	SEQ ID NO: 6199	RTT
6200	SEQ ID NO: 6200	RTT
6201	SEQ ID NO: 6201	RTT
6202	SEQ ID NO: 6202	RTT
6203	SEQ ID NO: 6203	RTT
6204	SEQ ID NO: 6204	RTT
6205	SEQ ID NO: 6205	RTT
6206	SEQ ID NO: 6206	RTT
6207	SEQ ID NO: 6207	RTT
6208	SEQ ID NO: 6208	RTT
6209	SEQ ID NO: 6209	RTT
6210	SEQ ID NO: 6210	RTT
6211	SEQ ID NO: 6211	RTT
6212	SEQ ID NO: 6212	RTT
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG;AGA PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG;AGA PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG;GGA PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)

Sequence Number	Sequence	Description
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)

Table 27

Sequence Number	Sequence	Description
6213	SEQ ID NO: 6213	PEgRNA spacer (TGA;TG PAM)
6214	SEQ ID NO: 6214	PEgRNA spacer (TGA;TG PAM)
6215	SEQ ID NO: 6215	PEgRNA spacer (TGA;TG PAM)
6216	SEQ ID NO: 6216	PEgRNA spacer (TGA;TG PAM)
6217	SEQ ID NO: 6217	PEgRNA spacer (TGA;TG PAM)
6218	SEQ ID NO: 6218	PEgRNA spacer (TGA;TG PAM)
6219	SEQ ID NO: 6219	PEgRNA spacer (TGA;TG PAM)
6220	AAG	PBS
6221	AAGA	PBS
6222	AAGAG	PBS
6223	AAGAGC	PBS
6224	AAGAGCT	PBS
6225	AAGAGCTG	PBS
6226	AAGAGCTGC	PBS
6227	SEQ ID NO: 6227	PBS
6228	SEQ ID NO: 6228	PBS
6229	SEQ ID NO: 6229	PBS
6230	SEQ ID NO: 6230	PBS
6231	SEQ ID NO: 6231	PBS
6232	SEQ ID NO: 6232	PBS
6233	SEQ ID NO: 6233	PBS
6234	SEQ ID NO: 6234	PBS
6235	SEQ ID NO: 6235	PBS
6236	SEQ ID NO: 6236	PBS
6237	SEQ ID NO: 6237	RTT
6238	SEQ ID NO: 6238	RTT
6239	SEQ ID NO: 6239	RTT
6240	SEQ ID NO: 6240	RTT
6241	SEQ ID NO: 6241	RTT
6242	SEQ ID NO: 6242	RTT
6243	SEQ ID NO: 6243	RTT
6244	SEQ ID NO: 6244	RTT
6245	SEQ ID NO: 6245	RTT
6246	SEQ ID NO: 6246	RTT
6247	SEQ ID NO: 6247	RTT
6248	SEQ ID NO: 6248	RTT
6249	SEQ ID NO: 6249	RTT
6250	SEQ ID NO: 6250	RTT
6251	SEQ ID NO: 6251	RTT
6252	SEQ ID NO: 6252	RTT
6253	SEQ ID NO: 6253	RTT
6254	SEQ ID NO: 6254	RTT
6255	SEQ ID NO: 6255	RTT
6256	SEQ ID NO: 6256	RTT
6257	SEQ ID NO: 6257	RTT
6258	SEQ ID NO: 6258	RTT
6259	SEQ ID NO: 6259	RTT
6260	SEQ ID NO: 6260	RTT
6261	SEQ ID NO: 6261	RTT
6262	SEQ ID NO: 6262	RTT
6263	SEQ ID NO: 6263	RTT
6264	SEQ ID NO: 6264	RTT
6265	SEQ ID NO: 6265	RTT
6266	SEQ ID NO: 6266	RTT
6267	SEQ ID NO: 6267	RTT
6268	SEQ ID NO: 6268	RTT
6269	SEQ ID NO: 6269	RTT
6270	SEQ ID NO: 6270	RTT
6271	SEQ ID NO: 6271	RTT
6272	SEQ ID NO: 6272	RTT
6273	SEQ ID NO: 6273	RTT
6274	SEQ ID NO: 6274	RTT
6275	SEQ ID NO: 6275	RTT
6276	SEQ ID NO: 6276	RTT
6277	SEQ ID NO: 6277	RTT
6278	SEQ ID NO: 6278	RTT
6279	SEQ ID NO: 6279	RTT
6280	SEQ ID NO: 6280	RTT
6281	SEQ ID NO: 6281	RTT
6282	SEQ ID NO: 6282	RTT
6283	SEQ ID NO: 6283	RTT
6284	SEQ ID NO: 6284	RTT
6285	SEQ ID NO: 6285	RTT
6286	SEQ ID NO: 6286	RTT
6287	SEQ ID NO: 6287	RTT
6288	SEQ ID NO: 6288	RTT
6289	SEQ ID NO: 6289	RTT
6290	SEQ ID NO: 6290	RTT
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)

Sequence Number	Sequence	Description
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG;GGG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG;AGG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG;GGA PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG;AGA PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG;CGA PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG;AGA PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)

Table 28

Sequence Number	Sequence	Description
6291	SEQ ID NO: 6291	PEgRNA spacer (TGA;TG PAM)
6292	SEQ ID NO: 6292	PEgRNA spacer (TGA;TG PAM)
6293	SEQ ID NO: 6293	PEgRNA spacer (TGA;TG PAM)
6294	SEQ ID NO: 6294	PEgRNA spacer (TGA;TG PAM)
6295	SEQ ID NO: 6295	PEgRNA spacer (TGA;TG PAM)
6296	SEQ ID NO: 6296	PEgRNA spacer (TGA;TG PAM)
6297	SEQ ID NO: 6297	PEgRNA spacer (TGA;TG PAM)
6298	TCA	PBS
6299	TCAG	PBS
6300	TCAGA	PBS
6301	TCAGAA	PBS
6302	TCAGAAA	PBS
6303	TCAGAAAA	PBS
6304	TCAGAAAAG	PBS
6305	SEQ ID NO: 6305	PBS
6306	SEQ ID NO: 6306	PBS
6307	SEQ ID NO: 6307	PBS
6308	SEQ ID NO: 6308	PBS
6309	SEQ ID NO: 6309	PBS
6310	SEQ ID NO: 6310	PBS
6311	SEQ ID NO: 6311	PBS
6312	SEQ ID NO: 6312	PBS
6313	SEQ ID NO: 6313	PBS
6314	SEQ ID NO: 6314	PBS

Sequence Number	Sequence	Description
6315	SEQ ID NO: 6315	RTT
6316	SEQ ID NO: 6316	RTT
6317	SEQ ID NO: 6317	RTT
6318	SEQ ID NO: 6318	RTT
6319	SEQ ID NO: 6319	RTT
6320	SEQ ID NO: 6320	RTT
6321	SEQ ID NO: 6321	RTT
6322	SEQ ID NO: 6322	RTT
6323	SEQ ID NO: 6323	RTT
6324	SEQ ID NO: 6324	RTT
6325	SEQ ID NO: 6325	RTT
6326	SEQ ID NO: 6326	RTT
6327	SEQ ID NO: 6327	RTT
6328	SEQ ID NO: 6328	RTT
6329	SEQ ID NO: 6329	RTT
6330	SEQ ID NO: 6330	RTT
6331	SEQ ID NO: 6331	RTT
6332	SEQ ID NO: 6332	RTT
6333	SEQ ID NO: 6333	RTT
6334	SEQ ID NO: 6334	RTT
6335	SEQ ID NO: 6335	RTT
6336	SEQ ID NO: 6336	RTT
6337	SEQ ID NO: 6337	RTT
6338	SEQ ID NO: 6338	RTT
6339	SEQ ID NO: 6339	RTT
6340	SEQ ID NO: 6340	RTT
6341	SEQ ID NO: 6341	RTT
6342	SEQ ID NO: 6342	RTT
6343	SEQ ID NO: 6343	RTT
6344	SEQ ID NO: 6344	RTT
6345	SEQ ID NO: 6345	RTT
6346	SEQ ID NO: 6346	RTT
6347	SEQ ID NO: 6347	RTT
6348	SEQ ID NO: 6348	RTT
6349	SEQ ID NO: 6349	RTT
6350	SEQ ID NO: 6350	RTT
6351	SEQ ID NO: 6351	RTT
6352	SEQ ID NO: 6352	RTT
6353	SEQ ID NO: 6353	RTT
6354	SEQ ID NO: 6354	RTT
6355	SEQ ID NO: 6355	RTT
6356	SEQ ID NO: 6356	RTT
6357	SEQ ID NO: 6357	RTT
6358	SEQ ID NO: 6358	RTT
6359	SEQ ID NO: 6359	RTT
6360	SEQ ID NO: 6360	RTT
6361	SEQ ID NO: 6361	RTT
6362	SEQ ID NO: 6362	RTT
6363	SEQ ID NO: 6363	RTT
6364	SEQ ID NO: 6364	RTT
6365	SEQ ID NO: 6365	RTT
6366	SEQ ID NO: 6366	RTT
6367	SEQ ID NO: 6367	RTT
6368	SEQ ID NO: 6368	RTT
6369	SEQ ID NO: 6369	RTT
6370	SEQ ID NO: 6370	RTT
6371	SEQ ID NO: 6371	RTT
6372	SEQ ID NO: 6372	RTT
6373	SEQ ID NO: 6373	RTT
6374	SEQ ID NO: 6374	RTT
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer
		(AG;AGG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG;TGG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG;TGG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG;TGG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG;TGG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG;AGA PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(GG;GGG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG;GGA PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG;CGA PAM)
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG;TGA PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG;AGG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
4175	SEQ ID NO: 4175	PE3 ngRNA spacer (AG;AGA PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG;AGG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG;TGG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG;TGG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG;TGG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG;AGG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG;TGG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG;GGG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG;TGG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG;TGG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG;GGG PAM)

Table 29

Sequence Number	Sequence	Description
6375	SEQ ID NO: 6375	PEgRNA spacer (GAG PAM)
6376	SEQ ID NO: 6376	PEgRNA spacer (GAG PAM)
6377	SEQ ID NO: 6377	PEgRNA spacer (GAG PAM)
6378	SEQ ID NO: 6378	PEgRNA spacer (GAG PAM)
6379	SEQ ID NO: 6379	PEgRNA spacer (GAG PAM)
6380	SEQ ID NO: 6380	PEgRNA spacer (GAG PAM)
6381	SEQ ID NO: 6381	PEgRNA spacer (GAG PAM)
5929	CAC	PBS
6382	CACA	PBS
6383	CACAG	PBS
6384	CACAGC	PBS
6385	CACAGC A	PBS
6386	CACAGC AA	PBS
6387	CACAGC AAC	PBS
6388	SEQ ID NO: 6388	PBS
6389	SEQ ID NO: 6389	PBS
6390	SEQ ID NO: 6390	PBS
6391	SEQ ID NO: 6391	PBS
6392	SEQ ID NO: 6392	PBS
6393	SEQ ID NO: 6393	PBS
6394	SEQ ID NO: 6394	PBS
6395	SEQ ID NO: 6395	PBS
6396	SEQ ID NO: 6396	PBS
6397	SEQ ID NO: 6397	PBS
6398	SEQ ID NO: 6398	RTT*93 (PAM silencing)
6399	SEQ ID NO: 6399	RTT
6400	SEQ ID NO: 6400	RTT*93 (PAM silencing)
6401	SEQ ID NO: 6401	RTT
6402	SEQ ID NO: 6402	RTT*93 (PAM silencing)
6403	SEQ ID NO: 6403	RTT
6404	SEQ ID NO: 6404	RTT
6405	SEQ ID NO: 6405	RTT*93 (PAM silencing)
6406	SEQ ID NO: 6406	RTT*93 (PAM silencing)
6407	SEQ ID NO: 6407	RTT
6408	SEQ ID NO: 6408	RTT
6409	SEQ ID NO: 6409	RTT*93 (PAM silencing)
6410	SEQ ID NO: 6410	RTT
6411	SEQ ID NO: 6411	RTT*93 (PAM silencing)
6412	SEQ ID NO: 6412	RTT
6413	SEQ ID NO: 6413	RTT*93 (PAM silencing)
6414	SEQ ID NO: 6414	RTT*93 (PAM silencing)
6415	SEQ ID NO: 6415	RTT
6416	SEQ ID NO: 6416	RTT*93 (PAM silencing)
6417	SEQ ID NO: 6417	RTT
6418	SEQ ID NO: 6418	RTT*93 (PAM silencing)
6419	SEQ ID NO: 6419	RTT
6420	SEQ ID NO: 6420	RTT*93 (PAM silencing)
6421	SEQ ID NO: 6421	RTT

Sequence Number	Sequence	Description
6422	SEQ ID NO: 6422	RTT*93 (PAM silencing)
6423	SEQ ID NO: 6423	RTT
6424	SEQ ID NO: 6424	RTT*93 (PAM silencing)
6425	SEQ ID NO: 6425	RTT
6426	SEQ ID NO: 6426	RTT*93 (PAM silencing)
6427	SEQ ID NO: 6427	RTT
6428	SEQ ID NO: 6428	RTT
6429	SEQ ID NO: 6429	RTT*93 (PAM silencing)
6430	SEQ ID NO: 6430	RTT*93 (PAM silencing)
6431	SEQ ID NO: 6431	RTT
6432	SEQ ID NO: 6432	RTT*93 (PAM silencing)
6433	SEQ ID NO: 6433	RTT
6434	SEQ ID NO: 6434	RTT*93 (PAM silencing)
6435	SEQ ID NO: 6435	RTT
6436	SEQ ID NO: 6436	RTT*93 (PAM silencing)
6437	SEQ ID NO: 6437	RTT
6438	SEQ ID NO: 6438	RTT
6439	SEQ ID NO: 6439	RTT*93 (PAM silencing)
6440	SEQ ID NO: 6440	RTT*93 (PAM silencing)
6441	SEQ ID NO: 6441	RTT
6442	SEQ ID NO: 6442	RTT
6443	SEQ ID NO: 6443	RTT*93 (PAM silencing)
6444	SEQ ID NO: 6444	RTT
6445	SEQ ID NO: 6445	RTT*93 (PAM silencing)
6446	SEQ ID NO: 6446	PE3 ngRNA spacer (AAG PAM)
6447	SEQ ID NO: 6447	PE3b*93 ngRNA spacer (CAG PAM)
6448	SEQ ID NO: 6448	PE3 ngRNA spacer (CAG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAG PAM)
6450	SEQ ID NO: 6450	PE3 ngRNA spacer (CAG PAM)
6451	SEQ ID NO: 6451	PE3 ngRNA spacer (CAG PAM)
6452	SEQ ID NO: 6452	PE3b*93 ngRNA spacer (CAG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAG PAM)
6453	SEQ ID NO: 6453	PE3 ngRNA spacer (AAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)
6456	SEQ ID NO: 6456	PE3 ngRNA spacer (AAG PAM)
6457	SEQ ID NO: 6457	PE3 ngRNA spacer (GAG PAM)

Table 30

Sequence Number	Sequence	Description
6458	SEQ ID NO: 6458	PEgRNA spacer (AAG;AAGG PAM)
6459	SEQ ID NO: 6459	PEgRNA spacer (AAG;AAGG PAM)
6460	SEQ ID NO: 6460	PEgRNA spacer (AAG;AAGG PAM)
6461	SEQ ID NO: 6461	PEgRNA spacer (AAG;AAGG PAM)
6462	SEQ ID NO: 6462	PEgRNA spacer (AAG;AAGG PAM)
6463	SEQ ID NO: 6463	PEgRNA spacer (AAG;AAGG PAM)
6464	SEQ ID NO: 6464	PEgRNA spacer (AAG;AAGG PAM)
6465	AGC	PBS
6466	AGCC	PBS
6467	AGCCA	PBS
6468	AGCCAC	PBS
6469	AGCCACA	PBS
6470	AGCCACAG	PBS
6471	AGCCACAGC	PBS
6472	SEQ ID NO: 6472	PBS
6473	SEQ ID NO: 6473	PBS
6474	SEQ ID NO: 6474	PBS
6475	SEQ ID NO: 6475	PBS
6476	SEQ ID NO: 6476	PBS
6477	SEQ ID NO: 6477	PBS
6478	SEQ ID NO: 6478	PBS
6479	SEQ ID NO: 6479	PBS
6480	SEQ ID NO: 6480	PBS
6481	SEQ ID NO: 6481	PBS
6482	SEQ ID NO: 6482	RTT
6483	SEQ ID NO: 6483	RTT*1 (PAM silencing)
6484	SEQ ID NO: 6484	RTT

Sequence Number	Sequence	Description
6485	SEQ ID NO: 6485	RTT*1 (PAM silencing)
6486	SEQ ID NO: 6486	RTT
6487	SEQ ID NO: 6487	RTT*1 (PAM silencing)
6488	SEQ ID NO: 6488	RTT*1 (PAM silencing)
6489	SEQ ID NO: 6489	RTT
6490	SEQ ID NO: 6490	RTT
6491	SEQ ID NO: 6491	RTT*1 (PAM silencing)
6492	SEQ ID NO: 6492	RTT*1 (PAM silencing)
6493	SEQ ID NO: 6493	RTT
6494	SEQ ID NO: 6494	RTT*1 (PAM silencing)
6495	SEQ ID NO: 6495	RTT
6496	SEQ ID NO: 6496	RTT*1 (PAM silencing)
6497	SEQ ID NO: 6497	RTT
6498	SEQ ID NO: 6498	RTT
6499	SEQ ID NO: 6499	RTT*1 (PAM silencing)
6500	SEQ ID NO: 6500	RTT
6501	SEQ ID NO: 6501	RTT*1 (PAM silencing)
6502	SEQ ID NO: 6502	RTT
6503	SEQ ID NO: 6503	RTT*1 (PAM silencing)
6504	SEQ ID NO: 6504	RTT
6505	SEQ ID NO: 6505	RTT*1 (PAM silencing)
6506	SEQ ID NO: 6506	RTT*1 (PAM silencing)
6507	SEQ ID NO: 6507	RTT
6508	SEQ ID NO: 6508	RTT
6509	SEQ ID NO: 6509	RTT*1 (PAM silencing)
6510	SEQ ID NO: 6510	RTT*1 (PAM silencing)

Sequence Number	Sequence	Description
6511	SEQ ID NO: 6511	RTT
6512	SEQ ID NO: 6512	RTT
6513	SEQ ID NO: 6513	RTT*1 (PAM silencing)
6514	SEQ ID NO: 6514	RTT*1 (PAM silencing)
6515	SEQ ID NO: 6515	RTT
6516	SEQ ID NO: 6516	RTT*1 (PAM silencing)
6517	SEQ ID NO: 6517	RTT
6518	SEQ ID NO: 6518	RTT
6519	SEQ ID NO: 6519	RTT*1 (PAM silencing)
6520	SEQ ID NO: 6520	RTT*1 (PAM silencing)
6521	SEQ ID NO: 6521	RTT
6522	SEQ ID NO: 6522	RTT*1 (PAM silencing)
6523	SEQ ID NO: 6523	RTT
6524	SEQ ID NO: 6524	RTT
6525	SEQ ID NO: 6525	RTT*1 (PAM silencing)
6526	SEQ ID NO: 6526	RTT
6527	SEQ ID NO: 6527	RTT*1 (PAM silencing)
6528	SEQ ID NO: 6528	RTT
6529	SEQ ID NO: 6529	RTT*1 (PAM silencing)
6530	SEQ ID NO: 6530	RTT
6531	SEQ ID NO: 6531	RTT*1 (PAM silencing)
6532	SEQ ID NO: 6532	RTT
6533	SEQ ID NO: 6533	RTT*1 (PAM silencing)
6534	SEQ ID NO: 6534	RTT*1 (PAM silencing)
6535	SEQ ID NO: 6535	RTT
6448	SEQ ID NO: 6448	PE3 ngRNA spacer (CAG PAM)

Sequence Number	Sequence	Description
93	SEQ ID NO: 93	PE3b ngRNA spacer (AGG;AG GG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GGG;GG GG PAM)
6457	SEQ ID NO: 6457	PE3 ngRNA spacer (GAG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GGG;GG GG PAM)
6446	SEQ ID NO: 6446	PE3 ngRNA spacer (AAG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAG;CA GG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GGG;GG GG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TGG;TG GG PAM)
6453	SEQ ID NO: 6453	PE3 ngRNA spacer (AAG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAG;CA GG PAM)
6456	SEQ ID NO: 6456	PE3 ngRNA spacer (AAG PAM)
6450	SEQ ID NO: 6450	PE3 ngRNA spacer (CAG PAM)
6536	SEQ ID NO: 6536	PE3 ngRNA spacer (ATGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (AGG;AG GG PAM)
6537	SEQ ID NO: 6537	PE3b*1 ngRNA spacer (CAG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAG;CA GG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG;CA GG PAM)
102	SEQ ID NO: 102	ngRNA (AGG;AG GG PAM)
101	SEQ ID NO: 101	ngRNA (TGG;TG GG PAM)
104	SEQ ID NO: 104	ngRNA (AGG;AG GG PAM)
105	SEQ ID NO: 105	ngRNA (GGG;GG GG PAM)
100	SEQ ID NO: 100	ngRNA (GGG;GG GG PAM)
109	SEQ ID NO: 109	ngRNA (GGG;GG GG PAM)
112	SEQ ID NO: 112	ngRNA (GGG;GG GG PAM)
117	SEQ ID NO: 117	ngRNA (AGG;AG GG PAM)
113	SEQ ID NO: 113	ngRNA (GGG;GG GG PAM)

Table 31

Sequence Number	Sequence	Description
6538	SEQ ID NO: 6538	PEgRNA spacer (GAG PAM)
6539	SEQ ID NO: 6539	PEgRNA spacer (GAG PAM)
6540	SEQ ID NO: 6540	PEgRNA spacer (GAG PAM)
6541	SEQ ID NO: 6541	PEgRNA spacer (GAG PAM)
6542	SEQ ID NO: 6542	PEgRNA spacer (GAG PAM)
6543	SEQ ID NO: 6543	PEgRNA spacer (GAG PAM)
6544	SEQ ID NO: 6544	PEgRNA spacer (GAG PAM)
6545	CTT	PBS
6546	CTTC	PBS
6547	CTTCT	PBS
6548	CTTCTC	PBS
6549	CTTCTC A	PBS
6550	CTTCTC AG	PBS
6551	CTTCTC AGC	PBS
6552	SEQ ID NO: 6552	PBS
6553	SEQ ID NO: 6553	PBS
6554	SEQ ID NO: 6554	PBS
6555	SEQ ID NO: 6555	PBS
6556	SEQ ID NO: 6556	PBS
6557	SEQ ID NO: 6557	PBS
6558	SEQ ID NO: 6558	PBS
6559	SEQ ID NO: 6559	PBS
6560	SEQ ID NO: 6560	PBS
6561	SEQ ID NO: 6561	PBS
6562	SEQ ID NO: 6562	RTT*93 (PAM silencing)
6563	SEQ ID NO: 6563	RTT
6564	SEQ ID NO: 6564	RTT*93 (PAM silencing)
6565	SEQ ID NO: 6565	RTT
6566	SEQ ID NO: 6566	RTT
6567	SEQ ID NO: 6567	RTT*93 (PAM silencing)
6568	SEQ ID NO: 6568	RTT
6569	SEQ ID NO: 6569	RTT*93 (PAM silencing)
6570	SEQ ID NO: 6570	RTT*93 (PAM silencing)
6571	SEQ ID NO: 6571	RTT
6572	SEQ ID NO: 6572	RTT*93 (PAM silencing)
6573	SEQ ID NO: 6573	RTT
6574	SEQ ID NO: 6574	RTT
6575	SEQ ID NO: 6575	RTT*93 (PAM silencing)
6576	SEQ ID NO: 6576	RTT*93 (PAM silencing)
6577	SEQ ID NO: 6577	RTT
6578	SEQ ID NO: 6578	RTT*93 (PAM silencing)
6579	SEQ ID NO: 6579	RTT
6580	SEQ ID NO: 6580	RTT*93 (PAM silencing)
6581	SEQ ID NO: 6581	RTT
6582	SEQ ID NO: 6582	RTT
6583	SEQ ID NO: 6583	RTT*93 (PAM silencing)
6584	SEQ ID NO: 6584	RTT*93 (PAM silencing)
6585	SEQ ID NO: 6585	RTT
6586	SEQ ID NO: 6586	RTT*93 (PAM silencing)
6587	SEQ ID NO: 6587	RTT
6588	SEQ ID NO: 6588	RTT
6589	SEQ ID NO: 6589	RTT*93 (PAM silencing)
6590	SEQ ID NO: 6590	RTT
6591	SEQ ID NO: 6591	RTT*93 (PAM silencing)
6592	SEQ ID NO: 6592	RTT*93 (PAM silencing)
6593	SEQ ID NO: 6593	RTT
6594	SEQ ID NO: 6594	RTT*93 (PAM silencing)
6595	SEQ ID NO: 6595	RTT

Sequence Number	Sequence	Description
6596	SEQ ID NO: 6596	RTT*93 (PAM silencing)
6597	SEQ ID NO: 6597	RTT
6598	SEQ ID NO: 6598	RTT*93 (PAM silencing)
6599	SEQ ID NO: 6599	RTT
6600	SEQ ID NO: 6600	RTT
6601	SEQ ID NO: 6601	RTT*93 (PAM silencing)
6602	SEQ ID NO: 6602	RTT*93 (PAM silencing)
6603	SEQ ID NO: 6603	RTT
6604	SEQ ID NO: 6604	RTT*93 (PAM silencing)
6605	SEQ ID NO: 6605	RTT
6606	SEQ ID NO: 6606	RTT*93 (PAM silencing)
6607	SEQ ID NO: 6607	RTT
6608	SEQ ID NO: 6608	RTT*93 (PAM silencing)
6609	SEQ ID NO: 6609	RTT
6610	SEQ ID NO: 6610	RTT
6611	SEQ ID NO: 6611	RTT*93 (PAM silencing)
6612	SEQ ID NO: 6612	RTT
6613	SEQ ID NO: 6613	RTT*93 (PAM silencing)
6614	SEQ ID NO: 6614	RTT*93 (PAM silencing)
6615	SEQ ID NO: 6615	RTT
6616	SEQ ID NO: 6616	RTT
6617	SEQ ID NO: 6617	RTT*93 (PAM silencing)
6618	SEQ ID NO: 6618	RTT
6619	SEQ ID NO: 6619	RTT*93 (PAM silencing)
6620	SEQ ID NO: 6620	RTT*93 (PAM silencing)
6621	SEQ ID NO: 6621	RTT
6622	SEQ ID NO: 6622	RTT*93 (PAM silencing)
6623	SEQ ID NO: 6623	RTT
6624	SEQ ID NO: 6624	RTT
6625	SEQ ID NO: 6625	RTT*93 (PAM silencing)
6626	SEQ ID NO: 6626	RTT
6627	SEQ ID NO: 6627	RTT*93 (PAM silencing)
6446	SEQ ID NO: 6446	PE3 ngRNA spacer (AAG PAM)
6448	SEQ ID NO: 6448	PE3 ngRNA spacer (CAG PAM)
6453	SEQ ID NO: 6453	PE3 ngRNA spacer (AAG PAM)
6457	SEQ ID NO: 6457	PE3 ngRNA spacer (GAG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAG PAM)
6456	SEQ ID NO: 6456	PE3 ngRNA spacer (AAG PAM)
6628	SEQ ID NO: 6628	PEgRNA spacer (GAG;GA GG PAM)
6629	SEQ ID NO: 6629	PEgRNA spacer (GAG;GA GG PAM)
6630	SEQ ID NO: 6630	PEgRNA spacer (GAG;GA GG PAM)
6631	SEQ ID NO: 6631	PEgRNA spacer (GAG;GA GG PAM)
6632	SEQ ID NO: 6632	PEgRNA spacer (GAG;GA GG PAM)
6633	SEQ ID NO: 6633	PEgRNA spacer (GAG;GA GG PAM)
6634	SEQ ID NO: 6634	PEgRNA spacer (GAG;GA GG PAM)
1735	GCC	PBS
6635	GCCT	PBS
6636	GCCTT	PBS
6637	GCCTTC	PBS
6638	GCCTTC T	PBS
6639	GCCTTC TC	PBS
6640	GCCTTC TCA	PBS
6641	SEQ ID NO: 6641	PBS
6642	SEQ ID NO: 6642	PBS
6643	SEQ ID NO: 6643	PBS
6644	SEQ ID NO: 6644	PBS
6645	SEQ ID NO: 6645	PBS
6646	SEQ ID NO: 6646	PBS
6647	SEQ ID NO: 6647	PBS
6648	SEQ ID NO: 6648	PBS
6649	SEQ ID NO: 6649	PBS
6650	SEQ ID NO: 6650	PBS
6651	SEQ ID NO: 6651	RTT
6652	SEQ ID NO: 6652	RTT*91 (PAM silencing)
6653	SEQ ID NO: 6653	RTT*88 (PAM silencing)

Table 32

Sequence Number	Sequence	Description
6654	SEQ ID NO: 6654	RTT*89 (PAM silencing)
6655	SEQ ID NO: 6655	RTT*92 (PAM silencing)
6656	SEQ ID NO: 6656	RTT*90 (PAM silencing)
6657	SEQ ID NO: 6657	RTT
6658	SEQ ID NO: 6658	RTT*88 (PAM silencing)
6659	SEQ ID NO: 6659	RTT*91 (PAM silencing)
6660	SEQ ID NO: 6660	RTT*90 (PAM silencing)
6661	SEQ ID NO: 6661	RTT*89 (PAM silencing)
6662	SEQ ID NO: 6662	RTT*92 (PAM silencing)
6663	SEQ ID NO: 6663	RTT
6664	SEQ ID NO: 6664	RTT*88 (PAM silencing)
6665	SEQ ID NO: 6665	RTT*91 (PAM silencing)
6666	SEQ ID NO: 6666	RTT*89 (PAM silencing)
6667	SEQ ID NO: 6667	RTT*92 (PAM silencing)
6668	SEQ ID NO: 6668	RTT*90 (PAM silencing)
6669	SEQ ID NO: 6669	RTT*88 (PAM silencing)
6670	SEQ ID NO: 6670	RTT*92 (PAM silencing)
6671	SEQ ID NO: 6671	RTT*91 (PAM silencing)
6672	SEQ ID NO: 6672	RTT*90 (PAM silencing)
6673	SEQ ID NO: 6673	RTT*89 (PAM silencing)
6674	SEQ ID NO: 6674	RTT
6675	SEQ ID NO: 6675	RTT*89 (PAM silencing)
6676	SEQ ID NO: 6676	RTT
6677	SEQ ID NO: 6677	RTT*92 (PAM silencing)
6678	SEQ ID NO: 6678	RTT*88 (PAM silencing)
6679	SEQ ID NO: 6679	RTT*91 (PAM silencing)
6680	SEQ ID NO: 6680	RTT*90 (PAM silencing)
6681	SEQ ID NO: 6681	RTT
6682	SEQ ID NO: 6682	RTT*88 (PAM silencing)
6683	SEQ ID NO: 6683	RTT*91 (PAM silencing)
6684	SEQ ID NO: 6684	RTT*89 (PAM silencing)
6685	SEQ ID NO: 6685	RTT*92 (PAM silencing)
6686	SEQ ID NO: 6686	RTT*90 (PAM silencing)
6687	SEQ ID NO: 6687	RTT*89 (PAM silencing)
6688	SEQ ID NO: 6688	RTT*88 (PAM silencing)
6689	SEQ ID NO: 6689	RTT*91 (PAM silencing)
6690	SEQ ID NO: 6690	RTT*90 (PAM silencing)
6691	SEQ ID NO: 6691	RTT*92 (PAM silencing)
6692	SEQ ID NO: 6692	RTT
6693	SEQ ID NO: 6693	RTT*89 (PAM silencing)
6694	SEQ ID NO: 6694	RTT*91 (PAM silencing)
6695	SEQ ID NO: 6695	RTT
6696	SEQ ID NO: 6696	RTT*90 (PAM silencing)
6697	SEQ ID NO: 6697	RTT*92 (PAM silencing)
6698	SEQ ID NO: 6698	RTT*88 (PAM silencing)
6699	SEQ ID NO: 6699	RTT*92 (PAM silencing)
6700	SEQ ID NO: 6700	RTT*89 (PAM silencing)
6701	SEQ ID NO: 6701	RTT*88 (PAM silencing)
6702	SEQ ID NO: 6702	RTT*90 (PAM silencing)
6703	SEQ ID NO: 6703	RTT
6704	SEQ ID NO: 6704	RTT*91 (PAM silencing)
6705	SEQ ID NO: 6705	RTT*91 (PAM silencing)
6706	SEQ ID NO: 6706	RTT*89 (PAM silencing)
6707	SEQ ID NO: 6707	RTT*88 (PAM silencing)
6708	SEQ ID NO: 6708	RTT*92 (PAM silencing)
6709	SEQ ID NO: 6709	RTT*90 (PAM silencing)
6710	SEQ ID NO: 6710	RTT
6711	SEQ ID NO: 6711	RTT*88 (PAM silencing)
6712	SEQ ID NO: 6712	RTT*92 (PAM silencing)
6713	SEQ ID NO: 6713	RTT
6714	SEQ ID NO: 6714	RTT*89 (PAM silencing)
6715	SEQ ID NO: 6715	RTT*90 (PAM silencing)
6716	SEQ ID NO: 6716	RTT*91 (PAM silencing)
6717	SEQ ID NO: 6717	RTT*90 (PAM silencing)
6718	SEQ ID NO: 6718	RTT*92 (PAM silencing)
6719	SEQ ID NO: 6719	RTT*88 (PAM silencing)
6720	SEQ ID NO: 6720	RTT
6721	SEQ ID NO: 6721	RTT*89 (PAM silencing)
6722	SEQ ID NO: 6722	RTT*91 (PAM silencing)

Sequence Number	Sequence	Description
6723	SEQ ID NO: 6723	RTT*91 (PAM silencing)
6724	SEQ ID NO: 6724	RTT*88 (PAM silencing)
6725	SEQ ID NO: 6725	RTT*90 (PAM silencing)
6726	SEQ ID NO: 6726	RTT*92 (PAM silencing)
6727	SEQ ID NO: 6727	RTT
6728	SEQ ID NO: 6728	RTT*89 (PAM silencing)
6729	SEQ ID NO: 6729	RTT*88 (PAM silencing)
6730	SEQ ID NO: 6730	RTT*91 (PAM silencing)
6731	SEQ ID NO: 6731	RTT
6732	SEQ ID NO: 6732	RTT*89 (PAM silencing)
6733	SEQ ID NO: 6733	RTT*92 (PAM silencing)
6734	SEQ ID NO: 6734	RTT*90 (PAM silencing)
6735	SEQ ID NO: 6735	RTT*89 (PAM silencing)
6736	SEQ ID NO: 6736	RTT*90 (PAM silencing)
6737	SEQ ID NO: 6737	RTT*92 (PAM silencing)
6738	SEQ ID NO: 6738	RTT
6739	SEQ ID NO: 6739	RTT*88 (PAM silencing)
6740	SEQ ID NO: 6740	RTT*91 (PAM silencing)
6741	SEQ ID NO: 6741	RTT*91 (PAM silencing)
6742	SEQ ID NO: 6742	RTT*89 (PAM silencing)
6743	SEQ ID NO: 6743	RTT*88 (PAM silencing)
6744	SEQ ID NO: 6744	RTT
6745	SEQ ID NO: 6745	RTT*92 (PAM silencing)

Sequence Number	Sequence	Description
6746	SEQ ID NO: 6746	RTT*90 (PAM silencing)
6747	SEQ ID NO: 6747	RTT*92 (PAM silencing)
6748	SEQ ID NO: 6748	RTT*91 (PAM silencing)
6749	SEQ ID NO: 6749	RTT*90 (PAM silencing)
6750	SEQ ID NO: 6750	RTT
6751	SEQ ID NO: 6751	RTT*89 (PAM silencing)
6752	SEQ ID NO: 6752	RTT*88 (PAM silencing)
6753	SEQ ID NO: 6753	RTT*89 (PAM silencing)
6754	SEQ ID NO: 6754	RTT*90 (PAM silencing)
6755	SEQ ID NO: 6755	RTT*91 (PAM silencing)
6756	SEQ ID NO: 6756	RTT*92 (PAM silencing)
6757	SEQ ID NO: 6757	RTT*88 (PAM silencing)
6758	SEQ ID NO: 6758	RTT
6759	SEQ ID NO: 6759	RTT*88 (PAM silencing)
6760	SEQ ID NO: 6760	RTT*90 (PAM silencing)
6761	SEQ ID NO: 6761	RTT*91 (PAM silencing)
6762	SEQ ID NO: 6762	RTT
6763	SEQ ID NO: 6763	RTT*92 (PAM silencing)
6764	SEQ ID NO: 6764	RTT*89 (PAM silencing)
6765	SEQ ID NO: 6765	RTT*91 (PAM silencing)
6766	SEQ ID NO: 6766	RTT*89 (PAM silencing)
6767	SEQ ID NO: 6767	RTT
6768	SEQ ID NO: 6768	RTT*90 (PAM silencing)

Sequence Number	Sequence	Description
6769	SEQ ID NO: 6769	RTT*92 (PAM silencing)
6770	SEQ ID NO: 6770	RTT*88 (PAM silencing)
6771	SEQ ID NO: 6771	RTT*89 (PAM silencing)
6772	SEQ ID NO: 6772	RTT*88 (PAM silencing)
6773	SEQ ID NO: 6773	RTT
6774	SEQ ID NO: 6774	RTT*91 (PAM silencing)
6775	SEQ ID NO: 6775	RTT*92 (PAM silencing)
6776	SEQ ID NO: 6776	RTT*90 (PAM silencing)
6777	SEQ ID NO: 6777	RTT*91 (PAM silencing)
6778	SEQ ID NO: 6778	RTT*88 (PAM silencing)
6779	SEQ ID NO: 6779	RTT
6780	SEQ ID NO: 6780	RTT*89 (PAM silencing)
6781	SEQ ID NO: 6781	RTT*92 (PAM silencing)
6782	SEQ ID NO: 6782	RTT*90 (PAM silencing)
6783	SEQ ID NO: 6783	RTT*88 (PAM silencing)
6784	SEQ ID NO: 6784	RTT*90 (PAM silencing)
6785	SEQ ID NO: 6785	RTT*89 (PAM silencing)
6786	SEQ ID NO: 6786	RTT*91 (PAM silencing)
6787	SEQ ID NO: 6787	RTT
6788	SEQ ID NO: 6788	RTT*92 (PAM silencing)
6789	SEQ ID NO: 6789	RTT*91 (PAM silencing)
6790	SEQ ID NO: 6790	RTT*88 (PAM silencing)
6791	SEQ ID NO: 6791	RTT*89 (PAM silencing)

Sequence Number	Sequence	Description
6792	SEQ ID NO: 6792	RTT*90 (PAM silencing)
6793	SEQ ID NO: 6793	RTT
6794	SEQ ID NO: 6794	RTT*92 (PAM silencing)
6795	SEQ ID NO: 6795	RTT*88 (PAM silencing)
6796	SEQ ID NO: 6796	RTT*89 (PAM silencing)
6797	SEQ ID NO: 6797	RTT*91 (PAM silencing)
6798	SEQ ID NO: 6798	RTT*92 (PAM silencing)
6799	SEQ ID NO: 6799	RTT*90 (PAM silencing)
6800	SEQ ID NO: 6800	RTT
6801	SEQ ID NO: 6801	RTT*92 (PAM silencing)
6802	SEQ ID NO: 6802	RTT*91 (PAM silencing)
6803	SEQ ID NO: 6803	RTT*88 (PAM silencing)
6804	SEQ ID NO: 6804	RTT*90 (PAM silencing)
6805	SEQ ID NO: 6805	RTT*89 (PAM silencing)
6806	SEQ ID NO: 6806	RTT
6807	SEQ ID NO: 6807	RTT*88 (PAM silencing)
6808	SEQ ID NO: 6808	RTT*91 (PAM silencing)
6809	SEQ ID NO: 6809	RTT*92 (PAM silencing)
6810	SEQ ID NO: 6810	RTT
6811	SEQ ID NO: 6811	RTT*90 (PAM silencing)
6812	SEQ ID NO: 6812	RTT*89 (PAM silencing)
6813	SEQ ID NO: 6813	RTT*90 (PAM silencing)
6814	SEQ ID NO: 6814	RTT
6815	SEQ ID NO: 6815	RTT*91 (PAM silencing)
6816	SEQ ID NO: 6816	RTT*88 (PAM silencing)
6817	SEQ ID NO: 6817	RTT*89 (PAM silencing)
6818	SEQ ID NO: 6818	RTT*92 (PAM silencing)
6819	SEQ ID NO: 6819	RTT*90 (PAM silencing)
6820	SEQ ID NO: 6820	RTT
6821	SEQ ID NO: 6821	RTT*88 (PAM silencing)
6822	SEQ ID NO: 6822	RTT*91 (PAM silencing)
6823	SEQ ID NO: 6823	RTT*89 (PAM silencing)
6824	SEQ ID NO: 6824	RTT*92 (PAM silencing)
6825	SEQ ID NO: 6825	RTT*90 (PAM silencing)
6826	SEQ ID NO: 6826	RTT*91 (PAM silencing)
6827	SEQ ID NO: 6827	RTT
6828	SEQ ID NO: 6828	RTT*89 (PAM silencing)
6829	SEQ ID NO: 6829	RTT*88 (PAM silencing)
6830	SEQ ID NO: 6830	RTT*92 (PAM silencing)
6831	SEQ ID NO: 6831	RTT*90 (PAM silencing)
6832	SEQ ID NO: 6832	RTT
6833	SEQ ID NO: 6833	RTT*92 (PAM silencing)
6834	SEQ ID NO: 6834	RTT*89 (PAM silencing)
6835	SEQ ID NO: 6835	RTT*91 (PAM silencing)
6836	SEQ ID NO: 6836	RTT*88 (PAM silencing)
6837	SEQ ID NO: 6837	RTT*92 (PAM silencing)
6838	SEQ ID NO: 6838	RTT
6839	SEQ ID NO: 6839	RTT*88 (PAM silencing)
6840	SEQ ID NO: 6840	RTT*90 (PAM silencing)
6841	SEQ ID NO: 6841	RTT*89 (PAM silencing)
6842	SEQ ID NO: 6842	RTT*91 (PAM silencing)
6843	SEQ ID NO: 6843	RTT
6844	SEQ ID NO: 6844	RTT*88 (PAM silencing)
6845	SEQ ID NO: 6845	RTT*91 (PAM silencing)
6846	SEQ ID NO: 6846	RTT*89 (PAM silencing)
6847	SEQ ID NO: 6847	RTT*90 (PAM silencing)
6848	SEQ ID NO: 6848	RTT*92 (PAM silencing)
6849	SEQ ID NO: 6849	RTT
6850	SEQ ID NO: 6850	RTT*91 (PAM silencing)
6851	SEQ ID NO: 6851	RTT*89 (PAM silencing)
6852	SEQ ID NO: 6852	RTT*88 (PAM silencing)
6853	SEQ ID NO: 6853	RTT*92 (PAM silencing)
6854	SEQ ID NO: 6854	RTT*90 (PAM silencing)
6855	SEQ ID NO: 6855	RTT*92 (PAM silencing)
6856	SEQ ID NO: 6856	RTT*91 (PAM silencing)
6857	SEQ ID NO: 6857	RTT
6858	SEQ ID NO: 6858	RTT*88 (PAM silencing)
6859	SEQ ID NO: 6859	RTT*90 (PAM silencing)
6860	SEQ ID NO: 6860	RTT*89 (PAM silencing)
6453	SEQ ID NO: 6453	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(AAG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GGG;GG GG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAG;CA GG PAM)
6456	SEQ ID NO: 6456	PE3 ngRNA spacer (AAG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GGG;GG GG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AGG;AG GG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAG;CA GG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TGG;TG GG PAM)
6448	SEQ ID NO: 6448	PE3 ngRNA spacer (CAG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAG;CA GG PAM)
6536	SEQ ID NO: 6536	PE3 ngRNA spacer (ATGG PAM)
6446	SEQ ID NO: 6446	PE3 ngRNA spacer (AAG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AGG;AG GG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GGG;GG GG PAM)
6457	SEQ ID NO: 6457	PE3 ngRNA spacer (GAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG;CA GG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
109	SEQ ID NO: 109	ngRNA (GGG;GG GG PAM)
105	SEQ ID NO: 105	ngRNA (GGG;GG GG PAM)
101	SEQ ID NO: 101	ngRNA (TGG;TG GG PAM)
104	SEQ ID NO: 104	ngRNA (AGG;AG GG PAM)
100	SEQ ID NO: 100	ngRNA (GGG;GG GG PAM)
102	SEQ ID NO: 102	ngRNA (AGG;AG GG PAM)
112	SEQ ID NO: 112	ngRNA (GGG;GG GG PAM)
117	SEQ ID NO: 117	ngRNA (AGG;AG GG PAM)
113	SEQ ID NO: 113	ngRNA (GGG;GG GG PAM)

Table 33

Sequence Number	Sequence	Description
6861	SEQ ID NO: 6861	PEgRNA spacer (GAG PAM)
6862	SEQ ID NO: 6862	PEgRNA spacer (GAG PAM)
6863	SEQ ID NO: 6863	PEgRNA spacer (GAG PAM)
6864	SEQ ID NO: 6864	PEgRNA spacer (GAG PAM)
6865	SEQ ID NO: 6865	PEgRNA spacer (GAG PAM)
6866	SEQ ID NO: 6866	PEgRNA spacer (GAG PAM)
6867	SEQ ID NO: 6867	PEgRNA spacer (GAG PAM)
6868	TCC	PBS
6869	TCCG	PBS
6870	TCCGC	PBS
6871	TCCGCC	PBS
6872	TCCGCC T	PBS
6873	TCCGCC TT	PBS
6874	TCCGCC TTC	PBS
6875	SEQ ID NO: 6875	PBS
6876	SEQ ID NO: 6876	PBS
6877	SEQ ID NO: 6877	PBS
6878	SEQ ID NO: 6878	PBS
6879	SEQ ID NO: 6879	PBS
6880	SEQ ID NO: 6880	PBS
6881	SEQ ID NO: 6881	PBS
6882	SEQ ID NO: 6882	PBS
6883	SEQ ID NO: 6883	PBS
6884	SEQ ID NO: 6884	PBS
6885	SEQ ID NO: 6885	RTT*84 (PAM silencing)
6886	SEQ ID NO: 6886	RTT
6887	SEQ ID NO: 6887	RTT*87 (PAM silencing)
6888	SEQ ID NO: 6888	RTT*85 (PAM silencing)
6889	SEQ ID NO: 6889	RTT*86 (PAM silencing)
6890	SEQ ID NO: 6890	RTT*86 (PAM silencing)
6891	SEQ ID NO: 6891	RTT*84 (PAM silencing)
6892	SEQ ID NO: 6892	RTT
6893	SEQ ID NO: 6893	RTT*85 (PAM silencing)
6894	SEQ ID NO: 6894	RTT*87 (PAM silencing)

Sequence Number	Sequence	Description
6895	SEQ ID NO: 6895	RTT*87 (PAM silencing)
6896	SEQ ID NO: 6896	RTT*84 (PAM silencing)
6897	SEQ ID NO: 6897	RTT*86 (PAM silencing)
6898	SEQ ID NO: 6898	RTT*85 (PAM silencing)
6899	SEQ ID NO: 6899	RTT
6900	SEQ ID NO: 6900	RTT*85 (PAM silencing)
6901	SEQ ID NO: 6901	RTT*84 (PAM silencing)
6902	SEQ ID NO: 6902	RTT*87 (PAM silencing)
6903	SEQ ID NO: 6903	RTT
6904	SEQ ID NO: 6904	RTT*86 (PAM silencing)
6905	SEQ ID NO: 6905	RTT*87 (PAM silencing)
6906	SEQ ID NO: 6906	RTT*86 (PAM silencing)
6907	SEQ ID NO: 6907	RTT
6908	SEQ ID NO: 6908	RTT*84 (PAM silencing)
6909	SEQ ID NO: 6909	RTT*85 (PAM silencing)
6910	SEQ ID NO: 6910	RTT*86 (PAM silencing)
6911	SEQ ID NO: 6911	RTT*85 (PAM silencing)
6912	SEQ ID NO: 6912	RTT*87 (PAM silencing)
6913	SEQ ID NO: 6913	RTT
6914	SEQ ID NO: 6914	RTT*84 (PAM silencing)
6915	SEQ ID NO: 6915	RTT*84 (PAM silencing)
6916	SEQ ID NO: 6916	RTT*85 (PAM silencing)
6917	SEQ ID NO: 6917	RTT*86 (PAM silencing)
6918	SEQ ID NO: 6918	RTT*87 (PAM silencing)
6919	SEQ ID NO: 6919	RTT
6920	SEQ ID NO: 6920	RTT*85 (PAM silencing)
6921	SEQ ID NO: 6921	RTT*86 (PAM silencing)
6922	SEQ ID NO: 6922	RTT
6923	SEQ ID NO: 6923	RTT*87 (PAM silencing)
6924	SEQ ID NO: 6924	RTT*84 (PAM silencing)
6925	SEQ ID NO: 6925	RTT*86 (PAM silencing)
6926	SEQ ID NO: 6926	RTT*84 (PAM silencing)
6927	SEQ ID NO: 6927	RTT*87 (PAM silencing)
6928	SEQ ID NO: 6928	RTT
6929	SEQ ID NO: 6929	RTT*85 (PAM silencing)
6930	SEQ ID NO: 6930	RTT*85 (PAM silencing)
6931	SEQ ID NO: 6931	RTT*87 (PAM silencing)
6932	SEQ ID NO: 6932	RTT
6933	SEQ ID NO: 6933	RTT*84 (PAM silencing)
6934	SEQ ID NO: 6934	RTT*86 (PAM silencing)
6935	SEQ ID NO: 6935	RTT*86 (PAM silencing)
6936	SEQ ID NO: 6936	RTT
6937	SEQ ID NO: 6937	RTT*84 (PAM silencing)
6938	SEQ ID NO: 6938	RTT*85 (PAM silencing)
6939	SEQ ID NO: 6939	RTT*87 (PAM silencing)
6940	SEQ ID NO: 6940	RTT
6941	SEQ ID NO: 6941	RTT*86 (PAM silencing)
6942	SEQ ID NO: 6942	RTT*85 (PAM silencing)
6943	SEQ ID NO: 6943	RTT*87 (PAM silencing)
6944	SEQ ID NO: 6944	RTT*84 (PAM silencing)
6945	SEQ ID NO: 6945	RTT*85 (PAM silencing)
6946	SEQ ID NO: 6946	RTT*87 (PAM silencing)
6947	SEQ ID NO: 6947	RTT
6948	SEQ ID NO: 6948	RTT*84 (PAM silencing)
6949	SEQ ID NO: 6949	RTT*86 (PAM silencing)
6950	SEQ ID NO: 6950	RTT
6951	SEQ ID NO: 6951	RTT*84 (PAM silencing)
6952	SEQ ID NO: 6952	RTT*86 (PAM silencing)
6953	SEQ ID NO: 6953	RTT*87 (PAM silencing)
6954	SEQ ID NO: 6954	RTT*85 (PAM silencing)
6955	SEQ ID NO: 6955	RTT*86 (PAM silencing)
6956	SEQ ID NO: 6956	RTT*85 (PAM silencing)
6957	SEQ ID NO: 6957	RTT*84 (PAM silencing)
6958	SEQ ID NO: 6958	RTT
6959	SEQ ID NO: 6959	RTT*87 (PAM silencing)
6960	SEQ ID NO: 6960	RTT*86 (PAM silencing)
6961	SEQ ID NO: 6961	RTT*85 (PAM silencing)
6962	SEQ ID NO: 6962	RTT*84 (PAM silencing)
6963	SEQ ID NO: 6963	RTT*87 (PAM silencing)
6964	SEQ ID NO: 6964	RTT

Sequence Number	Sequence	Description
6965	SEQ ID NO: 6965	RTT*87 (PAM silencing)
6966	SEQ ID NO: 6966	RTT
6967	SEQ ID NO: 6967	RTT*86 (PAM silencing)
6968	SEQ ID NO: 6968	RTT*85 (PAM silencing)
6969	SEQ ID NO: 6969	RTT*84 (PAM silencing)
6970	SEQ ID NO: 6970	RTT*87 (PAM silencing)
6971	SEQ ID NO: 6971	RTT*84 (PAM silencing)
6972	SEQ ID NO: 6972	RTT*86 (PAM silencing)
6973	SEQ ID NO: 6973	RTT
6974	SEQ ID NO: 6974	RTT*85 (PAM silencing)
6975	SEQ ID NO: 6975	RTT*85 (PAM silencing)
6976	SEQ ID NO: 6976	RTT*86 (PAM silencing)
6977	SEQ ID NO: 6977	RTT*87 (PAM silencing)
6978	SEQ ID NO: 6978	RTT*84 (PAM silencing)
6979	SEQ ID NO: 6979	RTT
6980	SEQ ID NO: 6980	RTT
6981	SEQ ID NO: 6981	RTT*87 (PAM silencing)
6982	SEQ ID NO: 6982	RTT*84 (PAM silencing)
6983	SEQ ID NO: 6983	RTT*86 (PAM silencing)
6984	SEQ ID NO: 6984	RTT*85 (PAM silencing)
6985	SEQ ID NO: 6985	RTT*87 (PAM silencing)
6986	SEQ ID NO: 6986	RTT*85 (PAM silencing)
6987	SEQ ID NO: 6987	RTT
6988	SEQ ID NO: 6988	RTT*86 (PAM silencing)
6989	SEQ ID NO: 6989	RTT*84 (PAM silencing)
6990	SEQ ID NO: 6990	RTT
6991	SEQ ID NO: 6991	RTT*86 (PAM silencing)
6992	SEQ ID NO: 6992	RTT*85 (PAM silencing)
6993	SEQ ID NO: 6993	RTT*84 (PAM silencing)
6994	SEQ ID NO: 6994	RTT*87 (PAM silencing)
6995	SEQ ID NO: 6995	RTT*86 (PAM silencing)
6996	SEQ ID NO: 6996	RTT*87 (PAM silencing)
6997	SEQ ID NO: 6997	RTT*85 (PAM silencing)
6998	SEQ ID NO: 6998	RTT*84 (PAM silencing)
6999	SEQ ID NO: 6999	RTT
7000	SEQ ID NO: 7000	RTT*85 (PAM silencing)
7001	SEQ ID NO: 7001	RTT*86 (PAM silencing)
7002	SEQ ID NO: 7002	RTT*87 (PAM silencing)
7003	SEQ ID NO: 7003	RTT
7004	SEQ ID NO: 7004	RTT*84 (PAM silencing)
7005	SEQ ID NO: 7005	RTT*86 (PAM silencing)
7006	SEQ ID NO: 7006	RTT*85 (PAM silencing)
7007	SEQ ID NO: 7007	RTT*87 (PAM silencing)
7008	SEQ ID NO: 7008	RTT*84 (PAM silencing)
7009	SEQ ID NO: 7009	RTT
7010	SEQ ID NO: 7010	RTT*84 (PAM silencing)
7011	SEQ ID NO: 7011	RTT*87 (PAM silencing)
7012	SEQ ID NO: 7012	RTT*85 (PAM silencing)
7013	SEQ ID NO: 7013	RTT*86 (PAM silencing)
7014	SEQ ID NO: 7014	RTT
7015	SEQ ID NO: 7015	RTT*84 (PAM silencing)
7016	SEQ ID NO: 7016	RTT*85 (PAM silencing)
7017	SEQ ID NO: 7017	RTT
7018	SEQ ID NO: 7018	RTT*86 (PAM silencing)
7019	SEQ ID NO: 7019	RTT*87 (PAM silencing)
7020	SEQ ID NO: 7020	RTT*87 (PAM silencing)
7021	SEQ ID NO: 7021	RTT
7022	SEQ ID NO: 7022	RTT*84 (PAM silencing)
7023	SEQ ID NO: 7023	RTT*86 (PAM silencing)
7024	SEQ ID NO: 7024	RTT*85 (PAM silencing)
7025	SEQ ID NO: 7025	RTT*87 (PAM silencing)
7026	SEQ ID NO: 7026	RTT*84 (PAM silencing)
7027	SEQ ID NO: 7027	RTT
7028	SEQ ID NO: 7028	RTT*86 (PAM silencing)
7029	SEQ ID NO: 7029	RTT*85 (PAM silencing)
7030	SEQ ID NO: 7030	RTT
7031	SEQ ID NO: 7031	RTT*85 (PAM silencing)
7032	SEQ ID NO: 7032	RTT*86 (PAM silencing)
7033	SEQ ID NO: 7033	RTT*84 (PAM silencing)
7034	SEQ ID NO: 7034	RTT*87 (PAM silencing)
7035	SEQ ID NO: 7035	RTT*86 (PAM silencing)

Sequence Number	Sequence	Description
7036	SEQ ID NO: 7036	RTT
7037	SEQ ID NO: 7037	RTT*85 (PAM silencing)
7038	SEQ ID NO: 7038	RTT*84 (PAM silencing)
7039	SEQ ID NO: 7039	RTT*87 (PAM silencing)
7040	SEQ ID NO: 7040	RTT*86 (PAM silencing)
7041	SEQ ID NO: 7041	RTT*84 (PAM silencing)
7042	SEQ ID NO: 7042	RTT*87 (PAM silencing)
7043	SEQ ID NO: 7043	RTT
7044	SEQ ID NO: 7044	RTT*85 (PAM silencing)
7045	SEQ ID NO: 7045	RTT*84 (PAM silencing)
7046	SEQ ID NO: 7046	RTT*86 (PAM silencing)
7047	SEQ ID NO: 7047	RTT
7048	SEQ ID NO: 7048	RTT*87 (PAM silencing)
7049	SEQ ID NO: 7049	RTT*85 (PAM silencing)
7050	SEQ ID NO: 7050	RTT
7051	SEQ ID NO: 7051	RTT*87 (PAM silencing)
7052	SEQ ID NO: 7052	RTT*85 (PAM silencing)
7053	SEQ ID NO: 7053	RTT*84 (PAM silencing)
7054	SEQ ID NO: 7054	RTT*86 (PAM silencing)
7055	SEQ ID NO: 7055	RTT*86 (PAM silencing)
7056	SEQ ID NO: 7056	RTT*85 (PAM silencing)
7057	SEQ ID NO: 7057	RTT*87 (PAM silencing)
7058	SEQ ID NO: 7058	RTT
7059	SEQ ID NO: 7059	RTT*84 (PAM silencing)
7060	SEQ ID NO: 7060	RTT*85 (PAM silencing)
7061	SEQ ID NO: 7061	RTT*87 (PAM silencing)
7062	SEQ ID NO: 7062	RTT*86 (PAM silencing)
7063	SEQ ID NO: 7063	RTT
7064	SEQ ID NO: 7064	RTT*84 (PAM silencing)
7065	SEQ ID NO: 7065	RTT*84 (PAM silencing)
7066	SEQ ID NO: 7066	RTT*86 (PAM silencing)
7067	SEQ ID NO: 7067	RTT
7068	SEQ ID NO: 7068	RTT*85 (PAM silencing)
7069	SEQ ID NO: 7069	RTT*87 (PAM silencing)
7070	SEQ ID NO: 7070	RTT
7071	SEQ ID NO: 7071	RTT*87 (PAM silencing)
7072	SEQ ID NO: 7072	RTT*86 (PAM silencing)
7073	SEQ ID NO: 7073	RTT*85 (PAM silencing)
7074	SEQ ID NO: 7074	RTT*84 (PAM silencing)
6457	SEQ ID NO: 6457	PE3 ngRNA spacer (GAG PAM)
6446	SEQ ID NO: 6446	PE3 ngRNA spacer (AAG PAM)
6448	SEQ ID NO: 6448	PE3 ngRNA spacer (CAG PAM)
6453	SEQ ID NO: 6453	PE3 ngRNA spacer (AAG PAM)
6456	SEQ ID NO: 6456	PE3 ngRNA spacer (AAG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)

Table 34

Sequence Number	Sequence	Description
7075	SEQ ID NO: 7075	PEgRNA spacer (CAG PAM)
7076	SEQ ID NO: 7076	PEgRNA spacer (CAG PAM)
7077	SEQ ID NO: 7077	PEgRNA spacer (CAG PAM)
7078	SEQ ID NO: 7078	PEgRNA spacer (CAG PAM)
7079	SEQ ID NO: 7079	PEgRNA spacer (CAG PAM)
7080	SEQ ID NO: 7080	PEgRNA spacer (CAG PAM)
7081	SEQ ID NO: 7081	PEgRNA spacer (CAG PAM)
7082	ACC	PBS
7083	ACCA	PBS
7084	ACCAT	PBS
7085	ACCATG	PBS
7086	ACCATGT	PBS
7087	ACCATGTT	PBS

Sequence Number	Sequence	Description
7088	ACCATGTTT	PBS
7089	SEQ ID NO: 7089	PBS
7090	SEQ ID NO: 7090	PBS
7091	SEQ ID NO: 7091	PBS
7092	SEQ ID NO: 7092	PBS
7093	SEQ ID NO: 7093	PBS
7094	SEQ ID NO: 7094	PBS
7095	SEQ ID NO: 7095	PBS
7096	SEQ ID NO: 7096	PBS
7097	SEQ ID NO: 7097	PBS
7098	SEQ ID NO: 7098	PBS
7099	SEQ ID NO: 7099	RTT
7100	SEQ ID NO: 7100	RTT
7101	SEQ ID NO: 7101	RTT
7102	SEQ ID NO: 7102	RTT
7103	SEQ ID NO: 7103	RTT
7104	SEQ ID NO: 7104	RTT
7105	SEQ ID NO: 7105	RTT
7106	SEQ ID NO: 7106	RTT
7107	SEQ ID NO: 7107	RTT
7108	SEQ ID NO: 7108	RTT
7109	SEQ ID NO: 7109	RTT
7110	SEQ ID NO: 7110	RTT
7111	SEQ ID NO: 7111	PE3 ngRNA spacer (GAG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG PAM)
7113	SEQ ID NO: 7113	PE3 ngRNA spacer (CAG PAM)
7114	SEQ ID NO: 7114	PE3 ngRNA spacer (AAG PAM)
7115	SEQ ID NO: 7115	PE3 ngRNA spacer (CAG PAM)
7116	SEQ ID NO: 7116	PE3 ngRNA spacer (CAG PAM)
7117	SEQ ID NO: 7117	PE3 ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
7118	SEQ ID NO: 7118	PE3 ngRNA spacer (CAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)

Table 35

Sequence Number	Sequence	Description
7119	SEQ ID NO: 7119	PEgRNA spacer (GAG;GA GG PAM)
7120	SEQ ID NO: 7120	PEgRNA spacer (GAG;GA GG PAM)
7121	SEQ ID NO: 7121	PEgRNA spacer (GAG;GA GG PAM)
7122	SEQ ID NO: 7122	PEgRNA spacer (GAG;GA GG PAM)
7123	SEQ ID NO: 7123	PEgRNA spacer (GAG;GA GG PAM)
7124	SEQ ID NO: 7124	PEgRNA spacer (GAG;GA GG PAM)
7125	SEQ ID NO: 7125	PEgRNA spacer (GAG;GA GG PAM)
4135	ACA	PBS
7126	ACAC	PBS
7127	ACACC	PBS
7128	ACACCA	PBS
7129	ACACCAT	PBS
7130	ACACCATG	PBS
7131	ACACCATGT	PBS
7132	SEQ ID NO: 7132	PBS
7133	SEQ ID NO: 7133	PBS
7134	SEQ ID NO: 7134	PBS
7135	SEQ ID NO: 7135	PBS
7136	SEQ ID NO: 7136	PBS
7137	SEQ ID NO: 7137	PBS
7138	SEQ ID NO: 7138	PBS
7139	SEQ ID NO: 7139	PBS
7140	SEQ ID NO: 7140	PBS
7141	SEQ ID NO: 7141	PBS
7142	SEQ ID NO: 7142	RTT
7143	SEQ ID NO: 7143	RTT
7144	SEQ ID NO: 7144	RTT
7145	SEQ ID NO: 7145	RTT
7146	SEQ ID NO: 7146	RTT
7147	SEQ ID NO: 7147	RTT
7148	SEQ ID NO: 7148	RTT
7149	SEQ ID NO: 7149	RTT
7150	SEQ ID NO: 7150	RTT
7151	SEQ ID NO: 7151	RTT
7152	SEQ ID NO: 7152	RTT
7153	SEQ ID NO: 7153	RTT
7154	SEQ ID NO: 7154	RTT
7155	SEQ ID NO: 7155	RTT
7118	SEQ ID NO: 7118	PE3 ngRNA spacer (CAG PAM)
7113	SEQ ID NO: 7113	PE3 ngRNA spacer (CAG PAM)
7111	SEQ ID NO: 7111	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (GAG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG;AAGG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TGG;TGG PAM)
7156	SEQ ID NO: 7156	PE3b ngRNA spacer (GTGG PAM)
7114	SEQ ID NO: 7114	PE3 ngRNA spacer (AAG PAM)
7157	SEQ ID NO: 7157	PE3b ngRNA spacer (CTGG PAM)
7117	SEQ ID NO: 7117	PE3 ngRNA spacer (CAG;CAGG PAM)
7158	SEQ ID NO: 7158	PE3 ngRNA spacer (CTGG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
7116	SEQ ID NO: 7116	PE3 ngRNA spacer (CAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG;CAGG PAM)
7159	SEQ ID NO: 7159	PE3b ngRNA spacer (TTGG PAM)
7115	SEQ ID NO: 7115	PE3 ngRNA spacer (CAG PAM)
2061	SEQ ID NO: 2061	ngRNA (TGG;TGG PAM)

Table 36

Sequence Number	Sequence	Description
7160	SEQ ID NO: 7160	PEgRNA spacer (AAG PAM)
7161	SEQ ID NO: 7161	PEgRNA spacer (AAG PAM)
7162	SEQ ID NO: 7162	PEgRNA spacer (AAG PAM)
7163	SEQ ID NO: 7163	PEgRNA spacer (AAG PAM)
7164	SEQ ID NO: 7164	PEgRNA spacer (AAG PAM)
7165	SEQ ID NO: 7165	PEgRNA spacer (AAG PAM)
7166	SEQ ID NO: 7166	PEgRNA spacer (AAG PAM)
7167	CTG	PBS
7168	CTGA	PBS
7169	CTGAA	PBS
7170	CTGAAC	PBS
7171	CTGAACA	PBS
7172	CTGAACAC	PBS
7173	CTGAACACC	PBS
7174	SEQ ID NO: 7174	PBS
7175	SEQ ID NO: 7175	PBS
7176	SEQ ID NO: 7176	PBS
7177	SEQ ID NO: 7177	PBS
7178	SEQ ID NO: 7178	PBS
7179	SEQ ID NO: 7179	PBS
7180	SEQ ID NO: 7180	PBS
7181	SEQ ID NO: 7181	PBS
7182	SEQ ID NO: 7182	PBS
7183	SEQ ID NO: 7183	PBS
7184	SEQ ID NO: 7184	RTT
7185	SEQ ID NO: 7185	RTT
7186	SEQ ID NO: 7186	RTT

Sequence Number	Sequence	Description
7187	SEQ ID NO: 7187	RTT
7188	SEQ ID NO: 7188	RTT
7189	SEQ ID NO: 7189	RTT
7190	SEQ ID NO: 7190	RTT
7191	SEQ ID NO: 7191	RTT
7192	SEQ ID NO: 7192	RTT
7193	SEQ ID NO: 7193	RTT
7194	SEQ ID NO: 7194	RTT
7195	SEQ ID NO: 7195	RTT
7196	SEQ ID NO: 7196	RTT
7197	SEQ ID NO: 7197	RTT
7198	SEQ ID NO: 7198	RTT
7199	SEQ ID NO: 7199	RTT
7200	SEQ ID NO: 7200	RTT
7201	SEQ ID NO: 7201	RTT
7111	SEQ ID NO: 7111	PE3 ngRNA spacer (GAG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG PAM)
7113	SEQ ID NO: 7113	PE3 ngRNA spacer (CAG PAM)
7114	SEQ ID NO: 7114	PE3 ngRNA spacer (AAG PAM)
7115	SEQ ID NO: 7115	PE3 ngRNA spacer (CAG PAM)
7116	SEQ ID NO: 7116	PE3 ngRNA spacer (CAG PAM)
7117	SEQ ID NO: 7117	PE3 ngRNA spacer (CAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (CAG PAM)
7118	SEQ ID NO: 7118	PE3 ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)

Table 37

Sequence Number	Sequence	Description
7202	SEQ ID NO: 7202	PEgRNA spacer (GAG PAM)
7203	SEQ ID NO: 7203	PEgRNA spacer (GAG PAM)
7204	SEQ ID NO: 7204	PEgRNA spacer (GAG PAM)
7205	SEQ ID NO: 7205	PEgRNA spacer (GAG PAM)
7206	SEQ ID NO: 7206	PEgRNA spacer (GAG PAM)
7207	SEQ ID NO: 7207	PEgRNA spacer (GAG PAM)
7208	SEQ ID NO: 7208	PEgRNA spacer (GAG PAM)
6868	TCC	PBS
7209	TCCT	PBS
7210	TCCTC	PBS
7211	TCCTCT	PBS
7212	TCCTCT G	PBS
7213	TCCTCT GA	PBS
7214	TCCTCT GAA	PBS
7215	SEQ ID NO: 7215	PBS
7216	SEQ ID NO: 7216	PBS
7217	SEQ ID NO: 7217	PBS
7218	SEQ ID NO: 7218	PBS
7219	SEQ ID NO: 7219	PBS
7220	SEQ ID NO: 7220	PBS
7221	SEQ ID NO: 7221	PBS
7222	SEQ ID NO: 7222	PBS
7223	SEQ ID NO: 7223	PBS
7224	SEQ ID NO: 7224	PBS
7225	SEQ ID NO: 7225	RTT
7226	SEQ ID NO: 7226	RTT
7227	SEQ ID NO: 7227	RTT
7228	SEQ ID NO: 7228	RTT
7229	SEQ ID NO: 7229	RTT
7230	SEQ ID NO: 7230	RTT
7231	SEQ ID NO: 7231	RTT
7232	SEQ ID NO: 7232	RTT
7233	SEQ ID NO: 7233	RTT
7234	SEQ ID NO: 7234	RTT
7235	SEQ ID NO: 7235	RTT
7236	SEQ ID NO: 7236	RTT
7237	SEQ ID NO: 7237	RTT
7238	SEQ ID NO: 7238	RTT
7239	SEQ ID NO: 7239	RTT
7240	SEQ ID NO: 7240	RTT
7241	SEQ ID NO: 7241	RTT
7242	SEQ ID NO: 7242	RTT
7243	SEQ ID NO: 7243	RTT
7244	SEQ ID NO: 7244	RTT
7245	SEQ ID NO: 7245	RTT
7246	SEQ ID NO: 7246	RTT
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG PAM)
7113	SEQ ID NO: 7113	PE3 ngRNA spacer (CAG PAM)
7111	SEQ ID NO: 7111	PE3 ngRNA
		spacer (GAG PAM)
7115	SEQ ID NO: 7115	PE3 ngRNA spacer (CAG PAM)
7116	SEQ ID NO: 7116	PE3 ngRNA spacer (CAG PAM)
7117	SEQ ID NO: 7117	PE3 ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)
7118	SEQ ID NO: 7118	PE3 ngRNA spacer (CAG PAM)
7114	SEQ ID NO: 7114	PE3 ngRNA spacer (AAG PAM)

Table 38

Sequence Number	Sequence	Description
7247	SEQ ID NO: 7247	PEgRNA spacer (AAG;AA GG PAM)
7248	SEQ ID NO: 7248	PEgRNA spacer (AAG;AA GG PAM)
7249	SEQ ID NO: 7249	PEgRNA spacer (AAG;AA GG PAM)
7250	SEQ ID NO: 7250	PEgRNA spacer (AAG;AA GG PAM)
7251	SEQ ID NO: 7251	PEgRNA spacer (AAG;AA GG PAM)
7252	SEQ ID NO: 7252	PEgRNA spacer (AAG;AA GG PAM)

Sequence Number	Sequence	Description
7253	SEQ ID NO: 7253	PEgRNA spacer (AAG;AAGG PAM)
7254	TAA	PBS
7255	TAAA	PBS
7256	TAAAC	PBS
7257	TAAACA	PBS
7258	TAAACAA	PBS
7259	TAAACAAA	PBS
7260	TAAACAAAT	PBS
7261	SEQ ID NO: 7261	PBS
7262	SEQ ID NO: 7262	PBS
7263	SEQ ID NO: 7263	PBS
7264	SEQ ID NO: 7264	PBS
7265	SEQ ID NO: 7265	PBS
7266	SEQ ID NO: 7266	PBS
7267	SEQ ID NO: 7267	PBS
7268	SEQ ID NO: 7268	PBS
7269	SEQ ID NO: 7269	PBS
7270	SEQ ID NO: 7270	PBS
7271	SEQ ID NO: 7271	RTT
7272	SEQ ID NO: 7272	RTT
7273	SEQ ID NO: 7273	RTT
7274	SEQ ID NO: 7274	RTT
7275	SEQ ID NO: 7275	RTT
7276	SEQ ID NO: 7276	RTT
7277	SEQ ID NO: 7277	RTT
7278	SEQ ID NO: 7278	RTT
7279	SEQ ID NO: 7279	RTT
7280	SEQ ID NO: 7280	RTT
7281	SEQ ID NO: 7281	RTT
7282	SEQ ID NO: 7282	RTT
7283	SEQ ID NO: 7283	RTT
7284	SEQ ID NO: 7284	RTT
7285	SEQ ID NO: 7285	RTT
7286	SEQ ID NO: 7286	RTT

Sequence Number	Sequence	Description
7287	SEQ ID NO: 7287	RTT
7288	SEQ ID NO: 7288	RTT
7289	SEQ ID NO: 7289	RTT
7290	SEQ ID NO: 7290	RTT
7291	SEQ ID NO: 7291	RTT
7292	SEQ ID NO: 7292	RTT
7293	SEQ ID NO: 7293	RTT
7294	SEQ ID NO: 7294	RTT
7295	SEQ ID NO: 7295	RTT
7296	SEQ ID NO: 7296	RTT
7297	SEQ ID NO: 7297	RTT
7298	SEQ ID NO: 7298	RTT
7299	SEQ ID NO: 7299	RTT
7300	SEQ ID NO: 7300	RTT
7301	SEQ ID NO: 7301	RTT
7302	SEQ ID NO: 7302	RTT
7303	SEQ ID NO: 7303	RTT
7304	SEQ ID NO: 7304	RTT
7305	SEQ ID NO: 7305	RTT
7306	SEQ ID NO: 7306	RTT
7307	SEQ ID NO: 7307	RTT
7117	SEQ ID NO: 7117	PE3 ngRNA spacer (CAG;CAGG PAM)
7118	SEQ ID NO: 7118	PE3 ngRNA spacer (CAG PAM)
7156	SEQ ID NO: 7156	PE3b ngRNA spacer (GTGG PAM)
7111	SEQ ID NO: 7111	PE3 ngRNA spacer (GAG PAM)
7113	SEQ ID NO: 7113	PE3 ngRNA spacer (CAG PAM)

Sequence Number	Sequence	Description
7158	SEQ ID NO: 7158	PE3 ngRNA spacer (CTGG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG;AAGG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG;CAGG PAM)
7159	SEQ ID NO: 7159	PE3b ngRNA spacer (TTGG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
7115	SEQ ID NO: 7115	PE3 ngRNA spacer (CAG PAM)
7114	SEQ ID NO: 7114	PE3 ngRNA spacer (AAG PAM)
7157	SEQ ID NO: 7157	PE3b ngRNA spacer (CTGG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TGG;TGGG PAM)
7116	SEQ ID NO: 7116	PE3 ngRNA spacer (CAG PAM)
2061	SEQ ID NO: 2061	ngRNA (TGG;TGGG PAM)

Table 39

Sequence Number	Sequence	Description
7308	SEQ ID NO: 7308	PEgRNA spacer (GAG PAM)
7309	SEQ ID NO: 7309	PEgRNA spacer (GAG PAM)
7310	SEQ ID NO: 7310	PEgRNA spacer

Sequence Number	Sequence	Description
		(GAG PAM)
7311	SEQ ID NO: 7311	PEgRNA spacer (GAG PAM)
7312	SEQ ID NO: 7312	PEgRNA spacer (GAG PAM)
7313	SEQ ID NO: 7313	PEgRNA spacer (GAG PAM)
7314	SEQ ID NO: 7314	PEgRNA spacer (GAG PAM)
305	CAG	PBS
7315	CAGT	PBS
7316	CAGTA	PBS
7317	CAGTAA	PBS
7318	CAGTAAA	PBS
7319	CAGTAAAC	PBS
7320	CAGTAAACA	PBS
7321	SEQ ID NO: 7321	PBS
7322	SEQ ID NO: 7322	PBS
7323	SEQ ID NO: 7323	PBS
7324	SEQ ID NO: 7324	PBS
7325	SEQ ID NO: 7325	PBS
7326	SEQ ID NO: 7326	PBS
7327	SEQ ID NO: 7327	PBS
7328	SEQ ID NO: 7328	PBS
7329	SEQ ID NO: 7329	PBS
7330	SEQ ID NO: 7330	PBS
7331	SEQ ID NO: 7331	RTT
7332	SEQ ID NO: 7332	RTT
7333	SEQ ID NO: 7333	RTT
7334	SEQ ID NO: 7334	RTT
7335	SEQ ID NO: 7335	RTT
7336	SEQ ID NO: 7336	RTT
7337	SEQ ID NO: 7337	RTT
7338	SEQ ID NO: 7338	RTT
7339	SEQ ID NO: 7339	RTT
7340	SEQ ID NO: 7340	RTT
7341	SEQ ID NO: 7341	RTT
7342	SEQ ID NO: 7342	RTT
7343	SEQ ID NO: 7343	RTT
7344	SEQ ID NO: 7344	RTT
7345	SEQ ID NO: 7345	RTT
7346	SEQ ID NO: 7346	RTT
7347	SEQ ID NO: 7347	RTT
7348	SEQ ID NO: 7348	RTT
7349	SEQ ID NO: 7349	RTT
7350	SEQ ID NO: 7350	RTT
7351	SEQ ID NO: 7351	RTT
7352	SEQ ID NO: 7352	RTT
7353	SEQ ID NO: 7353	RTT
7354	SEQ ID NO: 7354	RTT
7355	SEQ ID NO: 7355	RTT
7356	SEQ ID NO: 7356	RTT
7357	SEQ ID NO: 7357	RTT
7358	SEQ ID NO: 7358	RTT
7359	SEQ ID NO: 7359	RTT
7360	SEQ ID NO: 7360	RTT
7361	SEQ ID NO: 7361	RTT
7362	SEQ ID NO: 7362	RTT
7363	SEQ ID NO: 7363	RTT
7364	SEQ ID NO: 7364	RTT
7365	SEQ ID NO: 7365	RTT
7366	SEQ ID NO: 7366	RTT
7367	SEQ ID NO: 7367	RTT
7368	SEQ ID NO: 7368	RTT
7369	SEQ ID NO: 7369	RTT
7370	SEQ ID NO: 7370	RTT
7117	SEQ ID NO: 7117	PE3 ngRNA spacer
		(CAG PAM)
7116	SEQ ID NO: 7116	PE3 ngRNA spacer (CAG PAM)
7115	SEQ ID NO: 7115	PE3 ngRNA spacer (CAG PAM)
7114	SEQ ID NO: 7114	PE3 ngRNA spacer (AAG PAM)
7111	SEQ ID NO: 7111	PE3 ngRNA spacer (GAG PAM)
7118	SEQ ID NO: 7118	PE3 ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG PAM)
7113	SEQ ID NO: 7113	PE3 ngRNA spacer (CAG PAM)

Table 40

Sequence Number	Sequence	Description
7371	SEQ ID NO: 7371	PEgRNA spacer (CAG PAM)
7372	SEQ ID NO: 7372	PEgRNA spacer (CAG PAM)
7373	SEQ ID NO: 7373	PEgRNA spacer (CAG PAM)
7374	SEQ ID NO: 7374	PEgRNA spacer (CAG PAM)

Sequence Number	Sequence	Description
7375	SEQ ID NO: 7375	PEgRNA spacer (CAG PAM)
7376	SEQ ID NO: 7376	PEgRNA spacer (CAG PAM)
7377	SEQ ID NO: 7377	PEgRNA spacer (CAG PAM)
6545	CTT	PBS
6546	CTTC	PBS
7378	CTTCA	PBS
7379	CTTCAG	PBS
7380	CTTCAG T	PBS
7381	CTTCAG TA	PBS
7382	CTTCAG TAA	PBS
7383	SEQ ID NO: 7383	PBS
7384	SEQ ID NO: 7384	PBS
7385	SEQ ID NO: 7385	PBS
7386	SEQ ID NO: 7386	PBS
7387	SEQ ID NO: 7387	PBS
7388	SEQ ID NO: 7388	PBS
7389	SEQ ID NO: 7389	PBS
7390	SEQ ID NO: 7390	PBS
7391	SEQ ID NO: 7391	PBS
7392	SEQ ID NO: 7392	PBS
7393	SEQ ID NO: 7393	RTT
7394	SEQ ID NO: 7394	RTT
7395	SEQ ID NO: 7395	RTT
7396	SEQ ID NO: 7396	RTT
7397	SEQ ID NO: 7397	RTT
7398	SEQ ID NO: 7398	RTT
7399	SEQ ID NO: 7399	RTT
7400	SEQ ID NO: 7400	RTT
7401	SEQ ID NO: 7401	RTT
7402	SEQ ID NO: 7402	RTT
7403	SEQ ID NO: 7403	RTT
7404	SEQ ID NO: 7404	RTT

Sequence Number	Sequence	Description
7405	SEQ ID NO: 7405	RTT
7406	SEQ ID NO: 7406	RTT
7407	SEQ ID NO: 7407	RTT
7408	SEQ ID NO: 7408	RTT
7409	SEQ ID NO: 7409	RTT
7410	SEQ ID NO: 7410	RTT
7411	SEQ ID NO: 7411	RTT
7412	SEQ ID NO: 7412	RTT
7413	SEQ ID NO: 7413	RTT
7414	SEQ ID NO: 7414	RTT
7415	SEQ ID NO: 7415	RTT
7416	SEQ ID NO: 7416	RTT
7417	SEQ ID NO: 7417	RTT
7418	SEQ ID NO: 7418	RTT
7419	SEQ ID NO: 7419	RTT
7420	SEQ ID NO: 7420	RTT
7421	SEQ ID NO: 7421	RTT
7422	SEQ ID NO: 7422	RTT
7423	SEQ ID NO: 7423	RTT
7424	SEQ ID NO: 7424	RTT
7425	SEQ ID NO: 7425	RTT
7426	SEQ ID NO: 7426	RTT
7427	SEQ ID NO: 7427	RTT
7428	SEQ ID NO: 7428	RTT
7429	SEQ ID NO: 7429	RTT
7430	SEQ ID NO: 7430	RTT
7431	SEQ ID NO: 7431	RTT
7432	SEQ ID NO: 7432	RTT
7433	SEQ ID NO: 7433	RTT
7434	SEQ ID NO: 7434	RTT
7435	SEQ ID NO: 7435	RTT
7117	SEQ ID NO: 7117	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(CAG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG PAM)
7115	SEQ ID NO: 7115	PE3 ngRNA spacer (CAG PAM)
7113	SEQ ID NO: 7113	PE3 ngRNA spacer (CAG PAM)
7111	SEQ ID NO: 7111	PE3 ngRNA spacer (GAG PAM)
7118	SEQ ID NO: 7118	PE3 ngRNA spacer (CAG PAM)
7116	SEQ ID NO: 7116	PE3 ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)
7114	SEQ ID NO: 7114	PE3 ngRNA spacer (AAG PAM)

Table 41

Sequence Number	Sequence	Description
7436	SEQ ID NO: 7436	PEgRNA spacer (AAG PAM)
7437	SEQ ID NO: 7437	PEgRNA spacer (AAG PAM)
7438	SEQ ID NO: 7438	PEgRNA spacer (AAG PAM)
7439	SEQ ID NO: 7439	PEgRNA spacer (AAG PAM)

Sequence Number	Sequence	Description
7440	SEQ ID NO: 7440	PEgRNA spacer (AAG PAM)
7441	SEQ ID NO: 7441	PEgRNA spacer (AAG PAM)
7442	SEQ ID NO: 7442	PEgRNA spacer (AAG PAM)
7443	GTT	PBS
7444	GTTC	PBS
7445	GTTCA	PBS
7446	GTTCAG	PBS
7447	GTTCAG A	PBS
7448	GTTCAG AA	PBS
7449	GTTCAG AAA	PBS
7450	SEQ ID NO: 7450	PBS
7451	SEQ ID NO: 7451	PBS
7452	SEQ ID NO: 7452	PBS
7453	SEQ ID NO: 7453	PBS
7454	SEQ ID NO: 7454	PBS
7455	SEQ ID NO: 7455	PBS
7456	SEQ ID NO: 7456	PBS
7457	SEQ ID NO: 7457	PBS
7458	SEQ ID NO: 7458	PBS
7459	SEQ ID NO: 7459	PBS
7460	SEQ ID NO: 7460	RTT
7461	SEQ ID NO: 7461	RTT
7462	SEQ ID NO: 7462	RTT
7463	SEQ ID NO: 7463	RTT
7464	SEQ ID NO: 7464	RTT
7465	SEQ ID NO: 7465	RTT
7466	SEQ ID NO: 7466	RTT
7467	SEQ ID NO: 7467	RTT
7468	SEQ ID NO: 7468	RTT
7469	SEQ ID NO: 7469	RTT
7470	SEQ ID NO: 7470	RTT
7471	SEQ ID NO: 7471	RTT

Sequence Number	Sequence	Description
7472	SEQ ID NO: 7472	RTT
7473	SEQ ID NO: 7473	RTT
7474	SEQ ID NO: 7474	RTT
7475	SEQ ID NO: 7475	RTT
7476	SEQ ID NO: 7476	RTT
7477	SEQ ID NO: 7477	RTT
7478	SEQ ID NO: 7478	RTT
7479	SEQ ID NO: 7479	RTT
7480	SEQ ID NO: 7480	RTT
7481	SEQ ID NO: 7481	RTT
7482	SEQ ID NO: 7482	RTT
7483	SEQ ID NO: 7483	RTT
7484	SEQ ID NO: 7484	RTT
7485	SEQ ID NO: 7485	RTT
7486	SEQ ID NO: 7486	RTT
7487	SEQ ID NO: 7487	RTT
7488	SEQ ID NO: 7488	RTT
7489	SEQ ID NO: 7489	RTT
7490	SEQ ID NO: 7490	RTT
7491	SEQ ID NO: 7491	RTT
7492	SEQ ID NO: 7492	RTT
7493	SEQ ID NO: 7493	RTT
7494	SEQ ID NO: 7494	RTT
7495	SEQ ID NO: 7495	RTT
7496	SEQ ID NO: 7496	RTT
7497	SEQ ID NO: 7497	RTT
7498	SEQ ID NO: 7498	RTT
7499	SEQ ID NO: 7499	RTT
7500	SEQ ID NO: 7500	RTT
7501	SEQ ID NO: 7501	RTT
7502	SEQ ID NO: 7502	RTT
7503	SEQ ID NO: 7503	RTT
7504	SEQ ID NO: 7504	RTT

Sequence Number	Sequence	Description
7505	SEQ ID NO: 7505	RTT
7506	SEQ ID NO: 7506	RTT
7507	SEQ ID NO: 7507	RTT
7508	SEQ ID NO: 7508	RTT
7509	SEQ ID NO: 7509	RTT
7510	SEQ ID NO: 7510	RTT
7511	SEQ ID NO: 7511	RTT
7512	SEQ ID NO: 7512	RTT
7513	SEQ ID NO: 7513	RTT
7514	SEQ ID NO: 7514	RTT
7515	SEQ ID NO: 7515	RTT
7516	SEQ ID NO: 7516	RTT
7517	SEQ ID NO: 7517	RTT
7518	SEQ ID NO: 7518	RTT
7519	SEQ ID NO: 7519	RTT
7520	SEQ ID NO: 7520	RTT
7521	SEQ ID NO: 7521	RTT
7113	SEQ ID NO: 7113	PE3 ngRNA spacer (CAG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG PAM)
7115	SEQ ID NO: 7115	PE3 ngRNA spacer (CAG PAM)
7116	SEQ ID NO: 7116	PE3 ngRNA spacer (CAG PAM)
7117	SEQ ID NO: 7117	PE3 ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(CAG PAM)

Table 42

Sequence Number	Sequence	Description
7522	SEQ ID NO: 7522	PEgRNA spacer (AAG PAM)
7523	SEQ ID NO: 7523	PEgRNA spacer (AAG PAM)
7524	SEQ ID NO: 7524	PEgRNA spacer (AAG PAM)
7525	SEQ ID NO: 7525	PEgRNA spacer (AAG PAM)
7526	SEQ ID NO: 7526	PEgRNA spacer (AAG PAM)
7527	SEQ ID NO: 7527	PEgRNA spacer (AAG PAM)
7528	SEQ ID NO: 7528	PEgRNA spacer (AAG PAM)
7529	AAA	PBS
7530	AAAG	PBS
7531	AAAGG	PBS
7532	AAAGGT	PBS
7533	AAAGGTA	PBS
7534	AAAGGTAA	PBS
7535	AAAGGTAAC	PBS
7536	SEQ ID NO: 7536	PBS
7537	SEQ ID NO: 7537	PBS
7538	SEQ ID NO: 7538	PBS
7539	SEQ ID NO: 7539	PBS
7540	SEQ ID NO: 7540	PBS
7541	SEQ ID NO: 7541	PBS
7542	SEQ ID NO: 7542	PBS
7543	SEQ ID NO: 7543	PBS
7544	SEQ ID NO: 7544	PBS
7545	SEQ ID NO: 7545	PBS
7546	SEQ ID NO: 7546	RTT*46 (PAM silencing)
7547	SEQ ID NO: 7547	RTT
7548	SEQ ID NO: 7548	RTT*48 (PAM silencing)
7549	SEQ ID NO: 7549	RTT*49 (PAM silencing)
7550	SEQ ID NO: 7550	RTT*50 (PAM silencing)
7551	SEQ ID NO: 7551	RTT*54 (PAM silencing)
7552	SEQ ID NO: 7552	RTT*47 (PAM silencing)
7553	SEQ ID NO: 7553	RTT*52 (PAM silencing)
7554	SEQ ID NO: 7554	RTT*51 (PAM silencing)
7555	SEQ ID NO: 7555	RTT*53 (PAM silencing)
7556	SEQ ID NO: 7556	RTT*53 (PAM silencing)
7557	SEQ ID NO: 7557	RTT*50 (PAM silencing)
7558	SEQ ID NO: 7558	RTT
7559	SEQ ID NO: 7559	RTT*52 (PAM silencing)
7560	SEQ ID NO: 7560	RTT*54 (PAM silencing)
7561	SEQ ID NO: 7561	RTT*46 (PAM silencing)
7562	SEQ ID NO: 7562	RTT*48 (PAM silencing)
7563	SEQ ID NO: 7563	RTT*47 (PAM silencing)
7564	SEQ ID NO: 7564	RTT*49 (PAM silencing)
7565	SEQ ID NO: 7565	RTT*51 (PAM silencing)
7566	SEQ ID NO: 7566	RTT*50 (PAM silencing)
7567	SEQ ID NO: 7567	RTT*51 (PAM silencing)
7568	SEQ ID NO: 7568	RTT*52 (PAM silencing)
7569	SEQ ID NO: 7569	RTT*46 (PAM silencing)
7570	SEQ ID NO: 7570	RTT*54 (PAM silencing)
7571	SEQ ID NO: 7571	RTT*49 (PAM silencing)
7572	SEQ ID NO: 7572	RTT*47 (PAM silencing)
7573	SEQ ID NO: 7573	RTT*53 (PAM silencing)
7574	SEQ ID NO: 7574	RTT
7575	SEQ ID NO: 7575	RTT*48 (PAM silencing)
7576	SEQ ID NO: 7576	RTT*47 (PAM silencing)
7577	SEQ ID NO: 7577	RTT*48 (PAM silencing)
7578	SEQ ID NO: 7578	RTT*49 (PAM silencing)
7579	SEQ ID NO: 7579	RTT*52 (PAM silencing)
7580	SEQ ID NO: 7580	RTT*50 (PAM silencing)
7581	SEQ ID NO: 7581	RTT*51 (PAM silencing)
7582	SEQ ID NO: 7582	RTT*53 (PAM silencing)
7583	SEQ ID NO: 7583	RTT*54 (PAM silencing)
7584	SEQ ID NO: 7584	RTT*46 (PAM silencing)
7585	SEQ ID NO: 7585	RTT
7586	SEQ ID NO: 7586	RTT*53 (PAM silencing)
7587	SEQ ID NO: 7587	RTT*47 (PAM silencing)
7588	SEQ ID NO: 7588	RTT*50 (PAM silencing)
7589	SEQ ID NO: 7589	RTT*54 (PAM silencing)
7590	SEQ ID NO: 7590	RTT*51 (PAM silencing)
7591	SEQ ID NO: 7591	RTT*48 (PAM silencing)

Sequence Number	Sequence	Description
7592	SEQ ID NO: 7592	RTT*49 (PAM silencing)
7593	SEQ ID NO: 7593	RTT*52 (PAM silencing)
7594	SEQ ID NO: 7594	RTT
7595	SEQ ID NO: 7595	RTT*46 (PAM silencing)
7596	SEQ ID NO: 7596	RTT*51 (PAM silencing)
7597	SEQ ID NO: 7597	RTT*50 (PAM silencing)
7598	SEQ ID NO: 7598	RTT*48 (PAM silencing)
7599	SEQ ID NO: 7599	RTT*47 (PAM silencing)
7600	SEQ ID NO: 7600	RTT*52 (PAM silencing)
7601	SEQ ID NO: 7601	RTT*53 (PAM silencing)
7602	SEQ ID NO: 7602	RTT*46 (PAM silencing)
7603	SEQ ID NO: 7603	RTT*54 (PAM silencing)
7604	SEQ ID NO: 7604	RTT*49 (PAM silencing)
7605	SEQ ID NO: 7605	RTT
7606	SEQ ID NO: 7606	RTT*54 (PAM silencing)
7607	SEQ ID NO: 7607	RTT
7608	SEQ ID NO: 7608	RTT*51 (PAM silencing)
7609	SEQ ID NO: 7609	RTT*47 (PAM silencing)
7610	SEQ ID NO: 7610	RTT*48 (PAM silencing)
7611	SEQ ID NO: 7611	RTT*49 (PAM silencing)
7612	SEQ ID NO: 7612	RTT*53 (PAM silencing)
7613	SEQ ID NO: 7613	RTT*52 (PAM silencing)
7614	SEQ ID NO: 7614	RTT*50 (PAM silencing)
7615	SEQ ID NO: 7615	RTT*46 (PAM silencing)
7616	SEQ ID NO: 7616	RTT*46 (PAM silencing)
7617	SEQ ID NO: 7617	RTT*47 (PAM silencing)
7618	SEQ ID NO: 7618	RTT*52 (PAM silencing)
7619	SEQ ID NO: 7619	RTT*53 (PAM silencing)
7620	SEQ ID NO: 7620	RTT
7621	SEQ ID NO: 7621	RTT*54 (PAM silencing)
7622	SEQ ID NO: 7622	RTT*51 (PAM silencing)
7623	SEQ ID NO: 7623	RTT*48 (PAM silencing)
7624	SEQ ID NO: 7624	RTT*49 (PAM silencing)
7625	SEQ ID NO: 7625	RTT*50 (PAM silencing)
7626	SEQ ID NO: 7626	RTT*50 (PAM silencing)
7627	SEQ ID NO: 7627	RTT*54 (PAM silencing)
7628	SEQ ID NO: 7628	RTT*53 (PAM silencing)
7629	SEQ ID NO: 7629	RTT*48 (PAM silencing)
7630	SEQ ID NO: 7630	RTT*52 (PAM silencing)
7631	SEQ ID NO: 7631	RTT*47 (PAM silencing)
7632	SEQ ID NO: 7632	RTT
7633	SEQ ID NO: 7633	RTT*49 (PAM silencing)
7634	SEQ ID NO: 7634	RTT*46 (PAM silencing)
7635	SEQ ID NO: 7635	RTT*51 (PAM silencing)
7636	SEQ ID NO: 7636	RTT*50 (PAM silencing)
7637	SEQ ID NO: 7637	RTT*46 (PAM silencing)
7638	SEQ ID NO: 7638	RTT*51 (PAM silencing)
7639	SEQ ID NO: 7639	RTT*54 (PAM silencing)
7640	SEQ ID NO: 7640	RTT*49 (PAM silencing)
7641	SEQ ID NO: 7641	RTT*52 (PAM silencing)
7642	SEQ ID NO: 7642	RTT*47 (PAM silencing)
7643	SEQ ID NO: 7643	RTT*53 (PAM silencing)
7644	SEQ ID NO: 7644	RTT
7645	SEQ ID NO: 7645	RTT*48 (PAM silencing)
7646	SEQ ID NO: 7646	RTT*46 (PAM silencing)
7647	SEQ ID NO: 7647	RTT*51 (PAM silencing)
7648	SEQ ID NO: 7648	RTT*47 (PAM silencing)
7649	SEQ ID NO: 7649	RTT*50 (PAM silencing)
7650	SEQ ID NO: 7650	RTT*49 (PAM silencing)
7651	SEQ ID NO: 7651	RTT*54 (PAM silencing)
7652	SEQ ID NO: 7652	RTT*53 (PAM silencing)
7653	SEQ ID NO: 7653	RTT
7654	SEQ ID NO: 7654	RTT*48 (PAM silencing)
7655	SEQ ID NO: 7655	RTT*52 (PAM silencing)
7656	SEQ ID NO: 7656	RTT*53 (PAM silencing)
7657	SEQ ID NO: 7657	RTT*49 (PAM silencing)
7658	SEQ ID NO: 7658	RTT*51 (PAM silencing)
7659	SEQ ID NO: 7659	RTT
7660	SEQ ID NO: 7660	RTT*52 (PAM silencing)

Sequence Number	Sequence	Description
7661	SEQ ID NO: 7661	RTT*47 (PAM silencing)
7662	SEQ ID NO: 7662	RTT*50 (PAM silencing)
7663	SEQ ID NO: 7663	RTT*46 (PAM silencing)
7664	SEQ ID NO: 7664	RTT*54 (PAM silencing)
7665	SEQ ID NO: 7665	RTT*48 (PAM silencing)
7666	SEQ ID NO: 7666	RTT*53 (PAM silencing)
7667	SEQ ID NO: 7667	RTT*49 (PAM silencing)
7668	SEQ ID NO: 7668	RTT*51 (PAM silencing)
7669	SEQ ID NO: 7669	RTT*50 (PAM silencing)
7670	SEQ ID NO: 7670	RTT*52 (PAM silencing)
7671	SEQ ID NO: 7671	RTT
7672	SEQ ID NO: 7672	RTT*47 (PAM silencing)
7673	SEQ ID NO: 7673	RTT*54 (PAM silencing)
7674	SEQ ID NO: 7674	RTT*46 (PAM silencing)
7675	SEQ ID NO: 7675	RTT*48 (PAM silencing)
7676	SEQ ID NO: 7676	RTT*46 (PAM silencing)
7677	SEQ ID NO: 7677	RTT*47 (PAM silencing)
7678	SEQ ID NO: 7678	RTT*54 (PAM silencing)
7679	SEQ ID NO: 7679	RTT*48 (PAM silencing)
7680	SEQ ID NO: 7680	RTT*51 (PAM silencing)
7681	SEQ ID NO: 7681	RTT
7682	SEQ ID NO: 7682	RTT*50 (PAM silencing)
7683	SEQ ID NO: 7683	RTT*49 (PAM silencing)
7684	SEQ ID NO: 7684	RTT*53 (PAM silencing)
7685	SEQ ID NO: 7685	RTT*52 (PAM silencing)
7686	SEQ ID NO: 7686	RTT
7687	SEQ ID NO: 7687	RTT*51 (PAM silencing)
7688	SEQ ID NO: 7688	RTT*48 (PAM silencing)
7689	SEQ ID NO: 7689	RTT*52 (PAM silencing)
7690	SEQ ID NO: 7690	RTT*53 (PAM silencing)
7691	SEQ ID NO: 7691	RTT*50 (PAM silencing)
7692	SEQ ID NO: 7692	RTT*49 (PAM silencing)
7693	SEQ ID NO: 7693	RTT*54 (PAM silencing)
7694	SEQ ID NO: 7694	RTT*46 (PAM silencing)
7695	SEQ ID NO: 7695	RTT*47 (PAM silencing)
7696	SEQ ID NO: 7696	RTT
7697	SEQ ID NO: 7697	RTT*53 (PAM silencing)
7698	SEQ ID NO: 7698	RTT*51 (PAM silencing)
7699	SEQ ID NO: 7699	RTT*54 (PAM silencing)
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7701	SEQ ID NO: 7701	RTT*50 (PAM silencing)
7702	SEQ ID NO: 7702	RTT*52 (PAM silencing)
7703	SEQ ID NO: 7703	RTT*48 (PAM silencing)
7704	SEQ ID NO: 7704	RTT*46 (PAM silencing)
7705	SEQ ID NO: 7705	RTT*47 (PAM silencing)
7706	SEQ ID NO: 7706	RTT*54 (PAM silencing)
7707	SEQ ID NO: 7707	RTT*49 (PAM silencing)
7708	SEQ ID NO: 7708	RTT
7709	SEQ ID NO: 7709	RTT*46 (PAM silencing)
7710	SEQ ID NO: 7710	RTT*52 (PAM silencing)
7711	SEQ ID NO: 7711	RTT*51 (PAM silencing)
7712	SEQ ID NO: 7712	RTT*50 (PAM silencing)
7713	SEQ ID NO: 7713	RTT*53 (PAM silencing)
7714	SEQ ID NO: 7714	RTT*48 (PAM silencing)
7715	SEQ ID NO: 7715	RTT*47 (PAM silencing)
7716	SEQ ID NO: 7716	RTT
7717	SEQ ID NO: 7717	RTT*48 (PAM silencing)
7718	SEQ ID NO: 7718	RTT*50 (PAM silencing)
7719	SEQ ID NO: 7719	RTT*47 (PAM silencing)
7720	SEQ ID NO: 7720	RTT*51 (PAM silencing)
7721	SEQ ID NO: 7721	RTT*54 (PAM silencing)
7722	SEQ ID NO: 7722	RTT*53 (PAM silencing)
7723	SEQ ID NO: 7723	RTT*46 (PAM silencing)
7724	SEQ ID NO: 7724	RTT*52 (PAM silencing)
7725	SEQ ID NO: 7725	RTT*49 (PAM silencing)
7726	SEQ ID NO: 7726	RTT*51 (PAM silencing)
7727	SEQ ID NO: 7727	RTT*50 (PAM silencing)
7728	SEQ ID NO: 7728	RTT*46 (PAM silencing)
7729	SEQ ID NO: 7729	RTT*54 (PAM silencing)

Sequence Number	Sequence	Description
7730	SEQ ID NO: 7730	RTT*53 (PAM silencing)
7731	SEQ ID NO: 7731	RTT*47 (PAM silencing)
7732	SEQ ID NO: 7732	RTT*48 (PAM silencing)
7733	SEQ ID NO: 7733	RTT*49 (PAM silencing)
7734	SEQ ID NO: 7734	RTT*52 (PAM silencing)
7735	SEQ ID NO: 7735	RTT
7736	SEQ ID NO: 7736	RTT*47 (PAM silencing)
7737	SEQ ID NO: 7737	RTT
7738	SEQ ID NO: 7738	RTT*51 (PAM silencing)
7739	SEQ ID NO: 7739	RTT*52 (PAM silencing)
7740	SEQ ID NO: 7740	RTT*54 (PAM silencing)
7741	SEQ ID NO: 7741	RTT*46 (PAM silencing)
7742	SEQ ID NO: 7742	RTT*53 (PAM silencing)
7743	SEQ ID NO: 7743	RTT*49 (PAM silencing)
7744	SEQ ID NO: 7744	RTT*48 (PAM silencing)
7745	SEQ ID NO: 7745	RTT*50 (PAM silencing)
7746	SEQ ID NO: 7746	RTT*53 (PAM silencing)
7747	SEQ ID NO: 7747	RTT*54 (PAM silencing)
7748	SEQ ID NO: 7748	RTT*50 (PAM silencing)
7749	SEQ ID NO: 7749	RTT*49 (PAM silencing)
7750	SEQ ID NO: 7750	RTT*48 (PAM silencing)
7751	SEQ ID NO: 7751	RTT*51 (PAM silencing)
7752	SEQ ID NO: 7752	RTT*46 (PAM silencing)
7753	SEQ ID NO: 7753	RTT*52 (PAM silencing)
7754	SEQ ID NO: 7754	RTT
7755	SEQ ID NO: 7755	RTT*47 (PAM silencing)
7756	SEQ ID NO: 7756	RTT*50 (PAM silencing)
7757	SEQ ID NO: 7757	RTT*47 (PAM silencing)
7758	SEQ ID NO: 7758	RTT*46 (PAM silencing)
7759	SEQ ID NO: 7759	RTT*52 (PAM silencing)
7760	SEQ ID NO: 7760	RTT
7761	SEQ ID NO: 7761	RTT*51 (PAM silencing)
7762	SEQ ID NO: 7762	RTT*48 (PAM silencing)
7763	SEQ ID NO: 7763	RTT*49 (PAM silencing)
7764	SEQ ID NO: 7764	RTT*53 (PAM silencing)
7765	SEQ ID NO: 7765	RTT*54 (PAM silencing)
7766	SEQ ID NO: 7766	RTT*52 (PAM silencing)
7767	SEQ ID NO: 7767	RTT*54 (PAM silencing)
7768	SEQ ID NO: 7768	RTT*51 (PAM silencing)
7769	SEQ ID NO: 7769	RTT*53 (PAM silencing)
7770	SEQ ID NO: 7770	RTT*48 (PAM silencing)
7771	SEQ ID NO: 7771	RTT
7772	SEQ ID NO: 7772	RTT*46 (PAM silencing)
7773	SEQ ID NO: 7773	RTT*47 (PAM silencing)
7774	SEQ ID NO: 7774	RTT*50 (PAM silencing)
7775	SEQ ID NO: 7775	RTT*49 (PAM silencing)
7776	SEQ ID NO: 7776	RTT*47 (PAM silencing)
7777	SEQ ID NO: 7777	RTT*46 (PAM silencing)
7778	SEQ ID NO: 7778	RTT
7779	SEQ ID NO: 7779	RTT*53 (PAM silencing)
7780	SEQ ID NO: 7780	RTT*50 (PAM silencing)
7781	SEQ ID NO: 7781	RTT*49 (PAM silencing)
7782	SEQ ID NO: 7782	RTT*48 (PAM silencing)
7783	SEQ ID NO: 7783	RTT*51 (PAM silencing)
7784	SEQ ID NO: 7784	RTT*52 (PAM silencing)
7785	SEQ ID NO: 7785	RTT*54 (PAM silencing)
7786	SEQ ID NO: 7786	RTT*54 (PAM silencing)
7787	SEQ ID NO: 7787	RTT*48 (PAM silencing)
7788	SEQ ID NO: 7788	RTT
7789	SEQ ID NO: 7789	RTT*49 (PAM silencing)
7790	SEQ ID NO: 7790	RTT*52 (PAM silencing)
7791	SEQ ID NO: 7791	RTT*46 (PAM silencing)
7792	SEQ ID NO: 7792	RTT*51 (PAM silencing)
7793	SEQ ID NO: 7793	RTT*53 (PAM silencing)
7794	SEQ ID NO: 7794	RTT*50 (PAM silencing)
7795	SEQ ID NO: 7795	RTT*47 (PAM silencing)
7796	SEQ ID NO: 7796	RTT*50 (PAM silencing)
7797	SEQ ID NO: 7797	RTT*53 (PAM silencing)
7798	SEQ ID NO: 7798	RTT*46 (PAM silencing)

Sequence Number	Sequence	Description
7799	SEQ ID NO: 7799	RTT*47 (PAM silencing)
7800	SEQ ID NO: 7800	RTT*48 (PAM silencing)
7801	SEQ ID NO: 7801	RTT
7802	SEQ ID NO: 7802	RTT*49 (PAM silencing)
7803	SEQ ID NO: 7803	RTT*54 (PAM silencing)
7804	SEQ ID NO: 7804	RTT*51 (PAM silencing)
7805	SEQ ID NO: 7805	RTT*52 (PAM silencing)
7806	SEQ ID NO: 7806	RTT
7807	SEQ ID NO: 7807	RTT*48 (PAM silencing)
7808	SEQ ID NO: 7808	RTT*54 (PAM silencing)
7809	SEQ ID NO: 7809	RTT*53 (PAM silencing)
7810	SEQ ID NO: 7810	RTT*49 (PAM silencing)
7811	SEQ ID NO: 7811	RTT*47 (PAM silencing)
7812	SEQ ID NO: 7812	RTT*52 (PAM silencing)
7813	SEQ ID NO: 7813	RTT*46 (PAM silencing)
7814	SEQ ID NO: 7814	RTT*51 (PAM silencing)
7815	SEQ ID NO: 7815	RTT*50 (PAM silencing)
7816	SEQ ID NO: 7816	RTT*48 (PAM silencing)
7817	SEQ ID NO: 7817	RTT*46 (PAM silencing)
7818	SEQ ID NO: 7818	RTT*47 (PAM silencing)
7819	SEQ ID NO: 7819	RTT*54 (PAM silencing)
7820	SEQ ID NO: 7820	RTT*53 (PAM silencing)
7821	SEQ ID NO: 7821	RTT*51 (PAM silencing)
7822	SEQ ID NO: 7822	RTT
7823	SEQ ID NO: 7823	RTT*49 (PAM silencing)
7824	SEQ ID NO: 7824	RTT*52 (PAM silencing)
7825	SEQ ID NO: 7825	RTT*50 (PAM silencing)
7826	SEQ ID NO: 7826	RTT*48 (PAM silencing)
7827	SEQ ID NO: 7827	RTT*54 (PAM silencing)
7828	SEQ ID NO: 7828	RTT*50 (PAM silencing)
7829	SEQ ID NO: 7829	RTT
7830	SEQ ID NO: 7830	RTT*51 (PAM silencing)
7831	SEQ ID NO: 7831	RTT*47 (PAM silencing)
7832	SEQ ID NO: 7832	RTT*46 (PAM silencing)
7833	SEQ ID NO: 7833	RTT*53 (PAM silencing)
7834	SEQ ID NO: 7834	RTT*52 (PAM silencing)
7835	SEQ ID NO: 7835	RTT*49 (PAM silencing)
7836	SEQ ID NO: 7836	RTT*52 (PAM silencing)
7837	SEQ ID NO: 7837	RTT*48 (PAM silencing)
7838	SEQ ID NO: 7838	RTT*50 (PAM silencing)
7839	SEQ ID NO: 7839	RTT*47 (PAM silencing)
7840	SEQ ID NO: 7840	RTT
7841	SEQ ID NO: 7841	RTT*53 (PAM silencing)
7842	SEQ ID NO: 7842	RTT*49 (PAM silencing)
7843	SEQ ID NO: 7843	RTT*54 (PAM silencing)
7844	SEQ ID NO: 7844	RTT*46 (PAM silencing)
7845	SEQ ID NO: 7845	RTT*51 (PAM silencing)
7846	SEQ ID NO: 7846	RTT*51 (PAM silencing)
7847	SEQ ID NO: 7847	RTT*49 (PAM silencing)
7848	SEQ ID NO: 7848	RTT
7849	SEQ ID NO: 7849	RTT*46 (PAM silencing)
7850	SEQ ID NO: 7850	RTT*50 (PAM silencing)
7851	SEQ ID NO: 7851	RTT*54 (PAM silencing)
7852	SEQ ID NO: 7852	RTT*52 (PAM silencing)
7853	SEQ ID NO: 7853	RTT*53 (PAM silencing)
7854	SEQ ID NO: 7854	RTT*47 (PAM silencing)
7855	SEQ ID NO: 7855	RTT*48 (PAM silencing)
7856	SEQ ID NO: 7856	RTT*48 (PAM silencing)
7857	SEQ ID NO: 7857	RTT*51 (PAM silencing)
7858	SEQ ID NO: 7858	RTT*49 (PAM silencing)
7859	SEQ ID NO: 7859	RTT*53 (PAM silencing)
7860	SEQ ID NO: 7860	RTT*52 (PAM silencing)
7861	SEQ ID NO: 7861	RTT
7862	SEQ ID NO: 7862	RTT*54 (PAM silencing)
7863	SEQ ID NO: 7863	RTT*50 (PAM silencing)
7864	SEQ ID NO: 7864	RTT*47 (PAM silencing)
7865	SEQ ID NO: 7865	RTT*46 (PAM silencing)
7866	SEQ ID NO: 7866	RTT*48 (PAM silencing)
7867	SEQ ID NO: 7867	RTT*47 (PAM silencing)

Sequence Number	Sequence	Description
7868	SEQ ID NO: 7868	RTT*54 (PAM silencing)
7869	SEQ ID NO: 7869	RTT*53 (PAM silencing)
7870	SEQ ID NO: 7870	RTT*51 (PAM silencing)
7871	SEQ ID NO: 7871	RTT*52 (PAM silencing)
7872	SEQ ID NO: 7872	RTT*50 (PAM silencing)
7873	SEQ ID NO: 7873	RTT*49 (PAM silencing)
7874	SEQ ID NO: 7874	RTT*46 (PAM silencing)
7875	SEQ ID NO: 7875	RTT
7876	SEQ ID NO: 7876	RTT*48 (PAM silencing)
7877	SEQ ID NO: 7877	RTT
7878	SEQ ID NO: 7878	RTT*49 (PAM silencing)
7879	SEQ ID NO: 7879	RTT*47 (PAM silencing)
7880	SEQ ID NO: 7880	RTT*46 (PAM silencing)
7881	SEQ ID NO: 7881	RTT*54 (PAM silencing)
7882	SEQ ID NO: 7882	RTT*50 (PAM silencing)
7883	SEQ ID NO: 7883	RTT*52 (PAM silencing)
7884	SEQ ID NO: 7884	RTT*51 (PAM silencing)
7885	SEQ ID NO: 7885	RTT*53 (PAM silencing)
7886	SEQ ID NO: 7886	RTT*47 (PAM silencing)
7887	SEQ ID NO: 7887	RTT*54 (PAM silencing)
7888	SEQ ID NO: 7888	RTT*53 (PAM silencing)
7889	SEQ ID NO: 7889	RTT
7890	SEQ ID NO: 7890	RTT*52 (PAM silencing)

Sequence Number	Sequence	Description
7891	SEQ ID NO: 7891	RTT*50 (PAM silencing)
7892	SEQ ID NO: 7892	RTT*51 (PAM silencing)
7893	SEQ ID NO: 7893	RTT*46 (PAM silencing)
7894	SEQ ID NO: 7894	RTT*48 (PAM silencing)
7895	SEQ ID NO: 7895	RTT*49 (PAM silencing)
7896	SEQ ID NO: 7896	RTT*51 (PAM silencing)
7897	SEQ ID NO: 7897	RTT*49 (PAM silencing)
7898	SEQ ID NO: 7898	RTT*50 (PAM silencing)
7899	SEQ ID NO: 7899	RTT*47 (PAM silencing)
7900	SEQ ID NO: 7900	RTT
7901	SEQ ID NO: 7901	RTT*52 (PAM silencing)
7902	SEQ ID NO: 7902	RTT*48 (PAM silencing)
7903	SEQ ID NO: 7903	RTT*46 (PAM silencing)
7904	SEQ ID NO: 7904	RTT*53 (PAM silencing)
7905	SEQ ID NO: 7905	RTT*54 (PAM silencing)
7906	SEQ ID NO: 7906	RTT*52 (PAM silencing)
7907	SEQ ID NO: 7907	RTT*54 (PAM silencing)
7908	SEQ ID NO: 7908	RTT*51 (PAM silencing)
7909	SEQ ID NO: 7909	RTT*50 (PAM silencing)
7910	SEQ ID NO: 7910	RTT*47 (PAM silencing)
7911	SEQ ID NO: 7911	RTT*48 (PAM silencing)
7912	SEQ ID NO: 7912	RTT*53 (PAM silencing)

Sequence Number	Sequence	Description
7913	SEQ ID NO: 7913	RTT*46 (PAM silencing)
7914	SEQ ID NO: 7914	RTT*49 (PAM silencing)
7915	SEQ ID NO: 7915	RTT
7916	SEQ ID NO: 7916	RTT*47 (PAM silencing)
7917	SEQ ID NO: 7917	RTT*50 (PAM silencing)
7918	SEQ ID NO: 7918	RTT*49 (PAM silencing)
7919	SEQ ID NO: 7919	RTT*52 (PAM silencing)
7920	SEQ ID NO: 7920	RTT*46 (PAM silencing)
7921	SEQ ID NO: 7921	RTT*48 (PAM silencing)
7922	SEQ ID NO: 7922	RTT
7923	SEQ ID NO: 7923	RTT*51 (PAM silencing)
7924	SEQ ID NO: 7924	RTT*54 (PAM silencing)
7925	SEQ ID NO: 7925	RTT*53 (PAM silencing)
7926	SEQ ID NO: 7926	RTT*51 (PAM silencing)
7927	SEQ ID NO: 7927	RTT*46 (PAM silencing)
7928	SEQ ID NO: 7928	RTT*47 (PAM silencing)
7929	SEQ ID NO: 7929	RTT*53 (PAM silencing)
7930	SEQ ID NO: 7930	RTT*48 (PAM silencing)
7931	SEQ ID NO: 7931	RTT*52 (PAM silencing)
7932	SEQ ID NO: 7932	RTT
7933	SEQ ID NO: 7933	RTT*49 (PAM silencing)
7934	SEQ ID NO: 7934	RTT*54 (PAM silencing)
7935	SEQ ID NO: 7935	RTT*50 (PAM silencing)

Sequence Number	Sequence	Description
7936	SEQ ID NO: 7936	RTT*48 (PAM silencing)
7937	SEQ ID NO: 7937	RTT*53 (PAM silencing)
7938	SEQ ID NO: 7938	RTT*54 (PAM silencing)
7939	SEQ ID NO: 7939	RTT*49 (PAM silencing)
7940	SEQ ID NO: 7940	RTT*50 (PAM silencing)
7941	SEQ ID NO: 7941	RTT*51 (PAM silencing)
7942	SEQ ID NO: 7942	RTT
7943	SEQ ID NO: 7943	RTT*46 (PAM silencing)
7944	SEQ ID NO: 7944	RTT*52 (PAM silencing)
7945	SEQ ID NO: 7945	RTT*47 (PAM silencing)
7946	SEQ ID NO: 7946	RTT*49 (PAM silencing)
7947	SEQ ID NO: 7947	RTT*48 (PAM silencing)
7948	SEQ ID NO: 7948	RTT*54 (PAM silencing)
7949	SEQ ID NO: 7949	RTT*50 (PAM silencing)
7950	SEQ ID NO: 7950	RTT
7951	SEQ ID NO: 7951	RTT*53 (PAM silencing)
7952	SEQ ID NO: 7952	RTT*52 (PAM silencing)
7953	SEQ ID NO: 7953	RTT*46 (PAM silencing)
7954	SEQ ID NO: 7954	RTT*47 (PAM silencing)
7955	SEQ ID NO: 7955	RTT*51 (PAM silencing)
7956	SEQ ID NO: 7956	RTT*49 (PAM silencing)
7957	SEQ ID NO: 7957	RTT*46 (PAM silencing)
7958	SEQ ID NO: 7958	RTT*54 (PAM silencing)
7959	SEQ ID NO: 7959	RTT*52 (PAM silencing)
7960	SEQ ID NO: 7960	RTT*48 (PAM silencing)
7961	SEQ ID NO: 7961	RTT*51 (PAM silencing)
7962	SEQ ID NO: 7962	RTT
7963	SEQ ID NO: 7963	RTT*50 (PAM silencing)
7964	SEQ ID NO: 7964	RTT*53 (PAM silencing)
7965	SEQ ID NO: 7965	RTT*47 (PAM silencing)
7966	SEQ ID NO: 7966	RTT*49 (PAM silencing)
7967	SEQ ID NO: 7967	RTT*52 (PAM silencing)
7968	SEQ ID NO: 7968	RTT
7969	SEQ ID NO: 7969	RTT*53 (PAM silencing)
7970	SEQ ID NO: 7970	RTT*46 (PAM silencing)
7971	SEQ ID NO: 7971	RTT*51 (PAM silencing)
7972	SEQ ID NO: 7972	RTT*48 (PAM silencing)
7973	SEQ ID NO: 7973	RTT*47 (PAM silencing)
7974	SEQ ID NO: 7974	RTT*50 (PAM silencing)
7975	SEQ ID NO: 7975	RTT*54 (PAM silencing)
7976	SEQ ID NO: 7976	RTT*49 (PAM silencing)
7977	SEQ ID NO: 7977	RTT*48 (PAM silencing)
7978	SEQ ID NO: 7978	RTT*50 (PAM silencing)
7979	SEQ ID NO: 7979	RTT
7980	SEQ ID NO: 7980	RTT*47 (PAM silencing)
7981	SEQ ID NO: 7981	RTT*52 (PAM silencing)
7982	SEQ ID NO: 7982	RTT*53 (PAM silencing)
7983	SEQ ID NO: 7983	RTT*46 (PAM silencing)
7984	SEQ ID NO: 7984	RTT*51 (PAM silencing)
7985	SEQ ID NO: 7985	RTT*54 (PAM silencing)
7986	SEQ ID NO: 7986	RTT*51 (PAM silencing)
7987	SEQ ID NO: 7987	RTT
7988	SEQ ID NO: 7988	RTT*48 (PAM silencing)
7989	SEQ ID NO: 7989	RTT*54 (PAM silencing)
7990	SEQ ID NO: 7990	RTT*49 (PAM silencing)
7991	SEQ ID NO: 7991	RTT*47 (PAM silencing)
7992	SEQ ID NO: 7992	RTT*53 (PAM silencing)
7993	SEQ ID NO: 7993	RTT*50 (PAM silencing)
7994	SEQ ID NO: 7994	RTT*46 (PAM silencing)
7995	SEQ ID NO: 7995	RTT*52 (PAM silencing)
7996	SEQ ID NO: 7996	RTT*49 (PAM silencing)
7997	SEQ ID NO: 7997	RTT
7998	SEQ ID NO: 7998	RTT*47 (PAM silencing)
7999	SEQ ID NO: 7999	RTT*48 (PAM silencing)
8000	SEQ ID NO: 8000	RTT*46 (PAM silencing)
8001	SEQ ID NO: 8001	RTT*53 (PAM silencing)
8002	SEQ ID NO: 8002	RTT*54 (PAM silencing)
8003	SEQ ID NO: 8003	RTT*50 (PAM silencing)
8004	SEQ ID NO: 8004	RTT*52 (PAM silencing)

Sequence Number	Sequence	Description
8005	SEQ ID NO: 8005	RTT*51 (PAM silencing)
8006	SEQ ID NO: 8006	RTT*53 (PAM silencing)
8007	SEQ ID NO: 8007	RTT*50 (PAM silencing)
8008	SEQ ID NO: 8008	RTT*49 (PAM silencing)
8009	SEQ ID NO: 8009	RTT*48 (PAM silencing)
8010	SEQ ID NO: 8010	RTT*51 (PAM silencing)
8011	SEQ ID NO: 8011	RTT*52 (PAM silencing)
8012	SEQ ID NO: 8012	RTT*46 (PAM silencing)
8013	SEQ ID NO: 8013	RTT*47 (PAM silencing)
8014	SEQ ID NO: 8014	RTT
8015	SEQ ID NO: 8015	RTT*54 (PAM silencing)
8016	SEQ ID NO: 8016	RTT*54 (PAM silencing)
8017	SEQ ID NO: 8017	RTT*50 (PAM silencing)
8018	SEQ ID NO: 8018	RTT*52 (PAM silencing)
8019	SEQ ID NO: 8019	RTT*47 (PAM silencing)
8020	SEQ ID NO: 8020	RTT*51 (PAM silencing)
8021	SEQ ID NO: 8021	RTT*46 (PAM silencing)
8022	SEQ ID NO: 8022	RTT
8023	SEQ ID NO: 8023	RTT*53 (PAM silencing)
8024	SEQ ID NO: 8024	RTT*49 (PAM silencing)
8025	SEQ ID NO: 8025	RTT*48 (PAM silencing)
8026	SEQ ID NO: 8026	RTT*50 (PAM silencing)
8027	SEQ ID NO: 8027	RTT*47 (PAM silencing)

Sequence Number	Sequence	Description
8028	SEQ ID NO: 8028	RTT*52 (PAM silencing)
8029	SEQ ID NO: 8029	RTT*53 (PAM silencing)
8030	SEQ ID NO: 8030	RTT*48 (PAM silencing)
8031	SEQ ID NO: 8031	RTT
8032	SEQ ID NO: 8032	RTT*54 (PAM silencing)
8033	SEQ ID NO: 8033	RTT*46 (PAM silencing)
8034	SEQ ID NO: 8034	RTT*51 (PAM silencing)
8035	SEQ ID NO: 8035	RTT*49 (PAM silencing)
8036	SEQ ID NO: 8036	RTT
8037	SEQ ID NO: 8037	RTT*46 (PAM silencing)
8038	SEQ ID NO: 8038	RTT*49 (PAM silencing)
8039	SEQ ID NO: 8039	RTT*54 (PAM silencing)
8040	SEQ ID NO: 8040	RTT*51 (PAM silencing)
8041	SEQ ID NO: 8041	RTT*48 (PAM silencing)
8042	SEQ ID NO: 8042	RTT*52 (PAM silencing)
8043	SEQ ID NO: 8043	RTT*50 (PAM silencing)
8044	SEQ ID NO: 8044	RTT*53 (PAM silencing)
8045	SEQ ID NO: 8045	RTT*47 (PAM silencing)
8046	SEQ ID NO: 8046	RTT*49 (PAM silencing)
8047	SEQ ID NO: 8047	RTT*52 (PAM silencing)
8048	SEQ ID NO: 8048	RTT*51 (PAM silencing)
8049	SEQ ID NO: 8049	RTT*47 (PAM silencing)
8050	SEQ ID NO: 8050	RTT

Sequence Number	Sequence	Description
8051	SEQ ID NO: 8051	RTT*46 (PAM silencing)
8052	SEQ ID NO: 8052	RTT*54 (PAM silencing)
8053	SEQ ID NO: 8053	RTT*53 (PAM silencing)
8054	SEQ ID NO: 8054	RTT*48 (PAM silencing)
8055	SEQ ID NO: 8055	RTT*50 (PAM silencing)
8056	SEQ ID NO: 8056	RTT*53 (PAM silencing)
8057	SEQ ID NO: 8057	RTT*51 (PAM silencing)
8058	SEQ ID NO: 8058	RTT*50 (PAM silencing)
8059	SEQ ID NO: 8059	RTT*49 (PAM silencing)
8060	SEQ ID NO: 8060	RTT*46 (PAM silencing)
8061	SEQ ID NO: 8061	RTT*47 (PAM silencing)
8062	SEQ ID NO: 8062	RTT
8063	SEQ ID NO: 8063	RTT*54 (PAM silencing)
8064	SEQ ID NO: 8064	RTT*48 (PAM silencing)
8065	SEQ ID NO: 8065	RTT*52 (PAM silencing)
8066	SEQ ID NO: 8066	RTT*54 (PAM silencing)
8067	SEQ ID NO: 8067	RTT*49 (PAM silencing)
8068	SEQ ID NO: 8068	RTT*51 (PAM silencing)
8069	SEQ ID NO: 8069	RTT*48 (PAM silencing)
8070	SEQ ID NO: 8070	RTT*46 (PAM silencing)
8071	SEQ ID NO: 8071	RTT
8072	SEQ ID NO: 8072	RTT*52 (PAM silencing)
8073	SEQ ID NO: 8073	RTT*47 (PAM silencing)

Sequence Number	Sequence	Description
8074	SEQ ID NO: 8074	RTT*53 (PAM silencing)
8075	SEQ ID NO: 8075	RTT*50 (PAM silencing)
8076	SEQ ID NO: 8076	RTT*53 (PAM silencing)
8077	SEQ ID NO: 8077	RTT*52 (PAM silencing)
8078	SEQ ID NO: 8078	RTT
8079	SEQ ID NO: 8079	RTT*51 (PAM silencing)
8080	SEQ ID NO: 8080	RTT*48 (PAM silencing)
8081	SEQ ID NO: 8081	RTT*46 (PAM silencing)
8082	SEQ ID NO: 8082	RTT*47 (PAM silencing)
8083	SEQ ID NO: 8083	RTT*54 (PAM silencing)
8084	SEQ ID NO: 8084	RTT*49 (PAM silencing)
8085	SEQ ID NO: 8085	RTT*50 (PAM silencing)
8086	SEQ ID NO: 8086	RTT
8087	SEQ ID NO: 8087	RTT*51 (PAM silencing)
8088	SEQ ID NO: 8088	RTT*49 (PAM silencing)
8089	SEQ ID NO: 8089	RTT*52 (PAM silencing)
8090	SEQ ID NO: 8090	RTT*54 (PAM silencing)
8091	SEQ ID NO: 8091	RTT*46 (PAM silencing)
8092	SEQ ID NO: 8092	RTT*53 (PAM silencing)
8093	SEQ ID NO: 8093	RTT*47 (PAM silencing)
8094	SEQ ID NO: 8094	RTT*50 (PAM silencing)
8095	SEQ ID NO: 8095	RTT*48 (PAM silencing)
8096	SEQ ID NO: 8096	RTT*46 (PAM silencing)

Sequence Number	Sequence	Description
8097	SEQ ID NO: 8097	RTT*52 (PAM silencing)
8098	SEQ ID NO: 8098	RTT*54 (PAM silencing)
8099	SEQ ID NO: 8099	RTT*49 (PAM silencing)
8100	SEQ ID NO: 8100	RTT*47 (PAM silencing)
8101	SEQ ID NO: 8101	RTT*50 (PAM silencing)
8102	SEQ ID NO: 8102	RTT*53 (PAM silencing)
8103	SEQ ID NO: 8103	RTT
8104	SEQ ID NO: 8104	RTT*51 (PAM silencing)
8105	SEQ ID NO: 8105	RTT*48 (PAM silencing)
8106	SEQ ID NO: 8106	RTT
8107	SEQ ID NO: 8107	RTT*49 (PAM silencing)
8108	SEQ ID NO: 8108	RTT*53 (PAM silencing)
8109	SEQ ID NO: 8109	RTT*48 (PAM silencing)
8110	SEQ ID NO: 8110	RTT*46 (PAM silencing)
8111	SEQ ID NO: 8111	RTT*51 (PAM silencing)
8112	SEQ ID NO: 8112	RTT*47 (PAM silencing)
8113	SEQ ID NO: 8113	RTT*54 (PAM silencing)
8114	SEQ ID NO: 8114	RTT*52 (PAM silencing)
8115	SEQ ID NO: 8115	RTT*50 (PAM silencing)
8116	SEQ ID NO: 8116	RTT*50 (PAM silencing)
8117	SEQ ID NO: 8117	RTT*51 (PAM silencing)
8118	SEQ ID NO: 8118	RTT*49 (PAM silencing)
8119	SEQ ID NO: 8119	RTT

Sequence Number	Sequence	Description
8120	SEQ ID NO: 8120	RTT*47 (PAM silencing)
8121	SEQ ID NO: 8121	RTT*54 (PAM silencing)
8122	SEQ ID NO: 8122	RTT*48 (PAM silencing)
8123	SEQ ID NO: 8123	RTT*52 (PAM silencing)
8124	SEQ ID NO: 8124	RTT*53 (PAM silencing)
8125	SEQ ID NO: 8125	RTT*46 (PAM silencing)
8126	SEQ ID NO: 8126	RTT*49 (PAM silencing)
8127	SEQ ID NO: 8127	RTT
8128	SEQ ID NO: 8128	RTT*46 (PAM silencing)
8129	SEQ ID NO: 8129	RTT*54 (PAM silencing)
8130	SEQ ID NO: 8130	RTT*51 (PAM silencing)
8131	SEQ ID NO: 8131	RTT*52 (PAM silencing)
8132	SEQ ID NO: 8132	RTT*47 (PAM silencing)
8133	SEQ ID NO: 8133	RTT*48 (PAM silencing)
8134	SEQ ID NO: 8134	RTT*50 (PAM silencing)
8135	SEQ ID NO: 8135	RTT*53 (PAM silencing)
8136	SEQ ID NO: 8136	RTT*49 (PAM silencing)
8137	SEQ ID NO: 8137	RTT*52 (PAM silencing)
8138	SEQ ID NO: 8138	RTT*54 (PAM silencing)
8139	SEQ ID NO: 8139	RTT
8140	SEQ ID NO: 8140	RTT*48 (PAM silencing)
8141	SEQ ID NO: 8141	RTT*47 (PAM silencing)
8142	SEQ ID NO: 8142	RTT*51 (PAM silencing)

Sequence Number	Sequence	Description
8143	SEQ ID NO: 8143	RTT*50 (PAM silencing)
8144	SEQ ID NO: 8144	RTT*53 (PAM silencing)
8145	SEQ ID NO: 8145	RTT*46 (PAM silencing)
8146	SEQ ID NO: 8146	RTT
8147	SEQ ID NO: 8147	RTT*47 (PAM silencing)
8148	SEQ ID NO: 8148	RTT*54 (PAM silencing)
8149	SEQ ID NO: 8149	RTT*52 (PAM silencing)
8150	SEQ ID NO: 8150	RTT*48 (PAM silencing)
8151	SEQ ID NO: 8151	RTT*50 (PAM silencing)
8152	SEQ ID NO: 8152	RTT*51 (PAM silencing)
8153	SEQ ID NO: 8153	RTT*49 (PAM silencing)
8154	SEQ ID NO: 8154	RTT*53 (PAM silencing)
8155	SEQ ID NO: 8155	RTT*46 (PAM silencing)
8156	SEQ ID NO: 8156	RTT*46 (PAM silencing)
8157	SEQ ID NO: 8157	RTT*48 (PAM silencing)
8158	SEQ ID NO: 8158	RTT*54 (PAM silencing)
8159	SEQ ID NO: 8159	RTT*53 (PAM silencing)
8160	SEQ ID NO: 8160	RTT*50 (PAM silencing)
8161	SEQ ID NO: 8161	RTT*49 (PAM silencing)
8162	SEQ ID NO: 8162	RTT
8163	SEQ ID NO: 8163	RTT*51 (PAM silencing)
8164	SEQ ID NO: 8164	RTT*47 (PAM silencing)
8165	SEQ ID NO: 8165	RTT*52 (PAM silencing)
8166	SEQ ID NO: 8166	RTT*53 (PAM silencing)
8167	SEQ ID NO: 8167	RTT*46 (PAM silencing)
8168	SEQ ID NO: 8168	RTT*50 (PAM silencing)
8169	SEQ ID NO: 8169	RTT*51 (PAM silencing)
8170	SEQ ID NO: 8170	RTT*49 (PAM silencing)
8171	SEQ ID NO: 8171	RTT
8172	SEQ ID NO: 8172	RTT*54 (PAM silencing)
8173	SEQ ID NO: 8173	RTT*47 (PAM silencing)
8174	SEQ ID NO: 8174	RTT*52 (PAM silencing)
8175	SEQ ID NO: 8175	RTT*48 (PAM silencing)
8176	SEQ ID NO: 8176	RTT*50 (PAM silencing)
8177	SEQ ID NO: 8177	RTT*53 (PAM silencing)
8178	SEQ ID NO: 8178	RTT
8179	SEQ ID NO: 8179	RTT*48 (PAM silencing)
8180	SEQ ID NO: 8180	RTT*51 (PAM silencing)
8181	SEQ ID NO: 8181	RTT*46 (PAM silencing)
8182	SEQ ID NO: 8182	RTT*52 (PAM silencing)
8183	SEQ ID NO: 8183	RTT*47 (PAM silencing)
8184	SEQ ID NO: 8184	RTT*54 (PAM silencing)
8185	SEQ ID NO: 8185	RTT*49 (PAM silencing)
8186	SEQ ID NO: 8186	RTT*49 (PAM silencing)
8187	SEQ ID NO: 8187	RTT*47 (PAM silencing)
8188	SEQ ID NO: 8188	RTT*46 (PAM silencing)
8189	SEQ ID NO: 8189	RTT*53 (PAM silencing)
8190	SEQ ID NO: 8190	RTT*48 (PAM silencing)
8191	SEQ ID NO: 8191	RTT*54 (PAM silencing)
8192	SEQ ID NO: 8192	RTT*52 (PAM silencing)
8193	SEQ ID NO: 8193	RTT
8194	SEQ ID NO: 8194	RTT*50 (PAM silencing)
8195	SEQ ID NO: 8195	RTT*51 (PAM silencing)
8196	SEQ ID NO: 8196	RTT*46 (PAM silencing)
8197	SEQ ID NO: 8197	RTT*50 (PAM silencing)
8198	SEQ ID NO: 8198	RTT*49 (PAM silencing)
8199	SEQ ID NO: 8199	RTT*54 (PAM silencing)
8200	SEQ ID NO: 8200	RTT*48 (PAM silencing)
8201	SEQ ID NO: 8201	RTT
8202	SEQ ID NO: 8202	RTT*47 (PAM silencing)
8203	SEQ ID NO: 8203	RTT*53 (PAM silencing)
8204	SEQ ID NO: 8204	RTT*52 (PAM silencing)
8205	SEQ ID NO: 8205	RTT*51 (PAM silencing)
8206	SEQ ID NO: 8206	RTT
8207	SEQ ID NO: 8207	RTT*49 (PAM silencing)
8208	SEQ ID NO: 8208	RTT*46 (PAM silencing)
8209	SEQ ID NO: 8209	RTT*54 (PAM silencing)
8210	SEQ ID NO: 8210	RTT*52 (PAM silencing)
8211	SEQ ID NO: 8211	RTT*48 (PAM silencing)

Sequence Number	Sequence	Description
8212	SEQ ID NO: 8212	RTT*51 (PAM silencing)
8213	SEQ ID NO: 8213	RTT*47 (PAM silencing)
8214	SEQ ID NO: 8214	RTT*50 (PAM silencing)
8215	SEQ ID NO: 8215	RTT*53 (PAM silencing)
8216	SEQ ID NO: 8216	RTT
8217	SEQ ID NO: 8217	RTT*50 (PAM silencing)
8218	SEQ ID NO: 8218	RTT*47 (PAM silencing)
8219	SEQ ID NO: 8219	RTT*49 (PAM silencing)
8220	SEQ ID NO: 8220	RTT*52 (PAM silencing)
8221	SEQ ID NO: 8221	RTT*54 (PAM silencing)
8222	SEQ ID NO: 8222	RTT*51 (PAM silencing)
8223	SEQ ID NO: 8223	RTT*48 (PAM silencing)
8224	SEQ ID NO: 8224	RTT*46 (PAM silencing)
8225	SEQ ID NO: 8225	RTT*53 (PAM silencing)
8226	SEQ ID NO: 8226	RTT*53 (PAM silencing)
8227	SEQ ID NO: 8227	RTT*52 (PAM silencing)
8228	SEQ ID NO: 8228	RTT*47 (PAM silencing)
8229	SEQ ID NO: 8229	RTT*50 (PAM silencing)
8230	SEQ ID NO: 8230	RTT*46 (PAM silencing)
8231	SEQ ID NO: 8231	RTT*54 (PAM silencing)
8232	SEQ ID NO: 8232	RTT*49 (PAM silencing)
8233	SEQ ID NO: 8233	RTT
8234	SEQ ID NO: 8234	RTT*51 (PAM silencing)
8235	SEQ ID NO: 8235	RTT*48 (PAM silencing)
8236	SEQ ID NO: 8236	RTT*52 (PAM silencing)
8237	SEQ ID NO: 8237	RTT*51 (PAM silencing)
8238	SEQ ID NO: 8238	RTT
8239	SEQ ID NO: 8239	RTT*46 (PAM silencing)
8240	SEQ ID NO: 8240	RTT*54 (PAM silencing)
8241	SEQ ID NO: 8241	RTT*49 (PAM silencing)
8242	SEQ ID NO: 8242	RTT*50 (PAM silencing)
8243	SEQ ID NO: 8243	RTT*48 (PAM silencing)
8244	SEQ ID NO: 8244	RTT*53 (PAM silencing)
8245	SEQ ID NO: 8245	RTT*47 (PAM silencing)
8246	SEQ ID NO: 8246	RTT
8247	SEQ ID NO: 8247	RTT*48 (PAM silencing)
8248	SEQ ID NO: 8248	RTT*46 (PAM silencing)
8249	SEQ ID NO: 8249	RTT*50 (PAM silencing)
8250	SEQ ID NO: 8250	RTT*49 (PAM silencing)
8251	SEQ ID NO: 8251	RTT*51 (PAM silencing)
8252	SEQ ID NO: 8252	RTT*52 (PAM silencing)
8253	SEQ ID NO: 8253	RTT*53 (PAM silencing)
8254	SEQ ID NO: 8254	RTT*47 (PAM silencing)
8255	SEQ ID NO: 8255	RTT*54 (PAM silencing)
8256	SEQ ID NO: 8256	RTT*46 (PAM silencing)
8257	SEQ ID NO: 8257	RTT*48 (PAM silencing)
8258	SEQ ID NO: 8258	RTT*49 (PAM silencing)
8259	SEQ ID NO: 8259	RTT*47 (PAM silencing)
8260	SEQ ID NO: 8260	RTT*50 (PAM silencing)
8261	SEQ ID NO: 8261	RTT*52 (PAM silencing)
8262	SEQ ID NO: 8262	RTT
8263	SEQ ID NO: 8263	RTT*54 (PAM silencing)
8264	SEQ ID NO: 8264	RTT*51 (PAM silencing)
8265	SEQ ID NO: 8265	RTT*53 (PAM silencing)
8266	SEQ ID NO: 8266	RTT*54 (PAM silencing)
8267	SEQ ID NO: 8267	RTT*53 (PAM silencing)
8268	SEQ ID NO: 8268	RTT*46 (PAM silencing)
8269	SEQ ID NO: 8269	RTT*50 (PAM silencing)
8270	SEQ ID NO: 8270	RTT*52 (PAM silencing)
8271	SEQ ID NO: 8271	RTT
8272	SEQ ID NO: 8272	RTT*48 (PAM silencing)
8273	SEQ ID NO: 8273	RTT*47 (PAM silencing)
8274	SEQ ID NO: 8274	RTT*49 (PAM silencing)
8275	SEQ ID NO: 8275	RTT*51 (PAM silencing)
8276	SEQ ID NO: 8276	RTT*54 (PAM silencing)
8277	SEQ ID NO: 8277	RTT*46 (PAM silencing)
8278	SEQ ID NO: 8278	RTT*53 (PAM silencing)
8279	SEQ ID NO: 8279	RTT*51 (PAM silencing)
8280	SEQ ID NO: 8280	RTT*48 (PAM silencing)

Sequence Number	Sequence	Description
8281	SEQ ID NO: 8281	RTT*49 (PAM silencing)
8282	SEQ ID NO: 8282	RTT*47 (PAM silencing)
8283	SEQ ID NO: 8283	RTT
8284	SEQ ID NO: 8284	RTT*50 (PAM silencing)
8285	SEQ ID NO: 8285	RTT*52 (PAM silencing)
8286	SEQ ID NO: 8286	RTT*46 (PAM silencing)
8287	SEQ ID NO: 8287	RTT*53 (PAM silencing)
8288	SEQ ID NO: 8288	RTT*47 (PAM silencing)
8289	SEQ ID NO: 8289	RTT*52 (PAM silencing)
8290	SEQ ID NO: 8290	RTT*48 (PAM silencing)
8291	SEQ ID NO: 8291	RTT*50 (PAM silencing)
8292	SEQ ID NO: 8292	RTT*49 (PAM silencing)
8293	SEQ ID NO: 8293	RTT*54 (PAM silencing)
8294	SEQ ID NO: 8294	RTT
8295	SEQ ID NO: 8295	RTT*51 (PAM silencing)
8296	SEQ ID NO: 8296	RTT*54 (PAM silencing)
8297	SEQ ID NO: 8297	RTT*47 (PAM silencing)
8298	SEQ ID NO: 8298	RTT*52 (PAM silencing)
8299	SEQ ID NO: 8299	RTT*46 (PAM silencing)
8300	SEQ ID NO: 8300	RTT*48 (PAM silencing)
8301	SEQ ID NO: 8301	RTT*53 (PAM silencing)
8302	SEQ ID NO: 8302	RTT*49 (PAM silencing)
8303	SEQ ID NO: 8303	RTT*50 (PAM silencing)
8304	SEQ ID NO: 8304	RTT*51 (PAM silencing)
8305	SEQ ID NO: 8305	RTT
8306	SEQ ID NO: 8306	RTT
8307	SEQ ID NO: 8307	RTT*48 (PAM silencing)
8308	SEQ ID NO: 8308	RTT*52 (PAM silencing)
8309	SEQ ID NO: 8309	RTT*54 (PAM silencing)
8310	SEQ ID NO: 8310	RTT*51 (PAM silencing)
8311	SEQ ID NO: 8311	RTT*47 (PAM silencing)
8312	SEQ ID NO: 8312	RTT*53 (PAM silencing)
8313	SEQ ID NO: 8313	RTT*46 (PAM silencing)
8314	SEQ ID NO: 8314	RTT*50 (PAM silencing)
8315	SEQ ID NO: 8315	RTT*49 (PAM silencing)
8316	SEQ ID NO: 8316	RTT*47 (PAM silencing)
8317	SEQ ID NO: 8317	RTT*52 (PAM silencing)
8318	SEQ ID NO: 8318	RTT*46 (PAM silencing)
8319	SEQ ID NO: 8319	RTT*53 (PAM silencing)
8320	SEQ ID NO: 8320	RTT*50 (PAM silencing)
8321	SEQ ID NO: 8321	RTT
8322	SEQ ID NO: 8322	RTT*51 (PAM silencing)
8323	SEQ ID NO: 8323	RTT*48 (PAM silencing)
8324	SEQ ID NO: 8324	RTT*54 (PAM silencing)
8325	SEQ ID NO: 8325	RTT*49 (PAM silencing)
8326	SEQ ID NO: 8326	RTT*50 (PAM silencing)
8327	SEQ ID NO: 8327	RTT*53 (PAM silencing)
8328	SEQ ID NO: 8328	RTT*51 (PAM silencing)
8329	SEQ ID NO: 8329	RTT*52 (PAM silencing)
8330	SEQ ID NO: 8330	RTT*46 (PAM silencing)
8331	SEQ ID NO: 8331	RTT*49 (PAM silencing)
8332	SEQ ID NO: 8332	RTT*48 (PAM silencing)
8333	SEQ ID NO: 8333	RTT*54 (PAM silencing)
8334	SEQ ID NO: 8334	RTT*47 (PAM silencing)
8335	SEQ ID NO: 8335	RTT
8336	SEQ ID NO: 8336	RTT*48 (PAM silencing)
8337	SEQ ID NO: 8337	RTT*47 (PAM silencing)
8338	SEQ ID NO: 8338	RTT*53 (PAM silencing)
8339	SEQ ID NO: 8339	RTT*46 (PAM silencing)
8340	SEQ ID NO: 8340	RTT
8341	SEQ ID NO: 8341	RTT*54 (PAM silencing)
8342	SEQ ID NO: 8342	RTT*49 (PAM silencing)
8343	SEQ ID NO: 8343	RTT*52 (PAM silencing)
8344	SEQ ID NO: 8344	RTT*51 (PAM silencing)
8345	SEQ ID NO: 8345	RTT*50 (PAM silencing)
8346	SEQ ID NO: 8346	RTT*50 (PAM silencing)
8347	SEQ ID NO: 8347	RTT*46 (PAM silencing)
8348	SEQ ID NO: 8348	RTT*51 (PAM silencing)
8349	SEQ ID NO: 8349	RTT*47 (PAM silencing)

Sequence Number	Sequence	Description
8350	SEQ ID NO: 8350	RTT*49 (PAM silencing)
8351	SEQ ID NO: 8351	RTT*52 (PAM silencing)
8352	SEQ ID NO: 8352	RTT*54 (PAM silencing)
8353	SEQ ID NO: 8353	RTT
8354	SEQ ID NO: 8354	RTT*48 (PAM silencing)
8355	SEQ ID NO: 8355	RTT*53 (PAM silencing)
8356	SEQ ID NO: 8356	RTT*54 (PAM silencing)
8357	SEQ ID NO: 8357	RTT*47 (PAM silencing)
8358	SEQ ID NO: 8358	RTT*52 (PAM silencing)
8359	SEQ ID NO: 8359	RTT*48 (PAM silencing)
8360	SEQ ID NO: 8360	RTT*46 (PAM silencing)
8361	SEQ ID NO: 8361	RTT*51 (PAM silencing)
8362	SEQ ID NO: 8362	RTT
8363	SEQ ID NO: 8363	RTT*49 (PAM silencing)
8364	SEQ ID NO: 8364	RTT*50 (PAM silencing)
8365	SEQ ID NO: 8365	RTT*53 (PAM silencing)
8366	SEQ ID NO: 8366	PE3b*46 ngRNA spacer (AAG PAM)
8367	SEQ ID NO: 8367	PE3b*48 ngRNA spacer (CAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAG PAM)
8368	SEQ ID NO: 8368	PE3b*52 ngRNA spacer (AAG PAM)
8369	SEQ ID NO: 8369	PE3b*48 ngRNA spacer (AAG PAM)
8370	SEQ ID NO: 8370	PE3b*51 ngRNA spacer (AAG PAM)
8371	SEQ ID NO: 8371	PE3b*50 ngRNA spacer (AAG PAM)
8372	SEQ ID NO: 8372	PE3b*49 ngRNA spacer (AAG PAM)
8373	SEQ ID NO: 8373	PE3 ngRNA spacer (GAG PAM)
8374	SEQ ID NO: 8374	PE3 ngRNA spacer (GAG PAM)
8375	SEQ ID NO: 8375	PE3b*53 ngRNA spacer (AAG PAM)
8376	SEQ ID NO: 8376	PE3 ngRNA spacer (GAG PAM)
8377	SEQ ID NO: 8377	PE3 ngRNA spacer (GAG PAM)
8378	SEQ ID NO: 8378	PE3b*54 ngRNA spacer (AAG PAM)
8379	SEQ ID NO: 8379	PE3b*48 ngRNA spacer (CAG PAM)
8380	SEQ ID NO: 8380	PE3 ngRNA spacer (AAG PAM)
8381	SEQ ID NO: 8381	PE3b*47 ngRNA spacer (AAG PAM)

Table 43

Sequence Number	Sequence	Description
8382	SEQ ID NO: 8382	PEgRNA spacer (CAG PAM)
8383	SEQ ID NO: 8383	PEgRNA spacer (CAG PAM)
8384	SEQ ID NO: 8384	PEgRNA spacer (CAG PAM)
8385	SEQ ID NO: 8385	PEgRNA spacer (CAG PAM)
8386	SEQ ID NO: 8386	PEgRNA spacer (CAG PAM)
8387	SEQ ID NO: 8387	PEgRNA spacer (CAG PAM)
8388	SEQ ID NO: 8388	PEgRNA spacer (CAG PAM)
5929	CAC	PBS
8389	CACT	PBS
8390	CACTT	PBS
8391	CACTTG	PBS
8392	CACTTG G	PBS
8393	CACTTG GC	PBS
8394	CACTTG GCA	PBS
8395	SEQ ID NO: 8395	PBS
8396	SEQ ID NO: 8396	PBS
8397	SEQ ID NO: 8397	PBS
8398	SEQ ID NO: 8398	PBS
8399	SEQ ID NO: 8399	PBS
8400	SEQ ID NO: 8400	PBS
8401	SEQ ID NO: 8401	PBS
8402	SEQ ID NO: 8402	PBS

Sequence Number	Sequence	Description
8403	SEQ ID NO: 8403	PBS
8404	SEQ ID NO: 8404	PBS
8405	SEQ ID NO: 8405	RTT*55 (PAM silencing)
8406	SEQ ID NO: 8406	RTT
8407	SEQ ID NO: 8407	RTT*56 (PAM silencing)
8408	SEQ ID NO: 8408	RTT*56 (PAM silencing)
8409	SEQ ID NO: 8409	RTT
8410	SEQ ID NO: 8410	RTT*55 (PAM silencing)
8411	SEQ ID NO: 8411	RTT*56 (PAM silencing)
8412	SEQ ID NO: 8412	RTT
8413	SEQ ID NO: 8413	RTT*55 (PAM silencing)
8414	SEQ ID NO: 8414	RTT*55 (PAM silencing)
8415	SEQ ID NO: 8415	RTT*56 (PAM silencing)
8416	SEQ ID NO: 8416	RTT
8417	SEQ ID NO: 8417	RTT
8418	SEQ ID NO: 8418	RTT*55 (PAM silencing)
8419	SEQ ID NO: 8419	RTT*56 (PAM silencing)
8420	SEQ ID NO: 8420	RTT*56 (PAM silencing)
8421	SEQ ID NO: 8421	RTT
8422	SEQ ID NO: 8422	RTT*55 (PAM silencing)
8423	SEQ ID NO: 8423	RTT*55 (PAM silencing)
8424	SEQ ID NO: 8424	RTT*56 (PAM silencing)
8425	SEQ ID NO: 8425	RTT
8426	SEQ ID NO: 8426	RTT*55 (PAM silencing)
8427	SEQ ID NO: 8427	RTT
8428	SEQ ID NO: 8428	RTT*56 (PAM silencing)
8429	SEQ ID NO: 8429	RTT*56 (PAM silencing)
8430	SEQ ID NO: 8430	RTT
8431	SEQ ID NO: 8431	RTT*55 (PAM silencing)
8432	SEQ ID NO: 8432	RTT
8433	SEQ ID NO: 8433	RTT*55 (PAM silencing)
8434	SEQ ID NO: 8434	RTT*56 (PAM silencing)
8435	SEQ ID NO: 8435	RTT*55 (PAM silencing)
8436	SEQ ID NO: 8436	RTT
8437	SEQ ID NO: 8437	RTT*56 (PAM silencing)
8438	SEQ ID NO: 8438	RTT
8439	SEQ ID NO: 8439	RTT*56 (PAM silencing)
8440	SEQ ID NO: 8440	RTT*55 (PAM silencing)
8441	SEQ ID NO: 8441	RTT
8442	SEQ ID NO: 8442	RTT*56 (PAM silencing)
8443	SEQ ID NO: 8443	RTT*55 (PAM silencing)
8444	SEQ ID NO: 8444	RTT*55 (PAM silencing)
8445	SEQ ID NO: 8445	RTT
8446	SEQ ID NO: 8446	RTT*56 (PAM silencing)
8447	SEQ ID NO: 8447	RTT*55 (PAM silencing)
8448	SEQ ID NO: 8448	RTT*56 (PAM silencing)
8449	SEQ ID NO: 8449	RTT
8450	SEQ ID NO: 8450	RTT*56 (PAM silencing)
8451	SEQ ID NO: 8451	RTT*55 (PAM silencing)
8452	SEQ ID NO: 8452	RTT
8453	SEQ ID NO: 8453	RTT*55 (PAM silencing)
8454	SEQ ID NO: 8454	RTT*56 (PAM silencing)
8455	SEQ ID NO: 8455	RTT
8456	SEQ ID NO: 8456	RTT*55 (PAM silencing)
8457	SEQ ID NO: 8457	RTT
8458	SEQ ID NO: 8458	RTT*56 (PAM silencing)
8459	SEQ ID NO: 8459	RTT*56 (PAM silencing)
8460	SEQ ID NO: 8460	RTT
8461	SEQ ID NO: 8461	RTT*55 (PAM silencing)
8462	SEQ ID NO: 8462	RTT*56 (PAM silencing)
8463	SEQ ID NO: 8463	RTT*55 (PAM silencing)
8464	SEQ ID NO: 8464	RTT
8465	SEQ ID NO: 8465	RTT
8466	SEQ ID NO: 8466	RTT*56 (PAM silencing)
8467	SEQ ID NO: 8467	RTT*55 (PAM silencing)
8468	SEQ ID NO: 8468	RTT*56 (PAM silencing)
8469	SEQ ID NO: 8469	RTT
8470	SEQ ID NO: 8470	RTT*55 (PAM silencing)
8471	SEQ ID NO: 8471	RTT*55 (PAM silencing)
8472	SEQ ID NO: 8472	RTT*56 (PAM silencing)
8473	SEQ ID NO: 8473	RTT
8474	SEQ ID NO: 8474	RTT*55 (PAM silencing)
8475	SEQ ID NO: 8475	RTT
8476	SEQ ID NO: 8476	RTT*56 (PAM silencing)
8477	SEQ ID NO: 8477	RTT*55 (PAM silencing)

Sequence Number	Sequence	Description
8478	SEQ ID NO: 8478	RTT*56 (PAM silencing)
8479	SEQ ID NO: 8479	RTT
8480	SEQ ID NO: 8480	RTT*55 (PAM silencing)
8481	SEQ ID NO: 8481	RTT*56 (PAM silencing)
8482	SEQ ID NO: 8482	RTT
8483	SEQ ID NO: 8483	RTT*56 (PAM silencing)
8484	SEQ ID NO: 8484	RTT*55 (PAM silencing)
8485	SEQ ID NO: 8485	RTT
8486	SEQ ID NO: 8486	RTT*55 (PAM silencing)
8487	SEQ ID NO: 8487	RTT
8488	SEQ ID NO: 8488	RTT*56 (PAM silencing)
8489	SEQ ID NO: 8489	RTT*55 (PAM silencing)
8490	SEQ ID NO: 8490	RTT*56 (PAM silencing)
8491	SEQ ID NO: 8491	RTT
8492	SEQ ID NO: 8492	RTT*56 (PAM silencing)
8493	SEQ ID NO: 8493	RTT*55 (PAM silencing)
8494	SEQ ID NO: 8494	RTT
8495	SEQ ID NO: 8495	RTT*56 (PAM silencing)
8496	SEQ ID NO: 8496	RTT
8497	SEQ ID NO: 8497	RTT*55 (PAM silencing)
8498	SEQ ID NO: 8498	RTT*55 (PAM silencing)
8499	SEQ ID NO: 8499	RTT
8500	SEQ ID NO: 8500	RTT*56 (PAM silencing)
8501	SEQ ID NO: 8501	RTT*56 (PAM silencing)
8502	SEQ ID NO: 8502	RTT
8503	SEQ ID NO: 8503	RTT*55 (PAM silencing)
8504	SEQ ID NO: 8504	RTT*55 (PAM silencing)
8505	SEQ ID NO: 8505	RTT*56 (PAM silencing)
8506	SEQ ID NO: 8506	RTT
8507	SEQ ID NO: 8507	RTT*55 (PAM silencing)
8508	SEQ ID NO: 8508	RTT*56 (PAM silencing)
8509	SEQ ID NO: 8509	RTT
8510	SEQ ID NO: 8510	RTT
8511	SEQ ID NO: 8511	RTT*55 (PAM silencing)
8512	SEQ ID NO: 8512	RTT*56 (PAM silencing)
8513	SEQ ID NO: 8513	RTT*55 (PAM silencing)
8514	SEQ ID NO: 8514	RTT
8515	SEQ ID NO: 8515	RTT*56 (PAM silencing)
8516	SEQ ID NO: 8516	RTT*56 (PAM silencing)
8517	SEQ ID NO: 8517	RTT
8518	SEQ ID NO: 8518	RTT*55 (PAM silencing)
8519	SEQ ID NO: 8519	RTT*55 (PAM silencing)
8520	SEQ ID NO: 8520	RTT
8521	SEQ ID NO: 8521	RTT*56 (PAM silencing)
8522	SEQ ID NO: 8522	RTT
8523	SEQ ID NO: 8523	RTT*55 (PAM silencing)
8524	SEQ ID NO: 8524	RTT*56 (PAM silencing)
8525	SEQ ID NO: 8525	RTT*55 (PAM silencing)
8526	SEQ ID NO: 8526	RTT*56 (PAM silencing)
8527	SEQ ID NO: 8527	RTT
8528	SEQ ID NO: 8528	RTT*55 (PAM silencing)
8529	SEQ ID NO: 8529	RTT*56 (PAM silencing)
8530	SEQ ID NO: 8530	RTT
8531	SEQ ID NO: 8531	RTT*56 (PAM silencing)
8532	SEQ ID NO: 8532	RTT*55 (PAM silencing)
8533	SEQ ID NO: 8533	RTT
8534	SEQ ID NO: 8534	RTT*56 (PAM silencing)
8535	SEQ ID NO: 8535	RTT*55 (PAM silencing)
8536	SEQ ID NO: 8536	RTT
8537	SEQ ID NO: 8537	RTT*55 (PAM silencing)
8538	SEQ ID NO: 8538	RTT
8539	SEQ ID NO: 8539	RTT*56 (PAM silencing)
8540	SEQ ID NO: 8540	RTT*55 (PAM silencing)
8541	SEQ ID NO: 8541	RTT
8542	SEQ ID NO: 8542	RTT*56 (PAM silencing)
8543	SEQ ID NO: 8543	RTT*55 (PAM silencing)
8544	SEQ ID NO: 8544	RTT
8545	SEQ ID NO: 8545	RTT*56 (PAM silencing)
8546	SEQ ID NO: 8546	RTT*56 (PAM silencing)
8547	SEQ ID NO: 8547	RTT
8548	SEQ ID NO: 8548	RTT*55 (PAM silencing)
8549	SEQ ID NO: 8549	RTT*56 (PAM silencing)
8550	SEQ ID NO: 8550	RTT
8551	SEQ ID NO: 8551	RTT*55 (PAM silencing)
8552	SEQ ID NO: 8552	RTT*56 (PAM silencing)

Sequence Number	Sequence	Description
8553	SEQ ID NO: 8553	RTT
8554	SEQ ID NO: 8554	RTT*55 (PAM silencing)
8555	SEQ ID NO: 8555	RTT
8556	SEQ ID NO: 8556	RTT*56 (PAM silencing)
8557	SEQ ID NO: 8557	RTT*55 (PAM silencing)
8558	SEQ ID NO: 8558	RTT*56 (PAM silencing)
8559	SEQ ID NO: 8559	RTT
8560	SEQ ID NO: 8560	RTT*55 (PAM silencing)
8561	SEQ ID NO: 8561	RTT*56 (PAM silencing)
8562	SEQ ID NO: 8562	RTT*55 (PAM silencing)
8563	SEQ ID NO: 8563	RTT
8564	SEQ ID NO: 8564	RTT
8565	SEQ ID NO: 8565	RTT*56 (PAM silencing)
8566	SEQ ID NO: 8566	RTT*55 (PAM silencing)
8567	SEQ ID NO: 8567	RTT
8568	SEQ ID NO: 8568	RTT*56 (PAM silencing)
8569	SEQ ID NO: 8569	RTT*55 (PAM silencing)
8570	SEQ ID NO: 8570	RTT*55 (PAM silencing)
8571	SEQ ID NO: 8571	RTT
8572	SEQ ID NO: 8572	RTT*56 (PAM silencing)
8573	SEQ ID NO: 8573	RTT*55 (PAM silencing)
8574	SEQ ID NO: 8574	RTT*56 (PAM silencing)
8575	SEQ ID NO: 8575	RTT
8576	SEQ ID NO: 8576	RTT
8577	SEQ ID NO: 8577	RTT*55 (PAM silencing)
8578	SEQ ID NO: 8578	RTT*56 (PAM silencing)
8579	SEQ ID NO: 8579	RTT*56 (PAM silencing)
8580	SEQ ID NO: 8580	RTT
8581	SEQ ID NO: 8581	RTT*55 (PAM silencing)
8582	SEQ ID NO: 8582	RTT*56 (PAM silencing)
8583	SEQ ID NO: 8583	RTT
8584	SEQ ID NO: 8584	RTT*55 (PAM silencing)
8585	SEQ ID NO: 8585	RTT
8586	SEQ ID NO: 8586	RTT*55 (PAM silencing)
8587	SEQ ID NO: 8587	RTT*56 (PAM silencing)
8588	SEQ ID NO: 8588	RTT*55 (PAM silencing)
8589	SEQ ID NO: 8589	RTT*56 (PAM silencing)
8590	SEQ ID NO: 8590	RTT
8591	SEQ ID NO: 8591	RTT*55 (PAM silencing)
8592	SEQ ID NO: 8592	RTT
8593	SEQ ID NO: 8593	RTT*56 (PAM silencing)
8594	SEQ ID NO: 8594	RTT*55 (PAM silencing)
8595	SEQ ID NO: 8595	RTT*56 (PAM silencing)
8596	SEQ ID NO: 8596	RTT
8597	SEQ ID NO: 8597	RTT
8598	SEQ ID NO: 8598	RTT*55 (PAM silencing)
8599	SEQ ID NO: 8599	RTT*56 (PAM silencing)
8600	SEQ ID NO: 8600	RTT*56 (PAM silencing)
8601	SEQ ID NO: 8601	RTT*55 (PAM silencing)
8602	SEQ ID NO: 8602	RTT
8603	SEQ ID NO: 8603	RTT*56 (PAM silencing)
8604	SEQ ID NO: 8604	RTT*55 (PAM silencing)
8605	SEQ ID NO: 8605	RTT
8606	SEQ ID NO: 8606	RTT
8607	SEQ ID NO: 8607	RTT*56 (PAM silencing)
8608	SEQ ID NO: 8608	RTT*55 (PAM silencing)
8609	SEQ ID NO: 8609	RTT*56 (PAM silencing)
8610	SEQ ID NO: 8610	RTT*55 (PAM silencing)
8611	SEQ ID NO: 8611	RTT
8612	SEQ ID NO: 8612	RTT*56 (PAM silencing)
8613	SEQ ID NO: 8613	RTT
8614	SEQ ID NO: 8614	RTT*55 (PAM silencing)
8615	SEQ ID NO: 8615	RTT*55 (PAM silencing)
8616	SEQ ID NO: 8616	RTT*56 (PAM silencing)
8617	SEQ ID NO: 8617	RTT
8618	SEQ ID NO: 8618	RTT*56 (PAM silencing)
8619	SEQ ID NO: 8619	RTT
8620	SEQ ID NO: 8620	RTT*55 (PAM silencing)
8621	SEQ ID NO: 8621	RTT
8622	SEQ ID NO: 8622	RTT*56 (PAM silencing)
8623	SEQ ID NO: 8623	RTT*55 (PAM silencing)
8624	SEQ ID NO: 8624	RTT*56 (PAM silencing)
8625	SEQ ID NO: 8625	RTT*55 (PAM silencing)
8626	SEQ ID NO: 8626	RTT
8627	SEQ ID NO: 8627	RTT

Sequence Number	Sequence	Description
8628	SEQ ID NO: 8628	RTT*55 (PAM silencing)
8629	SEQ ID NO: 8629	RTT*56 (PAM silencing)
8630	SEQ ID NO: 8630	RTT
8631	SEQ ID NO: 8631	RTT*56 (PAM silencing)
8632	SEQ ID NO: 8632	RTT*55 (PAM silencing)
8633	SEQ ID NO: 8633	RTT*55 (PAM silencing)
8634	SEQ ID NO: 8634	RTT*56 (PAM silencing)
8635	SEQ ID NO: 8635	RTT
8636	SEQ ID NO: 8636	RTT*55 (PAM silencing)
8637	SEQ ID NO: 8637	RTT
8638	SEQ ID NO: 8638	RTT*56 (PAM silencing)
8639	SEQ ID NO: 8639	RTT
8640	SEQ ID NO: 8640	RTT*56 (PAM silencing)
8641	SEQ ID NO: 8641	RTT*55 (PAM silencing)
8642	SEQ ID NO: 8642	RTT*56 (PAM silencing)
8643	SEQ ID NO: 8643	RTT
8644	SEQ ID NO: 8644	RTT*55 (PAM silencing)
8645	SEQ ID NO: 8645	RTT*56 (PAM silencing)
8646	SEQ ID NO: 8646	RTT
8647	SEQ ID NO: 8647	RTT*55 (PAM silencing)
8648	SEQ ID NO: 8648	RTT*55 (PAM silencing)
8649	SEQ ID NO: 8649	RTT
8650	SEQ ID NO: 8650	RTT*56 (PAM silencing)
8651	SEQ ID NO: 8651	RTT
8652	SEQ ID NO: 8652	RTT*56 (PAM silencing)
8653	SEQ ID NO: 8653	RTT*55 (PAM silencing)
8654	SEQ ID NO: 8654	RTT*56 (PAM silencing)
8655	SEQ ID NO: 8655	RTT
8656	SEQ ID NO: 8656	RTT*55 (PAM silencing)
8657	SEQ ID NO: 8657	RTT
8658	SEQ ID NO: 8658	RTT*55 (PAM silencing)
8659	SEQ ID NO: 8659	RTT*56 (PAM silencing)
8660	SEQ ID NO: 8660	RTT*55 (PAM silencing)
8661	SEQ ID NO: 8661	RTT
8662	SEQ ID NO: 8662	RTT*56 (PAM silencing)
8663	SEQ ID NO: 8663	RTT*56 (PAM silencing)
8664	SEQ ID NO: 8664	RTT
8665	SEQ ID NO: 8665	RTT*55 (PAM silencing)
8666	SEQ ID NO: 8666	RTT*56 (PAM silencing)
8667	SEQ ID NO: 8667	RTT*55 (PAM silencing)
8668	SEQ ID NO: 8668	RTT
8669	SEQ ID NO: 8669	RTT
8670	SEQ ID NO: 8670	RTT*56 (PAM silencing)
8671	SEQ ID NO: 8671	RTT*55 (PAM silencing)
8672	SEQ ID NO: 8672	RTT
8673	SEQ ID NO: 8673	RTT*55 (PAM silencing)
8674	SEQ ID NO: 8674	RTT*56 (PAM silencing)
8377	SEQ ID NO: 8377	PE3 ngRNA spacer (GAG PAM)
8380	SEQ ID NO: 8380	PE3 ngRNA spacer (AAG PAM)
8376	SEQ ID NO: 8376	PE3 ngRNA spacer (GAG PAM)
8675	SEQ ID NO: 8675	PE3b*55 ngRNA spacer (AAG PAM)
8373	SEQ ID NO: 8373	PE3 ngRNA spacer (GAG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG PAM)
8374	SEQ ID NO: 8374	PE3 ngRNA spacer (GAG PAM)

Table 44

Sequence Number	Sequence	Description
8676	SEQ ID NO: 8676	PEgRNA spacer (CAG;CAGG PAM)
8677	SEQ ID NO: 8677	PEgRNA spacer (CAG;CAGG PAM)
8678	SEQ ID NO: 8678	PEgRNA spacer (CAG;CAGG PAM)
8679	SEQ ID NO: 8679	PEgRNA spacer (CAG;CAGG PAM)
8680	SEQ ID NO: 8680	PEgRNA spacer (CAG;CAGG PAM)
8681	SEQ ID NO: 8681	PEgRNA spacer (CAG;CAGG PAM)
8682	SEQ ID NO: 8682	PEgRNA spacer (CAG;CAGG PAM)
7167	CTG	PBS
8683	CTGG	PBS
8684	CTGGA	PBS

Sequence Number	Sequence	Description
8685	CTGGAA	PBS
8686	CTGGAA C	PBS
8687	CTGGAA CA	PBS
8688	CTGGAA CAC	PBS
8689	SEQ ID NO: 8689	PBS
8690	SEQ ID NO: 8690	PBS
8691	SEQ ID NO: 8691	PBS
8692	SEQ ID NO: 8692	PBS
8693	SEQ ID NO: 8693	PBS
8694	SEQ ID NO: 8694	PBS
8695	SEQ ID NO: 8695	PBS
8696	SEQ ID NO: 8696	PBS
8697	SEQ ID NO: 8697	PBS
8698	SEQ ID NO: 8698	PBS
8699	SEQ ID NO: 8699	RTT*64 (PAM silencing)
8700	SEQ ID NO: 8700	RTT*66 (PAM silencing)
8701	SEQ ID NO: 8701	RTT*60 (PAM silencing)
8702	SEQ ID NO: 8702	RTT*67 (PAM silencing)
8703	SEQ ID NO: 8703	RTT*61 (PAM silencing)
8704	SEQ ID NO: 8704	RTT*63 (PAM silencing)
8705	SEQ ID NO: 8705	RTT*58 (PAM silencing)
8706	SEQ ID NO: 8706	RTT*62 (PAM silencing)
8707	SEQ ID NO: 8707	RTT*65 (PAM silencing)
8708	SEQ ID NO: 8708	RTT*59 (PAM silencing)
8709	SEQ ID NO: 8709	RTT*57 (PAM silencing)
8710	SEQ ID NO: 8710	RTT
8711	SEQ ID NO: 8711	RTT*59 (PAM silencing)
8712	SEQ ID NO: 8712	RTT*64 (PAM silencing)
8713	SEQ ID NO: 8713	RTT*58 (PAM silencing)
8714	SEQ ID NO: 8714	RTT*66 (PAM silencing)
8715	SEQ ID NO: 8715	RTT*67 (PAM silencing)
8716	SEQ ID NO: 8716	RTT*65 (PAM silencing)
8717	SEQ ID NO: 8717	RTT*63 (PAM silencing)
8718	SEQ ID NO: 8718	RTT
8719	SEQ ID NO: 8719	RTT*60 (PAM silencing)
8720	SEQ ID NO: 8720	RTT*61 (PAM silencing)
8721	SEQ ID NO: 8721	RTT*62 (PAM silencing)
8722	SEQ ID NO: 8722	RTT*57 (PAM silencing)
8723	SEQ ID NO: 8723	RTT*57 (PAM silencing)
8724	SEQ ID NO: 8724	RTT*67 (PAM silencing)
8725	SEQ ID NO: 8725	RTT*58 (PAM silencing)
8726	SEQ ID NO: 8726	RTT*66 (PAM silencing)
8727	SEQ ID NO: 8727	RTT*65 (PAM silencing)
8728	SEQ ID NO: 8728	RTT*62 (PAM silencing)
8729	SEQ ID NO: 8729	RTT*64 (PAM silencing)
8730	SEQ ID NO: 8730	RTT
8731	SEQ ID NO: 8731	RTT*60 (PAM silencing)
8732	SEQ ID NO: 8732	RTT*61 (PAM silencing)
8733	SEQ ID NO: 8733	RTT*59 (PAM silencing)
8734	SEQ ID NO: 8734	RTT*63 (PAM silencing)
8735	SEQ ID NO: 8735	RTT*61 (PAM silencing)
8736	SEQ ID NO: 8736	RTT*65 (PAM silencing)
8737	SEQ ID NO: 8737	RTT*62 (PAM silencing)
8738	SEQ ID NO: 8738	RTT*58 (PAM silencing)
8739	SEQ ID NO: 8739	RTT*60 (PAM silencing)
8740	SEQ ID NO: 8740	RTT*64 (PAM silencing)
8741	SEQ ID NO: 8741	RTT*63 (PAM silencing)
8742	SEQ ID NO: 8742	RTT*57 (PAM silencing)
8743	SEQ ID NO: 8743	RTT
8744	SEQ ID NO: 8744	RTT*59 (PAM silencing)
8745	SEQ ID NO: 8745	RTT*66 (PAM silencing)
8746	SEQ ID NO: 8746	RTT*67 (PAM silencing)
8747	SEQ ID NO: 8747	RTT*61 (PAM silencing)
8748	SEQ ID NO: 8748	RTT*65 (PAM silencing)
8749	SEQ ID NO: 8749	RTT*57 (PAM silencing)
8750	SEQ ID NO: 8750	RTT*58 (PAM silencing)
8751	SEQ ID NO: 8751	RTT*62 (PAM silencing)
8752	SEQ ID NO: 8752	RTT
8753	SEQ ID NO: 8753	RTT*66 (PAM silencing)
8754	SEQ ID NO: 8754	RTT*60 (PAM silencing)
8755	SEQ ID NO: 8755	RTT*63 (PAM silencing)
8756	SEQ ID NO: 8756	RTT*59 (PAM silencing)
8757	SEQ ID NO: 8757	RTT*67 (PAM silencing)

Sequence Number	Sequence	Description
8758	SEQ ID NO: 8758	RTT*64 (PAM silencing)
8759	SEQ ID NO: 8759	RTT*62 (PAM silencing)
8760	SEQ ID NO: 8760	RTT*64 (PAM silencing)
8761	SEQ ID NO: 8761	RTT*57 (PAM silencing)
8762	SEQ ID NO: 8762	RTT*67 (PAM silencing)
8763	SEQ ID NO: 8763	RTT*66 (PAM silencing)
8764	SEQ ID NO: 8764	RTT
8765	SEQ ID NO: 8765	RTT*60 (PAM silencing)
8766	SEQ ID NO: 8766	RTT*61 (PAM silencing)
8767	SEQ ID NO: 8767	RTT*58 (PAM silencing)
8769	SEQ ID NO: 8769	RTT*65 (PAM silencing)
8770	SEQ ID NO: 8770	RTT*63 (PAM silencing)
8771	SEQ ID NO: 8771	RTT*65 (PAM silencing)
8772	SEQ ID NO: 8772	RTT*60 (PAM silencing)
8773	SEQ ID NO: 8773	RTT*58 (PAM silencing)
8774	SEQ ID NO: 8774	RTT*59 (PAM silencing)
8775	SEQ ID NO: 8775	RTT*61 (PAM silencing)
8776	SEQ ID NO: 8776	RTT*67 (PAM silencing)
8777	SEQ ID NO: 8777	RTT*63 (PAM silencing)
8778	SEQ ID NO: 8778	RTT*57 (PAM silencing)
8779	SEQ ID NO: 8779	RTT*62 (PAM silencing)
8780	SEQ ID NO: 8780	RTT
8781	SEQ ID NO: 8781	RTT*64 (PAM silencing)
8782	SEQ ID NO: 8782	RTT*66 (PAM silencing)
8783	SEQ ID NO: 8783	RTT*59 (PAM silencing)
8784	SEQ ID NO: 8784	RTT*63 (PAM silencing)
8785	SEQ ID NO: 8785	RTT*66 (PAM silencing)
8786	SEQ ID NO: 8786	RTT*65 (PAM silencing)
8787	SEQ ID NO: 8787	RTT*67 (PAM silencing)
8788	SEQ ID NO: 8788	RTT*61 (PAM silencing)
8789	SEQ ID NO: 8789	RTT*64 (PAM silencing)
8790	SEQ ID NO: 8790	RTT*62 (PAM silencing)
8791	SEQ ID NO: 8791	RTT*58 (PAM silencing)
8792	SEQ ID NO: 8792	RTT*60 (PAM silencing)
8793	SEQ ID NO: 8793	RTT*57 (PAM silencing)
8794	SEQ ID NO: 8794	RTT
8795	SEQ ID NO: 8795	RTT*64 (PAM silencing)
8796	SEQ ID NO: 8796	RTT
8797	SEQ ID NO: 8797	RTT*60 (PAM silencing)
8798	SEQ ID NO: 8798	RTT*62 (PAM silencing)
8799	SEQ ID NO: 8799	RTT*65 (PAM silencing)
8800	SEQ ID NO: 8800	RTT*59 (PAM silencing)
8801	SEQ ID NO: 8801	RTT*66 (PAM silencing)
8802	SEQ ID NO: 8802	RTT*67 (PAM silencing)
8803	SEQ ID NO: 8803	RTT*63 (PAM silencing)
8804	SEQ ID NO: 8804	RTT*58 (PAM silencing)
8805	SEQ ID NO: 8805	RTT*61 (PAM silencing)
8806	SEQ ID NO: 8806	RTT*57 (PAM silencing)
8807	SEQ ID NO: 8807	RTT*64 (PAM silencing)
8808	SEQ ID NO: 8808	RTT*63 (PAM silencing)
8809	SEQ ID NO: 8809	RTT*67 (PAM silencing)
8810	SEQ ID NO: 8810	RTT*59 (PAM silencing)
8811	SEQ ID NO: 8811	RTT*62 (PAM silencing)
8812	SEQ ID NO: 8812	RTT*66 (PAM silencing)
8813	SEQ ID NO: 8813	RTT*60 (PAM silencing)
8814	SEQ ID NO: 8814	RTT*58 (PAM silencing)
8815	SEQ ID NO: 8815	RTT
8816	SEQ ID NO: 8816	RTT*61 (PAM silencing)
8817	SEQ ID NO: 8817	RTT*57 (PAM silencing)
8818	SEQ ID NO: 8818	RTT*65 (PAM silencing)
8819	SEQ ID NO: 8819	RTT*59 (PAM silencing)
8820	SEQ ID NO: 8820	RTT*58 (PAM silencing)
8821	SEQ ID NO: 8821	RTT*66 (PAM silencing)
8822	SEQ ID NO: 8822	RTT*63 (PAM silencing)
8823	SEQ ID NO: 8823	RTT*65 (PAM silencing)
8824	SEQ ID NO: 8824	RTT*61 (PAM silencing)
8825	SEQ ID NO: 8825	RTT*60 (PAM silencing)
8826	SEQ ID NO: 8826	RTT*67 (PAM silencing)

Sequence Number	Sequence	Description
8827	SEQ ID NO: 8827	RTT*64 (PAM silencing)
8828	SEQ ID NO: 8828	RTT
8829	SEQ ID NO: 8829	RTT*62 (PAM silencing)
8830	SEQ ID NO: 8830	RTT*57 (PAM silencing)
8831	SEQ ID NO: 8831	RTT*61 (PAM silencing)
8832	SEQ ID NO: 8832	RTT*66 (PAM silencing)
8833	SEQ ID NO: 8833	RTT*62 (PAM silencing)
8834	SEQ ID NO: 8834	RTT*63 (PAM silencing)
8835	SEQ ID NO: 8835	RTT*59 (PAM silencing)
8836	SEQ ID NO: 8836	RTT*57 (PAM silencing)
8837	SEQ ID NO: 8837	RTT*64 (PAM silencing)
8838	SEQ ID NO: 8838	RTT*65 (PAM silencing)
8839	SEQ ID NO: 8839	RTT*58 (PAM silencing)
8840	SEQ ID NO: 8840	RTT
8841	SEQ ID NO: 8841	RTT*67 (PAM silencing)
8842	SEQ ID NO: 8842	RTT*60 (PAM silencing)
8843	SEQ ID NO: 8843	RTT*61 (PAM silencing)
8844	SEQ ID NO: 8844	RTT*60 (PAM silencing)
8845	SEQ ID NO: 8845	RTT*63 (PAM silencing)
8846	SEQ ID NO: 8846	RTT*59 (PAM silencing)
8847	SEQ ID NO: 8847	RTT*67 (PAM silencing)
8848	SEQ ID NO: 8848	RTT*66 (PAM silencing)
8849	SEQ ID NO: 8849	RTT*64 (PAM silencing)
8850	SEQ ID NO: 8850	RTT
8851	SEQ ID NO: 8851	RTT*65 (PAM silencing)
8852	SEQ ID NO: 8852	RTT*57 (PAM silencing)
8853	SEQ ID NO: 8853	RTT*58 (PAM silencing)
8854	SEQ ID NO: 8854	RTT*62 (PAM silencing)
8855	SEQ ID NO: 8855	RTT*57 (PAM silencing)
8856	SEQ ID NO: 8856	RTT*61 (PAM silencing)
8857	SEQ ID NO: 8857	RTT
8858	SEQ ID NO: 8858	RTT*62 (PAM silencing)
8859	SEQ ID NO: 8859	RTT*58 (PAM silencing)
8860	SEQ ID NO: 8860	RTT*64 (PAM silencing)
8861	SEQ ID NO: 8861	RTT*65 (PAM silencing)
8862	SEQ ID NO: 8862	RTT*63 (PAM silencing)
8863	SEQ ID NO: 8863	RTT*67 (PAM silencing)
8864	SEQ ID NO: 8864	RTT*60 (PAM silencing)
8865	SEQ ID NO: 8865	RTT*66 (PAM silencing)
8866	SEQ ID NO: 8866	RTT*59 (PAM silencing)
8867	SEQ ID NO: 8867	RTT*64 (PAM silencing)
8868	SEQ ID NO: 8868	RTT*66 (PAM silencing)
8869	SEQ ID NO: 8869	RTT*62 (PAM silencing)
8870	SEQ ID NO: 8870	RTT*67 (PAM silencing)
8871	SEQ ID NO: 8871	RTT*63 (PAM silencing)
8872	SEQ ID NO: 8872	RTT*57 (PAM silencing)
8873	SEQ ID NO: 8873	RTT*59 (PAM silencing)
8874	SEQ ID NO: 8874	RTT
8875	SEQ ID NO: 8875	RTT*65 (PAM silencing)
8876	SEQ ID NO: 8876	RTT*61 (PAM silencing)
8877	SEQ ID NO: 8877	RTT*58 (PAM silencing)
8878	SEQ ID NO: 8878	RTT*60 (PAM silencing)
8879	SEQ ID NO: 8879	RTT*57 (PAM silencing)
8880	SEQ ID NO: 8880	RTT*63 (PAM silencing)
8881	SEQ ID NO: 8881	RTT*59 (PAM silencing)
8882	SEQ ID NO: 8882	RTT*62 (PAM silencing)
8883	SEQ ID NO: 8883	RTT
8884	SEQ ID NO: 8884	RTT*58 (PAM silencing)
8885	SEQ ID NO: 8885	RTT*61 (PAM silencing)
8886	SEQ ID NO: 8886	RTT*66 (PAM silencing)
8887	SEQ ID NO: 8887	RTT*60 (PAM silencing)
8888	SEQ ID NO: 8888	RTT*67 (PAM silencing)
8889	SEQ ID NO: 8889	RTT*65 (PAM silencing)
8890	SEQ ID NO: 8890	RTT*64 (PAM silencing)
8891	SEQ ID NO: 8891	RTT*67 (PAM silencing)
8892	SEQ ID NO: 8892	RTT*59 (PAM silencing)
8893	SEQ ID NO: 8893	RTT
8894	SEQ ID NO: 8894	RTT*66 (PAM silencing)
8895	SEQ ID NO: 8895	RTT*58 (PAM silencing)

Sequence Number	Sequence	Description
8896	SEQ ID NO: 8896	RTT*60 (PAM silencing)
8897	SEQ ID NO: 8897	RTT*64 (PAM silencing)
8898	SEQ ID NO: 8898	RTT*65 (PAM silencing)
8899	SEQ ID NO: 8899	RTT*61 (PAM silencing)
8900	SEQ ID NO: 8900	RTT*62 (PAM silencing)
8901	SEQ ID NO: 8901	RTT*57 (PAM silencing)
8902	SEQ ID NO: 8902	RTT*63 (PAM silencing)
8903	SEQ ID NO: 8903	RTT*60 (PAM silencing)
8904	SEQ ID NO: 8904	RTT*66 (PAM silencing)
8905	SEQ ID NO: 8905	RTT*63 (PAM silencing)
8906	SEQ ID NO: 8906	RTT*65 (PAM silencing)
8907	SEQ ID NO: 8907	RTT*59 (PAM silencing)
8908	SEQ ID NO: 8908	RTT*67 (PAM silencing)
8909	SEQ ID NO: 8909	RTT*58 (PAM silencing)
8910	SEQ ID NO: 8910	RTT
8911	SEQ ID NO: 8911	RTT*64 (PAM silencing)
8912	SEQ ID NO: 8912	RTT*61 (PAM silencing)
8913	SEQ ID NO: 8913	RTT*57 (PAM silencing)
8914	SEQ ID NO: 8914	RTT*62 (PAM silencing)
8915	SEQ ID NO: 8915	RTT*67 (PAM silencing)
8916	SEQ ID NO: 8916	RTT*61 (PAM silencing)
8917	SEQ ID NO: 8917	RTT*62 (PAM silencing)
8918	SEQ ID NO: 8918	RTT

Sequence Number	Sequence	Description
8919	SEQ ID NO: 8919	RTT*58 (PAM silencing)
8920	SEQ ID NO: 8920	RTT*60 (PAM silencing)
8921	SEQ ID NO: 8921	RTT*66 (PAM silencing)
8922	SEQ ID NO: 8922	RTT*65 (PAM silencing)
8923	SEQ ID NO: 8923	RTT*64 (PAM silencing)
8924	SEQ ID NO: 8924	RTT*57 (PAM silencing)
8925	SEQ ID NO: 8925	RTT*59 (PAM silencing)
8926	SEQ ID NO: 8926	RTT*63 (PAM silencing)
8927	SEQ ID NO: 8927	RTT*65 (PAM silencing)
8928	SEQ ID NO: 8928	RTT*64 (PAM silencing)
8929	SEQ ID NO: 8929	RTT*67 (PAM silencing)
8930	SEQ ID NO: 8930	RTT*66 (PAM silencing)
8931	SEQ ID NO: 8931	RTT*58 (PAM silencing)
8932	SEQ ID NO: 8932	RTT*59 (PAM silencing)
8933	SEQ ID NO: 8933	RTT*63 (PAM silencing)
8934	SEQ ID NO: 8934	RTT*60 (PAM silencing)
8935	SEQ ID NO: 8935	RTT
8936	SEQ ID NO: 8936	RTT*61 (PAM silencing)
8937	SEQ ID NO: 8937	RTT*62 (PAM silencing)
8938	SEQ ID NO: 8938	RTT*57 (PAM silencing)
8939	SEQ ID NO: 8939	RTT*58 (PAM silencing)
8940	SEQ ID NO: 8940	RTT*63 (PAM silencing)

Sequence Number	Sequence	Description
8941	SEQ ID NO: 8941	RTT*57 (PAM silencing)
8942	SEQ ID NO: 8942	RTT*64 (PAM silencing)
8943	SEQ ID NO: 8943	RTT*66 (PAM silencing)
8944	SEQ ID NO: 8944	RTT*62 (PAM silencing)
8945	SEQ ID NO: 8945	RTT*65 (PAM silencing)
8946	SEQ ID NO: 8946	RTT
8947	SEQ ID NO: 8947	RTT*61 (PAM silencing)
8948	SEQ ID NO: 8948	RTT*67 (PAM silencing)
8949	SEQ ID NO: 8949	RTT*60 (PAM silencing)
8950	SEQ ID NO: 8950	RTT*59 (PAM silencing)
8951	SEQ ID NO: 8951	RTT*62 (PAM silencing)
8952	SEQ ID NO: 8952	RTT*61 (PAM silencing)
8953	SEQ ID NO: 8953	RTT*58 (PAM silencing)
8954	SEQ ID NO: 8954	RTT*59 (PAM silencing)
8955	SEQ ID NO: 8955	RTT*64 (PAM silencing)
8956	SEQ ID NO: 8956	RTT*60 (PAM silencing)
8957	SEQ ID NO: 8957	RTT*67 (PAM silencing)
8958	SEQ ID NO: 8958	RTT
8959	SEQ ID NO: 8959	RTT*65 (PAM silencing)
8960	SEQ ID NO: 8960	RTT*63 (PAM silencing)
8961	SEQ ID NO: 8961	RTT*57 (PAM silencing)
8962	SEQ ID NO: 8962	RTT*66 (PAM silencing)
8963	SEQ ID NO: 8963	RTT*59 (PAM silencing)

Sequence Number	Sequence	Description
8964	SEQ ID NO: 8964	RTT
8965	SEQ ID NO: 8965	RTT*58 (PAM silencing)
8966	SEQ ID NO: 8966	RTT*62 (PAM silencing)
8967	SEQ ID NO: 8967	RTT*65 (PAM silencing)
8968	SEQ ID NO: 8968	RTT*63 (PAM silencing)
8969	SEQ ID NO: 8969	RTT*57 (PAM silencing)
8970	SEQ ID NO: 8970	RTT*60 (PAM silencing)
8971	SEQ ID NO: 8971	RTT*66 (PAM silencing)
8972	SEQ ID NO: 8972	RTT*64 (PAM silencing)
8973	SEQ ID NO: 8973	RTT*67 (PAM silencing)
8974	SEQ ID NO: 8974	RTT*61 (PAM silencing)
8975	SEQ ID NO: 8975	RTT*67 (PAM silencing)
8976	SEQ ID NO: 8976	RTT*66 (PAM silencing)
8977	SEQ ID NO: 8977	RTT*58 (PAM silencing)
8978	SEQ ID NO: 8978	RTT*64 (PAM silencing)
8979	SEQ ID NO: 8979	RTT
8980	SEQ ID NO: 8980	RTT*63 (PAM silencing)
8981	SEQ ID NO: 8981	RTT*65 (PAM silencing)
8982	SEQ ID NO: 8982	RTT*59 (PAM silencing)
8983	SEQ ID NO: 8983	RTT*57 (PAM silencing)
8984	SEQ ID NO: 8984	RTT*61 (PAM silencing)
8985	SEQ ID NO: 8985	RTT*62 (PAM silencing)
8986	SEQ ID NO: 8986	RTT*60 (PAM silencing)
8987	SEQ ID NO: 8987	RTT*59 (PAM silencing)
8988	SEQ ID NO: 8988	RTT*64 (PAM silencing)
8989	SEQ ID NO: 8989	RTT*61 (PAM silencing)
8990	SEQ ID NO: 8990	RTT*62 (PAM silencing)
8991	SEQ ID NO: 8991	RTT*58 (PAM silencing)
8992	SEQ ID NO: 8992	RTT*66 (PAM silencing)
8993	SEQ ID NO: 8993	RTT
8994	SEQ ID NO: 8994	RTT*60 (PAM silencing)
8995	SEQ ID NO: 8995	RTT*63 (PAM silencing)
8996	SEQ ID NO: 8996	RTT*67 (PAM silencing)
8997	SEQ ID NO: 8997	RTT*65 (PAM silencing)
8998	SEQ ID NO: 8998	RTT*57 (PAM silencing)
8999	SEQ ID NO: 8999	RTT*61 (PAM silencing)
9000	SEQ ID NO: 9000	RTT*57 (PAM silencing)
9001	SEQ ID NO: 9001	RTT*59 (PAM silencing)
9002	SEQ ID NO: 9002	RTT*60 (PAM silencing)
9003	SEQ ID NO: 9003	RTT*63 (PAM silencing)
9004	SEQ ID NO: 9004	RTT*66 (PAM silencing)
9005	SEQ ID NO: 9005	RTT*58 (PAM silencing)
9006	SEQ ID NO: 9006	RTT*67 (PAM silencing)
9007	SEQ ID NO: 9007	RTT
9008	SEQ ID NO: 9008	RTT*64 (PAM silencing)
9009	SEQ ID NO: 9009	RTT*65 (PAM silencing)
9010	SEQ ID NO: 9010	RTT*62 (PAM silencing)
9011	SEQ ID NO: 9011	RTT*65 (PAM silencing)
9012	SEQ ID NO: 9012	RTT*60 (PAM silencing)
9013	SEQ ID NO: 9013	RTT*66 (PAM silencing)
9014	SEQ ID NO: 9014	RTT*63 (PAM silencing)
9015	SEQ ID NO: 9015	RTT
9016	SEQ ID NO: 9016	RTT*59 (PAM silencing)
9017	SEQ ID NO: 9017	RTT*64 (PAM silencing)
9018	SEQ ID NO: 9018	RTT*57 (PAM silencing)
9019	SEQ ID NO: 9019	RTT*67 (PAM silencing)
9020	SEQ ID NO: 9020	RTT*58 (PAM silencing)
9021	SEQ ID NO: 9021	RTT*61 (PAM silencing)
9022	SEQ ID NO: 9022	RTT*62 (PAM silencing)
9023	SEQ ID NO: 9023	RTT*58 (PAM silencing)
9024	SEQ ID NO: 9024	RTT*66 (PAM silencing)
9025	SEQ ID NO: 9025	RTT*67 (PAM silencing)
9026	SEQ ID NO: 9026	RTT*64 (PAM silencing)
9027	SEQ ID NO: 9027	RTT*62 (PAM silencing)
9028	SEQ ID NO: 9028	RTT*59 (PAM silencing)
9029	SEQ ID NO: 9029	RTT*60 (PAM silencing)
9030	SEQ ID NO: 9030	RTT*65 (PAM silencing)
9031	SEQ ID NO: 9031	RTT*63 (PAM silencing)

Sequence Number	Sequence	Description
9032	SEQ ID NO: 9032	RTT*61 (PAM silencing)
9033	SEQ ID NO: 9033	RTT
9034	SEQ ID NO: 9034	RTT*57 (PAM silencing)
9035	SEQ ID NO: 9035	RTT*58 (PAM silencing)
9036	SEQ ID NO: 9036	RTT*67 (PAM silencing)
9037	SEQ ID NO: 9037	RTT*66 (PAM silencing)
9038	SEQ ID NO: 9038	RTT*59 (PAM silencing)
9039	SEQ ID NO: 9039	RTT*62 (PAM silencing)
9040	SEQ ID NO: 9040	RTT*63 (PAM silencing)
9041	SEQ ID NO: 9041	RTT*64 (PAM silencing)
9042	SEQ ID NO: 9042	RTT*61 (PAM silencing)
9043	SEQ ID NO: 9043	RTT*65 (PAM silencing)
9044	SEQ ID NO: 9044	RTT*57 (PAM silencing)
9045	SEQ ID NO: 9045	RTT
9046	SEQ ID NO: 9046	RTT*60 (PAM silencing)
9047	SEQ ID NO: 9047	RTT*64 (PAM silencing)
9048	SEQ ID NO: 9048	RTT
9049	SEQ ID NO: 9049	RTT*60 (PAM silencing)
9050	SEQ ID NO: 9050	RTT*63 (PAM silencing)
9051	SEQ ID NO: 9051	RTT*66 (PAM silencing)
9052	SEQ ID NO: 9052	RTT*67 (PAM silencing)
9053	SEQ ID NO: 9053	RTT*62 (PAM silencing)
9054	SEQ ID NO: 9054	RTT*59 (PAM silencing)
9055	SEQ ID NO: 9055	RTT*61 (PAM silencing)
9056	SEQ ID NO: 9056	RTT*58 (PAM silencing)
9057	SEQ ID NO: 9057	RTT*57 (PAM silencing)
9058	SEQ ID NO: 9058	RTT*65 (PAM silencing)
9059	SEQ ID NO: 9059	RTT*64 (PAM silencing)
9060	SEQ ID NO: 9060	RTT
9061	SEQ ID NO: 9061	RTT*57 (PAM silencing)
9062	SEQ ID NO: 9062	RTT*62 (PAM silencing)
9063	SEQ ID NO: 9063	RTT*59 (PAM silencing)
9064	SEQ ID NO: 9064	RTT*63 (PAM silencing)
9065	SEQ ID NO: 9065	RTT*61 (PAM silencing)
9066	SEQ ID NO: 9066	RTT*67 (PAM silencing)
9067	SEQ ID NO: 9067	RTT*65 (PAM silencing)
9068	SEQ ID NO: 9068	RTT*58 (PAM silencing)
9069	SEQ ID NO: 9069	RTT*60 (PAM silencing)
9070	SEQ ID NO: 9070	RTT*66 (PAM silencing)
9071	SEQ ID NO: 9071	RTT*58 (PAM silencing)
9072	SEQ ID NO: 9072	RTT*66 (PAM silencing)
9073	SEQ ID NO: 9073	RTT
9074	SEQ ID NO: 9074	RTT*60 (PAM silencing)
9075	SEQ ID NO: 9075	RTT*64 (PAM silencing)
9076	SEQ ID NO: 9076	RTT*63 (PAM silencing)
9077	SEQ ID NO: 9077	RTT*57 (PAM silencing)
9078	SEQ ID NO: 9078	RTT*62 (PAM silencing)
9079	SEQ ID NO: 9079	RTT*65 (PAM silencing)
9080	SEQ ID NO: 9080	RTT*59 (PAM silencing)
9081	SEQ ID NO: 9081	RTT*67 (PAM silencing)
9082	SEQ ID NO: 9082	RTT*61 (PAM silencing)
9083	SEQ ID NO: 9083	RTT*57 (PAM silencing)
9084	SEQ ID NO: 9084	RTT*64 (PAM silencing)
9085	SEQ ID NO: 9085	RTT*59 (PAM silencing)
9086	SEQ ID NO: 9086	RTT*67 (PAM silencing)
9087	SEQ ID NO: 9087	RTT*66 (PAM silencing)
9088	SEQ ID NO: 9088	RTT*58 (PAM silencing)
9089	SEQ ID NO: 9089	RTT*65 (PAM silencing)
9090	SEQ ID NO: 9090	RTT*61 (PAM silencing)
9091	SEQ ID NO: 9091	RTT*63 (PAM silencing)
9092	SEQ ID NO: 9092	RTT
9093	SEQ ID NO: 9093	RTT*60 (PAM silencing)
9094	SEQ ID NO: 9094	RTT*62 (PAM silencing)
9095	SEQ ID NO: 9095	RTT
9096	SEQ ID NO: 9096	RTT*66 (PAM silencing)
9097	SEQ ID NO: 9097	RTT*62 (PAM silencing)
9098	SEQ ID NO: 9098	RTT*60 (PAM silencing)
9099	SEQ ID NO: 9099	RTT*64 (PAM silencing)
9100	SEQ ID NO: 9100	RTT*67 (PAM silencing)

Sequence Number	Sequence	Description
9101	SEQ ID NO: 9101	RTT*63 (PAM silencing)
9102	SEQ ID NO: 9102	RTT*59 (PAM silencing)
9103	SEQ ID NO: 9103	RTT*58 (PAM silencing)
9104	SEQ ID NO: 9104	RTT*61 (PAM silencing)
9105	SEQ ID NO: 9105	RTT*65 (PAM silencing)
9106	SEQ ID NO: 9106	RTT*57 (PAM silencing)
9107	SEQ ID NO: 9107	RTT*62 (PAM silencing)
9108	SEQ ID NO: 9108	RTT
9109	SEQ ID NO: 9109	RTT*66 (PAM silencing)
9110	SEQ ID NO: 9110	RTT*61 (PAM silencing)
9111	SEQ ID NO: 9111	RTT*67 (PAM silencing)
9112	SEQ ID NO: 9112	RTT*59 (PAM silencing)
9113	SEQ ID NO: 9113	RTT*65 (PAM silencing)
9114	SEQ ID NO: 9114	RTT*63 (PAM silencing)
9115	SEQ ID NO: 9115	RTT*64 (PAM silencing)
9116	SEQ ID NO: 9116	RTT*57 (PAM silencing)
9117	SEQ ID NO: 9117	RTT*58 (PAM silencing)
9118	SEQ ID NO: 9118	RTT*60 (PAM silencing)
9119	SEQ ID NO: 9119	RTT*59 (PAM silencing)
9120	SEQ ID NO: 9120	RTT*65 (PAM silencing)
9121	SEQ ID NO: 9121	RTT*61 (PAM silencing)
9122	SEQ ID NO: 9122	RTT*62 (PAM silencing)
9123	SEQ ID NO: 9123	RTT*63 (PAM silencing)
9124	SEQ ID NO: 9124	RTT
9125	SEQ ID NO: 9125	RTT*57 (PAM silencing)
9126	SEQ ID NO: 9126	RTT*67 (PAM silencing)
9127	SEQ ID NO: 9127	RTT*58 (PAM silencing)
9128	SEQ ID NO: 9128	RTT*64 (PAM silencing)
9129	SEQ ID NO: 9129	RTT*60 (PAM silencing)
9130	SEQ ID NO: 9130	RTT*66 (PAM silencing)
9131	SEQ ID NO: 9131	RTT*62 (PAM silencing)
9132	SEQ ID NO: 9132	RTT*64 (PAM silencing)
9133	SEQ ID NO: 9133	RTT*67 (PAM silencing)
9134	SEQ ID NO: 9134	RTT*59 (PAM silencing)
9135	SEQ ID NO: 9135	RTT*65 (PAM silencing)
9136	SEQ ID NO: 9136	RTT
9137	SEQ ID NO: 9137	RTT*58 (PAM silencing)
9138	SEQ ID NO: 9138	RTT*63 (PAM silencing)
9139	SEQ ID NO: 9139	RTT*66 (PAM silencing)
9140	SEQ ID NO: 9140	RTT*61 (PAM silencing)
9141	SEQ ID NO: 9141	RTT*60 (PAM silencing)
9142	SEQ ID NO: 9142	RTT*57 (PAM silencing)
9143	SEQ ID NO: 9143	RTT*62 (PAM silencing)
9144	SEQ ID NO: 9144	RTT
9145	SEQ ID NO: 9145	RTT*67 (PAM silencing)
9146	SEQ ID NO: 9146	RTT*64 (PAM silencing)
9147	SEQ ID NO: 9147	RTT*60 (PAM silencing)
9148	SEQ ID NO: 9148	RTT*61 (PAM silencing)
9149	SEQ ID NO: 9149	RTT*63 (PAM silencing)
9150	SEQ ID NO: 9150	RTT*65 (PAM silencing)
9151	SEQ ID NO: 9151	RTT*57 (PAM silencing)
9152	SEQ ID NO: 9152	RTT*59 (PAM silencing)
9153	SEQ ID NO: 9153	RTT*58 (PAM silencing)
9154	SEQ ID NO: 9154	RTT*66 (PAM silencing)
9155	SEQ ID NO: 9155	RTT*60 (PAM silencing)
9156	SEQ ID NO: 9156	RTT*63 (PAM silencing)
9157	SEQ ID NO: 9157	RTT*61 (PAM silencing)
9158	SEQ ID NO: 9158	RTT*59 (PAM silencing)
9159	SEQ ID NO: 9159	RTT*65 (PAM silencing)
9160	SEQ ID NO: 9160	RTT*57 (PAM silencing)
9161	SEQ ID NO: 9161	RTT*67 (PAM silencing)
9162	SEQ ID NO: 9162	RTT*64 (PAM silencing)
9163	SEQ ID NO: 9163	RTT
9164	SEQ ID NO: 9164	RTT*62 (PAM silencing)
9165	SEQ ID NO: 9165	RTT*66 (PAM silencing)
9166	SEQ ID NO: 9166	RTT*58 (PAM silencing)
9167	SEQ ID NO: 9167	RTT*67 (PAM silencing)

Sequence Number	Sequence	Description
9168	SEQ ID NO: 9168	RTT*65 (PAM silencing)
9169	SEQ ID NO: 9169	RTT*57 (PAM silencing)
9170	SEQ ID NO: 9170	RTT*62 (PAM silencing)
9171	SEQ ID NO: 9171	RTT*58 (PAM silencing)
9172	SEQ ID NO: 9172	RTT*66 (PAM silencing)
9173	SEQ ID NO: 9173	RTT*60 (PAM silencing)
9174	SEQ ID NO: 9174	RTT*63 (PAM silencing)
9175	SEQ ID NO: 9175	RTT*64 (PAM silencing)
9176	SEQ ID NO: 9176	RTT*61 (PAM silencing)
9177	SEQ ID NO: 9177	RTT
9178	SEQ ID NO: 9178	RTT*59 (PAM silencing)
9179	SEQ ID NO: 9179	RTT*64 (PAM silencing)
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9185	SEQ ID NO: 9185	RTT*62 (PAM silencing)
9186	SEQ ID NO: 9186	RTT*65 (PAM silencing)
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9189	SEQ ID NO: 9189	RTT*63 (PAM silencing)
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9191	SEQ ID NO: 9191	RTT*63 (PAM silencing)
9192	SEQ ID NO: 9192	RTT*65 (PAM silencing)
9193	SEQ ID NO: 9193	RTT*59 (PAM silencing)
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9195	SEQ ID NO: 9195	RTT*60 (PAM silencing)
9196	SEQ ID NO: 9196	RTT*58 (PAM silencing)
9197	SEQ ID NO: 9197	RTT*57 (PAM silencing)
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9201	SEQ ID NO: 9201	RTT*62 (PAM silencing)
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9204	SEQ ID NO: 9204	RTT*67 (PAM silencing)
9205	SEQ ID NO: 9205	RTT*58 (PAM silencing)
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9209	SEQ ID NO: 9209	RTT*63 (PAM silencing)
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9211	SEQ ID NO: 9211	RTT*65 (PAM silencing)
9212	SEQ ID NO: 9212	RTT*59 (PAM silencing)
9213	SEQ ID NO: 9213	RTT*62 (PAM silencing)
9214	SEQ ID NO: 9214	RTT*61 (PAM silencing)
9215	SEQ ID NO: 9215	RTT*63 (PAM silencing)
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9218	SEQ ID NO: 9218	RTT*65 (PAM silencing)
9219	SEQ ID NO: 9219	RTT*62 (PAM silencing)
9220	SEQ ID NO: 9220	RTT*57 (PAM silencing)
9221	SEQ ID NO: 9221	RTT*60 (PAM silencing)
9222	SEQ ID NO: 9222	RTT*61 (PAM silencing)
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9230	SEQ ID NO: 9230	RTT*58 (PAM silencing)
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9232	SEQ ID NO: 9232	RTT*61 (PAM silencing)
9233	SEQ ID NO: 9233	RTT
9234	SEQ ID NO: 9234	RTT*65 (PAM silencing)
9235	SEQ ID NO: 9235	RTT*66 (PAM silencing)
9236	SEQ ID NO: 9236	RTT*57 (PAM silencing)

Sequence Number	Sequence	Description
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9238	SEQ ID NO: 9238	RTT*62 (PAM silencing)
9239	SEQ ID NO: 9239	RTT*57 (PAM silencing)
9240	SEQ ID NO: 9240	RTT*63 (PAM silencing)
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9242	SEQ ID NO: 9242	RTT*58 (PAM silencing)
9243	SEQ ID NO: 9243	RTT*67 (PAM silencing)
9244	SEQ ID NO: 9244	RTT*59 (PAM silencing)
9245	SEQ ID NO: 9245	RTT*61 (PAM silencing)
9246	SEQ ID NO: 9246	RTT*62 (PAM silencing)
9247	SEQ ID NO: 9247	RTT*60 (PAM silencing)
9248	SEQ ID NO: 9248	RTT*64 (PAM silencing)
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9250	SEQ ID NO: 9250	RTT*65 (PAM silencing)
9251	SEQ ID NO: 9251	RTT*57 (PAM silencing)
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9253	SEQ ID NO: 9253	RTT*63 (PAM silencing)
9254	SEQ ID NO: 9254	RTT*67 (PAM silencing)
9255	SEQ ID NO: 9255	RTT*62 (PAM silencing)
9256	SEQ ID NO: 9256	RTT*58 (PAM silencing)
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9265	SEQ ID NO: 9265	RTT*67 (PAM silencing)
9266	SEQ ID NO: 9266	RTT*57 (PAM silencing)
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9269	SEQ ID NO: 9269	RTT*66 (PAM silencing)
9270	SEQ ID NO: 9270	RTT*58 (PAM silencing)
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9272	SEQ ID NO: 9272	RTT*62 (PAM silencing)
9273	SEQ ID NO: 9273	RTT*61 (PAM silencing)
9274	SEQ ID NO: 9274	RTT*63 (PAM silencing)
9275	SEQ ID NO: 9275	RTT*67 (PAM silencing)
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9277	SEQ ID NO: 9277	RTT*66 (PAM silencing)
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9288	SEQ ID NO: 9288	RTT*59 (PAM silencing)
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9301	SEQ ID NO: 9301	RTT*65 (PAM silencing)
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9303	SEQ ID NO: 9303	RTT*61 (PAM silencing)
9304	SEQ ID NO: 9304	RTT*59 (PAM silencing)
9305	SEQ ID NO: 9305	RTT*64 (PAM silencing)

Sequence Number	Sequence	Description
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9308	SEQ ID NO: 9308	RTT*63 (PAM silencing)
9309	SEQ ID NO: 9309	RTT*62 (PAM silencing)
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9311	SEQ ID NO: 9311	RTT*66 (PAM silencing)
9312	SEQ ID NO: 9312	RTT*65 (PAM silencing)
9313	SEQ ID NO: 9313	RTT*67 (PAM silencing)
9314	SEQ ID NO: 9314	RTT
9315	SEQ ID NO: 9315	RTT*61 (PAM silencing)
9316	SEQ ID NO: 9316	RTT*62 (PAM silencing)
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9330	SEQ ID NO: 9330	RTT*58 (PAM silencing)
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9332	SEQ ID NO: 9332	RTT*64 (PAM silencing)
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9335	SEQ ID NO: 9335	RTT*62 (PAM silencing)
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9343	SEQ ID NO: 9343	RTT*60 (PAM silencing)
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9345	SEQ ID NO: 9345	RTT*61 (PAM silencing)
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9348	SEQ ID NO: 9348	RTT*64 (PAM silencing)
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9352	SEQ ID NO: 9352	RTT*66 (PAM silencing)
9353	SEQ ID NO: 9353	RTT*58 (PAM silencing)
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9369	SEQ ID NO: 9369	RTT
9370	SEQ ID NO: 9370	RTT*60 (PAM silencing)
9371	SEQ ID NO: 9371	RTT*60 (PAM silencing)
9372	SEQ ID NO: 9372	RTT*67 (PAM silencing)
9373	SEQ ID NO: 9373	RTT*64 (PAM silencing)

Sequence Number	Sequence	Description
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9387	SEQ ID NO: 9387	RTT*64 (PAM silencing)
9388	SEQ ID NO: 9388	RTT*58 (PAM silencing)
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9394	SEQ ID NO: 9394	RTT*66 (PAM silencing)
9395	SEQ ID NO: 9395	RTT*67 (PAM silencing)
9396	SEQ ID NO: 9396	RTT*66 (PAM silencing)
9397	SEQ ID NO: 9397	RTT*65 (PAM silencing)
9398	SEQ ID NO: 9398	RTT*58 (PAM silencing)
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9404	SEQ ID NO: 9404	RTT*64 (PAM silencing)
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9406	SEQ ID NO: 9406	RTT*62 (PAM silencing)
9407	SEQ ID NO: 9407	RTT*58 (PAM silencing)
9408	SEQ ID NO: 9408	RTT*67 (PAM silencing)
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9418	SEQ ID NO: 9418	RTT*61 (PAM silencing)
9419	SEQ ID NO: 9419	RTT*61 (PAM silencing)
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9421	SEQ ID NO: 9421	RTT*59 (PAM silencing)
9422	SEQ ID NO: 9422	RTT*67 (PAM silencing)
9423	SEQ ID NO: 9423	RTT*65 (PAM silencing)
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9427	SEQ ID NO: 9427	RTT*63 (PAM silencing)
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9430	SEQ ID NO: 9430	RTT*62 (PAM silencing)
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9432	SEQ ID NO: 9432	RTT*62 (PAM silencing)
9433	SEQ ID NO: 9433	RTT*63 (PAM silencing)
9434	SEQ ID NO: 9434	RTT*65 (PAM silencing)
9435	SEQ ID NO: 9435	RTT
9436	SEQ ID NO: 9436	RTT*57 (PAM silencing)
9437	SEQ ID NO: 9437	RTT*67 (PAM silencing)
9438	SEQ ID NO: 9438	RTT*66 (PAM silencing)
9439	SEQ ID NO: 9439	RTT*58 (PAM silencing)
9440	SEQ ID NO: 9440	RTT*60 (PAM silencing)
9441	SEQ ID NO: 9441	RTT*64 (PAM silencing)
9442	SEQ ID NO: 9442	RTT*61 (PAM silencing)

Sequence Number	Sequence	Description
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9448	SEQ ID NO: 9448	RTT*66 (PAM silencing)
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9450	SEQ ID NO: 9450	RTT*57 (PAM silencing)
9451	SEQ ID NO: 9451	RTT*62 (PAM silencing)
9452	SEQ ID NO: 9452	RTT*63 (PAM silencing)
9453	SEQ ID NO: 9453	RTT*64 (PAM silencing)
9454	SEQ ID NO: 9454	RTT*67 (PAM silencing)
9455	SEQ ID NO: 9455	RTT*60 (PAM silencing)
9456	SEQ ID NO: 9456	RTT*66 (PAM silencing)
9457	SEQ ID NO: 9457	RTT*59 (PAM silencing)
9458	SEQ ID NO: 9458	RTT*58 (PAM silencing)
9459	SEQ ID NO: 9459	RTT*65 (PAM silencing)
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9461	SEQ ID NO: 9461	RTT*64 (PAM silencing)
9462	SEQ ID NO: 9462	RTT*62 (PAM silencing)
9463	SEQ ID NO: 9463	RTT*63 (PAM silencing)
9464	SEQ ID NO: 9464	RTT*57 (PAM silencing)
9465	SEQ ID NO: 9465	RTT*67 (PAM silencing)
9466	SEQ ID NO: 9466	RTT*61 (PAM silencing)
9467	SEQ ID NO: 9467	RTT
9468	SEQ ID NO: 9468	RTT*63 (PAM silencing)
9469	SEQ ID NO: 9469	RTT*67 (PAM silencing)
9470	SEQ ID NO: 9470	RTT*64 (PAM silencing)
9471	SEQ ID NO: 9471	RTT*66 (PAM silencing)
9472	SEQ ID NO: 9472	RTT*58 (PAM silencing)
9473	SEQ ID NO: 9473	RTT*62 (PAM silencing)
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9483	SEQ ID NO: 9483	RTT*62 (PAM silencing)
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9488	SEQ ID NO: 9488	RTT*58 (PAM silencing)
9489	SEQ ID NO: 9489	RTT*66 (PAM silencing)
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9493	SEQ ID NO: 9493	RTT*64 (PAM silencing)
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9495	SEQ ID NO: 9495	RTT*58 (PAM silencing)
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9497	SEQ ID NO: 9497	RTT*65 (PAM silencing)
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9505	SEQ ID NO: 9505	RTT*63 (PAM silencing)
9506	SEQ ID NO: 9506	RTT
9507	SEQ ID NO: 9507	RTT*60 (PAM silencing)
9508	SEQ ID NO: 9508	RTT*62 (PAM silencing)
9509	SEQ ID NO: 9509	RTT*66 (PAM silencing)
9510	SEQ ID NO: 9510	RTT*58 (PAM silencing)
9511	SEQ ID NO: 9511	RTT*59 (PAM silencing)

Sequence Number	Sequence	Description
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9514	SEQ ID NO: 9514	RTT*57 (PAM silencing)
9515	SEQ ID NO: 9515	RTT*60 (PAM silencing)
9516	SEQ ID NO: 9516	RTT*57 (PAM silencing)
9517	SEQ ID NO: 9517	RTT*62 (PAM silencing)
9518	SEQ ID NO: 9518	RTT*61 (PAM silencing)
9519	SEQ ID NO: 9519	RTT
9520	SEQ ID NO: 9520	RTT*67 (PAM silencing)
9521	SEQ ID NO: 9521	RTT*63 (PAM silencing)
9522	SEQ ID NO: 9522	RTT*65 (PAM silencing)
9523	SEQ ID NO: 9523	RTT*64 (PAM silencing)
9524	SEQ ID NO: 9524	RTT*66 (PAM silencing)
9525	SEQ ID NO: 9525	RTT*58 (PAM silencing)
9526	SEQ ID NO: 9526	RTT*59 (PAM silencing)
9527	SEQ ID NO: 9527	RTT*57 (PAM silencing)
9528	SEQ ID NO: 9528	RTT*61 (PAM silencing)
9529	SEQ ID NO: 9529	RTT*58 (PAM silencing)
9530	SEQ ID NO: 9530	RTT*67 (PAM silencing)
9531	SEQ ID NO: 9531	RTT*65 (PAM silencing)
9532	SEQ ID NO: 9532	RTT*66 (PAM silencing)
9533	SEQ ID NO: 9533	RTT*59 (PAM silencing)
9534	SEQ ID NO: 9534	RTT*60 (PAM silencing)
9535	SEQ ID NO: 9535	RTT*62 (PAM silencing)
9536	SEQ ID NO: 9536	RTT*63 (PAM silencing)
9537	SEQ ID NO: 9537	RTT*64 (PAM silencing)
9538	SEQ ID NO: 9538	RTT
9539	SEQ ID NO: 9539	RTT*57 (PAM silencing)
9540	SEQ ID NO: 9540	RTT*64 (PAM silencing)
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9542	SEQ ID NO: 9542	RTT*58 (PAM silencing)
9543	SEQ ID NO: 9543	RTT*65 (PAM silencing)
9544	SEQ ID NO: 9544	RTT*63 (PAM silencing)
9545	SEQ ID NO: 9545	RTT*62 (PAM silencing)
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9556	SEQ ID NO: 9556	RTT*64 (PAM silencing)
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9558	SEQ ID NO: 9558	RTT*66 (PAM silencing)
9559	SEQ ID NO: 9559	RTT*65 (PAM silencing)
9560	SEQ ID NO: 9560	RTT*62 (PAM silencing)
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9562	SEQ ID NO: 9562	RTT
9563	SEQ ID NO: 9563	RTT
9564	SEQ ID NO: 9564	RTT*64 (PAM silencing)
9565	SEQ ID NO: 9565	RTT*67 (PAM silencing)
9566	SEQ ID NO: 9566	RTT*66 (PAM silencing)
9567	SEQ ID NO: 9567	RTT*63 (PAM silencing)
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9569	SEQ ID NO: 9569	RTT*58 (PAM silencing)
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9571	SEQ ID NO: 9571	RTT*62 (PAM silencing)
9572	SEQ ID NO: 9572	RTT*57 (PAM silencing)
9573	SEQ ID NO: 9573	RTT*65 (PAM silencing)
9574	SEQ ID NO: 9574	RTT*60 (PAM silencing)
9575	SEQ ID NO: 9575	RTT*58 (PAM silencing)
9576	SEQ ID NO: 9576	RTT
9577	SEQ ID NO: 9577	RTT*63 (PAM silencing)
9578	SEQ ID NO: 9578	RTT*57 (PAM silencing)
9579	SEQ ID NO: 9579	RTT*61 (PAM silencing)

Sequence Number	Sequence	Description
9580	SEQ ID NO: 9580	RTT*59 (PAM silencing)
9581	SEQ ID NO: 9581	RTT*65 (PAM silencing)
9582	SEQ ID NO: 9582	RTT*64 (PAM silencing)
9583	SEQ ID NO: 9583	RTT*60 (PAM silencing)
9584	SEQ ID NO: 9584	RTT*62 (PAM silencing)
9585	SEQ ID NO: 9585	RTT*66 (PAM silencing)
9586	SEQ ID NO: 9586	RTT*67 (PAM silencing)
9587	SEQ ID NO: 9587	RTT*66 (PAM silencing)
9588	SEQ ID NO: 9588	RTT*64 (PAM silencing)
9589	SEQ ID NO: 9589	RTT*62 (PAM silencing)
9590	SEQ ID NO: 9590	RTT*61 (PAM silencing)
9591	SEQ ID NO: 9591	RTT*65 (PAM silencing)
9592	SEQ ID NO: 9592	RTT*58 (PAM silencing)
9593	SEQ ID NO: 9593	RTT
9594	SEQ ID NO: 9594	RTT*57 (PAM silencing)
9595	SEQ ID NO: 9595	RTT*59 (PAM silencing)
9596	SEQ ID NO: 9596	RTT*60 (PAM silencing)
9597	SEQ ID NO: 9597	RTT*63 (PAM silencing)
9598	SEQ ID NO: 9598	RTT*67 (PAM silencing)
9599	SEQ ID NO: 9599	RTT*62 (PAM silencing)
9600	SEQ ID NO: 9600	RTT*58 (PAM silencing)
9601	SEQ ID NO: 9601	RTT*67 (PAM silencing)
9602	SEQ ID NO: 9602	RTT*57 (PAM silencing)
9603	SEQ ID NO: 9603	RTT*60 (PAM silencing)
9604	SEQ ID NO: 9604	RTT
9605	SEQ ID NO: 9605	RTT*61 (PAM silencing)
9606	SEQ ID NO: 9606	RTT*63 (PAM silencing)
9607	SEQ ID NO: 9607	RTT*65 (PAM silencing)
9608	SEQ ID NO: 9608	RTT*66 (PAM silencing)
9609	SEQ ID NO: 9609	RTT*59 (PAM silencing)
9610	SEQ ID NO: 9610	RTT*64 (PAM silencing)
9611	SEQ ID NO: 9611	RTT
9612	SEQ ID NO: 9612	RTT*59 (PAM silencing)
9613	SEQ ID NO: 9613	RTT*67 (PAM silencing)
9614	SEQ ID NO: 9614	RTT*63 (PAM silencing)
9615	SEQ ID NO: 9615	RTT*66 (PAM silencing)
9616	SEQ ID NO: 9616	RTT*65 (PAM silencing)
9617	SEQ ID NO: 9617	RTT*60 (PAM silencing)
9618	SEQ ID NO: 9618	RTT*64 (PAM silencing)
9619	SEQ ID NO: 9619	RTT*62 (PAM silencing)
9620	SEQ ID NO: 9620	RTT*61 (PAM silencing)
9621	SEQ ID NO: 9621	RTT*57 (PAM silencing)
9622	SEQ ID NO: 9622	RTT*58 (PAM silencing)
9623	SEQ ID NO: 9623	RTT*64 (PAM silencing)
9624	SEQ ID NO: 9624	RTT*66 (PAM silencing)
9625	SEQ ID NO: 9625	RTT*67 (PAM silencing)
9626	SEQ ID NO: 9626	RTT*62 (PAM silencing)
9627	SEQ ID NO: 9627	RTT*59 (PAM silencing)
9628	SEQ ID NO: 9628	RTT*57 (PAM silencing)
9629	SEQ ID NO: 9629	RTT*63 (PAM silencing)
9630	SEQ ID NO: 9630	RTT*65 (PAM silencing)
9631	SEQ ID NO: 9631	RTT*60 (PAM silencing)
9632	SEQ ID NO: 9632	RTT
9633	SEQ ID NO: 9633	RTT*61 (PAM silencing)
9634	SEQ ID NO: 9634	RTT*58 (PAM silencing)
9635	SEQ ID NO: 9635	RTT*65 (PAM silencing)
9636	SEQ ID NO: 9636	RTT*60 (PAM silencing)
9637	SEQ ID NO: 9637	RTT*64 (PAM silencing)
9638	SEQ ID NO: 9638	RTT*61 (PAM silencing)
9639	SEQ ID NO: 9639	RTT*67 (PAM silencing)
9640	SEQ ID NO: 9640	RTT*66 (PAM silencing)
9641	SEQ ID NO: 9641	RTT*62 (PAM silencing)
9642	SEQ ID NO: 9642	RTT*59 (PAM silencing)
9643	SEQ ID NO: 9643	RTT
9644	SEQ ID NO: 9644	RTT*57 (PAM silencing)
9645	SEQ ID NO: 9645	RTT*63 (PAM silencing)
9646	SEQ ID NO: 9646	RTT*58 (PAM silencing)
9647	SEQ ID NO: 9647	RTT*59 (PAM silencing)

Sequence Number	Sequence	Description
9648	SEQ ID NO: 9648	RTT*61 (PAM silencing)
9649	SEQ ID NO: 9649	RTT*63 (PAM silencing)
9650	SEQ ID NO: 9650	RTT*57 (PAM silencing)
9651	SEQ ID NO: 9651	RTT*62 (PAM silencing)
9652	SEQ ID NO: 9652	RTT*67 (PAM silencing)
9653	SEQ ID NO: 9653	RTT*64 (PAM silencing)
9654	SEQ ID NO: 9654	RTT*66 (PAM silencing)
9655	SEQ ID NO: 9655	RTT*58 (PAM silencing)
9656	SEQ ID NO: 9656	RTT*65 (PAM silencing)
9657	SEQ ID NO: 9657	RTT
9658	SEQ ID NO: 9658	RTT*60 (PAM silencing)
9659	SEQ ID NO: 9659	RTT*67 (PAM silencing)
9660	SEQ ID NO: 9660	RTT*62 (PAM silencing)
9661	SEQ ID NO: 9661	RTT*59 (PAM silencing)
9662	SEQ ID NO: 9662	RTT*58 (PAM silencing)
9663	SEQ ID NO: 9663	RTT*64 (PAM silencing)
9664	SEQ ID NO: 9664	RTT*63 (PAM silencing)
9665	SEQ ID NO: 9665	RTT
9666	SEQ ID NO: 9666	RTT*65 (PAM silencing)
9667	SEQ ID NO: 9667	RTT*61 (PAM silencing)
9668	SEQ ID NO: 9668	RTT*57 (PAM silencing)
9669	SEQ ID NO: 9669	RTT*60 (PAM silencing)
9670	SEQ ID NO: 9670	RTT*66 (PAM silencing)

Sequence Number	Sequence	Description
9671	SEQ ID NO: 9671	RTT*62 (PAM silencing)
9672	SEQ ID NO: 9672	RTT*59 (PAM silencing)
9673	SEQ ID NO: 9673	RTT*63 (PAM silencing)
9674	SEQ ID NO: 9674	RTT*58 (PAM silencing)
9675	SEQ ID NO: 9675	RTT*57 (PAM silencing)
9676	SEQ ID NO: 9676	RTT
9677	SEQ ID NO: 9677	RTT*60 (PAM silencing)
9678	SEQ ID NO: 9678	RTT*66 (PAM silencing)
9679	SEQ ID NO: 9679	RTT*67 (PAM silencing)
9680	SEQ ID NO: 9680	RTT*64 (PAM silencing)
9681	SEQ ID NO: 9681	RTT*65 (PAM silencing)
9682	SEQ ID NO: 9682	RTT*61 (PAM silencing)
9683	SEQ ID NO: 9683	RTT*65 (PAM silencing)
9684	SEQ ID NO: 9684	RTT*67 (PAM silencing)
9685	SEQ ID NO: 9685	RTT*59 (PAM silencing)
9686	SEQ ID NO: 9686	RTT*66 (PAM silencing)
9687	SEQ ID NO: 9687	RTT
9688	SEQ ID NO: 9688	RTT*63 (PAM silencing)
9689	SEQ ID NO: 9689	RTT*61 (PAM silencing)
9690	SEQ ID NO: 9690	RTT*60 (PAM silencing)
9691	SEQ ID NO: 9691	RTT*57 (PAM silencing)
9692	SEQ ID NO: 9692	RTT*58 (PAM silencing)
9693	SEQ ID NO: 9693	RTT*64 (PAM silencing)

Sequence Number	Sequence	Description
9694	SEQ ID NO: 9694	RTT*62 (PAM silencing)
9695	SEQ ID NO: 9695	RTT*57 (PAM silencing)
9696	SEQ ID NO: 9696	RTT*62 (PAM silencing)
9697	SEQ ID NO: 9697	RTT*64 (PAM silencing)
9698	SEQ ID NO: 9698	RTT*60 (PAM silencing)
9699	SEQ ID NO: 9699	RTT*67 (PAM silencing)
9700	SEQ ID NO: 9700	RTT*63 (PAM silencing)
9701	SEQ ID NO: 9701	RTT*65 (PAM silencing)
9702	SEQ ID NO: 9702	RTT
9703	SEQ ID NO: 9703	RTT*66 (PAM silencing)
9704	SEQ ID NO: 9704	RTT*58 (PAM silencing)
9705	SEQ ID NO: 9705	RTT*61 (PAM silencing)
9706	SEQ ID NO: 9706	RTT*59 (PAM silencing)
9707	SEQ ID NO: 9707	RTT*63 (PAM silencing)
9708	SEQ ID NO: 9708	RTT*65 (PAM silencing)
9709	SEQ ID NO: 9709	RTT
9710	SEQ ID NO: 9710	RTT*59 (PAM silencing)
9711	SEQ ID NO: 9711	RTT*58 (PAM silencing)
9712	SEQ ID NO: 9712	RTT*60 (PAM silencing)
9713	SEQ ID NO: 9713	RTT*66 (PAM silencing)
9714	SEQ ID NO: 9714	RTT*61 (PAM silencing)
9715	SEQ ID NO: 9715	RTT*67 (PAM silencing)
9716	SEQ ID NO: 9716	RTT*62 (PAM silencing)

Sequence Number	Sequence	Description
9717	SEQ ID NO: 9717	RTT*57 (PAM silencing)
9718	SEQ ID NO: 9718	RTT*64 (PAM silencing)
9719	SEQ ID NO: 9719	RTT*63 (PAM silencing)
9720	SEQ ID NO: 9720	RTT*57 (PAM silencing)
9721	SEQ ID NO: 9721	RTT*66 (PAM silencing)
9722	SEQ ID NO: 9722	RTT*59 (PAM silencing)
9723	SEQ ID NO: 9723	RTT*67 (PAM silencing)
9724	SEQ ID NO: 9724	RTT*58 (PAM silencing)
9725	SEQ ID NO: 9725	RTT*61 (PAM silencing)
9726	SEQ ID NO: 9726	RTT*65 (PAM silencing)
9727	SEQ ID NO: 9727	RTT*60 (PAM silencing)
9728	SEQ ID NO: 9728	RTT*62 (PAM silencing)
9729	SEQ ID NO: 9729	RTT*64 (PAM silencing)
9730	SEQ ID NO: 9730	RTT
9731	SEQ ID NO: 9731	RTT*63 (PAM silencing)
9732	SEQ ID NO: 9732	RTT*57 (PAM silencing)
9733	SEQ ID NO: 9733	RTT*58 (PAM silencing)
9734	SEQ ID NO: 9734	RTT*59 (PAM silencing)
9735	SEQ ID NO: 9735	RTT*64 (PAM silencing)
9736	SEQ ID NO: 9736	RTT*67 (PAM silencing)
9737	SEQ ID NO: 9737	RTT*66 (PAM silencing)
9738	SEQ ID NO: 9738	RTT*60 (PAM silencing)
9739	SEQ ID NO: 9739	RTT*65 (PAM silencing)
9740	SEQ ID NO: 9740	RTT
9741	SEQ ID NO: 9741	RTT*61 (PAM silencing)
9742	SEQ ID NO: 9742	RTT*62 (PAM silencing)
9743	SEQ ID NO: 9743	RTT*60 (PAM silencing)
9744	SEQ ID NO: 9744	RTT*61 (PAM silencing)
9745	SEQ ID NO: 9745	RTT*57 (PAM silencing)
9746	SEQ ID NO: 9746	RTT*66 (PAM silencing)
9747	SEQ ID NO: 9747	RTT*62 (PAM silencing)
9748	SEQ ID NO: 9748	RTT
9749	SEQ ID NO: 9749	RTT*64 (PAM silencing)
9750	SEQ ID NO: 9750	RTT*59 (PAM silencing)
9751	SEQ ID NO: 9751	RTT*67 (PAM silencing)
9752	SEQ ID NO: 9752	RTT*58 (PAM silencing)
9753	SEQ ID NO: 9753	RTT*65 (PAM silencing)
9754	SEQ ID NO: 9754	RTT*63 (PAM silencing)
9755	SEQ ID NO: 9755	RTT*60 (PAM silencing)
9756	SEQ ID NO: 9756	RTT*64 (PAM silencing)
9757	SEQ ID NO: 9757	RTT*65 (PAM silencing)
9758	SEQ ID NO: 9758	RTT*66 (PAM silencing)
9759	SEQ ID NO: 9759	RTT*57 (PAM silencing)
9760	SEQ ID NO: 9760	RTT*67 (PAM silencing)
9761	SEQ ID NO: 9761	RTT*59 (PAM silencing)
9762	SEQ ID NO: 9762	RTT*63 (PAM silencing)
9763	SEQ ID NO: 9763	RTT
9764	SEQ ID NO: 9764	RTT*61 (PAM silencing)
9765	SEQ ID NO: 9765	RTT*62 (PAM silencing)
9766	SEQ ID NO: 9766	RTT*58 (PAM silencing)
9767	SEQ ID NO: 9767	RTT*67 (PAM silencing)
9768	SEQ ID NO: 9768	RTT
9769	SEQ ID NO: 9769	RTT*58 (PAM silencing)
9770	SEQ ID NO: 9770	RTT*65 (PAM silencing)
9771	SEQ ID NO: 9771	RTT*61 (PAM silencing)
9772	SEQ ID NO: 9772	RTT*66 (PAM silencing)
9773	SEQ ID NO: 9773	RTT*62 (PAM silencing)
9774	SEQ ID NO: 9774	RTT*60 (PAM silencing)
9775	SEQ ID NO: 9775	RTT*63 (PAM silencing)
9776	SEQ ID NO: 9776	RTT*64 (PAM silencing)
9777	SEQ ID NO: 9777	RTT*59 (PAM silencing)
9778	SEQ ID NO: 9778	RTT*57 (PAM silencing)
9779	SEQ ID NO: 9779	RTT
9780	SEQ ID NO: 9780	RTT*66 (PAM silencing)
9781	SEQ ID NO: 9781	RTT*67 (PAM silencing)
9782	SEQ ID NO: 9782	RTT*57 (PAM silencing)
9783	SEQ ID NO: 9783	RTT*62 (PAM silencing)
9784	SEQ ID NO: 9784	RTT*60 (PAM silencing)

Sequence Number	Sequence	Description
9785	SEQ ID NO: 9785	RTT*64 (PAM silencing)
9786	SEQ ID NO: 9786	RTT*65 (PAM silencing)
9787	SEQ ID NO: 9787	RTT*63 (PAM silencing)
9788	SEQ ID NO: 9788	RTT*58 (PAM silencing)
9789	SEQ ID NO: 9789	RTT*59 (PAM silencing)
9790	SEQ ID NO: 9790	RTT*61 (PAM silencing)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAG;CA GG PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAG PAM)
9791	SEQ ID NO: 9791	PE3 ngRNA spacer (GCGG PAM)
9792	SEQ ID NO: 9792	PE3b*65 ngRNA spacer (ATGG;G TGG PAM)
7158	SEQ ID NO: 7158	PE3 ngRNA spacer (CTGG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TGG;TG GG PAM)
8380	SEQ ID NO: 8380	PE3 ngRNA spacer (AAG;AA GG PAM)
9793	SEQ ID NO: 9793	PE3b*59 ngRNA spacer (GTGG PAM)
9794	SEQ ID NO: 9794	PE3b*66 ngRNA spacer (CTGG PAM)
9795	SEQ ID NO: 9795	PE3b*60 ngRNA spacer (CTGG PAM)
9796	SEQ ID NO: 9796	PE3b*66 ngRNA spacer (ATGG;G TGG PAM)
9797	SEQ ID NO: 9797	PE3b*61 ngRNA spacer (CTGG PAM)
9798	SEQ ID NO: 9798	PE3b*62 ngRNA spacer (CTGG PAM)
9799	SEQ ID NO: 9799	PE3 ngRNA spacer (GTGG PAM)
9800	SEQ ID NO: 9800	PE3b*64 ngRNA spacer (ATGG;G TGG PAM)
8373	SEQ ID NO: 8373	PE3 ngRNA spacer (GAG PAM)
9801	SEQ ID NO: 9801	PE3b*57 ngRNA spacer (GTGG PAM)
9802	SEQ ID NO: 9802	PE3b*57 ngRNA spacer (CTGG PAM)
8376	SEQ ID NO: 8376	PE3 ngRNA spacer (GAG;GA GG PAM)
9803	SEQ ID NO: 9803	PE3 ngRNA spacer (CTGG PAM)
9804	SEQ ID NO: 9804	PE3b*63 ngRNA spacer (CTGG PAM)
9805	SEQ ID NO: 9805	PE3b*59 ngRNA spacer (CTGG PAM)
9806	SEQ ID NO: 9806	PE3b*65 ngRNA spacer (CTGG PAM)
8377	SEQ ID NO: 8377	PE3 ngRNA spacer (GAG PAM)
9807	SEQ ID NO: 9807	PE3b*58 ngRNA spacer (GTGG PAM)
7157	SEQ ID NO: 7157	PE3b ngRNA spacer (CTGG PAM)
9808	SEQ ID NO: 9808	PE3b*67 ngRNA spacer (CTGG PAM)
7156	SEQ ID NO: 7156	PE3b ngRNA spacer (GTGG PAM)
9809	SEQ ID NO: 9809	PE3 ngRNA spacer (GTGG PAM)
9810	SEQ ID NO: 9810	PE3b*64 ngRNA spacer (CTGG PAM)
9811	SEQ ID NO: 9811	PE3b*67 ngRNA spacer (ATGG;G TGG PAM)
9812	SEQ ID NO: 9812	PE3b*58 ngRNA spacer (CTGG PAM)
8374	SEQ ID NO: 8374	PE3 ngRNA spacer (GAG PAM)
2061	SEQ ID NO: 2061	ngRNA (TGG;TG GG PAM)

Table 45

Sequence Number	Sequence	Description
9813	SEQ ID NO: 9813	PEgRNA spacer (GG;GGT GGT PAM)
9814	SEQ ID NO: 9814	PEgRNA spacer

Sequence Number	Sequence	Description
		(GG;GGT GGT PAM)
9815	SEQ ID NO: 9815	PEgRNA spacer (GG;GGT GGT PAM)
9816	SEQ ID NO: 9816	PEgRNA spacer (GG;GGT GGT PAM)
9817	SEQ ID NO: 9817	PEgRNA spacer (GG;GGT GGT PAM)
9818	SEQ ID NO: 9818	PEgRNA spacer (GG;GGT GGT PAM)
9819	SEQ ID NO: 9819	PEgRNA spacer (GG;GGT GGT PAM)
9820	ATG	PBS
9821	ATGA	PBS
9822	ATGAC	PBS
9823	ATGACC	PBS
9824	ATGACC A	PBS
9825	ATGACC AG	PBS
9826	ATGACC AGA	PBS
9827	SEQ ID NO: 9827	PBS
9828	SEQ ID NO: 9828	PBS
9829	SEQ ID NO: 9829	PBS
9830	SEQ ID NO: 9830	PBS
9831	SEQ ID NO: 9831	PBS
9832	SEQ ID NO: 9832	PBS
9833	SEQ ID NO: 9833	PBS
9834	SEQ ID NO: 9834	PBS
9835	SEQ ID NO: 9835	PBS
9836	SEQ ID NO: 9836	PBS
9837	SEQ ID NO: 9837	RTT*97 (PAM silencing)
9838	SEQ ID NO: 9838	RTT*98 (PAM silencing)
9839	SEQ ID NO: 9839	RTT

Sequence Number	Sequence	Description
9840	SEQ ID NO: 9840	RTT
9841	SEQ ID NO: 9841	RTT*97 (PAM silencing)
9842	SEQ ID NO: 9842	RTT*98 (PAM silencing)
9843	SEQ ID NO: 9843	RTT
9844	SEQ ID NO: 9844	RTT*97 (PAM silencing)
9845	SEQ ID NO: 9845	RTT*98 (PAM silencing)
9846	SEQ ID NO: 9846	RTT
9847	SEQ ID NO: 9847	RTT*98 (PAM silencing)
9848	SEQ ID NO: 9848	RTT*97 (PAM silencing)
9849	SEQ ID NO: 9849	RTT*97 (PAM silencing)
9850	SEQ ID NO: 9850	RTT
9851	SEQ ID NO: 9851	RTT*98 (PAM silencing)
9852	SEQ ID NO: 9852	RTT
9853	SEQ ID NO: 9853	RTT*97 (PAM silencing)
9854	SEQ ID NO: 9854	RTT*98 (PAM silencing)
9855	SEQ ID NO: 9855	RTT*98 (PAM silencing)
9856	SEQ ID NO: 9856	RTT*97 (PAM silencing)
9857	SEQ ID NO: 9857	RTT
9858	SEQ ID NO: 9858	RTT*97 (PAM silencing)
9859	SEQ ID NO: 9859	RTT
9860	SEQ ID NO: 9860	RTT*98 (PAM silencing)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAGGAT PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG;GGG GGG PAM)

Sequence Number	Sequence	Description
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG;GGC AAT PAM)
9861	SEQ ID NO: 9861	PE3b*98 ngRNA spacer (CAGGAT PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG;AGA ATG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
75	SEQ ID NO: 75	PE3 ngRNA spacer (TG PAM)
71	SEQ ID NO: 71	PE3 ngRNA spacer (GG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG;AGC ATG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)

Sequence Number	Sequence	Description
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
9862	SEQ ID NO: 9862	PE3b*97 ngRNA spacer (CAGGAT PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
6453	SEQ ID NO: 6453	PE3 ngRNA spacer (AAGAA T PAM)
67	SEQ ID NO: 67	PE3 ngRNA spacer (AG;AGG ATG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG;TGG GGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG;GGG GCG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG;GGC GTG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
109	SEQ ID NO: 109	ngRNA (GG;GGG GCG PAM)
108	SEQ ID NO: 108	ngRNA (GG PAM)
100	SEQ ID NO: 100	ngRNA (GG;GGG GGG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
101	SEQ ID NO: 101	ngRNA (TG;TGG GGG PAM)
102	SEQ ID NO: 102	ngRNA (AG PAM)
106	SEQ ID NO: 106	ngRNA (AG;AGG ATG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
112	SEQ ID NO: 112	ngRNA (GG;GGG GCG PAM)
111	SEQ ID NO: 111	ngRNA (AG;AGG ATG PAM)

Table 46

Sequence Number	Sequence	Description
9863	SEQ ID NO: 9863	PEgRNA spacer (GG PAM)
9864	SEQ ID NO: 9864	PEgRNA spacer (GG PAM)
9865	SEQ ID NO: 9865	PEgRNA spacer (GG PAM)
9866	SEQ ID NO: 9866	PEgRNA spacer (GG PAM)
9867	SEQ ID NO: 9867	PEgRNA spacer (GG PAM)
9868	SEQ ID NO: 9868	PEgRNA spacer (GG PAM)
9869	SEQ ID NO: 9869	PEgRNA spacer (GG PAM)
9870	AGG	PBS
9871	AGGA	PBS
9872	AGGAT	PBS
9873	AGGATG	PBS
9874	AGGATG A	PBS
9875	AGGATG AC	PBS
9876	AGGATG ACC	PBS
9877	SEQ ID NO: 9877	PBS
9878	SEQ ID NO: 9878	PBS
9879	SEQ ID NO: 9879	PBS
9880	SEQ ID NO: 9880	PBS
9881	SEQ ID NO: 9881	PBS
9882	SEQ ID NO: 9882	PBS
9883	SEQ ID NO: 9883	PBS
9884	SEQ ID NO: 9884	PBS
9885	SEQ ID NO: 9885	PBS
9886	SEQ ID NO: 9886	PBS

Sequence Number	Sequence	Description
9887	SEQ ID NO: 9887	RTT
9888	SEQ ID NO: 9888	RTT
9889	SEQ ID NO: 9889	RTT
9890	SEQ ID NO: 9890	RTT
9891	SEQ ID NO: 9891	RTT
9892	SEQ ID NO: 9892	RTT
9893	SEQ ID NO: 9893	RTT
9894	SEQ ID NO: 9894	RTT
9895	SEQ ID NO: 9895	RTT
9896	SEQ ID NO: 9896	RTT
9897	SEQ ID NO: 9897	RTT
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(AG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
67	SEQ ID NO: 67	PE3 ngRNA spacer (AG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
71	SEQ ID NO: 71	PE3 ngRNA spacer (GG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer

Sequence Number	Sequence	Description
		(GG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
106	SEQ ID NO: 106	ngRNA (AG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
102	SEQ ID NO: 102	ngRNA (AG PAM)
108	SEQ ID NO: 108	ngRNA (GG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)
111	SEQ ID NO: 111	ngRNA (AG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)

Sequence Number	Sequence	Description
118	SEQ ID NO: 118	ngRNA (GG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)

Table 47

Sequence Number	Sequence	Description
9898	SEQ ID NO: 9898	PEgRNA spacer (TG PAM)
9899	SEQ ID NO: 9899	PEgRNA spacer (TG PAM)
9900	SEQ ID NO: 9900	PEgRNA spacer (TG PAM)
9901	SEQ ID NO: 9901	PEgRNA spacer (TG PAM)
9902	SEQ ID NO: 9902	PEgRNA spacer (TG PAM)
9903	SEQ ID NO: 9903	PEgRNA spacer (TG PAM)
9904	SEQ ID NO: 9904	PEgRNA spacer (TG PAM)
7082	ACC	PBS
7083	ACCA	PBS
9905	ACCAG	PBS
9906	ACCAGG	PBS
9907	ACCAGG A	PBS
9908	ACCAGG AT	PBS
9909	ACCAGG ATG	PBS
9910	SEQ ID NO: 9910	PBS
9911	SEQ ID NO: 9911	PBS
9912	SEQ ID NO: 9912	PBS
9913	SEQ ID NO: 9913	PBS
9914	SEQ ID NO: 9914	PBS
9915	SEQ ID NO: 9915	PBS
9916	SEQ ID NO: 9916	PBS
9917	SEQ ID NO: 9917	PBS
9918	SEQ ID NO: 9918	PBS
9919	SEQ ID NO: 9919	PBS
9920	SEQ ID NO: 9920	RTT
9921	SEQ ID NO: 9921	RTT
9922	SEQ ID NO: 9922	RTT
9923	SEQ ID NO: 9923	RTT
9924	SEQ ID NO: 9924	RTT
9925	SEQ ID NO: 9925	RTT
9926	SEQ ID NO: 9926	RTT
9927	SEQ ID NO: 9927	RTT
9928	SEQ ID NO: 9928	RTT
9929	SEQ ID NO: 9929	RTT
9930	SEQ ID NO: 9930	RTT
9931	SEQ ID NO: 9931	RTT
9932	SEQ ID NO: 9932	RTT
9933	SEQ ID NO: 9933	RTT
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
67	SEQ ID NO: 67	PE3 ngRNA spacer (AG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(GG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
108	SEQ ID NO: 108	ngRNA (GG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
102	SEQ ID NO: 102	ngRNA (AG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
106	SEQ ID NO: 106	ngRNA (AG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)
111	SEQ ID NO: 111	ngRNA (AG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)

Table 48

Sequence Number	Sequence	Description
9934	SEQ ID NO: 9934	PEgRNA spacer (TG PAM)
9935	SEQ ID NO: 9935	PEgRNA spacer (TG PAM)
9936	SEQ ID NO: 9936	PEgRNA spacer (TG PAM)
9937	SEQ ID NO: 9937	PEgRNA spacer (TG PAM)
9938	SEQ ID NO: 9938	PEgRNA spacer (TG PAM)
9939	SEQ ID NO: 9939	PEgRNA spacer (TG PAM)
9940	SEQ ID NO: 9940	PEgRNA spacer (TG PAM)
7082	ACC	PBS
7083	ACCA	PBS
9941	ACCAC	PBS
9942	ACCACC	PBS
9943	ACCACC A	PBS
9944	ACCACC AG	PBS
9945	ACCACC AGG	PBS
9946	SEQ ID NO: 9946	PBS
9947	SEQ ID NO: 9947	PBS
9948	SEQ ID NO: 9948	PBS
9949	SEQ ID NO: 9949	PBS
9950	SEQ ID NO: 9950	PBS
9951	SEQ ID NO: 9951	PBS
9952	SEQ ID NO: 9952	PBS
9953	SEQ ID NO: 9953	PBS
9954	SEQ ID NO: 9954	PBS
9955	SEQ ID NO: 9955	PBS
9956	SEQ ID NO: 9956	RTT
9957	SEQ ID NO: 9957	RTT
9958	SEQ ID NO: 9958	RTT
9959	SEQ ID NO: 9959	RTT
9960	SEQ ID NO: 9960	RTT
9961	SEQ ID NO: 9961	RTT
9962	SEQ ID NO: 9962	RTT

Sequence Number	Sequence	Description
9963	SEQ ID NO: 9963	RTT
9964	SEQ ID NO: 9964	RTT
9965	SEQ ID NO: 9965	RTT
9966	SEQ ID NO: 9966	RTT
9967	SEQ ID NO: 9967	RTT
9968	SEQ ID NO: 9968	RTT
9969	SEQ ID NO: 9969	RTT
9970	SEQ ID NO: 9970	RTT
9971	SEQ ID NO: 9971	RTT
9972	SEQ ID NO: 9972	RTT
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)

Sequence Number	Sequence	Description
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
108	SEQ ID NO: 108	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
102	SEQ ID NO: 102	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)

Table 49

Sequence Number	Sequence	Description
9973	SEQ ID NO: 9973	PEgRNA spacer (GG PAM)
9974	SEQ ID NO: 9974	PEgRNA spacer (GG PAM)
9975	SEQ ID NO: 9975	PEgRNA spacer (GG PAM)
9976	SEQ ID NO: 9976	PEgRNA spacer (GG PAM)
9977	SEQ ID NO: 9977	PEgRNA spacer (GG PAM)
9978	SEQ ID NO: 9978	PEgRNA spacer (GG PAM)
9979	SEQ ID NO: 9979	PEgRNA spacer (GG PAM)
1536	GCA	PBS
1537	GCAA	PBS
9980	GCAAC	PBS
9981	GCAACC	PBS
9982	GCAACCA	PBS
9983	GCAACCAC	PBS
9984	GCAACCACC	PBS
9985	SEQ ID NO: 9985	PBS
9986	SEQ ID NO: 9986	PBS
9987	SEQ ID NO: 9987	PBS
9988	SEQ ID NO: 9988	PBS
9989	SEQ ID NO: 9989	PBS
9990	SEQ ID NO: 9990	PBS
9991	SEQ ID NO: 9991	PBS
9992	SEQ ID NO: 9992	PBS
9993	SEQ ID NO: 9993	PBS
9994	SEQ ID NO: 9994	PBS
9995	SEQ ID NO: 9995	RTT
9996	SEQ ID NO: 9996	RTT
9997	SEQ ID NO: 9997	RTT
9998	SEQ ID NO: 9998	RTT
9999	SEQ ID NO: 9999	RTT
10000	SEQ ID NO: 10000	RTT
10001	SEQ ID NO: 10001	RTT

Sequence Number	Sequence	Description
10002	SEQ ID NO: 10002	RTT
10003	SEQ ID NO: 10003	RTT
10004	SEQ ID NO: 10004	RTT
10005	SEQ ID NO: 10005	RTT
10006	SEQ ID NO: 10006	RTT
10007	SEQ ID NO: 10007	RTT
10008	SEQ ID NO: 10008	RTT
10009	SEQ ID NO: 10009	RTT
10010	SEQ ID NO: 10010	RTT
10011	SEQ ID NO: 10011	RTT
10012	SEQ ID NO: 10012	RTT
10013	SEQ ID NO: 10013	RTT
10014	SEQ ID NO: 10014	RTT
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
69	SEQ ID NO: 69	PE3 ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
108	SEQ ID NO: 108	ngRNA (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
102	SEQ ID NO: 102	ngRNA (AG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Table 50

Sequence Number	Sequence	Description
10015	SEQ ID NO: 10015	PEgRNA spacer (GG PAM)
10016	SEQ ID NO: 10016	PEgRNA spacer (GG PAM)
10017	SEQ ID NO: 10017	PEgRNA spacer (GG PAM)
10018	SEQ ID NO: 10018	PEgRNA spacer (GG PAM)
10019	SEQ ID NO: 10019	PEgRNA spacer (GG PAM)
10020	SEQ ID NO: 10020	PEgRNA spacer (GG PAM)
10021	SEQ ID NO: 10021	PEgRNA spacer (GG PAM)
6298	TCA	PBS
6299	TCAG	PBS
10022	TCAGC	PBS
10023	TCAGCC	PBS
10024	TCAGCC A	PBS
10025	TCAGCC AC	PBS
10026	TCAGCC ACA	PBS
10027	SEQ ID NO: 10027	PBS
10028	SEQ ID NO: 10028	PBS
10029	SEQ ID NO: 10029	PBS
10030	SEQ ID NO: 10030	PBS
10031	SEQ ID NO: 10031	PBS
10032	SEQ ID NO: 10032	PBS
10033	SEQ ID NO: 10033	PBS
10034	SEQ ID NO: 10034	PBS
10035	SEQ ID NO: 10035	PBS
10036	SEQ ID NO: 10036	PBS
10037	SEQ ID NO: 10037	RTT
10038	SEQ ID NO: 10038	RTT
10039	SEQ ID NO: 10039	RTT
10040	SEQ ID NO: 10040	RTT
10041	SEQ ID NO: 10041	RTT
10042	SEQ ID NO: 10042	RTT
10043	SEQ ID NO: 10043	RTT
10044	SEQ ID NO: 10044	RTT
10045	SEQ ID NO: 10045	RTT
10046	SEQ ID NO: 10046	RTT
10047	SEQ ID NO: 10047	RTT
10048	SEQ ID NO: 10048	RTT
10049	SEQ ID NO: 10049	RTT
10050	SEQ ID NO: 10050	RTT
10051	SEQ ID NO: 10051	RTT
10052	SEQ ID NO: 10052	RTT
10053	SEQ ID NO: 10053	RTT
10054	SEQ ID NO: 10054	RTT
10055	SEQ ID NO: 10055	RTT
10056	SEQ ID NO: 10056	RTT
10057	SEQ ID NO: 10057	RTT
10058	SEQ ID NO: 10058	RTT
10059	SEQ ID NO: 10059	RTT
10060	SEQ ID NO: 10060	RTT
10061	SEQ ID NO: 10061	RTT
10062	SEQ ID NO: 10062	RTT
10063	SEQ ID NO: 10063	RTT
10064	SEQ ID NO: 10064	RTT
10065	SEQ ID NO: 10065	RTT
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)

Sequence Number	Sequence	Description
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
60	SEQ ID NO: 60	PE3 ngRNA spacer (AG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
108	SEQ ID NO: 108	ngRNA (GG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
102	SEQ ID NO: 102	ngRNA (AG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Table 51

Sequence Number	Sequence	Description
10066	SEQ ID NO: 10066	PEgRNA spacer (AG PAM)
10067	SEQ ID NO: 10067	PEgRNA spacer (AG PAM)
10068	SEQ ID NO: 10068	PEgRNA spacer (AG PAM)
10069	SEQ ID NO: 10069	PEgRNA spacer (AG PAM)
10070	SEQ ID NO: 10070	PEgRNA spacer (AG PAM)
10071	SEQ ID NO: 10071	PEgRNA spacer (AG PAM)
10072	SEQ ID NO: 10072	PEgRNA spacer (AG PAM)
10073	CTC	PBS
10074	CTCC	PBS
10075	CTCCG	PBS
10076	CTCCGC	PBS
10077	CTCCGCC	PBS
10078	CTCCGCCT	PBS
10079	CTCCGCCTT	PBS
10080	SEQ ID NO: 10080	PBS
10081	SEQ ID NO: 10081	PBS
10082	SEQ ID NO: 10082	PBS
10083	SEQ ID NO: 10083	PBS
10084	SEQ ID NO: 10084	PBS
10085	SEQ ID NO: 10085	PBS
10086	SEQ ID NO: 10086	PBS
10087	SEQ ID NO: 10087	PBS
10088	SEQ ID NO: 10088	PBS
10089	SEQ ID NO: 10089	PBS
10090	SEQ ID NO: 10090	RTT*15 (PAM silencing)
10091	SEQ ID NO: 10091	RTT*14 (PAM silencing)
10092	SEQ ID NO: 10092	RTT
10093	SEQ ID NO: 10093	RTT*13 (PAM silencing)
10094	SEQ ID NO: 10094	RTT*12 (PAM silencing)
10095	SEQ ID NO: 10095	RTT*15 (PAM silencing)
10096	SEQ ID NO: 10096	RTT*13 (PAM silencing)
10097	SEQ ID NO: 10097	RTT*14 (PAM silencing)
10098	SEQ ID NO: 10098	RTT
10099	SEQ ID NO: 10099	RTT*12 (PAM silencing)
10100	SEQ ID NO: 10100	RTT
10101	SEQ ID NO: 10101	RTT*14 (PAM silencing)
10102	SEQ ID NO: 10102	RTT*12 (PAM silencing)
10103	SEQ ID NO: 10103	RTT*13 (PAM silencing)
10104	SEQ ID NO: 10104	RTT*15 (PAM silencing)
10105	SEQ ID NO: 10105	RTT*12 (PAM silencing)
10106	SEQ ID NO: 10106	RTT*14 (PAM silencing)

Sequence Number	Sequence	Description
10107	SEQ ID NO: 10107	RTT*13 (PAM silencing)
10108	SEQ ID NO: 10108	RTT*15 (PAM silencing)
10109	SEQ ID NO: 10109	RTT
10110	SEQ ID NO: 10110	RTT*14 (PAM silencing)
10111	SEQ ID NO: 10111	RTT
10112	SEQ ID NO: 10112	RTT*13 (PAM silencing)
10113	SEQ ID NO: 10113	RTT*15 (PAM silencing)
10114	SEQ ID NO: 10114	RTT*12 (PAM silencing)
10115	SEQ ID NO: 10115	RTT*13 (PAM silencing)
10116	SEQ ID NO: 10116	RTT*14 (PAM silencing)
10117	SEQ ID NO: 10117	RTT*15 (PAM silencing)
10118	SEQ ID NO: 10118	RTT*12 (PAM silencing)
10119	SEQ ID NO: 10119	RTT
10120	SEQ ID NO: 10120	RTT
10121	SEQ ID NO: 10121	RTT*12 (PAM silencing)
10122	SEQ ID NO: 10122	RTT*14 (PAM silencing)
10123	SEQ ID NO: 10123	RTT*13 (PAM silencing)
10124	SEQ ID NO: 10124	RTT*15 (PAM silencing)
10125	SEQ ID NO: 10125	RTT*13 (PAM silencing)
10126	SEQ ID NO: 10126	RTT
10127	SEQ ID NO: 10127	RTT*15 (PAM silencing)
10128	SEQ ID NO: 10128	RTT*14 (PAM silencing)
10129	SEQ ID NO: 10129	RTT*12 (PAM silencing)
10130	SEQ ID NO: 10130	RTT*13 (PAM silencing)

Sequence Number	Sequence	Description
10131	SEQ ID NO: 10131	RTT
10132	SEQ ID NO: 10132	RTT*15 (PAM silencing)
10133	SEQ ID NO: 10133	RTT*14 (PAM silencing)
10134	SEQ ID NO: 10134	RTT*12 (PAM silencing)
10135	SEQ ID NO: 10135	RTT*13 (PAM silencing)
10136	SEQ ID NO: 10136	RTT*14 (PAM silencing)
10137	SEQ ID NO: 10137	RTT*15 (PAM silencing)
10138	SEQ ID NO: 10138	RTT
10139	SEQ ID NO: 10139	RTT*12 (PAM silencing)
10140	SEQ ID NO: 10140	RTT*15 (PAM silencing)
10141	SEQ ID NO: 10141	RTT*12 (PAM silencing)
10142	SEQ ID NO: 10142	RTT*14 (PAM silencing)
10143	SEQ ID NO: 10143	RTT*13 (PAM silencing)
10144	SEQ ID NO: 10144	RTT
10145	SEQ ID NO: 10145	RTT
10146	SEQ ID NO: 10146	RTT*12 (PAM silencing)
10147	SEQ ID NO: 10147	RTT*13 (PAM silencing)
10148	SEQ ID NO: 10148	RTT*15 (PAM silencing)
10149	SEQ ID NO: 10149	RTT*14 (PAM silencing)
10150	SEQ ID NO: 10150	RTT*15 (PAM silencing)
10151	SEQ ID NO: 10151	RTT
10152	SEQ ID NO: 10152	RTT*12 (PAM silencing)
10153	SEQ ID NO: 10153	RTT*13 (PAM silencing)
10154	SEQ ID NO: 10154	RTT*14 (PAM silencing)

Sequence Number	Sequence	Description
10155	SEQ ID NO: 10155	RTT*13 (PAM silencing)
10156	SEQ ID NO: 10156	RTT*15 (PAM silencing)
10157	SEQ ID NO: 10157	RTT*12 (PAM silencing)
10158	SEQ ID NO: 10158	RTT*14 (PAM silencing)
10159	SEQ ID NO: 10159	RTT
10160	SEQ ID NO: 10160	RTT*14 (PAM silencing)
10161	SEQ ID NO: 10161	RTT*13 (PAM silencing)
10162	SEQ ID NO: 10162	RTT
10163	SEQ ID NO: 10163	RTT*15 (PAM silencing)
10164	SEQ ID NO: 10164	RTT*12 (PAM silencing)
10165	SEQ ID NO: 10165	RTT*13 (PAM silencing)
10166	SEQ ID NO: 10166	RTT
10167	SEQ ID NO: 10167	RTT*12 (PAM silencing)
10168	SEQ ID NO: 10168	RTT*15 (PAM silencing)
10169	SEQ ID NO: 10169	RTT*14 (PAM silencing)
10170	SEQ ID NO: 10170	RTT
10171	SEQ ID NO: 10171	RTT*15 (PAM silencing)
10172	SEQ ID NO: 10172	RTT*14 (PAM silencing)
10173	SEQ ID NO: 10173	RTT*13 (PAM silencing)
10174	SEQ ID NO: 10174	RTT*12 (PAM silencing)
10175	SEQ ID NO: 10175	RTT*14 (PAM silencing)
10176	SEQ ID NO: 10176	RTT*13 (PAM silencing)
10177	SEQ ID NO: 10177	RTT*12 (PAM silencing)
10178	SEQ ID NO: 10178	RTT

Sequence Number	Sequence	Description
10179	SEQ ID NO: 10179	RTT*15 (PAM silencing)
10180	SEQ ID NO: 10180	RTT*12 (PAM silencing)
10181	SEQ ID NO: 10181	RTT
10182	SEQ ID NO: 10182	RTT*15 (PAM silencing)
10183	SEQ ID NO: 10183	RTT*14 (PAM silencing)
10184	SEQ ID NO: 10184	RTT*13 (PAM silencing)
10185	SEQ ID NO: 10185	RTT*15 (PAM silencing)
10186	SEQ ID NO: 10186	RTT
10187	SEQ ID NO: 10187	RTT*14 (PAM silencing)
10188	SEQ ID NO: 10188	RTT*13 (PAM silencing)
10189	SEQ ID NO: 10189	RTT*12 (PAM silencing)
10190	SEQ ID NO: 10190	RTT
10191	SEQ ID NO: 10191	RTT*13 (PAM silencing)
10192	SEQ ID NO: 10192	RTT*15 (PAM silencing)
10193	SEQ ID NO: 10193	RTT*14 (PAM silencing)
10194	SEQ ID NO: 10194	RTT*12 (PAM silencing)
10195	SEQ ID NO: 10195	RTT*13 (PAM silencing)
10196	SEQ ID NO: 10196	RTT*15 (PAM silencing)
10197	SEQ ID NO: 10197	RTT*14 (PAM silencing)
10198	SEQ ID NO: 10198	RTT*12 (PAM silencing)
10199	SEQ ID NO: 10199	RTT
10200	SEQ ID NO: 10200	RTT*13 (PAM silencing)
10201	SEQ ID NO: 10201	RTT*14 (PAM silencing)
10202	SEQ ID NO: 10202	RTT*15 (PAM silencing)
10203	SEQ ID NO: 10203	RTT*12 (PAM silencing)
10204	SEQ ID NO: 10204	RTT
10205	SEQ ID NO: 10205	RTT*15 (PAM silencing)
10206	SEQ ID NO: 10206	RTT
10207	SEQ ID NO: 10207	RTT*12 (PAM silencing)
10208	SEQ ID NO: 10208	RTT*13 (PAM silencing)
10209	SEQ ID NO: 10209	RTT*14 (PAM silencing)
10210	SEQ ID NO: 10210	RTT
10211	SEQ ID NO: 10211	RTT*15 (PAM silencing)
10212	SEQ ID NO: 10212	RTT*13 (PAM silencing)
10213	SEQ ID NO: 10213	RTT*14 (PAM silencing)
10214	SEQ ID NO: 10214	RTT*12 (PAM silencing)
10215	SEQ ID NO: 10215	RTT*13 (PAM silencing)
10216	SEQ ID NO: 10216	RTT*12 (PAM silencing)
10217	SEQ ID NO: 10217	RTT*14 (PAM silencing)
10218	SEQ ID NO: 10218	RTT
10219	SEQ ID NO: 10219	RTT*15 (PAM silencing)
10220	SEQ ID NO: 10220	RTT*15 (PAM silencing)
10221	SEQ ID NO: 10221	RTT*13 (PAM silencing)
10222	SEQ ID NO: 10222	RTT*14 (PAM silencing)
10223	SEQ ID NO: 10223	RTT
10224	SEQ ID NO: 10224	RTT*12 (PAM silencing)
10225	SEQ ID NO: 10225	RTT*13 (PAM silencing)
10226	SEQ ID NO: 10226	RTT
10227	SEQ ID NO: 10227	RTT*12 (PAM silencing)
10228	SEQ ID NO: 10228	RTT*14 (PAM silencing)
10229	SEQ ID NO: 10229	RTT*15 (PAM silencing)
10230	SEQ ID NO: 10230	RTT*13 (PAM silencing)
10231	SEQ ID NO: 10231	RTT*12 (PAM silencing)
10232	SEQ ID NO: 10232	RTT*14 (PAM silencing)
10233	SEQ ID NO: 10233	RTT
10234	SEQ ID NO: 10234	RTT*15 (PAM silencing)
10235	SEQ ID NO: 10235	RTT
10236	SEQ ID NO: 10236	RTT*13 (PAM silencing)
10237	SEQ ID NO: 10237	RTT*12 (PAM silencing)
10238	SEQ ID NO: 10238	RTT*14 (PAM silencing)
10239	SEQ ID NO: 10239	RTT*15 (PAM silencing)
10240	SEQ ID NO: 10240	RTT*13 (PAM silencing)
10241	SEQ ID NO: 10241	RTT*14 (PAM silencing)
10242	SEQ ID NO: 10242	RTT
10243	SEQ ID NO: 10243	RTT*15 (PAM silencing)
10244	SEQ ID NO: 10244	RTT*12 (PAM silencing)
10245	SEQ ID NO: 10245	RTT*15 (PAM silencing)
10246	SEQ ID NO: 10246	RTT*14 (PAM silencing)
10247	SEQ ID NO: 10247	RTT*13 (PAM silencing)
10248	SEQ ID NO: 10248	RTT*12 (PAM silencing)
10249	SEQ ID NO: 10249	RTT

Sequence Number	Sequence	Description
10250	SEQ ID NO: 10250	RTT*15 (PAM silencing)
10251	SEQ ID NO: 10251	RTT
10252	SEQ ID NO: 10252	RTT*14 (PAM silencing)
10253	SEQ ID NO: 10253	RTT*13 (PAM silencing)
10254	SEQ ID NO: 10254	RTT*12 (PAM silencing)
10255	SEQ ID NO: 10255	RTT*12 (PAM silencing)
10256	SEQ ID NO: 10256	RTT
10257	SEQ ID NO: 10257	RTT*14 (PAM silencing)
10258	SEQ ID NO: 10258	RTT*13 (PAM silencing)
10259	SEQ ID NO: 10259	RTT*15 (PAM silencing)
10260	SEQ ID NO: 10260	RTT*13 (PAM silencing)
10261	SEQ ID NO: 10261	RTT*15 (PAM silencing)
10262	SEQ ID NO: 10262	RTT*12 (PAM silencing)
10263	SEQ ID NO: 10263	RTT*14 (PAM silencing)
10264	SEQ ID NO: 10264	RTT
10265	SEQ ID NO: 10265	RTT*15 (PAM silencing)
10266	SEQ ID NO: 10266	RTT
10267	SEQ ID NO: 10267	RTT*13 (PAM silencing)
10268	SEQ ID NO: 10268	RTT*12 (PAM silencing)
10269	SEQ ID NO: 10269	RTT*14 (PAM silencing)
10270	SEQ ID NO: 10270	RTT*13 (PAM silencing)
10271	SEQ ID NO: 10271	RTT*14 (PAM silencing)
10272	SEQ ID NO: 10272	RTT*12 (PAM silencing)
10273	SEQ ID NO: 10273	RTT*15 (PAM silencing)
10274	SEQ ID NO: 10274	RTT
10275	SEQ ID NO: 10275	RTT
10276	SEQ ID NO: 10276	RTT*14 (PAM silencing)
10277	SEQ ID NO: 10277	RTT*13 (PAM silencing)
10278	SEQ ID NO: 10278	RTT*15 (PAM silencing)
10279	SEQ ID NO: 10279	RTT*12 (PAM silencing)
10280	SEQ ID NO: 10280	RTT*15 (PAM silencing)
10281	SEQ ID NO: 10281	RTT
10282	SEQ ID NO: 10282	RTT*12 (PAM silencing)
10283	SEQ ID NO: 10283	RTT*14 (PAM silencing)
10284	SEQ ID NO: 10284	RTT*13 (PAM silencing)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
10285	SEQ ID NO: 10285	PE3b*13 ngRNA spacer (CG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer
		(GG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
10286	SEQ ID NO: 10286	PE3b*15 ngRNA spacer (CG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
10287	SEQ ID NO: 10287	PE3b*14 ngRNA spacer (CG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)

Sequence Number	Sequence	Description
10288	SEQ ID NO: 10288	PE3b*12 ngRNA spacer (CG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
90	SEQ ID NO: 90	PE3 ngRNA spacer (CG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
108	SEQ ID NO: 108	ngRNA (GG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
102	SEQ ID NO: 102	ngRNA (AG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)

Table 52

Sequence Number	Sequence	Description
10289	SEQ ID NO: 10289	PEgRNA spacer (TG PAM)
10290	SEQ ID NO: 10290	PEgRNA spacer (TG PAM)
10291	SEQ ID NO: 10291	PEgRNA spacer (TG PAM)
10292	SEQ ID NO: 10292	PEgRNA spacer (TG PAM)
10293	SEQ ID NO: 10293	PEgRNA spacer (TG PAM)
10294	SEQ ID NO: 10294	PEgRNA spacer (TG PAM)
10295	SEQ ID NO: 10295	PEgRNA spacer (TG PAM)
10073	CTC	PBS
10074	CTCC	PBS
10296	CTCCT	PBS
10297	CTCCTC	PBS
10298	CTCCTCT	PBS
10299	CTCCTCTC	PBS
10300	CTCCTCTCC	PBS
10301	SEQ ID NO: 10301	PBS
10302	SEQ ID NO: 10302	PBS
10303	SEQ ID NO: 10303	PBS
10304	SEQ ID NO: 10304	PBS
10305	SEQ ID NO: 10305	PBS
10306	SEQ ID NO: 10306	PBS
10307	SEQ ID NO: 10307	PBS
10308	SEQ ID NO: 10308	PBS
10309	SEQ ID NO: 10309	PBS
10310	SEQ ID NO: 10310	PBS
10311	SEQ ID NO: 10311	RTT
10312	SEQ ID NO: 10312	RTT
10313	SEQ ID NO: 10313	RTT
10314	SEQ ID NO: 10314	RTT
10315	SEQ ID NO: 10315	RTT
10316	SEQ ID NO: 10316	RTT
10317	SEQ ID NO: 10317	RTT
10318	SEQ ID NO: 10318	RTT
10319	SEQ ID NO: 10319	RTT
10320	SEQ ID NO: 10320	RTT
10321	SEQ ID NO: 10321	RTT
10322	SEQ ID NO: 10322	RTT
10323	SEQ ID NO: 10323	RTT
10324	SEQ ID NO: 10324	RTT
10325	SEQ ID NO: 10325	RTT
10326	SEQ ID NO: 10326	RTT
10327	SEQ ID NO: 10327	RTT
10328	SEQ ID NO: 10328	RTT
10329	SEQ ID NO: 10329	RTT
10330	SEQ ID NO: 10330	RTT
10331	SEQ ID NO: 10331	RTT
10332	SEQ ID NO: 10332	RTT
10333	SEQ ID NO: 10333	RTT

Sequence Number	Sequence	Description
10334	SEQ ID NO: 10334	RTT
10335	SEQ ID NO: 10335	RTT
10336	SEQ ID NO: 10336	RTT
10337	SEQ ID NO: 10337	RTT
10338	SEQ ID NO: 10338	RTT
10339	SEQ ID NO: 10339	RTT
10340	SEQ ID NO: 10340	RTT
10341	SEQ ID NO: 10341	RTT
10342	SEQ ID NO: 10342	RTT
10343	SEQ ID NO: 10343	RTT
10344	SEQ ID NO: 10344	RTT
10345	SEQ ID NO: 10345	RTT
10346	SEQ ID NO: 10346	RTT
10347	SEQ ID NO: 10347	RTT
10348	SEQ ID NO: 10348	RTT
10349	SEQ ID NO: 10349	RTT
10350	SEQ ID NO: 10350	RTT
10351	SEQ ID NO: 10351	RTT
10352	SEQ ID NO: 10352	RTT
10353	SEQ ID NO: 10353	RTT
10354	SEQ ID NO: 10354	RTT
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
77	SEQ ID NO: 77	PE3 ngRNA spacer (GG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
65	SEQ ID NO: 65	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
61	SEQ ID NO: 61	PE3 ngRNA spacer (GG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
108	SEQ ID NO: 108	ngRNA (GG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
102	SEQ ID NO: 102	ngRNA (AG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)

Sequence Number	Sequence	Description
105	SEQ ID NO: 105	ngRNA (GG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)

Table 53

Sequence Number	Sequence	Description
10355	SEQ ID NO: 10355	PEgRNA spacer (CG PAM)
10356	SEQ ID NO: 10356	PEgRNA spacer (CG PAM)
10357	SEQ ID NO: 10357	PEgRNA spacer (CG PAM)
10358	SEQ ID NO: 10358	PEgRNA spacer (CG PAM)
10359	SEQ ID NO: 10359	PEgRNA spacer (CG PAM)
10360	SEQ ID NO: 10360	PEgRNA spacer (CG PAM)
10361	SEQ ID NO: 10361	PEgRNA spacer (CG PAM)
10362	CGA	PBS
10363	CGAA	PBS
10364	CGAAG	PBS
10365	CGAAGA	PBS
10366	CGAAGA A	PBS
10367	CGAAGA AT	PBS
10368	CGAAGA ATG	PBS
10369	SEQ ID NO: 10369	PBS
10370	SEQ ID NO: 10370	PBS
10371	SEQ ID NO: 10371	PBS
10372	SEQ ID NO: 10372	PBS
10373	SEQ ID NO: 10373	PBS
10374	SEQ ID NO: 10374	PBS
10375	SEQ ID NO: 10375	PBS
10376	SEQ ID NO: 10376	PBS
10377	SEQ ID NO: 10377	PBS
10378	SEQ ID NO: 10378	PBS
10379	SEQ ID NO: 10379	RTT*78 (PAM silencing)
10380	SEQ ID NO: 10380	RTT*77 (PAM silencing)
10381	SEQ ID NO: 10381	RTT*79 (PAM silencing)
10382	SEQ ID NO: 10382	RTT
10383	SEQ ID NO: 10383	RTT*79 (PAM silencing)
10384	SEQ ID NO: 10384	RTT
10385	SEQ ID NO: 10385	RTT*78 (PAM silencing)
10386	SEQ ID NO: 10386	RTT*77 (PAM silencing)
10387	SEQ ID NO: 10387	RTT*77 (PAM silencing)
10388	SEQ ID NO: 10388	RTT
10389	SEQ ID NO: 10389	RTT*79 (PAM silencing)
10390	SEQ ID NO: 10390	RTT*78 (PAM silencing)
10391	SEQ ID NO: 10391	RTT*78 (PAM silencing)
10392	SEQ ID NO: 10392	RTT
10393	SEQ ID NO: 10393	RTT*79 (PAM silencing)
10394	SEQ ID NO: 10394	RTT*77 (PAM silencing)
10395	SEQ ID NO: 10395	RTT*79 (PAM silencing)
10396	SEQ ID NO: 10396	RTT
10397	SEQ ID NO: 10397	RTT*78 (PAM silencing)
10398	SEQ ID NO: 10398	RTT*77 (PAM silencing)
10399	SEQ ID NO: 10399	RTT
10400	SEQ ID NO: 10400	RTT*79 (PAM silencing)
10401	SEQ ID NO: 10401	RTT*77 (PAM silencing)
10402	SEQ ID NO: 10402	RTT*78 (PAM silencing)
10403	SEQ ID NO: 10403	RTT
10404	SEQ ID NO: 10404	RTT*77 (PAM silencing)
10405	SEQ ID NO: 10405	RTT*78 (PAM silencing)
10406	SEQ ID NO: 10406	RTT*79 (PAM silencing)
10407	SEQ ID NO: 10407	RTT*77 (PAM silencing)
10408	SEQ ID NO: 10408	RTT
10409	SEQ ID NO: 10409	RTT*78 (PAM silencing)
10410	SEQ ID NO: 10410	RTT*79 (PAM silencing)
10411	SEQ ID NO: 10411	RTT*79 (PAM silencing)
10412	SEQ ID NO: 10412	RTT
10413	SEQ ID NO: 10413	RTT*77 (PAM silencing)
10414	SEQ ID NO: 10414	RTT*78 (PAM silencing)
10415	SEQ ID NO: 10415	RTT*77 (PAM silencing)
10416	SEQ ID NO: 10416	RTT*79 (PAM silencing)
10417	SEQ ID NO: 10417	RTT*78 (PAM silencing)
10418	SEQ ID NO: 10418	RTT
10419	SEQ ID NO: 10419	RTT*78 (PAM silencing)
10420	SEQ ID NO: 10420	RTT
10421	SEQ ID NO: 10421	RTT*79 (PAM silencing)

Sequence Number	Sequence	Description
10422	SEQ ID NO: 10422	RTT*77 (PAM silencing)
10423	SEQ ID NO: 10423	RTT*78 (PAM silencing)
10424	SEQ ID NO: 10424	RTT
10425	SEQ ID NO: 10425	RTT*77 (PAM silencing)
10426	SEQ ID NO: 10426	RTT*79 (PAM silencing)
10427	SEQ ID NO: 10427	RTT*79 (PAM silencing)
10428	SEQ ID NO: 10428	RTT
10429	SEQ ID NO: 10429	RTT*78 (PAM silencing)
10430	SEQ ID NO: 10430	RTT*77 (PAM silencing)
10431	SEQ ID NO: 10431	RTT
10432	SEQ ID NO: 10432	RTT*78 (PAM silencing)
10433	SEQ ID NO: 10433	RTT*79 (PAM silencing)
10434	SEQ ID NO: 10434	RTT*77 (PAM silencing)
10435	SEQ ID NO: 10435	RTT*78 (PAM silencing)
10436	SEQ ID NO: 10436	RTT*77 (PAM silencing)
10437	SEQ ID NO: 10437	RTT*79 (PAM silencing)
10438	SEQ ID NO: 10438	RTT
10439	SEQ ID NO: 10439	RTT*77 (PAM silencing)
10440	SEQ ID NO: 10440	RTT*79 (PAM silencing)
10441	SEQ ID NO: 10441	RTT
10442	SEQ ID NO: 10442	RTT*78 (PAM silencing)
10443	SEQ ID NO: 10443	RTT*79 (PAM silencing)
10444	SEQ ID NO: 10444	RTT*77 (PAM silencing)
10445	SEQ ID NO: 10445	RTT
10446	SEQ ID NO: 10446	RTT*78 (PAM silencing)
10447	SEQ ID NO: 10447	RTT*77 (PAM silencing)
10448	SEQ ID NO: 10448	RTT
10449	SEQ ID NO: 10449	RTT*79 (PAM silencing)
10450	SEQ ID NO: 10450	RTT*78 (PAM silencing)
10451	SEQ ID NO: 10451	RTT*78 (PAM silencing)
10452	SEQ ID NO: 10452	RTT
10453	SEQ ID NO: 10453	RTT*79 (PAM silencing)
10454	SEQ ID NO: 10454	RTT*77 (PAM silencing)
10455	SEQ ID NO: 10455	RTT
10456	SEQ ID NO: 10456	RTT*78 (PAM silencing)
10457	SEQ ID NO: 10457	RTT*79 (PAM silencing)
10458	SEQ ID NO: 10458	RTT*77 (PAM silencing)
10459	SEQ ID NO: 10459	RTT
10460	SEQ ID NO: 10460	RTT*77 (PAM silencing)
10461	SEQ ID NO: 10461	RTT*79 (PAM silencing)
10462	SEQ ID NO: 10462	RTT*78 (PAM silencing)
10463	SEQ ID NO: 10463	RTT*77 (PAM silencing)
10464	SEQ ID NO: 10464	RTT*78 (PAM silencing)
10465	SEQ ID NO: 10465	RTT*79 (PAM silencing)
10466	SEQ ID NO: 10466	RTT
10467	SEQ ID NO: 10467	RTT*77 (PAM silencing)
10468	SEQ ID NO: 10468	RTT
10469	SEQ ID NO: 10469	RTT*79 (PAM silencing)
10470	SEQ ID NO: 10470	RTT*78 (PAM silencing)
10471	SEQ ID NO: 10471	RTT*78 (PAM silencing)
10472	SEQ ID NO: 10472	RTT*77 (PAM silencing)
10473	SEQ ID NO: 10473	RTT
10474	SEQ ID NO: 10474	RTT*79 (PAM silencing)
10475	SEQ ID NO: 10475	RTT*78 (PAM silencing)
10476	SEQ ID NO: 10476	RTT
10477	SEQ ID NO: 10477	RTT*79 (PAM silencing)
10478	SEQ ID NO: 10478	RTT*77 (PAM silencing)
10479	SEQ ID NO: 10479	RTT*77 (PAM silencing)
10480	SEQ ID NO: 10480	RTT
10481	SEQ ID NO: 10481	RTT*78 (PAM silencing)
10482	SEQ ID NO: 10482	RTT*79 (PAM silencing)
10483	SEQ ID NO: 10483	RTT*78 (PAM silencing)
10484	SEQ ID NO: 10484	RTT*77 (PAM silencing)
10485	SEQ ID NO: 10485	RTT*79 (PAM silencing)
10486	SEQ ID NO: 10486	RTT
10487	SEQ ID NO: 10487	RTT*79 (PAM silencing)
10488	SEQ ID NO: 10488	RTT
10489	SEQ ID NO: 10489	RTT*78 (PAM silencing)
10490	SEQ ID NO: 10490	RTT*77 (PAM silencing)
10491	SEQ ID NO: 10491	RTT*79 (PAM silencing)
10492	SEQ ID NO: 10492	RTT*77 (PAM silencing)
10493	SEQ ID NO: 10493	RTT

Sequence Number	Sequence	Description
10494	SEQ ID NO: 10494	RTT*78 (PAM silencing)
10495	SEQ ID NO: 10495	RTT*78 (PAM silencing)
10496	SEQ ID NO: 10496	RTT*79 (PAM silencing)
10497	SEQ ID NO: 10497	RTT
10498	SEQ ID NO: 10498	RTT*77 (PAM silencing)
10499	SEQ ID NO: 10499	RTT*78 (PAM silencing)
10500	SEQ ID NO: 10500	RTT
10501	SEQ ID NO: 10501	RTT*79 (PAM silencing)
10502	SEQ ID NO: 10502	RTT*77 (PAM silencing)
10503	SEQ ID NO: 10503	RTT*79 (PAM silencing)
10504	SEQ ID NO: 10504	RTT
10505	SEQ ID NO: 10505	RTT*78 (PAM silencing)
10506	SEQ ID NO: 10506	RTT*77 (PAM silencing)
10507	SEQ ID NO: 10507	RTT*79 (PAM silencing)
10508	SEQ ID NO: 10508	RTT
10509	SEQ ID NO: 10509	RTT*77 (PAM silencing)
10510	SEQ ID NO: 10510	RTT*78 (PAM silencing)
10511	SEQ ID NO: 10511	RTT*79 (PAM silencing)
10512	SEQ ID NO: 10512	RTT
10513	SEQ ID NO: 10513	RTT*78 (PAM silencing)
10514	SEQ ID NO: 10514	RTT*77 (PAM silencing)
10515	SEQ ID NO: 10515	RTT*78 (PAM silencing)
10516	SEQ ID NO: 10516	RTT*77 (PAM silencing)
10517	SEQ ID NO: 10517	RTT
10518	SEQ ID NO: 10518	RTT*79 (PAM silencing)
10519	SEQ ID NO: 10519	RTT*77 (PAM silencing)
10520	SEQ ID NO: 10520	RTT*79 (PAM silencing)
10521	SEQ ID NO: 10521	RTT
10522	SEQ ID NO: 10522	RTT*78 (PAM silencing)
10523	SEQ ID NO: 10523	RTT*78 (PAM silencing)
10524	SEQ ID NO: 10524	RTT*77 (PAM silencing)
10525	SEQ ID NO: 10525	RTT
10526	SEQ ID NO: 10526	RTT*79 (PAM silencing)
10527	SEQ ID NO: 10527	RTT*77 (PAM silencing)
10528	SEQ ID NO: 10528	RTT*79 (PAM silencing)
10529	SEQ ID NO: 10529	RTT
10530	SEQ ID NO: 10530	RTT*78 (PAM silencing)
10531	SEQ ID NO: 10531	RTT*78 (PAM silencing)
10532	SEQ ID NO: 10532	RTT*77 (PAM silencing)
10533	SEQ ID NO: 10533	RTT
10534	SEQ ID NO: 10534	RTT*79 (PAM silencing)
10535	SEQ ID NO: 10535	RTT*77 (PAM silencing)
10536	SEQ ID NO: 10536	RTT*78 (PAM silencing)
10537	SEQ ID NO: 10537	RTT
10538	SEQ ID NO: 10538	RTT*79 (PAM silencing)
10539	SEQ ID NO: 10539	RTT*78 (PAM silencing)
10540	SEQ ID NO: 10540	RTT*79 (PAM silencing)
10541	SEQ ID NO: 10541	RTT
10542	SEQ ID NO: 10542	RTT*77 (PAM silencing)
10543	SEQ ID NO: 10543	RTT*79 (PAM silencing)
10544	SEQ ID NO: 10544	RTT*78 (PAM silencing)
10545	SEQ ID NO: 10545	RTT*77 (PAM silencing)
10546	SEQ ID NO: 10546	RTT
10547	SEQ ID NO: 10547	RTT*79 (PAM silencing)
10548	SEQ ID NO: 10548	RTT
10549	SEQ ID NO: 10549	RTT*78 (PAM silencing)
10550	SEQ ID NO: 10550	RTT*77 (PAM silencing)
10551	SEQ ID NO: 10551	RTT*79 (PAM silencing)
10552	SEQ ID NO: 10552	RTT*77 (PAM silencing)
10553	SEQ ID NO: 10553	RTT
10554	SEQ ID NO: 10554	RTT*78 (PAM silencing)
10555	SEQ ID NO: 10555	RTT*78 (PAM silencing)
10556	SEQ ID NO: 10556	RTT*77 (PAM silencing)
10557	SEQ ID NO: 10557	RTT*79 (PAM silencing)
10558	SEQ ID NO: 10558	RTT
10559	SEQ ID NO: 10559	RTT*78 (PAM silencing)
10560	SEQ ID NO: 10560	RTT*77 (PAM silencing)
10561	SEQ ID NO: 10561	RTT*79 (PAM silencing)
10562	SEQ ID NO: 10562	RTT
10563	SEQ ID NO: 10563	RTT*79 (PAM silencing)
10564	SEQ ID NO: 10564	RTT*78 (PAM silencing)
10565	SEQ ID NO: 10565	RTT

Sequence Number	Sequence	Description
10566	SEQ ID NO: 10566	RTT*77 (PAM silencing)
10567	SEQ ID NO: 10567	RTT
10568	SEQ ID NO: 10568	RTT*77 (PAM silencing)
10569	SEQ ID NO: 10569	RTT*78 (PAM silencing)
10570	SEQ ID NO: 10570	RTT*79 (PAM silencing)
10571	SEQ ID NO: 10571	RTT*79 (PAM silencing)
10572	SEQ ID NO: 10572	RTT
10573	SEQ ID NO: 10573	RTT*77 (PAM silencing)
10574	SEQ ID NO: 10574	RTT*78 (PAM silencing)
10575	SEQ ID NO: 10575	RTT*78 (PAM silencing)
10576	SEQ ID NO: 10576	RTT*77 (PAM silencing)
10577	SEQ ID NO: 10577	RTT*79 (PAM silencing)
10578	SEQ ID NO: 10578	RTT
10579	SEQ ID NO: 10579	RTT*77 (PAM silencing)
10580	SEQ ID NO: 10580	RTT*78 (PAM silencing)
10581	SEQ ID NO: 10581	RTT
10582	SEQ ID NO: 10582	RTT*79 (PAM silencing)
10583	SEQ ID NO: 10583	RTT*78 (PAM silencing)
10584	SEQ ID NO: 10584	RTT*79 (PAM silencing)
10585	SEQ ID NO: 10585	RTT*77 (PAM silencing)
10586	SEQ ID NO: 10586	RTT
10587	SEQ ID NO: 10587	RTT*78 (PAM silencing)
10588	SEQ ID NO: 10588	RTT
10589	SEQ ID NO: 10589	RTT*79 (PAM silencing)
10590	SEQ ID NO: 10590	RTT*77 (PAM silencing)
10591	SEQ ID NO: 10591	RTT
10592	SEQ ID NO: 10592	RTT*77 (PAM silencing)
10593	SEQ ID NO: 10593	RTT*78 (PAM silencing)
10594	SEQ ID NO: 10594	RTT*79 (PAM silencing)
10595	SEQ ID NO: 10595	RTT*78 (PAM silencing)
10596	SEQ ID NO: 10596	RTT
10597	SEQ ID NO: 10597	RTT*79 (PAM silencing)
10598	SEQ ID NO: 10598	RTT*77 (PAM silencing)
10599	SEQ ID NO: 10599	RTT*77 (PAM silencing)
10600	SEQ ID NO: 10600	RTT*78 (PAM silencing)
10601	SEQ ID NO: 10601	RTT
10602	SEQ ID NO: 10602	RTT*79 (PAM silencing)
10603	SEQ ID NO: 10603	RTT*78 (PAM silencing)
10604	SEQ ID NO: 10604	RTT*79 (PAM silencing)
10605	SEQ ID NO: 10605	RTT
10606	SEQ ID NO: 10606	RTT*77 (PAM silencing)
10607	SEQ ID NO: 10607	RTT*77 (PAM silencing)
10608	SEQ ID NO: 10608	RTT*79 (PAM silencing)
10609	SEQ ID NO: 10609	RTT
10610	SEQ ID NO: 10610	RTT*78 (PAM silencing)
10611	SEQ ID NO: 10611	RTT*79 (PAM silencing)
10612	SEQ ID NO: 10612	RTT*78 (PAM silencing)
10613	SEQ ID NO: 10613	RTT*77 (PAM silencing)
10614	SEQ ID NO: 10614	RTT
10615	SEQ ID NO: 10615	RTT*78 (PAM silencing)
10616	SEQ ID NO: 10616	RTT
10617	SEQ ID NO: 10617	RTT*79 (PAM silencing)
10618	SEQ ID NO: 10618	RTT*77 (PAM silencing)
10619	SEQ ID NO: 10619	RTT*77 (PAM silencing)
10620	SEQ ID NO: 10620	RTT
10621	SEQ ID NO: 10621	RTT*79 (PAM silencing)
10622	SEQ ID NO: 10622	RTT*78 (PAM silencing)
78	SEQ ID NO: 78	PE3 ngRNA spacer (CG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
10623	SEQ ID NO: 10623	PE3b*77 ngRNA spacer (TG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
10624	SEQ ID NO: 10624	PE3b*79 ngRNA spacer (TG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
10625	SEQ ID NO: 10625	PE3b*78 ngRNA spacer (AG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG PAM)
10626	SEQ ID NO: 10626	PE3b*78 ngRNA spacer (CG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
64	SEQ ID NO: 64	PE3 ngRNA spacer (CG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
99	SEQ ID NO: 99	PE3 ngRNA spacer (TG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
10627	SEQ ID NO: 10627	PE3b*77 ngRNA spacer (AG PAM)
10628	SEQ ID NO: 10628	PE3b*79 ngRNA spacer (CG PAM)
10629	SEQ ID NO: 10629	PE3b*77 ngRNA spacer (CG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
10630	SEQ ID NO: 10630	PE3b*79 ngRNA spacer (AG PAM)
81	SEQ ID NO: 81	PE3 ngRNA spacer (AG PAM)
10631	SEQ ID NO: 10631	PE3b*78 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)

Table 54

Sequence Number	Sequence	Description
10632	SEQ ID NO: 10632	PEgRNA spacer (TG PAM)
10633	SEQ ID NO: 10633	PEgRNA spacer (TG PAM)
10634	SEQ ID NO: 10634	PEgRNA spacer (TG PAM)
10635	SEQ ID NO: 10635	PEgRNA spacer (TG PAM)
10636	SEQ ID NO: 10636	PEgRNA spacer (TG PAM)
10637	SEQ ID NO: 10637	PEgRNA spacer (TG PAM)
10638	SEQ ID NO: 10638	PEgRNA spacer (TG PAM)
10639	GGG	PBS
10640	GGGG	PBS
10641	GGGGC	PBS
10642	GGGGCG	PBS
10643	GGGGCGT	PBS

Sequence Number	Sequence	Description
10644	GGGGCG TG	PBS
10645	GGGGCG TGT	PBS
10646	SEQ ID NO: 10646	PBS
10647	SEQ ID NO: 10647	PBS
10648	SEQ ID NO: 10648	PBS
10649	SEQ ID NO: 10649	PBS
10650	SEQ ID NO: 10650	PBS
10651	SEQ ID NO: 10651	PBS
10652	SEQ ID NO: 10652	PBS
10653	SEQ ID NO: 10653	PBS
10654	SEQ ID NO: 10654	PBS
10655	SEQ ID NO: 10655	PBS
10656	SEQ ID NO: 10656	RTT
10657	SEQ ID NO: 10657	RTT
10658	SEQ ID NO: 10658	RTT
10659	SEQ ID NO: 10659	RTT
10660	SEQ ID NO: 10660	RTT
10661	SEQ ID NO: 10661	RTT
10662	SEQ ID NO: 10662	RTT
10663	SEQ ID NO: 10663	RTT
10664	SEQ ID NO: 10664	RTT
10665	SEQ ID NO: 10665	RTT
10666	SEQ ID NO: 10666	RTT
10667	SEQ ID NO: 10667	RTT
10668	SEQ ID NO: 10668	RTT
10669	SEQ ID NO: 10669	RTT
10670	SEQ ID NO: 10670	RTT
10671	SEQ ID NO: 10671	RTT
10672	SEQ ID NO: 10672	RTT
10673	SEQ ID NO: 10673	RTT
10674	SEQ ID NO: 10674	RTT
10675	SEQ ID NO: 10675	RTT
10676	SEQ ID NO: 10676	RTT

Sequence Number	Sequence	Description
10677	SEQ ID NO: 10677	RTT
10678	SEQ ID NO: 10678	RTT
10679	SEQ ID NO: 10679	RTT
10680	SEQ ID NO: 10680	RTT
10681	SEQ ID NO: 10681	RTT
10682	SEQ ID NO: 10682	RTT
10683	SEQ ID NO: 10683	RTT
10684	SEQ ID NO: 10684	RTT
10685	SEQ ID NO: 10685	RTT
10686	SEQ ID NO: 10686	RTT
10687	SEQ ID NO: 10687	RTT
10688	SEQ ID NO: 10688	RTT
10689	SEQ ID NO: 10689	RTT
10690	SEQ ID NO: 10690	RTT
10691	SEQ ID NO: 10691	RTT
10692	SEQ ID NO: 10692	RTT
10693	SEQ ID NO: 10693	RTT
10694	SEQ ID NO: 10694	RTT
10695	SEQ ID NO: 10695	RTT
10696	SEQ ID NO: 10696	RTT
10697	SEQ ID NO: 10697	RTT
10698	SEQ ID NO: 10698	RTT
10699	SEQ ID NO: 10699	RTT
10700	SEQ ID NO: 10700	RTT
10701	SEQ ID NO: 10701	RTT
10702	SEQ ID NO: 10702	RTT
10703	SEQ ID NO: 10703	RTT
10704	SEQ ID NO: 10704	RTT
10705	SEQ ID NO: 10705	RTT
10706	SEQ ID NO: 10706	RTT
10707	SEQ ID NO: 10707	RTT
10708	SEQ ID NO: 10708	RTT
10709	SEQ ID NO: 10709	RTT

Sequence Number	Sequence	Description
10710	SEQ ID NO: 10710	RTT
10711	SEQ ID NO: 10711	RTT
10712	SEQ ID NO: 10712	RTT
10713	SEQ ID NO: 10713	RTT
10714	SEQ ID NO: 10714	RTT
10715	SEQ ID NO: 10715	RTT
10716	SEQ ID NO: 10716	RTT
10717	SEQ ID NO: 10717	RTT
10718	SEQ ID NO: 10718	RTT
10719	SEQ ID NO: 10719	RTT
10720	SEQ ID NO: 10720	RTT
10721	SEQ ID NO: 10721	RTT
10722	SEQ ID NO: 10722	RTT
10723	SEQ ID NO: 10723	RTT
10724	SEQ ID NO: 10724	RTT
10725	SEQ ID NO: 10725	RTT
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (AG PAM)
72	SEQ ID NO: 72	PE3 ngRNA spacer (GG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GG PAM)
85	SEQ ID NO: 85	PE3 ngRNA spacer (GG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(AG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG PAM)
100	SEQ ID NO: 100	ngRNA (GG PAM)
109	SEQ ID NO: 109	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
101	SEQ ID NO: 101	ngRNA (TG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
110	SEQ ID NO: 110	ngRNA (GG PAM)
105	SEQ ID NO: 105	ngRNA (GG PAM)
113	SEQ ID NO: 113	ngRNA (GG PAM)
118	SEQ ID NO: 118	ngRNA (GG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Sequence Number	Sequence	Description
1527	SEQ ID NO: 1527	ngRNA (AG PAM)
112	SEQ ID NO: 112	ngRNA (GG PAM)

Table 55

Sequence Number	Sequence	Description
10726	SEQ ID NO: 10726	PEgRNA spacer (TG PAM)
10727	SEQ ID NO: 10727	PEgRNA spacer (TG PAM)
10728	SEQ ID NO: 10728	PEgRNA spacer (TG PAM)
10729	SEQ ID NO: 10729	PEgRNA spacer (TG PAM)
10730	SEQ ID NO: 10730	PEgRNA spacer (TG PAM)
10731	SEQ ID NO: 10731	PEgRNA spacer (TG PAM)
10732	SEQ ID NO: 10732	PEgRNA spacer (TG PAM)
6465	AGC	PBS
10733	AGCA	PBS
10734	AGCAT	PBS
10735	AGCATG	PBS
10736	AGCATG G	PBS
10737	AGCATG GG	PBS
10738	AGCATG GGG	PBS
10739	SEQ ID NO: 10739	PBS
10740	SEQ ID NO: 10740	PBS
10741	SEQ ID NO: 10741	PBS
10742	SEQ ID NO: 10742	PBS
10743	SEQ ID NO: 10743	PBS
10744	SEQ ID NO: 10744	PBS
10745	SEQ ID NO: 10745	PBS
10746	SEQ ID NO: 10746	PBS
10747	SEQ ID NO: 10747	PBS
10748	SEQ ID NO: 10748	PBS
10749	SEQ ID NO: 10749	RTT
10750	SEQ ID NO: 10750	RTT
10751	SEQ ID NO: 10751	RTT

Sequence Number	Sequence	Description
10752	SEQ ID NO: 10752	RTT
10753	SEQ ID NO: 10753	RTT
10754	SEQ ID NO: 10754	RTT
10755	SEQ ID NO: 10755	RTT
10756	SEQ ID NO: 10756	RTT
10757	SEQ ID NO: 10757	RTT
10758	SEQ ID NO: 10758	RTT
10759	SEQ ID NO: 10759	RTT
10760	SEQ ID NO: 10760	RTT
10761	SEQ ID NO: 10761	RTT
10762	SEQ ID NO: 10762	RTT
10763	SEQ ID NO: 10763	RTT
10764	SEQ ID NO: 10764	RTT
10765	SEQ ID NO: 10765	RTT
10766	SEQ ID NO: 10766	RTT
10767	SEQ ID NO: 10767	RTT
10768	SEQ ID NO: 10768	RTT
10769	SEQ ID NO: 10769	RTT
10770	SEQ ID NO: 10770	RTT
10771	SEQ ID NO: 10771	RTT
10772	SEQ ID NO: 10772	RTT
10773	SEQ ID NO: 10773	RTT
10774	SEQ ID NO: 10774	RTT
10775	SEQ ID NO: 10775	RTT
10776	SEQ ID NO: 10776	RTT
10777	SEQ ID NO: 10777	RTT
10778	SEQ ID NO: 10778	RTT
10779	SEQ ID NO: 10779	RTT
10780	SEQ ID NO: 10780	RTT
10781	SEQ ID NO: 10781	RTT
10782	SEQ ID NO: 10782	RTT
10783	SEQ ID NO: 10783	RTT
10784	SEQ ID NO: 10784	RTT

Sequence Number	Sequence	Description
10785	SEQ ID NO: 10785	RTT
10786	SEQ ID NO: 10786	RTT
10787	SEQ ID NO: 10787	RTT
10788	SEQ ID NO: 10788	RTT
10789	SEQ ID NO: 10789	RTT
10790	SEQ ID NO: 10790	RTT
10791	SEQ ID NO: 10791	RTT
10792	SEQ ID NO: 10792	RTT
10793	SEQ ID NO: 10793	RTT
10794	SEQ ID NO: 10794	RTT
10795	SEQ ID NO: 10795	RTT
10796	SEQ ID NO: 10796	RTT
10797	SEQ ID NO: 10797	RTT
10798	SEQ ID NO: 10798	RTT
10799	SEQ ID NO: 10799	RTT
10800	SEQ ID NO: 10800	RTT
10801	SEQ ID NO: 10801	RTT
10802	SEQ ID NO: 10802	RTT
10803	SEQ ID NO: 10803	RTT
10804	SEQ ID NO: 10804	RTT
10805	SEQ ID NO: 10805	RTT
10806	SEQ ID NO: 10806	RTT
10807	SEQ ID NO: 10807	RTT
10808	SEQ ID NO: 10808	RTT
10809	SEQ ID NO: 10809	RTT
10810	SEQ ID NO: 10810	RTT
10811	SEQ ID NO: 10811	RTT
10812	SEQ ID NO: 10812	RTT
10813	SEQ ID NO: 10813	RTT
10814	SEQ ID NO: 10814	RTT
10815	SEQ ID NO: 10815	RTT
10816	SEQ ID NO: 10816	RTT
10817	SEQ ID NO: 10817	RTT

Sequence Number	Sequence	Description
10818	SEQ ID NO: 10818	RTT
10819	SEQ ID NO: 10819	RTT
10820	SEQ ID NO: 10820	RTT
10821	SEQ ID NO: 10821	RTT
10822	SEQ ID NO: 10822	RTT
10823	SEQ ID NO: 10823	RTT
10824	SEQ ID NO: 10824	RTT
10825	SEQ ID NO: 10825	RTT
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
1217	SEQ ID NO: 1217	PE3 ngRNA spacer (TG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)

Sequence Number	Sequence	Description
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Table 56

Sequence Number	Sequence	Description
10826	SEQ ID NO: 10826	PEgRNA spacer (TG PAM)
10827	SEQ ID NO: 10827	PEgRNA spacer (TG PAM)
10828	SEQ ID NO: 10828	PEgRNA spacer (TG PAM)
10829	SEQ ID NO: 10829	PEgRNA spacer (TG PAM)
10830	SEQ ID NO: 10830	PEgRNA spacer (TG PAM)
10831	SEQ ID NO: 10831	PEgRNA spacer (TG PAM)
10832	SEQ ID NO: 10832	PEgRNA spacer (TG PAM)
10833	AGA	PBS
10834	AGAG	PBS
10835	AGAGC	PBS
10836	AGAGCA	PBS
10837	AGAGCAT	PBS
10838	AGAGCATG	PBS
10839	AGAGCATGG	PBS
10840	SEQ ID NO: 10840	PBS
10841	SEQ ID NO: 10841	PBS
10842	SEQ ID NO: 10842	PBS
10843	SEQ ID NO: 10843	PBS
10844	SEQ ID NO: 10844	PBS
10845	SEQ ID NO: 10845	PBS
10846	SEQ ID NO: 10846	PBS
10847	SEQ ID NO: 10847	PBS
10848	SEQ ID NO: 10848	PBS
10849	SEQ ID NO: 10849	PBS
10850	SEQ ID NO: 10850	RTT*112 (PAM silencing)
10851	SEQ ID NO: 10851	RTT*111 (PAM silencing)
10852	SEQ ID NO: 10852	RTT
10853	SEQ ID NO: 10853	RTT*113 (PAM silencing)
10854	SEQ ID NO: 10854	RTT*113 (PAM silencing)
10855	SEQ ID NO: 10855	RTT*111 (PAM silencing)
10856	SEQ ID NO: 10856	RTT
10857	SEQ ID NO: 10857	RTT*112 (PAM silencing)
10858	SEQ ID NO: 10858	RTT*111 (PAM silencing)
10859	SEQ ID NO: 10859	RTT*113 (PAM silencing)
10860	SEQ ID NO: 10860	RTT
10861	SEQ ID NO: 10861	RTT*112 (PAM silencing)
10862	SEQ ID NO: 10862	RTT*111 (PAM silencing)
10863	SEQ ID NO: 10863	RTT*113 (PAM silencing)
10864	SEQ ID NO: 10864	RTT*112 (PAM silencing)
10865	SEQ ID NO: 10865	RTT
10866	SEQ ID NO: 10866	RTT
10867	SEQ ID NO: 10867	RTT*111 (PAM silencing)
10868	SEQ ID NO: 10868	RTT*112 (PAM silencing)
10869	SEQ ID NO: 10869	RTT*113 (PAM silencing)
10870	SEQ ID NO: 10870	RTT
10871	SEQ ID NO: 10871	RTT*113 (PAM silencing)
10872	SEQ ID NO: 10872	RTT*111 (PAM silencing)
10873	SEQ ID NO: 10873	RTT*112 (PAM silencing)
10874	SEQ ID NO: 10874	RTT*112 (PAM silencing)

Sequence Number	Sequence	Description
10875	SEQ ID NO: 10875	RTT*113 (PAM silencing)
10876	SEQ ID NO: 10876	RTT*111 (PAM silencing)
10877	SEQ ID NO: 10877	RTT
10878	SEQ ID NO: 10878	RTT*113 (PAM silencing)
10879	SEQ ID NO: 10879	RTT*111 (PAM silencing)
10880	SEQ ID NO: 10880	RTT*112 (PAM silencing)
10881	SEQ ID NO: 10881	RTT
10882	SEQ ID NO: 10882	RTT*113 (PAM silencing)
10883	SEQ ID NO: 10883	RTT
10884	SEQ ID NO: 10884	RTT*112 (PAM silencing)
10885	SEQ ID NO: 10885	RTT*111 (PAM silencing)
10886	SEQ ID NO: 10886	RTT*113 (PAM silencing)
10887	SEQ ID NO: 10887	RTT*112 (PAM silencing)
10888	SEQ ID NO: 10888	RTT
10889	SEQ ID NO: 10889	RTT*111 (PAM silencing)
10890	SEQ ID NO: 10890	RTT*111 (PAM silencing)
10891	SEQ ID NO: 10891	RTT*112 (PAM silencing)
10892	SEQ ID NO: 10892	RTT
10893	SEQ ID NO: 10893	RTT*113 (PAM silencing)
10894	SEQ ID NO: 10894	RTT
10895	SEQ ID NO: 10895	RTT*112 (PAM silencing)
10896	SEQ ID NO: 10896	RTT*111 (PAM silencing)
10897	SEQ ID NO: 10897	RTT*113 (PAM silencing)
10898	SEQ ID NO: 10898	RTT
10899	SEQ ID NO: 10899	RTT*113 (PAM silencing)
10900	SEQ ID NO: 10900	RTT*112 (PAM silencing)
10901	SEQ ID NO: 10901	RTT*111 (PAM silencing)
10902	SEQ ID NO: 10902	RTT*111 (PAM silencing)
10903	SEQ ID NO: 10903	RTT*113 (PAM silencing)
10904	SEQ ID NO: 10904	RTT
10905	SEQ ID NO: 10905	RTT*112 (PAM silencing)
10906	SEQ ID NO: 10906	RTT*111 (PAM silencing)
10907	SEQ ID NO: 10907	RTT
10908	SEQ ID NO: 10908	RTT*113 (PAM silencing)
10909	SEQ ID NO: 10909	RTT*112 (PAM silencing)
10910	SEQ ID NO: 10910	RTT*111 (PAM silencing)
10911	SEQ ID NO: 10911	RTT
10912	SEQ ID NO: 10912	RTT*112 (PAM silencing)
10913	SEQ ID NO: 10913	RTT*113 (PAM silencing)
10914	SEQ ID NO: 10914	RTT*113 (PAM silencing)
10915	SEQ ID NO: 10915	RTT*112 (PAM silencing)
10916	SEQ ID NO: 10916	RTT
10917	SEQ ID NO: 10917	RTT*111 (PAM silencing)
10918	SEQ ID NO: 10918	RTT*112 (PAM silencing)
10919	SEQ ID NO: 10919	RTT
10920	SEQ ID NO: 10920	RTT*111 (PAM silencing)
10921	SEQ ID NO: 10921	RTT*113 (PAM silencing)
10922	SEQ ID NO: 10922	RTT
10923	SEQ ID NO: 10923	RTT*113 (PAM silencing)
10924	SEQ ID NO: 10924	RTT*112 (PAM silencing)
10925	SEQ ID NO: 10925	RTT*111 (PAM silencing)
10926	SEQ ID NO: 10926	RTT*112 (PAM silencing)
10927	SEQ ID NO: 10927	RTT
10928	SEQ ID NO: 10928	RTT*113 (PAM silencing)
10929	SEQ ID NO: 10929	RTT*111 (PAM silencing)
10930	SEQ ID NO: 10930	RTT*111 (PAM silencing)
10931	SEQ ID NO: 10931	RTT*112 (PAM silencing)
10932	SEQ ID NO: 10932	RTT*113 (PAM silencing)
10933	SEQ ID NO: 10933	RTT
10934	SEQ ID NO: 10934	RTT*112 (PAM silencing)
10935	SEQ ID NO: 10935	RTT*111 (PAM silencing)
10936	SEQ ID NO: 10936	RTT*113 (PAM silencing)
10937	SEQ ID NO: 10937	RTT
10938	SEQ ID NO: 10938	RTT
10939	SEQ ID NO: 10939	RTT*113 (PAM silencing)
10940	SEQ ID NO: 10940	RTT*112 (PAM silencing)
10941	SEQ ID NO: 10941	RTT*111 (PAM silencing)
10942	SEQ ID NO: 10942	RTT*112 (PAM silencing)
10943	SEQ ID NO: 10943	RTT
10944	SEQ ID NO: 10944	RTT*113 (PAM silencing)
10945	SEQ ID NO: 10945	RTT*111 (PAM silencing)
10946	SEQ ID NO: 10946	RTT*113 (PAM silencing)

Sequence Number	Sequence	Description
10947	SEQ ID NO: 10947	RTT*111 (PAM silencing)
10948	SEQ ID NO: 10948	RTT*112 (PAM silencing)
10949	SEQ ID NO: 10949	RTT
10950	SEQ ID NO: 10950	RTT
10951	SEQ ID NO: 10951	RTT*113 (PAM silencing)
10952	SEQ ID NO: 10952	RTT*111 (PAM silencing)
10953	SEQ ID NO: 10953	RTT*112 (PAM silencing)
10954	SEQ ID NO: 10954	RTT*113 (PAM silencing)
10955	SEQ ID NO: 10955	RTT
10956	SEQ ID NO: 10956	RTT*111 (PAM silencing)
10957	SEQ ID NO: 10957	RTT*112 (PAM silencing)
10958	SEQ ID NO: 10958	RTT
10959	SEQ ID NO: 10959	RTT*112 (PAM silencing)
10960	SEQ ID NO: 10960	RTT*113 (PAM silencing)
10961	SEQ ID NO: 10961	RTT*111 (PAM silencing)
10962	SEQ ID NO: 10962	RTT*112 (PAM silencing)
10963	SEQ ID NO: 10963	RTT*111 (PAM silencing)
10964	SEQ ID NO: 10964	RTT
10965	SEQ ID NO: 10965	RTT*113 (PAM silencing)
10966	SEQ ID NO: 10966	RTT*111 (PAM silencing)
10967	SEQ ID NO: 10967	RTT
10968	SEQ ID NO: 10968	RTT*112 (PAM silencing)
10969	SEQ ID NO: 10969	RTT*113 (PAM silencing)
10970	SEQ ID NO: 10970	RTT*112 (PAM silencing)
10971	SEQ ID NO: 10971	RTT*111 (PAM silencing)
10972	SEQ ID NO: 10972	RTT*113 (PAM silencing)
10973	SEQ ID NO: 10973	RTT
10974	SEQ ID NO: 10974	RTT*113 (PAM silencing)
10975	SEQ ID NO: 10975	RTT
10976	SEQ ID NO: 10976	RTT*112 (PAM silencing)
10977	SEQ ID NO: 10977	RTT*111 (PAM silencing)
10978	SEQ ID NO: 10978	RTT*112 (PAM silencing)
10979	SEQ ID NO: 10979	RTT*111 (PAM silencing)
10980	SEQ ID NO: 10980	RTT*113 (PAM silencing)
10981	SEQ ID NO: 10981	RTT
10982	SEQ ID NO: 10982	RTT*111 (PAM silencing)
10983	SEQ ID NO: 10983	RTT*113 (PAM silencing)
10984	SEQ ID NO: 10984	RTT
10985	SEQ ID NO: 10985	RTT*112 (PAM silencing)
10986	SEQ ID NO: 10986	RTT*113 (PAM silencing)
10987	SEQ ID NO: 10987	RTT
10988	SEQ ID NO: 10988	RTT*111 (PAM silencing)
10989	SEQ ID NO: 10989	RTT*112 (PAM silencing)
10990	SEQ ID NO: 10990	RTT*112 (PAM silencing)
10991	SEQ ID NO: 10991	RTT*113 (PAM silencing)
10992	SEQ ID NO: 10992	RTT
10993	SEQ ID NO: 10993	RTT*111 (PAM silencing)
10994	SEQ ID NO: 10994	RTT*111 (PAM silencing)
10995	SEQ ID NO: 10995	RTT
10996	SEQ ID NO: 10996	RTT*113 (PAM silencing)
10997	SEQ ID NO: 10997	RTT*112 (PAM silencing)
10998	SEQ ID NO: 10998	RTT
10999	SEQ ID NO: 10999	RTT*111 (PAM silencing)
11000	SEQ ID NO: 11000	RTT*113 (PAM silencing)
11001	SEQ ID NO: 11001	RTT*112 (PAM silencing)
11002	SEQ ID NO: 11002	RTT*112 (PAM silencing)
11003	SEQ ID NO: 11003	RTT
11004	SEQ ID NO: 11004	RTT*111 (PAM silencing)
11005	SEQ ID NO: 11005	RTT*113 (PAM silencing)
11006	SEQ ID NO: 11006	RTT*113 (PAM silencing)
11007	SEQ ID NO: 11007	RTT
11008	SEQ ID NO: 11008	RTT*111 (PAM silencing)
11009	SEQ ID NO: 11009	RTT*112 (PAM silencing)
11010	SEQ ID NO: 11010	RTT*111 (PAM silencing)
11011	SEQ ID NO: 11011	RTT*113 (PAM silencing)
11012	SEQ ID NO: 11012	RTT*112 (PAM silencing)
11013	SEQ ID NO: 11013	RTT
11014	SEQ ID NO: 11014	RTT*111 (PAM silencing)
11015	SEQ ID NO: 11015	RTT*112 (PAM silencing)
11016	SEQ ID NO: 11016	RTT*113 (PAM silencing)
11017	SEQ ID NO: 11017	RTT
11018	SEQ ID NO: 11018	RTT*112 (PAM silencing)

Sequence Number	Sequence	Description
11019	SEQ ID NO: 11019	RTT
11020	SEQ ID NO: 11020	RTT*111 (PAM silencing)
11021	SEQ ID NO: 11021	RTT*113 (PAM silencing)
11022	SEQ ID NO: 11022	RTT*111 (PAM silencing)
11023	SEQ ID NO: 11023	RTT*112 (PAM silencing)
11024	SEQ ID NO: 11024	RTT*113 (PAM silencing)
11025	SEQ ID NO: 11025	RTT
11026	SEQ ID NO: 11026	RTT*111 (PAM silencing)
11027	SEQ ID NO: 11027	RTT*112 (PAM silencing)
11028	SEQ ID NO: 11028	RTT
11029	SEQ ID NO: 11029	RTT*113 (PAM silencing)
11030	SEQ ID NO: 11030	RTT*111 (PAM silencing)
11031	SEQ ID NO: 11031	RTT*112 (PAM silencing)
11032	SEQ ID NO: 11032	RTT*113 (PAM silencing)
11033	SEQ ID NO: 11033	RTT
11034	SEQ ID NO: 11034	RTT*113 (PAM silencing)
11035	SEQ ID NO: 11035	RTT
11036	SEQ ID NO: 11036	RTT*112 (PAM silencing)
11037	SEQ ID NO: 11037	RTT*111 (PAM silencing)
11038	SEQ ID NO: 11038	RTT
11039	SEQ ID NO: 11039	RTT*113 (PAM silencing)
11040	SEQ ID NO: 11040	RTT*112 (PAM silencing)
11041	SEQ ID NO: 11041	RTT*111 (PAM silencing)
11042	SEQ ID NO: 11042	RTT*113 (PAM silencing)
11043	SEQ ID NO: 11043	RTT*112 (PAM silencing)
11044	SEQ ID NO: 11044	RTT
11045	SEQ ID NO: 11045	RTT*111 (PAM silencing)
11046	SEQ ID NO: 11046	RTT
11047	SEQ ID NO: 11047	RTT*113 (PAM silencing)
11048	SEQ ID NO: 11048	RTT*112 (PAM silencing)
11049	SEQ ID NO: 11049	RTT*111 (PAM silencing)
11050	SEQ ID NO: 11050	RTT*112 (PAM silencing)
11051	SEQ ID NO: 11051	RTT*113 (PAM silencing)
11052	SEQ ID NO: 11052	RTT*111 (PAM silencing)
11053	SEQ ID NO: 11053	RTT
11054	SEQ ID NO: 11054	RTT*113 (PAM silencing)
11055	SEQ ID NO: 11055	RTT*112 (PAM silencing)
11056	SEQ ID NO: 11056	RTT
11057	SEQ ID NO: 11057	RTT*111 (PAM silencing)
11058	SEQ ID NO: 11058	RTT*113 (PAM silencing)
11059	SEQ ID NO: 11059	RTT*112 (PAM silencing)
11060	SEQ ID NO: 11060	RTT
11061	SEQ ID NO: 11061	RTT*111 (PAM silencing)
11062	SEQ ID NO: 11062	RTT*112 (PAM silencing)
11063	SEQ ID NO: 11063	RTT
11064	SEQ ID NO: 11064	RTT*113 (PAM silencing)
11065	SEQ ID NO: 11065	RTT*111 (PAM silencing)
11066	SEQ ID NO: 11066	RTT
11067	SEQ ID NO: 11067	RTT*111 (PAM silencing)
11068	SEQ ID NO: 11068	RTT*113 (PAM silencing)
11069	SEQ ID NO: 11069	RTT*112 (PAM silencing)
11070	SEQ ID NO: 11070	RTT*111 (PAM silencing)
11071	SEQ ID NO: 11071	RTT*113 (PAM silencing)
11072	SEQ ID NO: 11072	RTT
11073	SEQ ID NO: 11073	RTT*112 (PAM silencing)
11074	SEQ ID NO: 11074	RTT
11075	SEQ ID NO: 11075	RTT*113 (PAM silencing)
11076	SEQ ID NO: 11076	RTT*111 (PAM silencing)
11077	SEQ ID NO: 11077	RTT*112 (PAM silencing)
11078	SEQ ID NO: 11078	RTT*111 (PAM silencing)
11079	SEQ ID NO: 11079	RTT*112 (PAM silencing)
11080	SEQ ID NO: 11080	RTT*113 (PAM silencing)
11081	SEQ ID NO: 11081	RTT
11082	SEQ ID NO: 11082	RTT
11083	SEQ ID NO: 11083	RTT*113 (PAM silencing)
11084	SEQ ID NO: 11084	RTT*112 (PAM silencing)
11085	SEQ ID NO: 11085	RTT*111 (PAM silencing)
11086	SEQ ID NO: 11086	RTT*113 (PAM silencing)
11087	SEQ ID NO: 11087	RTT*112 (PAM silencing)
11088	SEQ ID NO: 11088	RTT
11089	SEQ ID NO: 11089	RTT*111 (PAM silencing)
11090	SEQ ID NO: 11090	RTT

Sequence Number	Sequence	Description
11091	SEQ ID NO: 11091	RTT*112 (PAM silencing)
11092	SEQ ID NO: 11092	RTT*111 (PAM silencing)
11093	SEQ ID NO: 11093	RTT*113 (PAM silencing)
11094	SEQ ID NO: 11094	RTT*112 (PAM silencing)
11095	SEQ ID NO: 11095	RTT*111 (PAM silencing)
11096	SEQ ID NO: 11096	RTT*113 (PAM silencing)
11097	SEQ ID NO: 11097	RTT
11098	SEQ ID NO: 11098	RTT
11099	SEQ ID NO: 11099	RTT*111 (PAM silencing)
11100	SEQ ID NO: 11100	RTT*113 (PAM silencing)
11101	SEQ ID NO: 11101	RTT*112 (PAM silencing)
11102	SEQ ID NO: 11102	RTT*111 (PAM silencing)
11103	SEQ ID NO: 11103	RTT*113 (PAM silencing)
11104	SEQ ID NO: 11104	RTT*112 (PAM silencing)
11105	SEQ ID NO: 11105	RTT
11106	SEQ ID NO: 11106	RTT*112 (PAM silencing)
11107	SEQ ID NO: 11107	RTT*111 (PAM silencing)
11108	SEQ ID NO: 11108	RTT
11109	SEQ ID NO: 11109	RTT*113 (PAM silencing)
11110	SEQ ID NO: 11110	RTT*111 (PAM silencing)
11111	SEQ ID NO: 11111	RTT*113 (PAM silencing)
11112	SEQ ID NO: 11112	RTT
11113	SEQ ID NO: 11113	RTT*112 (PAM silencing)
11114	SEQ ID NO: 11114	RTT
11115	SEQ ID NO: 11115	RTT*112 (PAM silencing)
11116	SEQ ID NO: 11116	RTT*111 (PAM silencing)
11117	SEQ ID NO: 11117	RTT*113 (PAM silencing)
11118	SEQ ID NO: 11118	RTT*111 (PAM silencing)
11119	SEQ ID NO: 11119	RTT
11120	SEQ ID NO: 11120	RTT*113 (PAM silencing)
11121	SEQ ID NO: 11121	RTT*112 (PAM silencing)
11122	SEQ ID NO: 11122	RTT
11123	SEQ ID NO: 11123	RTT*112 (PAM silencing)
11124	SEQ ID NO: 11124	RTT*113 (PAM silencing)
11125	SEQ ID NO: 11125	RTT*111 (PAM silencing)
11126	SEQ ID NO: 11126	RTT*111 (PAM silencing)
11127	SEQ ID NO: 11127	RTT*112 (PAM silencing)
11128	SEQ ID NO: 11128	RTT*113 (PAM silencing)
11129	SEQ ID NO: 11129	RTT
11130	SEQ ID NO: 11130	RTT*112 (PAM silencing)
11131	SEQ ID NO: 11131	RTT*113 (PAM silencing)
11132	SEQ ID NO: 11132	RTT
11133	SEQ ID NO: 11133	RTT*111 (PAM silencing)
11134	SEQ ID NO: 11134	RTT*112 (PAM silencing)
11135	SEQ ID NO: 11135	RTT*111 (PAM silencing)
11136	SEQ ID NO: 11136	RTT
11137	SEQ ID NO: 11137	RTT*113 (PAM silencing)
11138	SEQ ID NO: 11138	RTT
11139	SEQ ID NO: 11139	RTT*111 (PAM silencing)
11140	SEQ ID NO: 11140	RTT*112 (PAM silencing)
11141	SEQ ID NO: 11141	RTT*113 (PAM silencing)
11142	SEQ ID NO: 11142	RTT
11143	SEQ ID NO: 11143	RTT*112 (PAM silencing)
11144	SEQ ID NO: 11144	RTT*111 (PAM silencing)
11145	SEQ ID NO: 11145	RTT*113 (PAM silencing)
11146	SEQ ID NO: 11146	RTT*112 (PAM silencing)
11147	SEQ ID NO: 11147	RTT*111 (PAM silencing)
11148	SEQ ID NO: 11148	RTT*113 (PAM silencing)
11149	SEQ ID NO: 11149	RTT
11150	SEQ ID NO: 11150	RTT
11151	SEQ ID NO: 11151	RTT*111 (PAM silencing)
11152	SEQ ID NO: 11152	RTT*113 (PAM silencing)
11153	SEQ ID NO: 11153	RTT*112 (PAM silencing)
11154	SEQ ID NO: 11154	RTT*112 (PAM silencing)
11155	SEQ ID NO: 11155	RTT*111 (PAM silencing)
11156	SEQ ID NO: 11156	RTT*113 (PAM silencing)
11157	SEQ ID NO: 11157	RTT
11158	SEQ ID NO: 11158	RTT
11159	SEQ ID NO: 11159	RTT*112 (PAM silencing)
11160	SEQ ID NO: 11160	RTT*113 (PAM silencing)
11161	SEQ ID NO: 11161	RTT*111 (PAM silencing)
11162	SEQ ID NO: 11162	RTT*111 (PAM silencing)

Sequence Number	Sequence	Description
11163	SEQ ID NO: 11163	RTT*112 (PAM silencing)
11164	SEQ ID NO: 11164	RTT*113 (PAM silencing)
11165	SEQ ID NO: 11165	RTT
1217	SEQ ID NO: 1217	PE3 ngRNA spacer (TG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
11166	SEQ ID NO: 11166	PE3b*111 ngRNA spacer (AG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
91	SEQ ID NO: 91	PE3 ngRNA spacer (AG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
11167	SEQ ID NO: 11167	PE3b*113 ngRNA spacer (AG PAM)
11168	SEQ ID NO: 11168	PE3b*112 ngRNA spacer (AG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
11169	SEQ ID NO: 11169	PE3b*112 ngRNA spacer (AG PAM)
97	SEQ ID NO: 97	PE3 ngRNA spacer (AG PAM)
11170	SEQ ID NO: 11170	PE3b*113 ngRNA spacer (AG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
11171	SEQ ID NO: 11171	PE3b*111 ngRNA spacer (AG PAM)
1240	SEQ ID NO: 1240	PE3 ngRNA spacer (AG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Table 57

Sequence Number	Sequence	Description
11172	SEQ ID NO: 11172	PEgRNA spacer (TG PAM)
11173	SEQ ID NO: 11173	PEgRNA spacer (TG PAM)
11174	SEQ ID NO: 11174	PEgRNA spacer (TG PAM)
11175	SEQ ID NO: 11175	PEgRNA spacer (TG PAM)
11176	SEQ ID NO: 11176	PEgRNA spacer (TG PAM)
11177	SEQ ID NO: 11177	PEgRNA spacer (TG PAM)
11178	SEQ ID NO: 11178	PEgRNA spacer (TG PAM)
2024	AAC	PBS
2025	AACA	PBS
2026	AACAC	PBS
11179	AACACA	PBS
11180	AACACAA	PBS

Sequence Number	Sequence	Description
11181	AACACA AA	PBS
11182	AACACA AAG	PBS
11183	SEQ ID NO: 11183	PBS
11184	SEQ ID NO: 11184	PBS
11185	SEQ ID NO: 11185	PBS
11186	SEQ ID NO: 11186	PBS
11187	SEQ ID NO: 11187	PBS
11188	SEQ ID NO: 11188	PBS
11189	SEQ ID NO: 11189	PBS
11190	SEQ ID NO: 11190	PBS
11191	SEQ ID NO: 11191	PBS
11192	SEQ ID NO: 11192	PBS
11193	SEQ ID NO: 11193	RTT
11194	SEQ ID NO: 11194	RTT
11195	SEQ ID NO: 11195	RTT
11196	SEQ ID NO: 11196	RTT
11197	SEQ ID NO: 11197	RTT
11198	SEQ ID NO: 11198	RTT
11199	SEQ ID NO: 11199	RTT
11200	SEQ ID NO: 11200	RTT
11201	SEQ ID NO: 11201	RTT
11202	SEQ ID NO: 11202	RTT
11203	SEQ ID NO: 11203	RTT
11204	SEQ ID NO: 11204	RTT
11205	SEQ ID NO: 11205	RTT
11206	SEQ ID NO: 11206	RTT
11207	SEQ ID NO: 11207	RTT
11208	SEQ ID NO: 11208	RTT
11209	SEQ ID NO: 11209	RTT
11210	SEQ ID NO: 11210	RTT
11211	SEQ ID NO: 11211	RTT
11212	SEQ ID NO: 11212	RTT
11213	SEQ ID NO: 11213	RTT

Sequence Number	Sequence	Description
11214	SEQ ID NO: 11214	RTT
11215	SEQ ID NO: 11215	RTT
11216	SEQ ID NO: 11216	RTT
11217	SEQ ID NO: 11217	RTT
11218	SEQ ID NO: 11218	RTT
11219	SEQ ID NO: 11219	RTT
11220	SEQ ID NO: 11220	RTT
11221	SEQ ID NO: 11221	RTT
11222	SEQ ID NO: 11222	RTT
11223	SEQ ID NO: 11223	RTT
11224	SEQ ID NO: 11224	RTT
11225	SEQ ID NO: 11225	RTT
11226	SEQ ID NO: 11226	RTT
11227	SEQ ID NO: 11227	RTT
11228	SEQ ID NO: 11228	RTT
11229	SEQ ID NO: 11229	RTT
11230	SEQ ID NO: 11230	RTT
11231	SEQ ID NO: 11231	RTT
11232	SEQ ID NO: 11232	RTT
11233	SEQ ID NO: 11233	RTT
11234	SEQ ID NO: 11234	RTT
11235	SEQ ID NO: 11235	RTT
11236	SEQ ID NO: 11236	RTT
11237	SEQ ID NO: 11237	RTT
11238	SEQ ID NO: 11238	RTT
11239	SEQ ID NO: 11239	RTT
11240	SEQ ID NO: 11240	RTT
11241	SEQ ID NO: 11241	RTT
11242	SEQ ID NO: 11242	RTT
11243	SEQ ID NO: 11243	RTT
11244	SEQ ID NO: 11244	RTT
11245	SEQ ID NO: 11245	RTT
11246	SEQ ID NO: 11246	RTT

Sequence Number	Sequence	Description
11247	SEQ ID NO: 11247	RTT
11248	SEQ ID NO: 11248	RTT
11249	SEQ ID NO: 11249	RTT
11250	SEQ ID NO: 11250	RTT
11251	SEQ ID NO: 11251	RTT
11252	SEQ ID NO: 11252	RTT
11253	SEQ ID NO: 11253	RTT
11254	SEQ ID NO: 11254	RTT
11255	SEQ ID NO: 11255	RTT
11256	SEQ ID NO: 11256	RTT
11257	SEQ ID NO: 11257	RTT
11258	SEQ ID NO: 11258	RTT
11259	SEQ ID NO: 11259	RTT
11260	SEQ ID NO: 11260	RTT
11261	SEQ ID NO: 11261	RTT
11262	SEQ ID NO: 11262	RTT
11263	SEQ ID NO: 11263	RTT
11264	SEQ ID NO: 11264	RTT
11265	SEQ ID NO: 11265	RTT
11266	SEQ ID NO: 11266	RTT
11267	SEQ ID NO: 11267	RTT
11268	SEQ ID NO: 11268	RTT
11269	SEQ ID NO: 11269	RTT
11270	SEQ ID NO: 11270	RTT
11271	SEQ ID NO: 11271	RTT
11272	SEQ ID NO: 11272	RTT
11273	SEQ ID NO: 11273	RTT
11274	SEQ ID NO: 11274	RTT
11275	SEQ ID NO: 11275	RTT
11276	SEQ ID NO: 11276	RTT
11277	SEQ ID NO: 11277	RTT
11278	SEQ ID NO: 11278	RTT
70	SEQ ID NO: 70	PE3b ngRNA spacer

Sequence Number	Sequence	Description
		(GG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
1240	SEQ ID NO: 1240	PE3 ngRNA spacer (AG PAM)
1217	SEQ ID NO: 1217	PE3 ngRNA spacer (TG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
79	SEQ ID NO: 79	PE3b ngRNA spacer (TG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
1239	SEQ ID NO: 1239	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
1220	SEQ ID NO: 1220	PE3 ngRNA spacer (TG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
1243	SEQ ID NO: 1243	PE3 ngRNA spacer (AG PAM)
1222	SEQ ID NO: 1222	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(GG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
1525	SEQ ID NO: 1525	ngRNA (AG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG PAM)

Sequence Number	Sequence	Description
117	SEQ ID NO: 117	ngRNA (AG PAM)
1528	SEQ ID NO: 1528	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Table 58

Sequence Number	Sequence	Description
11279	SEQ ID NO: 11279	PEgRNA spacer (GG PAM)
11280	SEQ ID NO: 11280	PEgRNA spacer (GG PAM)
11281	SEQ ID NO: 11281	PEgRNA spacer (GG PAM)
11282	SEQ ID NO: 11282	PEgRNA spacer (GG PAM)
11283	SEQ ID NO: 11283	PEgRNA spacer (GG PAM)
11284	SEQ ID NO: 11284	PEgRNA spacer (GG PAM)
11285	SEQ ID NO: 11285	PEgRNA spacer (GG PAM)
5632	GGC	PBS
11286	GGCA	PBS
11287	GGCAA	PBS
11288	GGCAAT	PBS
11289	GGCAAT G	PBS
11290	GGCAAT GA	PBS
11291	GGCAAT GAA	PBS
11292	SEQ ID NO: 11292	PBS
11293	SEQ ID NO: 11293	PBS
11294	SEQ ID NO: 11294	PBS
11295	SEQ ID NO: 11295	PBS
11296	SEQ ID NO: 11296	PBS
11297	SEQ ID NO: 11297	PBS
11298	SEQ ID NO: 11298	PBS
11299	SEQ ID NO: 11299	PBS

Sequence Number	Sequence	Description
11300	SEQ ID NO: 11300	PBS
11301	SEQ ID NO: 11301	PBS
11302	SEQ ID NO: 11302	RTT
11303	SEQ ID NO: 11303	RTT
11304	SEQ ID NO: 11304	RTT
11305	SEQ ID NO: 11305	RTT
11306	SEQ ID NO: 11306	RTT
11307	SEQ ID NO: 11307	RTT
11308	SEQ ID NO: 11308	RTT
11309	SEQ ID NO: 11309	RTT
11310	SEQ ID NO: 11310	RTT
11311	SEQ ID NO: 11311	RTT
11312	SEQ ID NO: 11312	RTT
11313	SEQ ID NO: 11313	RTT
11314	SEQ ID NO: 11314	RTT
11315	SEQ ID NO: 11315	RTT
11316	SEQ ID NO: 11316	RTT
11317	SEQ ID NO: 11317	RTT
11318	SEQ ID NO: 11318	RTT
11319	SEQ ID NO: 11319	RTT
11320	SEQ ID NO: 11320	RTT
11321	SEQ ID NO: 11321	RTT
11322	SEQ ID NO: 11322	RTT
11323	SEQ ID NO: 11323	RTT
11324	SEQ ID NO: 11324	RTT
11325	SEQ ID NO: 11325	RTT
11326	SEQ ID NO: 11326	RTT
11327	SEQ ID NO: 11327	RTT
11328	SEQ ID NO: 11328	RTT
11329	SEQ ID NO: 11329	RTT
11330	SEQ ID NO: 11330	RTT
11331	SEQ ID NO: 11331	RTT
11332	SEQ ID NO: 11332	RTT

Sequence Number	Sequence	Description
11333	SEQ ID NO: 11333	RTT
11334	SEQ ID NO: 11334	RTT
11335	SEQ ID NO: 11335	RTT
11336	SEQ ID NO: 11336	RTT
11337	SEQ ID NO: 11337	RTT
11338	SEQ ID NO: 11338	RTT
11339	SEQ ID NO: 11339	RTT
11340	SEQ ID NO: 11340	RTT
11341	SEQ ID NO: 11341	RTT
11342	SEQ ID NO: 11342	RTT
11343	SEQ ID NO: 11343	RTT
11344	SEQ ID NO: 11344	RTT
11345	SEQ ID NO: 11345	RTT
11346	SEQ ID NO: 11346	RTT
11347	SEQ ID NO: 11347	RTT
11348	SEQ ID NO: 11348	RTT
11349	SEQ ID NO: 11349	RTT
11350	SEQ ID NO: 11350	RTT
11351	SEQ ID NO: 11351	RTT
11352	SEQ ID NO: 11352	RTT
11353	SEQ ID NO: 11353	RTT
11354	SEQ ID NO: 11354	RTT
11355	SEQ ID NO: 11355	RTT
11356	SEQ ID NO: 11356	RTT
11357	SEQ ID NO: 11357	RTT
11358	SEQ ID NO: 11358	RTT
11359	SEQ ID NO: 11359	RTT
11360	SEQ ID NO: 11360	RTT
11361	SEQ ID NO: 11361	RTT
11362	SEQ ID NO: 11362	RTT
11363	SEQ ID NO: 11363	RTT
11364	SEQ ID NO: 11364	RTT
11365	SEQ ID NO: 11365	RTT

Sequence Number	Sequence	Description
11366	SEQ ID NO: 11366	RTT
11367	SEQ ID NO: 11367	RTT
11368	SEQ ID NO: 11368	RTT
11369	SEQ ID NO: 11369	RTT
11370	SEQ ID NO: 11370	RTT
11371	SEQ ID NO: 11371	RTT
11372	SEQ ID NO: 11372	RTT
11373	SEQ ID NO: 11373	RTT
11374	SEQ ID NO: 11374	RTT
11375	SEQ ID NO: 11375	RTT
11376	SEQ ID NO: 11376	RTT
11377	SEQ ID NO: 11377	RTT
11378	SEQ ID NO: 11378	RTT
11379	SEQ ID NO: 11379	RTT
11380	SEQ ID NO: 11380	RTT
11381	SEQ ID NO: 11381	RTT
11382	SEQ ID NO: 11382	RTT
11383	SEQ ID NO: 11383	RTT
11384	SEQ ID NO: 11384	RTT
11385	SEQ ID NO: 11385	RTT
11386	SEQ ID NO: 11386	RTT
11387	SEQ ID NO: 11387	RTT
11388	SEQ ID NO: 11388	RTT
11389	SEQ ID NO: 11389	RTT
11390	SEQ ID NO: 11390	RTT
11391	SEQ ID NO: 11391	RTT
11392	SEQ ID NO: 11392	RTT
1217	SEQ ID NO: 1217	PE3 ngRNA spacer (TG PAM)
1222	SEQ ID NO: 1222	PE3 ngRNA spacer (GG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(AG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GG PAM)
1240	SEQ ID NO: 1240	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
1243	SEQ ID NO: 1243	PE3 ngRNA spacer (AG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
1843	SEQ ID NO: 1843	PE3 ngRNA spacer (TG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
1239	SEQ ID NO: 1239	PE3 ngRNA spacer (AG PAM)
1220	SEQ ID NO: 1220	PE3 ngRNA spacer (TG PAM)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG PAM)
1238	SEQ ID NO: 1238	PE3 ngRNA spacer (AG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
1525	SEQ ID NO: 1525	ngRNA (AG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
1528	SEQ ID NO: 1528	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Table 59

Sequence Number	Sequence	Description
11393	SEQ ID NO: 11393	PEgRNA spacer (TG PAM)
11394	SEQ ID NO: 11394	PEgRNA spacer (TG PAM)
11395	SEQ ID NO: 11395	PEgRNA spacer (TG PAM)
11396	SEQ ID NO: 11396	PEgRNA spacer (TG PAM)
11397	SEQ ID NO: 11397	PEgRNA spacer (TG PAM)
11398	SEQ ID NO: 11398	PEgRNA spacer (TG PAM)
11399	SEQ ID NO: 11399	PEgRNA spacer (TG PAM)
4183	CCA	PBS
11400	CCAG	PBS
11401	CCAGG	PBS
11402	CCAGGG	PBS
11403	CCAGGGC	PBS
11404	CCAGGGCA	PBS
11405	CCAGGGCAA	PBS
11406	SEQ ID NO: 11406	PBS
11407	SEQ ID NO: 11407	PBS
11408	SEQ ID NO: 11408	PBS
11409	SEQ ID NO: 11409	PBS
11410	SEQ ID NO: 11410	PBS
11411	SEQ ID NO: 11411	PBS
11412	SEQ ID NO: 11412	PBS
11413	SEQ ID NO: 11413	PBS
11414	SEQ ID NO: 11414	PBS
11415	SEQ ID NO: 11415	PBS
11416	SEQ ID NO: 11416	RTT*75 (PAM silencing)
11417	SEQ ID NO: 11417	RTT*73 (PAM silencing)

Sequence Number	Sequence	Description
11418	SEQ ID NO: 11418	RTT
11419	SEQ ID NO: 11419	RTT*74 (PAM silencing)
11420	SEQ ID NO: 11420	RTT*70 (PAM silencing)
11421	SEQ ID NO: 11421	RTT*70 (PAM silencing)
11422	SEQ ID NO: 11422	RTT
11423	SEQ ID NO: 11423	RTT*75 (PAM silencing)
11424	SEQ ID NO: 11424	RTT*73 (PAM silencing)
11425	SEQ ID NO: 11425	RTT*74 (PAM silencing)
11426	SEQ ID NO: 11426	RTT*70 (PAM silencing)
11427	SEQ ID NO: 11427	RTT
11428	SEQ ID NO: 11428	RTT*74 (PAM silencing)
11429	SEQ ID NO: 11429	RTT*73 (PAM silencing)
11430	SEQ ID NO: 11430	RTT*75 (PAM silencing)
11431	SEQ ID NO: 11431	RTT*70 (PAM silencing)
11432	SEQ ID NO: 11432	RTT*74 (PAM silencing)
11433	SEQ ID NO: 11433	RTT*73 (PAM silencing)
11434	SEQ ID NO: 11434	RTT*75 (PAM silencing)
11435	SEQ ID NO: 11435	RTT
11436	SEQ ID NO: 11436	RTT*70 (PAM silencing)
11437	SEQ ID NO: 11437	RTT*73 (PAM silencing)
11438	SEQ ID NO: 11438	RTT*75 (PAM silencing)
11439	SEQ ID NO: 11439	RTT*74 (PAM silencing)
11440	SEQ ID NO: 11440	RTT
11441	SEQ ID NO: 11441	RTT*74 (PAM silencing)
11442	SEQ ID NO: 11442	RTT*73 (PAM silencing)
11443	SEQ ID NO: 11443	RTT
11444	SEQ ID NO: 11444	RTT*75 (PAM silencing)
11445	SEQ ID NO: 11445	RTT*70 (PAM silencing)
11446	SEQ ID NO: 11446	RTT*73 (PAM silencing)
11447	SEQ ID NO: 11447	RTT
11448	SEQ ID NO: 11448	RTT*74 (PAM silencing)
11449	SEQ ID NO: 11449	RTT*75 (PAM silencing)
11450	SEQ ID NO: 11450	RTT*70 (PAM silencing)
11451	SEQ ID NO: 11451	RTT*70 (PAM silencing)
11452	SEQ ID NO: 11452	RTT*75 (PAM silencing)
11453	SEQ ID NO: 11453	RTT*73 (PAM silencing)
11454	SEQ ID NO: 11454	RTT
11455	SEQ ID NO: 11455	RTT*74 (PAM silencing)
11456	SEQ ID NO: 11456	RTT*73 (PAM silencing)
11457	SEQ ID NO: 11457	RTT
11458	SEQ ID NO: 11458	RTT*74 (PAM silencing)
11459	SEQ ID NO: 11459	RTT*75 (PAM silencing)
11460	SEQ ID NO: 11460	RTT*70 (PAM silencing)
11461	SEQ ID NO: 11461	RTT*70 (PAM silencing)
11462	SEQ ID NO: 11462	RTT*75 (PAM silencing)
11463	SEQ ID NO: 11463	RTT*73 (PAM silencing)
11464	SEQ ID NO: 11464	RTT*74 (PAM silencing)
11465	SEQ ID NO: 11465	RTT
11466	SEQ ID NO: 11466	RTT*74 (PAM silencing)
11467	SEQ ID NO: 11467	RTT*70 (PAM silencing)
11468	SEQ ID NO: 11468	RTT*75 (PAM silencing)
11469	SEQ ID NO: 11469	RTT
11470	SEQ ID NO: 11470	RTT*73 (PAM silencing)
11471	SEQ ID NO: 11471	RTT
11472	SEQ ID NO: 11472	RTT*70 (PAM silencing)
11473	SEQ ID NO: 11473	RTT*75 (PAM silencing)
11474	SEQ ID NO: 11474	RTT*74 (PAM silencing)
11475	SEQ ID NO: 11475	RTT*73 (PAM silencing)
11476	SEQ ID NO: 11476	RTT*73 (PAM silencing)
11477	SEQ ID NO: 11477	RTT
11478	SEQ ID NO: 11478	RTT*70 (PAM silencing)
11479	SEQ ID NO: 11479	RTT*75 (PAM silencing)
11480	SEQ ID NO: 11480	RTT*74 (PAM silencing)
11481	SEQ ID NO: 11481	RTT*73 (PAM silencing)
11482	SEQ ID NO: 11482	RTT*75 (PAM silencing)
11483	SEQ ID NO: 11483	RTT*70 (PAM silencing)
11484	SEQ ID NO: 11484	RTT
11485	SEQ ID NO: 11485	RTT*74 (PAM silencing)
11486	SEQ ID NO: 11486	RTT*70 (PAM silencing)
11487	SEQ ID NO: 11487	RTT*73 (PAM silencing)
11488	SEQ ID NO: 11488	RTT
11489	SEQ ID NO: 11489	RTT*75 (PAM silencing)

Sequence Number	Sequence	Description
11490	SEQ ID NO: 11490	RTT*74 (PAM silencing)
11491	SEQ ID NO: 11491	RTT
11492	SEQ ID NO: 11492	RTT*70 (PAM silencing)
11493	SEQ ID NO: 11493	RTT*75 (PAM silencing)
11494	SEQ ID NO: 11494	RTT*74 (PAM silencing)
11495	SEQ ID NO: 11495	RTT*73 (PAM silencing)
11496	SEQ ID NO: 11496	RTT*74 (PAM silencing)
11497	SEQ ID NO: 11497	RTT*73 (PAM silencing)
11498	SEQ ID NO: 11498	RTT
11499	SEQ ID NO: 11499	RTT*70 (PAM silencing)
11500	SEQ ID NO: 11500	RTT*75 (PAM silencing)
11501	SEQ ID NO: 11501	RTT*73 (PAM silencing)
11502	SEQ ID NO: 11502	RTT*70 (PAM silencing)
11503	SEQ ID NO: 11503	RTT
11504	SEQ ID NO: 11504	RTT*74 (PAM silencing)
11505	SEQ ID NO: 11505	RTT*75 (PAM silencing)
11506	SEQ ID NO: 11506	RTT*70 (PAM silencing)
11507	SEQ ID NO: 11507	RTT*75 (PAM silencing)
11508	SEQ ID NO: 11508	RTT
11509	SEQ ID NO: 11509	RTT*74 (PAM silencing)
11510	SEQ ID NO: 11510	RTT*73 (PAM silencing)
11511	SEQ ID NO: 11511	RTT*75 (PAM silencing)
11512	SEQ ID NO: 11512	RTT*73 (PAM silencing)
11513	SEQ ID NO: 11513	RTT*74 (PAM silencing)
11514	SEQ ID NO: 11514	RTT
11515	SEQ ID NO: 11515	RTT*70 (PAM silencing)
11516	SEQ ID NO: 11516	RTT
11517	SEQ ID NO: 11517	RTT*75 (PAM silencing)
11518	SEQ ID NO: 11518	RTT*70 (PAM silencing)
11519	SEQ ID NO: 11519	RTT*73 (PAM silencing)
11520	SEQ ID NO: 11520	RTT*74 (PAM silencing)
11521	SEQ ID NO: 11521	RTT
11522	SEQ ID NO: 11522	RTT*75 (PAM silencing)
11523	SEQ ID NO: 11523	RTT*74 (PAM silencing)
11524	SEQ ID NO: 11524	RTT*73 (PAM silencing)
11525	SEQ ID NO: 11525	RTT*70 (PAM silencing)
11526	SEQ ID NO: 11526	RTT
11527	SEQ ID NO: 11527	RTT*75 (PAM silencing)
11528	SEQ ID NO: 11528	RTT*70 (PAM silencing)
11529	SEQ ID NO: 11529	RTT*73 (PAM silencing)
11530	SEQ ID NO: 11530	RTT*74 (PAM silencing)
11531	SEQ ID NO: 11531	RTT*70 (PAM silencing)
11532	SEQ ID NO: 11532	RTT*73 (PAM silencing)
11533	SEQ ID NO: 11533	RTT*75 (PAM silencing)
11534	SEQ ID NO: 11534	RTT*74 (PAM silencing)
11535	SEQ ID NO: 11535	RTT
11536	SEQ ID NO: 11536	RTT
11537	SEQ ID NO: 11537	RTT*73 (PAM silencing)
11538	SEQ ID NO: 11538	RTT*70 (PAM silencing)
11539	SEQ ID NO: 11539	RTT*74 (PAM silencing)
11540	SEQ ID NO: 11540	RTT*75 (PAM silencing)
11541	SEQ ID NO: 11541	RTT*73 (PAM silencing)
11542	SEQ ID NO: 11542	RTT*70 (PAM silencing)
11543	SEQ ID NO: 11543	RTT*75 (PAM silencing)
11544	SEQ ID NO: 11544	RTT*74 (PAM silencing)
11545	SEQ ID NO: 11545	RTT
11546	SEQ ID NO: 11546	RTT
11547	SEQ ID NO: 11547	RTT*74 (PAM silencing)
11548	SEQ ID NO: 11548	RTT*73 (PAM silencing)
11549	SEQ ID NO: 11549	RTT*70 (PAM silencing)
11550	SEQ ID NO: 11550	RTT*75 (PAM silencing)
11551	SEQ ID NO: 11551	RTT*73 (PAM silencing)
11552	SEQ ID NO: 11552	RTT*70 (PAM silencing)
11553	SEQ ID NO: 11553	RTT*75 (PAM silencing)
11554	SEQ ID NO: 11554	RTT
11555	SEQ ID NO: 11555	RTT*74 (PAM silencing)
11556	SEQ ID NO: 11556	RTT*74 (PAM silencing)
11557	SEQ ID NO: 11557	RTT*70 (PAM silencing)
11558	SEQ ID NO: 11558	RTT
11559	SEQ ID NO: 11559	RTT*75 (PAM silencing)

Sequence Number	Sequence	Description
11560	SEQ ID NO: 11560	RTT*73 (PAM silencing)
11561	SEQ ID NO: 11561	RTT*75 (PAM silencing)
11562	SEQ ID NO: 11562	RTT*70 (PAM silencing)
11563	SEQ ID NO: 11563	RTT*73 (PAM silencing)
11564	SEQ ID NO: 11564	RTT*74 (PAM silencing)
11565	SEQ ID NO: 11565	RTT
11566	SEQ ID NO: 11566	RTT*70 (PAM silencing)
11567	SEQ ID NO: 11567	RTT*74 (PAM silencing)
11568	SEQ ID NO: 11568	RTT
11569	SEQ ID NO: 11569	RTT*75 (PAM silencing)
11570	SEQ ID NO: 11570	RTT*73 (PAM silencing)
11571	SEQ ID NO: 11571	RTT
11572	SEQ ID NO: 11572	RTT*70 (PAM silencing)
11573	SEQ ID NO: 11573	RTT*75 (PAM silencing)
11574	SEQ ID NO: 11574	RTT*74 (PAM silencing)
11575	SEQ ID NO: 11575	RTT*73 (PAM silencing)
11576	SEQ ID NO: 11576	RTT*73 (PAM silencing)
11577	SEQ ID NO: 11577	RTT
11578	SEQ ID NO: 11578	RTT*74 (PAM silencing)
11579	SEQ ID NO: 11579	RTT*70 (PAM silencing)
11580	SEQ ID NO: 11580	RTT*75 (PAM silencing)
11581	SEQ ID NO: 11581	RTT*70 (PAM silencing)
11582	SEQ ID NO: 11582	RTT*73 (PAM silencing)
11583	SEQ ID NO: 11583	RTT
11584	SEQ ID NO: 11584	RTT*75 (PAM silencing)
11585	SEQ ID NO: 11585	RTT*74 (PAM silencing)
11586	SEQ ID NO: 11586	RTT*70 (PAM silencing)
11587	SEQ ID NO: 11587	RTT*75 (PAM silencing)
11588	SEQ ID NO: 11588	RTT*73 (PAM silencing)
11589	SEQ ID NO: 11589	RTT*74 (PAM silencing)
11590	SEQ ID NO: 11590	RTT
11591	SEQ ID NO: 11591	RTT*73 (PAM silencing)
11592	SEQ ID NO: 11592	RTT*70 (PAM silencing)
11593	SEQ ID NO: 11593	RTT*75 (PAM silencing)
11594	SEQ ID NO: 11594	RTT*74 (PAM silencing)
11595	SEQ ID NO: 11595	RTT
11596	SEQ ID NO: 11596	RTT*70 (PAM silencing)
11597	SEQ ID NO: 11597	RTT*75 (PAM silencing)
11598	SEQ ID NO: 11598	RTT
11599	SEQ ID NO: 11599	RTT*74 (PAM silencing)
11600	SEQ ID NO: 11600	RTT*73 (PAM silencing)
11601	SEQ ID NO: 11601	RTT*75 (PAM silencing)
11602	SEQ ID NO: 11602	RTT
11603	SEQ ID NO: 11603	RTT*73 (PAM silencing)
11604	SEQ ID NO: 11604	RTT*70 (PAM silencing)
11605	SEQ ID NO: 11605	RTT*74 (PAM silencing)
11606	SEQ ID NO: 11606	RTT
11607	SEQ ID NO: 11607	RTT*75 (PAM silencing)
11608	SEQ ID NO: 11608	RTT*74 (PAM silencing)
11609	SEQ ID NO: 11609	RTT*73 (PAM silencing)
11610	SEQ ID NO: 11610	RTT*70 (PAM silencing)
11611	SEQ ID NO: 11611	RTT*70 (PAM silencing)
11612	SEQ ID NO: 11612	RTT*75 (PAM silencing)
11613	SEQ ID NO: 11613	RTT*74 (PAM silencing)
11614	SEQ ID NO: 11614	RTT*73 (PAM silencing)
11615	SEQ ID NO: 11615	RTT
11616	SEQ ID NO: 11616	RTT*74 (PAM silencing)
11617	SEQ ID NO: 11617	RTT*70 (PAM silencing)
11618	SEQ ID NO: 11618	RTT*75 (PAM silencing)
11619	SEQ ID NO: 11619	RTT
11620	SEQ ID NO: 11620	RTT*73 (PAM silencing)
11621	SEQ ID NO: 11621	RTT*70 (PAM silencing)
11622	SEQ ID NO: 11622	RTT*75 (PAM silencing)
11623	SEQ ID NO: 11623	RTT*73 (PAM silencing)
11624	SEQ ID NO: 11624	RTT*74 (PAM silencing)
11625	SEQ ID NO: 11625	RTT
11626	SEQ ID NO: 11626	RTT
11627	SEQ ID NO: 11627	RTT*75 (PAM silencing)
11628	SEQ ID NO: 11628	RTT*74 (PAM silencing)
11629	SEQ ID NO: 11629	RTT*70 (PAM silencing)
11630	SEQ ID NO: 11630	RTT*73 (PAM silencing)

Sequence Number	Sequence	Description
11631	SEQ ID NO: 11631	RTT*73 (PAM silencing)
11632	SEQ ID NO: 11632	RTT*70 (PAM silencing)
11633	SEQ ID NO: 11633	RTT*75 (PAM silencing)
11634	SEQ ID NO: 11634	RTT
11635	SEQ ID NO: 11635	RTT*74 (PAM silencing)
11636	SEQ ID NO: 11636	RTT*74 (PAM silencing)
11637	SEQ ID NO: 11637	RTT*75 (PAM silencing)
11638	SEQ ID NO: 11638	RTT
11639	SEQ ID NO: 11639	RTT*73 (PAM silencing)
11640	SEQ ID NO: 11640	RTT*70 (PAM silencing)
11641	SEQ ID NO: 11641	RTT*73 (PAM silencing)
11642	SEQ ID NO: 11642	RTT*70 (PAM silencing)
11643	SEQ ID NO: 11643	RTT*75 (PAM silencing)
11644	SEQ ID NO: 11644	RTT
11645	SEQ ID NO: 11645	RTT*74 (PAM silencing)
11646	SEQ ID NO: 11646	RTT*75 (PAM silencing)
11647	SEQ ID NO: 11647	RTT*73 (PAM silencing)
11648	SEQ ID NO: 11648	RTT*70 (PAM silencing)
11649	SEQ ID NO: 11649	RTT
11650	SEQ ID NO: 11650	RTT*74 (PAM silencing)
11651	SEQ ID NO: 11651	RTT
11652	SEQ ID NO: 11652	RTT*70 (PAM silencing)
11653	SEQ ID NO: 11653	RTT*73 (PAM silencing)
11654	SEQ ID NO: 11654	RTT*74 (PAM silencing)
11655	SEQ ID NO: 11655	RTT*75 (PAM silencing)
11656	SEQ ID NO: 11656	RTT*75 (PAM silencing)
11657	SEQ ID NO: 11657	RTT*74 (PAM silencing)
11658	SEQ ID NO: 11658	RTT*73 (PAM silencing)
11659	SEQ ID NO: 11659	RTT*70 (PAM silencing)
11660	SEQ ID NO: 11660	RTT
11661	SEQ ID NO: 11661	RTT
11662	SEQ ID NO: 11662	RTT*74 (PAM silencing)
11663	SEQ ID NO: 11663	RTT*73 (PAM silencing)
11664	SEQ ID NO: 11664	RTT*70 (PAM silencing)
11665	SEQ ID NO: 11665	RTT*75 (PAM silencing)
11666	SEQ ID NO: 11666	RTT*74 (PAM silencing)
11667	SEQ ID NO: 11667	RTT*75 (PAM silencing)
11668	SEQ ID NO: 11668	RTT*73 (PAM silencing)
11669	SEQ ID NO: 11669	RTT
11670	SEQ ID NO: 11670	RTT*70 (PAM silencing)
11671	SEQ ID NO: 11671	RTT*70 (PAM silencing)
11672	SEQ ID NO: 11672	RTT*75 (PAM silencing)
11673	SEQ ID NO: 11673	RTT
11674	SEQ ID NO: 11674	RTT*73 (PAM silencing)
11675	SEQ ID NO: 11675	RTT*74 (PAM silencing)
11676	SEQ ID NO: 11676	RTT*73 (PAM silencing)
11677	SEQ ID NO: 11677	RTT
11678	SEQ ID NO: 11678	RTT*75 (PAM silencing)
11679	SEQ ID NO: 11679	RTT*70 (PAM silencing)
11680	SEQ ID NO: 11680	RTT*74 (PAM silencing)
11681	SEQ ID NO: 11681	RTT*74 (PAM silencing)
11682	SEQ ID NO: 11682	RTT*75 (PAM silencing)
11683	SEQ ID NO: 11683	RTT*70 (PAM silencing)
11684	SEQ ID NO: 11684	RTT
11685	SEQ ID NO: 11685	RTT*73 (PAM silencing)
11686	SEQ ID NO: 11686	RTT*70 (PAM silencing)
11687	SEQ ID NO: 11687	RTT*73 (PAM silencing)
11688	SEQ ID NO: 11688	RTT*74 (PAM silencing)
11689	SEQ ID NO: 11689	RTT
11690	SEQ ID NO: 11690	RTT*75 (PAM silencing)
11691	SEQ ID NO: 11691	RTT
11692	SEQ ID NO: 11692	RTT*74 (PAM silencing)
11693	SEQ ID NO: 11693	RTT*75 (PAM silencing)
11694	SEQ ID NO: 11694	RTT*70 (PAM silencing)
11695	SEQ ID NO: 11695	RTT*73 (PAM silencing)
11696	SEQ ID NO: 11696	RTT*73 (PAM silencing)
11697	SEQ ID NO: 11697	RTT*74 (PAM silencing)
11698	SEQ ID NO: 11698	RTT*70 (PAM silencing)
11699	SEQ ID NO: 11699	RTT
11700	SEQ ID NO: 11700	RTT*75 (PAM silencing)
11701	SEQ ID NO: 11701	RTT*75 (PAM silencing)

Sequence Number	Sequence	Description
11702	SEQ ID NO: 11702	RTT*73 (PAM silencing)
11703	SEQ ID NO: 11703	RTT*70 (PAM silencing)
11704	SEQ ID NO: 11704	RTT*74 (PAM silencing)
11705	SEQ ID NO: 11705	RTT
11706	SEQ ID NO: 11706	RTT
11707	SEQ ID NO: 11707	RTT*73 (PAM silencing)
11708	SEQ ID NO: 11708	RTT*70 (PAM silencing)
11709	SEQ ID NO: 11709	RTT*75 (PAM silencing)
11710	SEQ ID NO: 11710	RTT*74 (PAM silencing)
11711	SEQ ID NO: 11711	RTT*75 (PAM silencing)
11712	SEQ ID NO: 11712	RTT*74 (PAM silencing)
11713	SEQ ID NO: 11713	RTT*70 (PAM silencing)
11714	SEQ ID NO: 11714	RTT
11715	SEQ ID NO: 11715	RTT*73 (PAM silencing)
11716	SEQ ID NO: 11716	RTT*70 (PAM silencing)
11717	SEQ ID NO: 11717	RTT*73 (PAM silencing)
11718	SEQ ID NO: 11718	RTT*74 (PAM silencing)
11719	SEQ ID NO: 11719	RTT
11720	SEQ ID NO: 11720	RTT*75 (PAM silencing)
11721	SEQ ID NO: 11721	RTT
11722	SEQ ID NO: 11722	RTT*73 (PAM silencing)
11723	SEQ ID NO: 11723	RTT*74 (PAM silencing)
11724	SEQ ID NO: 11724	RTT*75 (PAM silencing)
11725	SEQ ID NO: 11725	RTT*70 (PAM silencing)
11726	SEQ ID NO: 11726	RTT*74 (PAM silencing)
11727	SEQ ID NO: 11727	RTT
11728	SEQ ID NO: 11728	RTT*70 (PAM silencing)
11729	SEQ ID NO: 11729	RTT*73 (PAM silencing)
11730	SEQ ID NO: 11730	RTT*75 (PAM silencing)
11731	SEQ ID NO: 11731	RTT*75 (PAM silencing)
11732	SEQ ID NO: 11732	RTT*70 (PAM silencing)
11733	SEQ ID NO: 11733	RTT*74 (PAM silencing)
11734	SEQ ID NO: 11734	RTT*73 (PAM silencing)
11735	SEQ ID NO: 11735	RTT
11736	SEQ ID NO: 11736	RTT*74 (PAM silencing)
11737	SEQ ID NO: 11737	RTT*75 (PAM silencing)
11738	SEQ ID NO: 11738	RTT*70 (PAM silencing)
11739	SEQ ID NO: 11739	RTT*73 (PAM silencing)
11740	SEQ ID NO: 11740	RTT
11741	SEQ ID NO: 11741	RTT
11742	SEQ ID NO: 11742	RTT*74 (PAM silencing)
11743	SEQ ID NO: 11743	RTT*70 (PAM silencing)
11744	SEQ ID NO: 11744	RTT*73 (PAM silencing)
11745	SEQ ID NO: 11745	RTT*75 (PAM silencing)
11746	SEQ ID NO: 11746	RTT*70 (PAM silencing)
11747	SEQ ID NO: 11747	RTT*75 (PAM silencing)
11748	SEQ ID NO: 11748	RTT
11749	SEQ ID NO: 11749	RTT*73 (PAM silencing)
11750	SEQ ID NO: 11750	RTT*74 (PAM silencing)
11751	SEQ ID NO: 11751	RTT*75 (PAM silencing)
11752	SEQ ID NO: 11752	RTT
11753	SEQ ID NO: 11753	RTT*70 (PAM silencing)
11754	SEQ ID NO: 11754	RTT*74 (PAM silencing)
11755	SEQ ID NO: 11755	RTT*73 (PAM silencing)
11756	SEQ ID NO: 11756	RTT*74 (PAM silencing)
11757	SEQ ID NO: 11757	RTT*75 (PAM silencing)
11758	SEQ ID NO: 11758	RTT*73 (PAM silencing)
11759	SEQ ID NO: 11759	RTT*70 (PAM silencing)
11760	SEQ ID NO: 11760	RTT
11761	SEQ ID NO: 11761	RTT*74 (PAM silencing)
11762	SEQ ID NO: 11762	RTT*70 (PAM silencing)
11763	SEQ ID NO: 11763	RTT*75 (PAM silencing)
11764	SEQ ID NO: 11764	RTT*73 (PAM silencing)
11765	SEQ ID NO: 11765	RTT
11766	SEQ ID NO: 11766	RTT
11767	SEQ ID NO: 11767	RTT*74 (PAM silencing)
11768	SEQ ID NO: 11768	RTT*75 (PAM silencing)
11769	SEQ ID NO: 11769	RTT*73 (PAM silencing)
11770	SEQ ID NO: 11770	RTT*70 (PAM silencing)
11771	SEQ ID NO: 11771	RTT
11772	SEQ ID NO: 11772	RTT*75 (PAM silencing)
11773	SEQ ID NO: 11773	RTT*73 (PAM silencing)

Sequence Number	Sequence	Description
11774	SEQ ID NO: 11774	RTT*70 (PAM silencing)
11775	SEQ ID NO: 11775	RTT*74 (PAM silencing)
11776	SEQ ID NO: 11776	RTT*75 (PAM silencing)
11777	SEQ ID NO: 11777	RTT
11778	SEQ ID NO: 11778	RTT*74 (PAM silencing)
11779	SEQ ID NO: 11779	RTT*73 (PAM silencing)
11780	SEQ ID NO: 11780	RTT*70 (PAM silencing)
11781	SEQ ID NO: 11781	RTT*73 (PAM silencing)
11782	SEQ ID NO: 11782	RTT*75 (PAM silencing)
11783	SEQ ID NO: 11783	RTT
11784	SEQ ID NO: 11784	RTT*74 (PAM silencing)
11785	SEQ ID NO: 11785	RTT*70 (PAM silencing)
11786	SEQ ID NO: 11786	RTT*73 (PAM silencing)
11787	SEQ ID NO: 11787	RTT*74 (PAM silencing)
11788	SEQ ID NO: 11788	RTT*70 (PAM silencing)
11789	SEQ ID NO: 11789	RTT*75 (PAM silencing)
11790	SEQ ID NO: 11790	RTT
11791	SEQ ID NO: 11791	RTT*75 (PAM silencing)
11792	SEQ ID NO: 11792	RTT*74 (PAM silencing)
11793	SEQ ID NO: 11793	RTT
11794	SEQ ID NO: 11794	RTT*73 (PAM silencing)
11795	SEQ ID NO: 11795	RTT*70 (PAM silencing)
11796	SEQ ID NO: 11796	RTT*75 (PAM silencing)
11797	SEQ ID NO: 11797	RTT*70 (PAM silencing)
11798	SEQ ID NO: 11798	RTT*74 (PAM silencing)
11799	SEQ ID NO: 11799	RTT
11800	SEQ ID NO: 11800	RTT*73 (PAM silencing)
11801	SEQ ID NO: 11801	RTT*74 (PAM silencing)
11802	SEQ ID NO: 11802	RTT*70 (PAM silencing)
11803	SEQ ID NO: 11803	RTT*75 (PAM silencing)
11804	SEQ ID NO: 11804	RTT
11805	SEQ ID NO: 11805	RTT*73 (PAM silencing)
11806	SEQ ID NO: 11806	RTT*73 (PAM silencing)
11807	SEQ ID NO: 11807	RTT
11808	SEQ ID NO: 11808	RTT*75 (PAM silencing)
11809	SEQ ID NO: 11809	RTT*70 (PAM silencing)
11810	SEQ ID NO: 11810	RTT*74 (PAM silencing)
11811	SEQ ID NO: 11811	RTT*73 (PAM silencing)
11812	SEQ ID NO: 11812	RTT
11813	SEQ ID NO: 11813	RTT*70 (PAM silencing)
11814	SEQ ID NO: 11814	RTT*75 (PAM silencing)
11815	SEQ ID NO: 11815	RTT*74 (PAM silencing)
11816	SEQ ID NO: 11816	RTT
11817	SEQ ID NO: 11817	RTT*74 (PAM silencing)
11818	SEQ ID NO: 11818	RTT*73 (PAM silencing)
11819	SEQ ID NO: 11819	RTT*70 (PAM silencing)
11820	SEQ ID NO: 11820	RTT*75 (PAM silencing)
11821	SEQ ID NO: 11821	RTT
11822	SEQ ID NO: 11822	RTT*75 (PAM silencing)
11823	SEQ ID NO: 11823	RTT*74 (PAM silencing)
11824	SEQ ID NO: 11824	RTT*70 (PAM silencing)
11825	SEQ ID NO: 11825	RTT*73 (PAM silencing)
11826	SEQ ID NO: 11826	RTT*74 (PAM silencing)
11827	SEQ ID NO: 11827	RTT*73 (PAM silencing)
11828	SEQ ID NO: 11828	RTT*70 (PAM silencing)
11829	SEQ ID NO: 11829	RTT*75 (PAM silencing)
11830	SEQ ID NO: 11830	RTT
11831	SEQ ID NO: 11831	RTT*73 (PAM silencing)
11832	SEQ ID NO: 11832	RTT*70 (PAM silencing)
11833	SEQ ID NO: 11833	RTT*74 (PAM silencing)
11834	SEQ ID NO: 11834	RTT*75 (PAM silencing)
11835	SEQ ID NO: 11835	RTT
11836	SEQ ID NO: 11836	RTT
11837	SEQ ID NO: 11837	RTT*73 (PAM silencing)
11838	SEQ ID NO: 11838	RTT*74 (PAM silencing)
11839	SEQ ID NO: 11839	RTT*75 (PAM silencing)
11840	SEQ ID NO: 11840	RTT*70 (PAM silencing)
11841	SEQ ID NO: 11841	RTT*73 (PAM silencing)
11842	SEQ ID NO: 11842	RTT*74 (PAM silencing)
11843	SEQ ID NO: 11843	RTT
11844	SEQ ID NO: 11844	RTT*70 (PAM silencing)

Sequence Number	Sequence	Description
11845	SEQ ID NO: 11845	RTT*75 (PAM silencing)
11846	SEQ ID NO: 11846	RTT*74 (PAM silencing)
11847	SEQ ID NO: 11847	RTT*70 (PAM silencing)
11848	SEQ ID NO: 11848	RTT*75 (PAM silencing)
11849	SEQ ID NO: 11849	RTT
11850	SEQ ID NO: 11850	RTT*73 (PAM silencing)
11851	SEQ ID NO: 11851	RTT*75 (PAM silencing)
11852	SEQ ID NO: 11852	RTT
11853	SEQ ID NO: 11853	RTT*73 (PAM silencing)
11854	SEQ ID NO: 11854	RTT*70 (PAM silencing)
11855	SEQ ID NO: 11855	RTT*74 (PAM silencing)
11856	SEQ ID NO: 11856	RTT*73 (PAM silencing)
11857	SEQ ID NO: 11857	RTT*74 (PAM silencing)
11858	SEQ ID NO: 11858	RTT
11859	SEQ ID NO: 11859	RTT*70 (PAM silencing)
11860	SEQ ID NO: 11860	RTT*75 (PAM silencing)
11861	SEQ ID NO: 11861	RTT*74 (PAM silencing)
11862	SEQ ID NO: 11862	RTT*70 (PAM silencing)
11863	SEQ ID NO: 11863	RTT*73 (PAM silencing)
11864	SEQ ID NO: 11864	RTT*75 (PAM silencing)
11865	SEQ ID NO: 11865	RTT
11866	SEQ ID NO: 11866	RTT*73 (PAM silencing)
11867	SEQ ID NO: 11867	RTT
11868	SEQ ID NO: 11868	RTT*70 (PAM silencing)
11869	SEQ ID NO: 11869	RTT*74 (PAM silencing)
11870	SEQ ID NO: 11870	RTT*75 (PAM silencing)
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AG PAM)
11871	SEQ ID NO: 11871	PE3b*75 ngRNA spacer (GG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
11872	SEQ ID NO: 11872	PE3b*75 ngRNA spacer (CG PAM)
1217	SEQ ID NO: 1217	PE3 ngRNA spacer (TG PAM)
11873	SEQ ID NO: 11873	PE3b*75 ngRNA spacer (GG PAM)
11874	SEQ ID NO: 11874	PE3b*73 ngRNA spacer (GG;TG PAM)
1238	SEQ ID NO: 1238	PE3 ngRNA spacer (AG PAM)
11875	SEQ ID NO: 11875	PE3b*74 ngRNA spacer (GG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
92	SEQ ID NO: 92	PE3b ngRNA spacer (GG PAM)
1222	SEQ ID NO: 1222	PE3 ngRNA spacer (GG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
11876	SEQ ID NO: 11876	PE3b*73 ngRNA spacer (CG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
11877	SEQ ID NO: 11877	PE3b*74 ngRNA spacer (GG PAM)
1243	SEQ ID NO: 1243	PE3 ngRNA spacer (AG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
11878	SEQ ID NO: 11878	PE3b*75 ngRNA spacer (AG PAM)
11879	SEQ ID NO: 11879	PE3b*74 ngRNA spacer (AG PAM)
11880	SEQ ID NO: 11880	PE3b*74 ngRNA spacer (CG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
1240	SEQ ID NO: 1240	PE3 ngRNA spacer (AG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer (AG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)

Sequence Number	Sequence	Description
11881	SEQ ID NO: 11881	PE3b*70 ngRNA spacer (AG PAM)
1220	SEQ ID NO: 1220	PE3 ngRNA spacer (TG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
11882	SEQ ID NO: 11882	PE3b*73 ngRNA spacer (AG PAM)
11883	SEQ ID NO: 11883	PE3b*70 ngRNA spacer (GG PAM)
1844	SEQ ID NO: 1844	PE3 ngRNA spacer (GG PAM)
1843	SEQ ID NO: 1843	PE3 ngRNA spacer (TG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
1845	SEQ ID NO: 1845	PE3 ngRNA spacer (TG PAM)
11884	SEQ ID NO: 11884	PE3b*73 ngRNA spacer (GG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
1239	SEQ ID NO: 1239	PE3 ngRNA spacer (AG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
103	SEQ ID NO: 103	ngRNA (GG PAM)
104	SEQ ID NO: 104	ngRNA (AG PAM)
1525	SEQ ID NO: 1525	ngRNA (AG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG PAM)
1958	SEQ ID NO: 1958	ngRNA (TG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG PAM)
117	SEQ ID NO: 117	ngRNA (AG PAM)
1959	SEQ ID NO: 1959	ngRNA (TG PAM)
1528	SEQ ID NO: 1528	ngRNA (AG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Table 60

Sequence Number	Sequence	Description
11885	SEQ ID NO: 11885	PEgRNA spacer (GG PAM)
11886	SEQ ID NO: 11886	PEgRNA spacer (GG PAM)
11887	SEQ ID NO: 11887	PEgRNA spacer (GG PAM)
11888	SEQ ID NO: 11888	PEgRNA spacer (GG PAM)
11889	SEQ ID NO: 11889	PEgRNA spacer (GG PAM)
11890	SEQ ID NO: 11890	PEgRNA spacer (GG PAM)
11891	SEQ ID NO: 11891	PEgRNA spacer (GG PAM)
5632	GGC	PBS
11892	GGCC	PBS
11893	GGCCC	PBS
11894	GGCCCA	PBS
11895	GGCCCAG	PBS
11896	GGCCCAGG	PBS
11897	GGCCCAGGG	PBS
11898	SEQ ID NO: 11898	PBS
11899	SEQ ID NO: 11899	PBS
11900	SEQ ID NO: 11900	PBS
11901	SEQ ID NO: 11901	PBS
11902	SEQ ID NO: 11902	PBS
11903	SEQ ID NO: 11903	PBS
11904	SEQ ID NO: 11904	PBS
11905	SEQ ID NO: 11905	PBS
11906	SEQ ID NO: 11906	PBS
11907	SEQ ID NO: 11907	PBS
11908	SEQ ID NO: 11908	RTT
11909	SEQ ID NO: 11909	RTT
11910	SEQ ID NO: 11910	RTT
11911	SEQ ID NO: 11911	RTT
11912	SEQ ID NO: 11912	RTT
11913	SEQ ID NO: 11913	RTT
11914	SEQ ID NO: 11914	RTT
11915	SEQ ID NO: 11915	RTT
11916	SEQ ID NO: 11916	RTT
11917	SEQ ID NO: 11917	RTT
11918	SEQ ID NO: 11918	RTT
11919	SEQ ID NO: 11919	RTT
11920	SEQ ID NO: 11920	RTT
11921	SEQ ID NO: 11921	RTT
11922	SEQ ID NO: 11922	RTT
11923	SEQ ID NO: 11923	RTT
11924	SEQ ID NO: 11924	RTT
11925	SEQ ID NO: 11925	RTT
11926	SEQ ID NO: 11926	RTT
11927	SEQ ID NO: 11927	RTT

Sequence Number	Sequence	Description
11928	SEQ ID NO: 11928	RTT
11929	SEQ ID NO: 11929	RTT
11930	SEQ ID NO: 11930	RTT
11931	SEQ ID NO: 11931	RTT
11932	SEQ ID NO: 11932	RTT
11933	SEQ ID NO: 11933	RTT
11934	SEQ ID NO: 11934	RTT
11935	SEQ ID NO: 11935	RTT
11936	SEQ ID NO: 11936	RTT
11937	SEQ ID NO: 11937	RTT
11938	SEQ ID NO: 11938	RTT
11939	SEQ ID NO: 11939	RTT
11940	SEQ ID NO: 11940	RTT
11941	SEQ ID NO: 11941	RTT
11942	SEQ ID NO: 11942	RTT
11943	SEQ ID NO: 11943	RTT
11944	SEQ ID NO: 11944	RTT
11945	SEQ ID NO: 11945	RTT
11946	SEQ ID NO: 11946	RTT
11947	SEQ ID NO: 11947	RTT
11948	SEQ ID NO: 11948	RTT
11949	SEQ ID NO: 11949	RTT
11950	SEQ ID NO: 11950	RTT
11951	SEQ ID NO: 11951	RTT
11952	SEQ ID NO: 11952	RTT
11953	SEQ ID NO: 11953	RTT
11954	SEQ ID NO: 11954	RTT
11955	SEQ ID NO: 11955	RTT
11956	SEQ ID NO: 11956	RTT
11957	SEQ ID NO: 11957	RTT
11958	SEQ ID NO: 11958	RTT
11959	SEQ ID NO: 11959	RTT
11960	SEQ ID NO: 11960	RTT

Sequence Number	Sequence	Description
11961	SEQ ID NO: 11961	RTT
11962	SEQ ID NO: 11962	RTT
11963	SEQ ID NO: 11963	RTT
11964	SEQ ID NO: 11964	RTT
11965	SEQ ID NO: 11965	RTT
11966	SEQ ID NO: 11966	RTT
11967	SEQ ID NO: 11967	RTT
11968	SEQ ID NO: 11968	RTT
11969	SEQ ID NO: 11969	RTT
11970	SEQ ID NO: 11970	RTT
11971	SEQ ID NO: 11971	RTT
11972	SEQ ID NO: 11972	RTT
11973	SEQ ID NO: 11973	RTT
11974	SEQ ID NO: 11974	RTT
11975	SEQ ID NO: 11975	RTT
11976	SEQ ID NO: 11976	RTT
11977	SEQ ID NO: 11977	RTT
11978	SEQ ID NO: 11978	RTT
11979	SEQ ID NO: 11979	RTT
11980	SEQ ID NO: 11980	RTT
11981	SEQ ID NO: 11981	RTT
11982	SEQ ID NO: 11982	RTT
11983	SEQ ID NO: 11983	RTT
11984	SEQ ID NO: 11984	RTT
11985	SEQ ID NO: 11985	RTT
11986	SEQ ID NO: 11986	RTT
11987	SEQ ID NO: 11987	RTT
11988	SEQ ID NO: 11988	RTT
11989	SEQ ID NO: 11989	RTT
11990	SEQ ID NO: 11990	RTT
11991	SEQ ID NO: 11991	RTT
11992	SEQ ID NO: 11992	RTT
11993	SEQ ID NO: 11993	RTT

Sequence Number	Sequence	Description
11994	SEQ ID NO: 11994	RTT
11995	SEQ ID NO: 11995	RTT
11996	SEQ ID NO: 11996	RTT
11997	SEQ ID NO: 11997	RTT
11998	SEQ ID NO: 11998	RTT
733	SEQ ID NO: 733	PE3 ngRNA spacer (TG PAM)
1843	SEQ ID NO: 1843	PE3 ngRNA spacer (TG PAM)
1234	SEQ ID NO: 1234	PE3 ngRNA spacer (GG PAM)
1220	SEQ ID NO: 1220	PE3 ngRNA spacer (TG PAM)
293	SEQ ID NO: 293	PE3 ngRNA spacer (AG PAM)
294	SEQ ID NO: 294	PE3 ngRNA spacer (TG PAM)
1222	SEQ ID NO: 1222	PE3 ngRNA spacer (GG PAM)
62	SEQ ID NO: 62	PE3 ngRNA spacer (AG PAM)
1223	SEQ ID NO: 1223	PE3 ngRNA spacer (AG PAM)
1243	SEQ ID NO: 1243	PE3 ngRNA spacer (AG PAM)
378	SEQ ID NO: 378	PE3 ngRNA spacer (TG PAM)
1229	SEQ ID NO: 1229	PE3 ngRNA spacer (TG PAM)
1212	SEQ ID NO: 1212	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(AG PAM)
1238	SEQ ID NO: 1238	PE3 ngRNA spacer (AG PAM)
732	SEQ ID NO: 732	PE3 ngRNA spacer (TG PAM)
1228	SEQ ID NO: 1228	PE3 ngRNA spacer (TG PAM)
1239	SEQ ID NO: 1239	PE3 ngRNA spacer (AG PAM)
1844	SEQ ID NO: 1844	PE3 ngRNA spacer (GG PAM)
1240	SEQ ID NO: 1240	PE3 ngRNA spacer (AG PAM)
1214	SEQ ID NO: 1214	PE3 ngRNA spacer (AG PAM)
1845	SEQ ID NO: 1845	PE3 ngRNA spacer (TG PAM)
1233	SEQ ID NO: 1233	PE3 ngRNA spacer (TG PAM)
84	SEQ ID NO: 84	PE3b ngRNA spacer (GG PAM)
189	SEQ ID NO: 189	PE3 ngRNA spacer (AG PAM)
1217	SEQ ID NO: 1217	PE3 ngRNA spacer (TG PAM)
1213	SEQ ID NO: 1213	PE3 ngRNA spacer (AG PAM)
1958	SEQ ID NO: 1958	ngRNA (TG PAM)
1526	SEQ ID NO: 1526	ngRNA (AG PAM)
107	SEQ ID NO: 107	ngRNA (AG PAM)
1525	SEQ ID NO: 1525	ngRNA (AG PAM)
1528	SEQ ID NO: 1528	ngRNA (AG PAM)
1527	SEQ ID NO: 1527	ngRNA (AG PAM)
1959	SEQ ID NO: 1959	ngRNA (TG PAM)
114	SEQ ID NO: 114	ngRNA (AG PAM)

Table 61

Sequence Number	Sequence	Description
11999	SEQ ID NO: 11999	PEgRNA spacer (GG PAM)
12000	SEQ ID NO: 12000	PEgRNA spacer (GG PAM)
12001	SEQ ID NO: 12001	PEgRNA spacer (GG PAM)
12002	SEQ ID NO: 12002	PEgRNA spacer (GG PAM)
12003	SEQ ID NO: 12003	PEgRNA spacer (GG PAM)
12004	SEQ ID NO: 12004	PEgRNA spacer (GG PAM)
12005	SEQ ID NO: 12005	PEgRNA spacer (GG PAM)
12006	TTT	PBS
12007	TTTA	PBS
12008	TTTAG	PBS
12009	TTTAGA	PBS
12010	TTTAGA A	PBS
12011	TTTAGA AT	PBS
12012	TTTAGA ATT	PBS
12013	SEQ ID NO: 12013	PBS
12014	SEQ ID NO: 12014	PBS
12015	SEQ ID NO: 12015	PBS
12016	SEQ ID NO: 12016	PBS
12017	SEQ ID NO: 12017	PBS
12018	SEQ ID NO: 12018	PBS
12019	SEQ ID NO: 12019	PBS
12020	SEQ ID NO: 12020	PBS
12021	SEQ ID NO: 12021	PBS
12022	SEQ ID NO: 12022	PBS
12023	SEQ ID NO: 12023	RTT
12024	SEQ ID NO: 12024	RTT
12025	SEQ ID NO: 12025	RTT
12026	SEQ ID NO: 12026	RTT
12027	SEQ ID NO: 12027	RTT
12028	SEQ ID NO: 12028	RTT
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
2007	SEQ ID NO: 2007	PE3 ngRNA spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer

Sequence Number	Sequence	Description
		(AG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1991	SEQ ID NO: 1991	PE3 ngRNA spacer (TG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
2009	SEQ ID NO: 2009	PE3 ngRNA spacer (AG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)

Table 62

Sequence Number	Sequence	Description
12029	SEQ ID NO: 12029	PEgRNA spacer (TG PAM)
12030	SEQ ID NO: 12030	PEgRNA spacer (TG PAM)
12031	SEQ ID NO: 12031	PEgRNA spacer (TG PAM)
12032	SEQ ID NO: 12032	PEgRNA spacer (TG PAM)
12033	SEQ ID NO: 12033	PEgRNA spacer (TG PAM)
12034	SEQ ID NO: 12034	PEgRNA spacer (TG PAM)
12035	SEQ ID NO: 12035	PEgRNA spacer (TG PAM)
12036	TGT	PBS
12037	TGTT	PBS
12038	TGTTT	PBS
12039	TGTTTA	PBS
12040	TGTTTA G	PBS
12041	TGTTTA GA	PBS
12042	TGTTTA GAA	PBS
12043	SEQ ID NO: 12043	PBS
12044	SEQ ID NO: 12044	PBS
12045	SEQ ID NO: 12045	PBS
12046	SEQ ID NO: 12046	PBS
12047	SEQ ID NO: 12047	PBS
12048	SEQ ID NO: 12048	PBS
12049	SEQ ID NO: 12049	PBS
12050	SEQ ID NO: 12050	PBS
12051	SEQ ID NO: 12051	PBS
12052	SEQ ID NO: 12052	PBS
12053	SEQ ID NO: 12053	RTT
12054	SEQ ID NO: 12054	RTT
12055	SEQ ID NO: 12055	RTT
12056	SEQ ID NO: 12056	RTT
12057	SEQ ID NO: 12057	RTT
12058	SEQ ID NO: 12058	RTT
12059	SEQ ID NO: 12059	RTT
12060	SEQ ID NO: 12060	RTT
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2007	SEQ ID NO: 2007	PE3 ngRNA spacer (TG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
1991	SEQ ID NO: 1991	PE3 ngRNA spacer (TG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)

Table 63

Sequence Number	Sequence	Description
12061	SEQ ID NO: 12061	PEgRNA spacer (AG PAM)
12062	SEQ ID NO: 12062	PEgRNA spacer (AG PAM)
12063	SEQ ID NO: 12063	PEgRNA spacer (AG PAM)
12064	SEQ ID NO: 12064	PEgRNA spacer (AG PAM)
12065	SEQ ID NO: 12065	PEgRNA spacer (AG PAM)
12066	SEQ ID NO: 12066	PEgRNA spacer (AG PAM)
12067	SEQ ID NO: 12067	PEgRNA spacer (AG PAM)
387	TCT	PBS
12068	TCTG	PBS
12069	TCTGA	PBS
12070	TCTGAA	PBS
12071	TCTGAAC	PBS
12072	TCTGAACA	PBS
12073	TCTGAACAC	PBS
12074	SEQ ID NO: 12074	PBS
12075	SEQ ID NO: 12075	PBS
12076	SEQ ID NO: 12076	PBS
12077	SEQ ID NO: 12077	PBS
12078	SEQ ID NO: 12078	PBS
12079	SEQ ID NO: 12079	PBS
12080	SEQ ID NO: 12080	PBS
12081	SEQ ID NO: 12081	PBS
12082	SEQ ID NO: 12082	PBS
12083	SEQ ID NO: 12083	PBS
12084	SEQ ID NO: 12084	RTT
12085	SEQ ID NO: 12085	RTT
12086	SEQ ID NO: 12086	RTT
12087	SEQ ID NO: 12087	RTT
12088	SEQ ID NO: 12088	RTT
12089	SEQ ID NO: 12089	RTT
12090	SEQ ID NO: 12090	RTT
12091	SEQ ID NO: 12091	RTT
12092	SEQ ID NO: 12092	RTT
12093	SEQ ID NO: 12093	RTT
12094	SEQ ID NO: 12094	RTT
12095	SEQ ID NO: 12095	RTT
12096	SEQ ID NO: 12096	RTT
12097	SEQ ID NO: 12097	RTT
12098	SEQ ID NO: 12098	RTT
12099	SEQ ID NO: 12099	RTT
12100	SEQ ID NO: 12100	RTT
12101	SEQ ID NO: 12101	RTT
12102	SEQ ID NO: 12102	RTT
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer

Sequence Number	Sequence	Description
		(GG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
1991	SEQ ID NO: 1991	PE3 ngRNA spacer (TG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)

Table 64

Sequence Number	Sequence	Description
12103	SEQ ID NO: 12103	PEgRNA spacer (TG PAM)
12104	SEQ ID NO: 12104	PEgRNA spacer (TG PAM)
12105	SEQ ID NO: 12105	PEgRNA spacer (TG PAM)
12106	SEQ ID NO: 12106	PEgRNA spacer (TG PAM)
12107	SEQ ID NO: 12107	PEgRNA spacer (TG PAM)
12108	SEQ ID NO: 12108	PEgRNA spacer (TG PAM)
12109	SEQ ID NO: 12109	PEgRNA spacer (TG PAM)
10073	CTC	PBS
12110	CTCA	PBS
12111	CTCAC	PBS
12112	CTCACT	PBS
12113	CTCACT T	PBS
12114	CTCACT TC	PBS
12115	CTCACT TCC	PBS
12116	SEQ ID NO: 12116	PBS
12117	SEQ ID NO: 12117	PBS
12118	SEQ ID NO: 12118	PBS
12119	SEQ ID NO: 12119	PBS
12120	SEQ ID NO: 12120	PBS
12121	SEQ ID NO: 12121	PBS
12122	SEQ ID NO: 12122	PBS
12123	SEQ ID NO: 12123	PBS
12124	SEQ ID NO: 12124	PBS
12125	SEQ ID NO: 12125	PBS
12126	SEQ ID NO: 12126	RTT
12127	SEQ ID NO: 12127	RTT
12128	SEQ ID NO: 12128	RTT
12129	SEQ ID NO: 12129	RTT
12130	SEQ ID NO: 12130	RTT
12131	SEQ ID NO: 12131	RTT
12132	SEQ ID NO: 12132	RTT
12133	SEQ ID NO: 12133	RTT
12134	SEQ ID NO: 12134	RTT
12135	SEQ ID NO: 12135	RTT
12136	SEQ ID NO: 12136	RTT
12137	SEQ ID NO: 12137	RTT
12138	SEQ ID NO: 12138	RTT
12139	SEQ ID NO: 12139	RTT
12140	SEQ ID NO: 12140	RTT
12141	SEQ ID NO: 12141	RTT
12142	SEQ ID NO: 12142	RTT
12143	SEQ ID NO: 12143	RTT
12144	SEQ ID NO: 12144	RTT
12145	SEQ ID NO: 12145	RTT
12146	SEQ ID NO: 12146	RTT
12147	SEQ ID NO: 12147	RTT
12148	SEQ ID NO: 12148	RTT
12149	SEQ ID NO: 12149	RTT
12150	SEQ ID NO: 12150	RTT
12151	SEQ ID NO: 12151	RTT
12152	SEQ ID NO: 12152	RTT

Sequence Number	Sequence	Description
12153	SEQ ID NO: 12153	RTT
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)

Table 65

Sequence Number	Sequence	Description
12154	SEQ ID NO: 12154	PEgRNA spacer (AG PAM)
12155	SEQ ID NO: 12155	PEgRNA spacer (AG PAM)
12156	SEQ ID NO: 12156	PEgRNA spacer (AG PAM)
12157	SEQ ID NO: 12157	PEgRNA spacer (AG PAM)
12158	SEQ ID NO: 12158	PEgRNA spacer (AG PAM)
12159	SEQ ID NO: 12159	PEgRNA spacer (AG PAM)
12160	SEQ ID NO: 12160	PEgRNA spacer (AG PAM)
6298	TCA	PBS
6299	TCAG	PBS
12161	TCAGT	PBS
12162	TCAGTA	PBS
12163	TCAGTA A	PBS
12164	TCAGTA AA	PBS
12165	TCAGTA AAC	PBS
12166	SEQ ID NO: 12166	PBS
12167	SEQ ID NO: 12167	PBS
12168	SEQ ID NO: 12168	PBS
12169	SEQ ID NO: 12169	PBS
12170	SEQ ID NO: 12170	PBS
12171	SEQ ID NO: 12171	PBS
12172	SEQ ID NO: 12172	PBS
12173	SEQ ID NO: 12173	PBS
12174	SEQ ID NO: 12174	PBS
12175	SEQ ID NO: 12175	PBS

Sequence Number	Sequence	Description
12176	SEQ ID NO: 12176	RTT
12177	SEQ ID NO: 12177	RTT
12178	SEQ ID NO: 12178	RTT
12179	SEQ ID NO: 12179	RTT
12180	SEQ ID NO: 12180	RTT
12181	SEQ ID NO: 12181	RTT
12182	SEQ ID NO: 12182	RTT
12183	SEQ ID NO: 12183	RTT
12184	SEQ ID NO: 12184	RTT
12185	SEQ ID NO: 12185	RTT
12186	SEQ ID NO: 12186	RTT
12187	SEQ ID NO: 12187	RTT
12188	SEQ ID NO: 12188	RTT
12189	SEQ ID NO: 12189	RTT
12190	SEQ ID NO: 12190	RTT
12191	SEQ ID NO: 12191	RTT
12192	SEQ ID NO: 12192	RTT
12193	SEQ ID NO: 12193	RTT
12194	SEQ ID NO: 12194	RTT
12195	SEQ ID NO: 12195	RTT
12196	SEQ ID NO: 12196	RTT
12197	SEQ ID NO: 12197	RTT
12198	SEQ ID NO: 12198	RTT
12199	SEQ ID NO: 12199	RTT
12200	SEQ ID NO: 12200	RTT
12201	SEQ ID NO: 12201	RTT
12202	SEQ ID NO: 12202	RTT
12203	SEQ ID NO: 12203	RTT
12204	SEQ ID NO: 12204	RTT
12205	SEQ ID NO: 12205	RTT
12206	SEQ ID NO: 12206	RTT
12207	SEQ ID NO: 12207	RTT
12208	SEQ ID NO: 12208	RTT
12209	SEQ ID NO: 12209	RTT
12210	SEQ ID NO: 12210	RTT
12211	SEQ ID NO: 12211	RTT
12212	SEQ ID NO: 12212	RTT
12213	SEQ ID NO: 12213	RTT
12214	SEQ ID NO: 12214	RTT
12215	SEQ ID NO: 12215	RTT
12216	SEQ ID NO: 12216	RTT
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
1993	SEQ ID NO: 1993	PE3 ngRNA spacer (AG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA

Sequence Number	Sequence	Description
		spacer (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)

Table 66

Sequence Number	Sequence	Description
12217	SEQ ID NO: 12217	PEgRNA spacer (AG PAM)
12218	SEQ ID NO: 12218	PEgRNA spacer (AG PAM)
12219	SEQ ID NO: 12219	PEgRNA spacer (AG PAM)
12220	SEQ ID NO: 12220	PEgRNA spacer (AG PAM)
12221	SEQ ID NO: 12221	PEgRNA spacer (AG PAM)
12222	SEQ ID NO: 12222	PEgRNA spacer (AG PAM)
12223	SEQ ID NO: 12223	PEgRNA spacer (AG PAM)
4314	CCT	PBS
4315	CCTT	PBS
4316	CCTTC	PBS
12224	CCTTCA	PBS
12225	CCTTCA G	PBS
12226	CCTTCA GT	PBS
12227	CCTTCA GTA	PBS
12228	SEQ ID NO: 12228	PBS
12229	SEQ ID NO: 12229	PBS
12230	SEQ ID NO: 12230	PBS
12231	SEQ ID NO: 12231	PBS
12232	SEQ ID NO: 12232	PBS
12233	SEQ ID NO: 12233	PBS
12234	SEQ ID NO: 12234	PBS
12235	SEQ ID NO: 12235	PBS
12236	SEQ ID NO: 12236	PBS
12237	SEQ ID NO: 12237	PBS
12238	SEQ ID NO: 12238	RTT
12239	SEQ ID NO: 12239	RTT
12240	SEQ ID NO: 12240	RTT
12241	SEQ ID NO: 12241	RTT
12242	SEQ ID NO: 12242	RTT
12243	SEQ ID NO: 12243	RTT
12244	SEQ ID NO: 12244	RTT
12245	SEQ ID NO: 12245	RTT
12246	SEQ ID NO: 12246	RTT
12247	SEQ ID NO: 12247	RTT
12248	SEQ ID NO: 12248	RTT
12249	SEQ ID NO: 12249	RTT
12250	SEQ ID NO: 12250	RTT
12251	SEQ ID NO: 12251	RTT
12252	SEQ ID NO: 12252	RTT
12253	SEQ ID NO: 12253	RTT
12254	SEQ ID NO: 12254	RTT
12255	SEQ ID NO: 12255	RTT
12256	SEQ ID NO: 12256	RTT
12257	SEQ ID NO: 12257	RTT
12258	SEQ ID NO: 12258	RTT
12259	SEQ ID NO: 12259	RTT
12260	SEQ ID NO: 12260	RTT
12261	SEQ ID NO: 12261	RTT
12262	SEQ ID NO: 12262	RTT
12263	SEQ ID NO: 12263	RTT
12264	SEQ ID NO: 12264	RTT
12265	SEQ ID NO: 12265	RTT
12266	SEQ ID NO: 12266	RTT
12267	SEQ ID NO: 12267	RTT
12268	SEQ ID NO: 12268	RTT
12269	SEQ ID NO: 12269	RTT
12270	SEQ ID NO: 12270	RTT
12271	SEQ ID NO: 12271	RTT
12272	SEQ ID NO: 12272	RTT
12273	SEQ ID NO: 12273	RTT
12274	SEQ ID NO: 12274	RTT
12275	SEQ ID NO: 12275	RTT
12276	SEQ ID NO: 12276	RTT
12277	SEQ ID NO: 12277	RTT
12278	SEQ ID NO: 12278	RTT
12279	SEQ ID NO: 12279	RTT
12280	SEQ ID NO: 12280	RTT
12281	SEQ ID NO: 12281	RTT
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)

Sequence Number	Sequence	Description
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
1999	SEQ ID NO: 1999	PE3 ngRNA spacer (AG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
2002	SEQ ID NO: 2002	PE3 ngRNA spacer (TG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG PAM)
1996	SEQ ID NO: 1996	PE3 ngRNA spacer (AG PAM)
1995	SEQ ID NO: 1995	PE3 ngRNA spacer (AG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
061	SEQ ID NO: 2061	ngRNA (TG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)

Table 67

Sequence Number	Sequence	Description
12282	SEQ ID NO: 12282	PEgRNA spacer (AG PAM)
12283	SEQ ID NO: 12283	PEgRNA spacer (AG PAM)
12284	SEQ ID NO: 12284	PEgRNA spacer (AG PAM)
12285	SEQ ID NO: 12285	PEgRNA spacer (AG PAM)
12286	SEQ ID NO: 12286	PEgRNA spacer (AG PAM)
12287	SEQ ID NO: 12287	PEgRNA spacer (AG PAM)
12288	SEQ ID NO: 12288	PEgRNA spacer (AG PAM)
12289	GGT	PBS
12290	GGTT	PBS
12291	GGTTC	PBS
12292	GGTTCA	PBS
12293	GGTTCAG	PBS
12294	GGTTCAGA	PBS
12295	GGTTCAGAA	PBS
12296	SEQ ID NO: 12296	PBS
12297	SEQ ID NO: 12297	PBS
12298	SEQ ID NO: 12298	PBS
12299	SEQ ID NO: 12299	PBS
12300	SEQ ID NO: 12300	PBS
12301	SEQ ID NO: 12301	PBS
12302	SEQ ID NO: 12302	PBS
12303	SEQ ID NO: 12303	PBS
12304	SEQ ID NO: 12304	PBS
12305	SEQ ID NO: 12305	PBS
12306	SEQ ID NO: 12306	RTT
12307	SEQ ID NO: 12307	RTT
12308	SEQ ID NO: 12308	RTT
12309	SEQ ID NO: 12309	RTT
12310	SEQ ID NO: 12310	RTT
12311	SEQ ID NO: 12311	RTT
12312	SEQ ID NO: 12312	RTT
12313	SEQ ID NO: 12313	RTT
12314	SEQ ID NO: 12314	RTT
12315	SEQ ID NO: 12315	RTT
12316	SEQ ID NO: 12316	RTT
12317	SEQ ID NO: 12317	RTT

Sequence Number	Sequence	Description
12318	SEQ ID NO: 12318	RTT
12319	SEQ ID NO: 12319	RTT
12320	SEQ ID NO: 12320	RTT
12321	SEQ ID NO: 12321	RTT
12322	SEQ ID NO: 12322	RTT
12323	SEQ ID NO: 12323	RTT
12324	SEQ ID NO: 12324	RTT
12325	SEQ ID NO: 12325	RTT
12326	SEQ ID NO: 12326	RTT
12327	SEQ ID NO: 12327	RTT
12328	SEQ ID NO: 12328	RTT
12329	SEQ ID NO: 12329	RTT
12330	SEQ ID NO: 12330	RTT
12331	SEQ ID NO: 12331	RTT
12332	SEQ ID NO: 12332	RTT
12333	SEQ ID NO: 12333	RTT
12334	SEQ ID NO: 12334	RTT
12335	SEQ ID NO: 12335	RTT
12336	SEQ ID NO: 12336	RTT
12337	SEQ ID NO: 12337	RTT
12338	SEQ ID NO: 12338	RTT
12339	SEQ ID NO: 12339	RTT
12340	SEQ ID NO: 12340	RTT
12341	SEQ ID NO: 12341	RTT
12342	SEQ ID NO: 12342	RTT
12343	SEQ ID NO: 12343	RTT
12344	SEQ ID NO: 12344	RTT
12345	SEQ ID NO: 12345	RTT
12346	SEQ ID NO: 12346	RTT
12347	SEQ ID NO: 12347	RTT
12348	SEQ ID NO: 12348	RTT
12349	SEQ ID NO: 12349	RTT
12350	SEQ ID NO: 12350	RTT

Sequence Number	Sequence	Description
12351	SEQ ID NO: 12351	RTT
12352	SEQ ID NO: 12352	RTT
12353	SEQ ID NO: 12353	RTT
12354	SEQ ID NO: 12354	RTT
12355	SEQ ID NO: 12355	RTT
12356	SEQ ID NO: 12356	RTT
12357	SEQ ID NO: 12357	RTT
12358	SEQ ID NO: 12358	RTT
12359	SEQ ID NO: 12359	RTT
12360	SEQ ID NO: 12360	RTT
12361	SEQ ID NO: 12361	RTT
12362	SEQ ID NO: 12362	RTT
12363	SEQ ID NO: 12363	RTT
12364	SEQ ID NO: 12364	RTT
12365	SEQ ID NO: 12365	RTT
12366	SEQ ID NO: 12366	RTT
12367	SEQ ID NO: 12367	RTT
12368	SEQ ID NO: 12368	RTT
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)

Sequence Number	Sequence	Description
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)

Sequence Number	Sequence	Description
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)

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Sequence Number	Sequence	Description
12369	SEQ ID NO: 12369	PEgRNA spacer (TG PAM)
12370	SEQ ID NO: 12370	PEgRNA spacer (TG PAM)
12371	SEQ ID NO: 12371	PEgRNA spacer (TG PAM)
12372	SEQ ID NO: 12372	PEgRNA spacer (TG PAM)
12373	SEQ ID NO: 12373	PEgRNA spacer (TG PAM)
12374	SEQ ID NO: 12374	PEgRNA spacer (TG PAM)
12375	SEQ ID NO: 12375	PEgRNA spacer (TG PAM)
6298	TCA	PBS
6299	TCAG	PBS
12376	TCAGG	PBS
12377	TCAGGT	PBS
12378	TCAGGT T	PBS
12379	TCAGGT TC	PBS
12380	TCAGGT TCA	PBS
12381	SEQ ID NO: 12381	PBS
12382	SEQ ID NO: 12382	PBS
12383	SEQ ID NO: 12383	PBS
12384	SEQ ID NO: 12384	PBS
12385	SEQ ID NO: 12385	PBS
12386	SEQ ID NO: 12386	PBS
12387	SEQ ID NO: 12387	PBS
12388	SEQ ID NO: 12388	PBS
12389	SEQ ID NO: 12389	PBS
12390	SEQ ID NO: 12390	PBS
12391	SEQ ID NO: 12391	RTT
12392	SEQ ID NO: 12392	RTT
12393	SEQ ID NO: 12393	RTT
12394	SEQ ID NO: 12394	RTT
12395	SEQ ID NO: 12395	RTT
12396	SEQ ID NO: 12396	RTT
12397	SEQ ID NO: 12397	RTT
12398	SEQ ID NO: 12398	RTT
12399	SEQ ID NO: 12399	RTT
12400	SEQ ID NO: 12400	RTT
12401	SEQ ID NO: 12401	RTT
12402	SEQ ID NO: 12402	RTT
12403	SEQ ID NO: 12403	RTT
12404	SEQ ID NO: 12404	RTT
12405	SEQ ID NO: 12405	RTT
12406	SEQ ID NO: 12406	RTT
12407	SEQ ID NO: 12407	RTT
12408	SEQ ID NO: 12408	RTT
12409	SEQ ID NO: 12409	RTT
12410	SEQ ID NO: 12410	RTT
12411	SEQ ID NO: 12411	RTT
12412	SEQ ID NO: 12412	RTT
12413	SEQ ID NO: 12413	RTT
12414	SEQ ID NO: 12414	RTT
12415	SEQ ID NO: 12415	RTT
12416	SEQ ID NO: 12416	RTT
12417	SEQ ID NO: 12417	RTT
12418	SEQ ID NO: 12418	RTT
12419	SEQ ID NO: 12419	RTT
12420	SEQ ID NO: 12420	RTT
12421	SEQ ID NO: 12421	RTT
12422	SEQ ID NO: 12422	RTT
12423	SEQ ID NO: 12423	RTT
12424	SEQ ID NO: 12424	RTT
12425	SEQ ID NO: 12425	RTT
12426	SEQ ID NO: 12426	RTT
12427	SEQ ID NO: 12427	RTT
12428	SEQ ID NO: 12428	RTT
12429	SEQ ID NO: 12429	RTT
12430	SEQ ID NO: 12430	RTT
12431	SEQ ID NO: 12431	RTT
12432	SEQ ID NO: 12432	RTT
12433	SEQ ID NO: 12433	RTT
12434	SEQ ID NO: 12434	RTT
12435	SEQ ID NO: 12435	RTT
12436	SEQ ID NO: 12436	RTT
12437	SEQ ID NO: 12437	RTT
12438	SEQ ID NO: 12438	RTT
12439	SEQ ID NO: 12439	RTT
12440	SEQ ID NO: 12440	RTT
12441	SEQ ID NO: 12441	RTT
12442	SEQ ID NO: 12442	RTT
12443	SEQ ID NO: 12443	RTT

Sequence Number	Sequence	Description
12444	SEQ ID NO: 12444	RTT
12445	SEQ ID NO: 12445	RTT
12446	SEQ ID NO: 12446	RTT
12447	SEQ ID NO: 12447	RTT
12448	SEQ ID NO: 12448	RTT
12449	SEQ ID NO: 12449	RTT
12450	SEQ ID NO: 12450	RTT
12451	SEQ ID NO: 12451	RTT
12452	SEQ ID NO: 12452	RTT
12453	SEQ ID NO: 12453	RTT
12454	SEQ ID NO: 12454	RTT
12455	SEQ ID NO: 12455	RTT
12456	SEQ ID NO: 12456	RTT
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)
3268	SEQ ID NO: 3268	PE3 ngRNA spacer (AG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA spacer (AG PAM)
1997	SEQ ID NO: 1997	PE3 ngRNA spacer (AG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
3283	SEQ ID NO: 3283	PE3 ngRNA spacer (GG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
1992	SEQ ID NO: 1992	PE3 ngRNA spacer (GG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
4091	SEQ ID NO: 4091	ngRNA (AG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
2010	SEQ ID NO: 2010	ngRNA (AG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
4124	SEQ ID NO: 4124	ngRNA (AG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)

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Sequence Number	Sequence	Description
12457	SEQ ID NO: 12457	PEgRNA spacer (TG PAM)
12458	SEQ ID NO: 12458	PEgRNA spacer (TG PAM)
12459	SEQ ID NO: 12459	PEgRNA spacer (TG PAM)
12460	SEQ ID NO: 12460	PEgRNA spacer (TG PAM)
12461	SEQ ID NO: 12461	PEgRNA spacer (TG PAM)

Sequence Number	Sequence	Description
12462	SEQ ID NO: 12462	PEgRNA spacer (TG PAM)
12463	SEQ ID NO: 12463	PEgRNA spacer (TG PAM)
2135	GCT	PBS
12464	GCTT	PBS
12465	GCTTC	PBS
12466	GCTTCA	PBS
12467	GCTTCA G	PBS
12468	GCTTCA GG	PBS
12469	GCTTCA GGT	PBS
12470	SEQ ID NO: 12470	PBS
12471	SEQ ID NO: 12471	PBS
12472	SEQ ID NO: 12472	PBS
12473	SEQ ID NO: 12473	PBS
12474	SEQ ID NO: 12474	PBS
12475	SEQ ID NO: 12475	PBS
12476	SEQ ID NO: 12476	PBS
12477	SEQ ID NO: 12477	PBS
12478	SEQ ID NO: 12478	PBS
12479	SEQ ID NO: 12479	PBS
12480	SEQ ID NO: 12480	RTT
12481	SEQ ID NO: 12481	RTT
12482	SEQ ID NO: 12482	RTT
12483	SEQ ID NO: 12483	RTT
12484	SEQ ID NO: 12484	RTT
12485	SEQ ID NO: 12485	RTT
12486	SEQ ID NO: 12486	RTT
12487	SEQ ID NO: 12487	RTT
12488	SEQ ID NO: 12488	RTT
12489	SEQ ID NO: 12489	RTT
12490	SEQ ID NO: 12490	RTT
12491	SEQ ID NO: 12491	RTT
12492	SEQ ID NO: 12492	RTT
12493	SEQ ID NO: 12493	RTT
12494	SEQ ID NO: 12494	RTT

Sequence Number	Sequence	Description
12495	SEQ ID NO: 12495	RTT
12496	SEQ ID NO: 12496	RTT
12497	SEQ ID NO: 12497	RTT
12498	SEQ ID NO: 12498	RTT
12499	SEQ ID NO: 12499	RTT
12500	SEQ ID NO: 12500	RTT
12501	SEQ ID NO: 12501	RTT
12502	SEQ ID NO: 12502	RTT
12503	SEQ ID NO: 12503	RTT
12504	SEQ ID NO: 12504	RTT
12505	SEQ ID NO: 12505	RTT
12506	SEQ ID NO: 12506	RTT
12507	SEQ ID NO: 12507	RTT
12508	SEQ ID NO: 12508	RTT
12509	SEQ ID NO: 12509	RTT
12510	SEQ ID NO: 12510	RTT
12511	SEQ ID NO: 12511	RTT
12512	SEQ ID NO: 12512	RTT
12513	SEQ ID NO: 12513	RTT
12514	SEQ ID NO: 12514	RTT
12515	SEQ ID NO: 12515	RTT
12516	SEQ ID NO: 12516	RTT
12517	SEQ ID NO: 12517	RTT
12518	SEQ ID NO: 12518	RTT
12519	SEQ ID NO: 12519	RTT
12520	SEQ ID NO: 12520	RTT
12521	SEQ ID NO: 12521	RTT
12522	SEQ ID NO: 12522	RTT
12523	SEQ ID NO: 12523	RTT
12524	SEQ ID NO: 12524	RTT
12525	SEQ ID NO: 12525	RTT
12526	SEQ ID NO: 12526	RTT
12527	SEQ ID NO: 12527	RTT

Sequence Number	Sequence	Description
12528	SEQ ID NO: 12528	RTT
12529	SEQ ID NO: 12529	RTT
12530	SEQ ID NO: 12530	RTT
12531	SEQ ID NO: 12531	RTT
12532	SEQ ID NO: 12532	RTT
12533	SEQ ID NO: 12533	RTT
12534	SEQ ID NO: 12534	RTT
12535	SEQ ID NO: 12535	RTT
12536	SEQ ID NO: 12536	RTT
12537	SEQ ID NO: 12537	RTT
12538	SEQ ID NO: 12538	RTT
12539	SEQ ID NO: 12539	RTT
12540	SEQ ID NO: 12540	RTT
12541	SEQ ID NO: 12541	RTT
12542	SEQ ID NO: 12542	RTT
12543	SEQ ID NO: 12543	RTT
12544	SEQ ID NO: 12544	RTT
12545	SEQ ID NO: 12545	RTT
12546	SEQ ID NO: 12546	RTT
12547	SEQ ID NO: 12547	RTT
12548	SEQ ID NO: 12548	RTT
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
3282	SEQ ID NO: 3282	PE3 ngRNA spacer (AG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
3285	SEQ ID NO: 3285	PE3 ngRNA spacer (GG PAM)
2008	SEQ ID NO: 2008	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (AG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)
1989	SEQ ID NO: 1989	PE3 ngRNA spacer (AG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
3268	SEQ ID NO: 3268	PE3 ngRNA spacer (AG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
3283	SEQ ID NO: 3283	PE3 ngRNA spacer (GG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
4091	SEQ ID NO: 4091	ngRNA (AG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
4124	SEQ ID NO: 4124	ngRNA (AG PAM)

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Sequence Number	Sequence	Description
12549	SEQ ID NO: 12549	PEgRNA spacer (TG PAM)
12550	SEQ ID NO: 12550	PEgRNA spacer (TG PAM)
12551	SEQ ID NO: 12551	PEgRNA spacer (TG PAM)
12552	SEQ ID NO: 12552	PEgRNA spacer (TG PAM)
12553	SEQ ID NO: 12553	PEgRNA spacer (TG PAM)
12554	SEQ ID NO: 12554	PEgRNA spacer (TG PAM)
12555	SEQ ID NO: 12555	PEgRNA spacer (TG PAM)
2070	GTA	PBS
2071	GTAA	PBS
12556	GTAAC	PBS
12557	GTAACA	PBS
12558	GTAACAG	PBS
12559	GTAACAGC	PBS
12560	GTAACAGCA	PBS
12561	SEQ ID NO: 12561	PBS
12562	SEQ ID NO: 12562	PBS
12563	SEQ ID NO: 12563	PBS
12564	SEQ ID NO: 12564	PBS
12565	SEQ ID NO: 12565	PBS
12566	SEQ ID NO: 12566	PBS
12567	SEQ ID NO: 12567	PBS
12568	SEQ ID NO: 12568	PBS
12569	SEQ ID NO: 12569	PBS
12570	SEQ ID NO: 12570	PBS
12571	SEQ ID NO: 12571	RTT
12572	SEQ ID NO: 12572	RTT
12573	SEQ ID NO: 12573	RTT
12574	SEQ ID NO: 12574	RTT
12575	SEQ ID NO: 12575	RTT
12576	SEQ ID NO: 12576	RTT
12577	SEQ ID NO: 12577	RTT
12578	SEQ ID NO: 12578	RTT
12579	SEQ ID NO: 12579	RTT
12580	SEQ ID NO: 12580	RTT
12581	SEQ ID NO: 12581	RTT

Sequence Number	Sequence	Description
12582	SEQ ID NO: 12582	RTT
12583	SEQ ID NO: 12583	RTT
12584	SEQ ID NO: 12584	RTT
12585	SEQ ID NO: 12585	RTT
12586	SEQ ID NO: 12586	RTT
12587	SEQ ID NO: 12587	RTT
12588	SEQ ID NO: 12588	RTT
12589	SEQ ID NO: 12589	RTT
12590	SEQ ID NO: 12590	RTT
12591	SEQ ID NO: 12591	RTT
12592	SEQ ID NO: 12592	RTT
12593	SEQ ID NO: 12593	RTT
12594	SEQ ID NO: 12594	RTT
12595	SEQ ID NO: 12595	RTT
12596	SEQ ID NO: 12596	RTT
12597	SEQ ID NO: 12597	RTT
12598	SEQ ID NO: 12598	RTT
12599	SEQ ID NO: 12599	RTT
12600	SEQ ID NO: 12600	RTT
12601	SEQ ID NO: 12601	RTT
12602	SEQ ID NO: 12602	RTT
12603	SEQ ID NO: 12603	RTT
12604	SEQ ID NO: 12604	RTT
12605	SEQ ID NO: 12605	RTT
12606	SEQ ID NO: 12606	RTT
12607	SEQ ID NO: 12607	RTT
12608	SEQ ID NO: 12608	RTT
12609	SEQ ID NO: 12609	RTT
12610	SEQ ID NO: 12610	RTT
12611	SEQ ID NO: 12611	RTT
12612	SEQ ID NO: 12612	RTT
12613	SEQ ID NO: 12613	RTT
12614	SEQ ID NO: 12614	RTT
12615	SEQ ID NO: 12615	RTT
12616	SEQ ID NO: 12616	RTT
12617	SEQ ID NO: 12617	RTT
12618	SEQ ID NO: 12618	RTT
12619	SEQ ID NO: 12619	RTT
12620	SEQ ID NO: 12620	RTT
12621	SEQ ID NO: 12621	RTT
12622	SEQ ID NO: 12622	RTT
12623	SEQ ID NO: 12623	RTT
12624	SEQ ID NO: 12624	RTT
12625	SEQ ID NO: 12625	RTT
12626	SEQ ID NO: 12626	RTT
12627	SEQ ID NO: 12627	RTT
12628	SEQ ID NO: 12628	RTT
12629	SEQ ID NO: 12629	RTT
12630	SEQ ID NO: 12630	RTT
12631	SEQ ID NO: 12631	RTT
12632	SEQ ID NO: 12632	RTT
12633	SEQ ID NO: 12633	RTT
12634	SEQ ID NO: 12634	RTT
12635	SEQ ID NO: 12635	RTT
12636	SEQ ID NO: 12636	RTT
12637	SEQ ID NO: 12637	RTT
12638	SEQ ID NO: 12638	RTT
12639	SEQ ID NO: 12639	RTT
12640	SEQ ID NO: 12640	RTT
12641	SEQ ID NO: 12641	RTT
12642	SEQ ID NO: 12642	RTT
12643	SEQ ID NO: 12643	RTT
12644	SEQ ID NO: 12644	RTT
12645	SEQ ID NO: 12645	RTT
12646	SEQ ID NO: 12646	RTT
12647	SEQ ID NO: 12647	RTT
12648	SEQ ID NO: 12648	RTT
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
3260	SEQ ID NO: 3260	PE3 ngRNA spacer (AG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)
2001	SEQ ID NO: 2001	PE3 ngRNA spacer (GG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
3263	SEQ ID NO: 3263	PE3 ngRNA spacer (AG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
3270	SEQ ID NO: 3270	PE3 ngRNA spacer (GG PAM)
3283	SEQ ID NO: 3283	PE3 ngRNA spacer (GG PAM)

Sequence Number	Sequence	Description
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
3269	SEQ ID NO: 3269	PE3 ngRNA spacer (CG PAM)
3282	SEQ ID NO: 3282	PE3 ngRNA spacer (AG PAM)
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)
3266	SEQ ID NO: 3266	PE3 ngRNA spacer (TG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
3268	SEQ ID NO: 3268	PE3 ngRNA spacer (AG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
3285	SEQ ID NO: 3285	PE3 ngRNA spacer (GG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
4091	SEQ ID NO: 4091	ngRNA (AG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
4105	SEQ ID NO: 4105	ngRNA (AG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
4106	SEQ ID NO: 4106	ngRNA (CG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
4124	SEQ ID NO: 4124	ngRNA (AG PAM)

Table 71

Sequence Number	Sequence	Description
12649	SEQ ID NO: 12649	PEgRNA spacer (AG PAM)
12650	SEQ ID NO: 12650	PEgRNA spacer (AG PAM)
12651	SEQ ID NO: 12651	PEgRNA spacer (AG PAM)
12652	SEQ ID NO: 12652	PEgRNA spacer (AG PAM)
12653	SEQ ID NO: 12653	PEgRNA spacer (AG PAM)
12654	SEQ ID NO: 12654	PEgRNA spacer (AG PAM)
12655	SEQ ID NO: 12655	PEgRNA spacer (AG PAM)
200	CAA	PBS
12656	CAAA	PBS
12657	CAAAG	PBS
12658	CAAAGG	PBS
12659	CAAAGGT	PBS
12660	CAAAGGTA	PBS
12661	CAAAGGTAA	PBS
12662	SEQ ID NO: 12662	PBS
12663	SEQ ID NO: 12663	PBS
12664	SEQ ID NO: 12664	PBS
12665	SEQ ID NO: 12665	PBS
12666	SEQ ID NO: 12666	PBS
12667	SEQ ID NO: 12667	PBS
12668	SEQ ID NO: 12668	PBS
12669	SEQ ID NO: 12669	PBS
12670	SEQ ID NO: 12670	PBS
12671	SEQ ID NO: 12671	PBS
12672	SEQ ID NO: 12672	RTT
12673	SEQ ID NO: 12673	RTT*45 (PAM silencing)
12674	SEQ ID NO: 12674	RTT*45 (PAM silencing)
12675	SEQ ID NO: 12675	RTT
12676	SEQ ID NO: 12676	RTT*45 (PAM silencing)
12677	SEQ ID NO: 12677	RTT
12678	SEQ ID NO: 12678	RTT*45 (PAM silencing)
12679	SEQ ID NO: 12679	RTT
12680	SEQ ID NO: 12680	RTT*45 (PAM silencing)
12681	SEQ ID NO: 12681	RTT
12682	SEQ ID NO: 12682	RTT
12683	SEQ ID NO: 12683	RTT*45 (PAM silencing)
12684	SEQ ID NO: 12684	RTT*45 (PAM silencing)
12685	SEQ ID NO: 12685	RTT
12686	SEQ ID NO: 12686	RTT*45 (PAM silencing)

Sequence Number	Sequence	Description
12687	SEQ ID NO: 12687	RTT
12688	SEQ ID NO: 12688	RTT
12689	SEQ ID NO: 12689	RTT*45 (PAM silencing)
12690	SEQ ID NO: 12690	RTT*45 (PAM silencing)
12691	SEQ ID NO: 12691	RTT
12692	SEQ ID NO: 12692	RTT*45 (PAM silencing)
12693	SEQ ID NO: 12693	RTT
12694	SEQ ID NO: 12694	RTT
12695	SEQ ID NO: 12695	RTT*45 (PAM silencing)
12696	SEQ ID NO: 12696	RTT
12697	SEQ ID NO: 12697	RTT*45 (PAM silencing)
12698	SEQ ID NO: 12698	RTT*45 (PAM silencing)
12699	SEQ ID NO: 12699	RTT
12700	SEQ ID NO: 12700	RTT
12701	SEQ ID NO: 12701	RTT*45 (PAM silencing)
12702	SEQ ID NO: 12702	RTT
12703	SEQ ID NO: 12703	RTT*45 (PAM silencing)
12704	SEQ ID NO: 12704	RTT
12705	SEQ ID NO: 12705	RTT*45 (PAM silencing)
12706	SEQ ID NO: 12706	RTT*45 (PAM silencing)
12707	SEQ ID NO: 12707	RTT
12708	SEQ ID NO: 12708	RTT
12709	SEQ ID NO: 12709	RTT*45 (PAM silencing)
12710	SEQ ID NO: 12710	RTT*45 (PAM silencing)
12711	SEQ ID NO: 12711	RTT
12712	SEQ ID NO: 12712	RTT*45 (PAM silencing)
12713	SEQ ID NO: 12713	RTT
12714	SEQ ID NO: 12714	RTT
12715	SEQ ID NO: 12715	RTT*45 (PAM silencing)
12716	SEQ ID NO: 12716	RTT*45 (PAM silencing)
12717	SEQ ID NO: 12717	RTT
12718	SEQ ID NO: 12718	RTT
12719	SEQ ID NO: 12719	RTT*45 (PAM silencing)
12720	SEQ ID NO: 12720	RTT*45 (PAM silencing)
12721	SEQ ID NO: 12721	RTT
12722	SEQ ID NO: 12722	RTT*45 (PAM silencing)
12723	SEQ ID NO: 12723	RTT
12724	SEQ ID NO: 12724	RTT*45 (PAM silencing)
12725	SEQ ID NO: 12725	RTT
12726	SEQ ID NO: 12726	RTT*45 (PAM silencing)
12727	SEQ ID NO: 12727	RTT
12728	SEQ ID NO: 12728	RTT*45 (PAM silencing)
12729	SEQ ID NO: 12729	RTT
12730	SEQ ID NO: 12730	RTT
12731	SEQ ID NO: 12731	RTT*45 (PAM silencing)
12732	SEQ ID NO: 12732	RTT
12733	SEQ ID NO: 12733	RTT*45 (PAM silencing)
12734	SEQ ID NO: 12734	RTT*45 (PAM silencing)
12735	SEQ ID NO: 12735	RTT
12736	SEQ ID NO: 12736	RTT*45 (PAM silencing)
12737	SEQ ID NO: 12737	RTT
12738	SEQ ID NO: 12738	RTT
12739	SEQ ID NO: 12739	RTT*45 (PAM silencing)
12740	SEQ ID NO: 12740	RTT*45 (PAM silencing)
12741	SEQ ID NO: 12741	RTT
12742	SEQ ID NO: 12742	RTT
12743	SEQ ID NO: 12743	RTT*45 (PAM silencing)
12744	SEQ ID NO: 12744	RTT
12745	SEQ ID NO: 12745	RTT*45 (PAM silencing)
12746	SEQ ID NO: 12746	RTT
12747	SEQ ID NO: 12747	RTT*45 (PAM silencing)
12748	SEQ ID NO: 12748	RTT*45 (PAM silencing)
12749	SEQ ID NO: 12749	RTT
12750	SEQ ID NO: 12750	RTT*45 (PAM silencing)
12751	SEQ ID NO: 12751	RTT
12752	SEQ ID NO: 12752	RTT*45 (PAM silencing)
12753	SEQ ID NO: 12753	RTT
12754	SEQ ID NO: 12754	RTT*45 (PAM silencing)
12755	SEQ ID NO: 12755	RTT
12756	SEQ ID NO: 12756	RTT*45 (PAM silencing)
12757	SEQ ID NO: 12757	RTT
12758	SEQ ID NO: 12758	RTT*45 (PAM silencing)
12759	SEQ ID NO: 12759	RTT
12760	SEQ ID NO: 12760	RTT
12761	SEQ ID NO: 12761	RTT*45 (PAM silencing)
12762	SEQ ID NO: 12762	RTT
12763	SEQ ID NO: 12763	RTT*45 (PAM silencing)
12764	SEQ ID NO: 12764	RTT
12765	SEQ ID NO: 12765	RTT*45 (PAM silencing)
12766	SEQ ID NO: 12766	RTT

Sequence Number	Sequence	Description
12767	SEQ ID NO: 12767	RTT*45 (PAM silencing)
12768	SEQ ID NO: 12768	RTT
12769	SEQ ID NO: 12769	RTT*45 (PAM silencing)
12770	SEQ ID NO: 12770	RTT*45 (PAM silencing)
12771	SEQ ID NO: 12771	RTT
12772	SEQ ID NO: 12772	RTT
12773	SEQ ID NO: 12773	RTT*45 (PAM silencing)
12774	SEQ ID NO: 12774	RTT
12775	SEQ ID NO: 12775	RTT*45 (PAM silencing)
12776	SEQ ID NO: 12776	RTT*45 (PAM silencing)
12777	SEQ ID NO: 12777	RTT
12778	SEQ ID NO: 12778	RTT*45 (PAM silencing)
12779	SEQ ID NO: 12779	RTT
12780	SEQ ID NO: 12780	RTT
12781	SEQ ID NO: 12781	RTT*45 (PAM silencing)
12782	SEQ ID NO: 12782	RTT
12783	SEQ ID NO: 12783	RTT*45 (PAM silencing)
12784	SEQ ID NO: 12784	RTT*45 (PAM silencing)
12785	SEQ ID NO: 12785	RTT
12786	SEQ ID NO: 12786	RTT
12787	SEQ ID NO: 12787	RTT*45 (PAM silencing)
12788	SEQ ID NO: 12788	RTT*45 (PAM silencing)
12789	SEQ ID NO: 12789	RTT
12790	SEQ ID NO: 12790	RTT
12791	SEQ ID NO: 12791	RTT*45 (PAM silencing)
12792	SEQ ID NO: 12792	RTT*45 (PAM silencing)

Sequence Number	Sequence	Description
12793	SEQ ID NO: 12793	RTT
12794	SEQ ID NO: 12794	RTT
12795	SEQ ID NO: 12795	RTT*45 (PAM silencing)
12796	SEQ ID NO: 12796	RTT
12797	SEQ ID NO: 12797	RTT*45 (PAM silencing)
12798	SEQ ID NO: 12798	RTT*45 (PAM silencing)
12799	SEQ ID NO: 12799	RTT
12800	SEQ ID NO: 12800	RTT
12801	SEQ ID NO: 12801	RTT*45 (PAM silencing)
12802	SEQ ID NO: 12802	RTT
12803	SEQ ID NO: 12803	RTT*45 (PAM silencing)
12804	SEQ ID NO: 12804	RTT
12805	SEQ ID NO: 12805	RTT*45 (PAM silencing)
12806	SEQ ID NO: 12806	RTT*45 (PAM silencing)
12807	SEQ ID NO: 12807	RTT
12808	SEQ ID NO: 12808	RTT
12809	SEQ ID NO: 12809	RTT*45 (PAM silencing)
12810	SEQ ID NO: 12810	RTT
12811	SEQ ID NO: 12811	RTT*45 (PAM silencing)
12812	SEQ ID NO: 12812	RTT
12813	SEQ ID NO: 12813	RTT*45 (PAM silencing)
12814	SEQ ID NO: 12814	RTT*45 (PAM silencing)
12815	SEQ ID NO: 12815	RTT
12816	SEQ ID NO: 12816	RTT
12817	SEQ ID NO: 12817	RTT*45 (PAM silencing)
12818	SEQ ID NO: 12818	RTT
12819	SEQ ID NO: 12819	RTT*45 (PAM silencing)

Sequence Number	Sequence	Description
12820	SEQ ID NO: 12820	RTT*45 (PAM silencing)
12821	SEQ ID NO: 12821	RTT
12822	SEQ ID NO: 12822	RTT
12823	SEQ ID NO: 12823	RTT*45 (PAM silencing)
12824	SEQ ID NO: 12824	RTT
12825	SEQ ID NO: 12825	RTT*45 (PAM silencing)
12826	SEQ ID NO: 12826	RTT*45 (PAM silencing)
12827	SEQ ID NO: 12827	RTT
12828	SEQ ID NO: 12828	RTT
12829	SEQ ID NO: 12829	RTT*45 (PAM silencing)
12830	SEQ ID NO: 12830	RTT
12831	SEQ ID NO: 12831	RTT*45 (PAM silencing)
12832	SEQ ID NO: 12832	RTT
12833	SEQ ID NO: 12833	RTT*45 (PAM silencing)
12834	SEQ ID NO: 12834	RTT*45 (PAM silencing)
12835	SEQ ID NO: 12835	RTT
12836	SEQ ID NO: 12836	RTT*45 (PAM silencing)
12837	SEQ ID NO: 12837	RTT
3268	SEQ ID NO: 3268	PE3 ngRNA spacer (AG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
3282	SEQ ID NO: 3282	PE3 ngRNA spacer (AG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)

Sequence Number	Sequence	Description
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
1990	SEQ ID NO: 1990	PE3 ngRNA spacer (AG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
3266	SEQ ID NO: 3266	PE3 ngRNA spacer (TG PAM)
3270	SEQ ID NO: 3270	PE3 ngRNA spacer (GG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
3263	SEQ ID NO: 3263	PE3 ngRNA spacer (AG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
3279	SEQ ID NO: 3279	PE3 ngRNA spacer (TG PAM)
3285	SEQ ID NO: 3285	PE3 ngRNA spacer (GG PAM)
3295	SEQ ID NO: 3295	PE3 ngRNA spacer (GG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
12838	SEQ ID NO: 12838	PE3b*45 ngRNA spacer (AG PAM)
3260	SEQ ID NO: 3260	PE3 ngRNA spacer (AG PAM)
3269	SEQ ID NO: 3269	PE3 ngRNA spacer (CG PAM)
3283	SEQ ID NO: 3283	PE3 ngRNA spacer (GG PAM)
12839	SEQ ID NO: 12839	PE3b*45 ngRNA spacer (GG PAM)
12840	SEQ ID NO: 12840	PE3b*45 ngRNA spacer (TG PAM)
2014	SEQ ID NO: 2014	ngRNA (AG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
4110	SEQ ID NO: 4110	ngRNA (TG PAM)
4105	SEQ ID NO: 4105	ngRNA (AG PAM)
4106	SEQ ID NO: 4106	ngRNA (CG PAM)
4091	SEQ ID NO: 4091	ngRNA (AG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
4124	SEQ ID NO: 4124	ngRNA (AG PAM)

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Sequence Number	Sequence	Description
12841	SEQ ID NO: 12841	PEgRNA spacer (TG PAM)
12842	SEQ ID NO: 12842	PEgRNA spacer (TG PAM)
12843	SEQ ID NO: 12843	PEgRNA spacer (TG PAM)
12844	SEQ ID NO: 12844	PEgRNA spacer (TG PAM)
12845	SEQ ID NO: 12845	PEgRNA spacer (TG PAM)
12846	SEQ ID NO: 12846	PEgRNA spacer (TG PAM)
12847	SEQ ID NO: 12847	PEgRNA spacer (TG PAM)
5632	GGC	PBS
11286	GGCA	PBS
11287	GGCAA	PBS
12848	GGCAAA	PBS
12849	GGCAAAG	PBS
12850	GGCAAAGG	PBS
12851	GGCAAAGGT	PBS

Sequence Number	Sequence	Description
12852	SEQ ID NO: 12852	PBS
12853	SEQ ID NO: 12853	PBS
12854	SEQ ID NO: 12854	PBS
12855	SEQ ID NO: 12855	PBS
12856	SEQ ID NO: 12856	PBS
12857	SEQ ID NO: 12857	PBS
12858	SEQ ID NO: 12858	PBS
12859	SEQ ID NO: 12859	PBS
12860	SEQ ID NO: 12860	PBS
12861	SEQ ID NO: 12861	PBS
12862	SEQ ID NO: 12862	RTT
12863	SEQ ID NO: 12863	RTT
12864	SEQ ID NO: 12864	RTT
12865	SEQ ID NO: 12865	RTT
12866	SEQ ID NO: 12866	RTT
12867	SEQ ID NO: 12867	RTT
12868	SEQ ID NO: 12868	RTT
12869	SEQ ID NO: 12869	RTT
12870	SEQ ID NO: 12870	RTT
12871	SEQ ID NO: 12871	RTT
12872	SEQ ID NO: 12872	RTT
12873	SEQ ID NO: 12873	RTT
12874	SEQ ID NO: 12874	RTT
12875	SEQ ID NO: 12875	RTT
12876	SEQ ID NO: 12876	RTT
12877	SEQ ID NO: 12877	RTT
12878	SEQ ID NO: 12878	RTT
12879	SEQ ID NO: 12879	RTT
12880	SEQ ID NO: 12880	RTT
12881	SEQ ID NO: 12881	RTT
12882	SEQ ID NO: 12882	RTT
12883	SEQ ID NO: 12883	RTT
12884	SEQ ID NO: 12884	RTT

Sequence Number	Sequence	Description
12885	SEQ ID NO: 12885	RTT
12886	SEQ ID NO: 12886	RTT
12887	SEQ ID NO: 12887	RTT
12888	SEQ ID NO: 12888	RTT
12889	SEQ ID NO: 12889	RTT
12890	SEQ ID NO: 12890	RTT
12891	SEQ ID NO: 12891	RTT
12892	SEQ ID NO: 12892	RTT
12893	SEQ ID NO: 12893	RTT
12894	SEQ ID NO: 12894	RTT
12895	SEQ ID NO: 12895	RTT
12896	SEQ ID NO: 12896	RTT
12897	SEQ ID NO: 12897	RTT
12898	SEQ ID NO: 12898	RTT
12899	SEQ ID NO: 12899	RTT
12900	SEQ ID NO: 12900	RTT
12901	SEQ ID NO: 12901	RTT
12902	SEQ ID NO: 12902	RTT
12903	SEQ ID NO: 12903	RTT
12904	SEQ ID NO: 12904	RTT
12905	SEQ ID NO: 12905	RTT
12906	SEQ ID NO: 12906	RTT
12907	SEQ ID NO: 12907	RTT
12908	SEQ ID NO: 12908	RTT
12909	SEQ ID NO: 12909	RTT
12910	SEQ ID NO: 12910	RTT
12911	SEQ ID NO: 12911	RTT
12912	SEQ ID NO: 12912	RTT
12913	SEQ ID NO: 12913	RTT
12914	SEQ ID NO: 12914	RTT
12915	SEQ ID NO: 12915	RTT
12916	SEQ ID NO: 12916	RTT
12917	SEQ ID NO: 12917	RTT

Sequence Number	Sequence	Description
12918	SEQ ID NO: 12918	RTT
12919	SEQ ID NO: 12919	RTT
12920	SEQ ID NO: 12920	RTT
12921	SEQ ID NO: 12921	RTT
12922	SEQ ID NO: 12922	RTT
12923	SEQ ID NO: 12923	RTT
12924	SEQ ID NO: 12924	RTT
12925	SEQ ID NO: 12925	RTT
12926	SEQ ID NO: 12926	RTT
12927	SEQ ID NO: 12927	RTT
12928	SEQ ID NO: 12928	RTT
12929	SEQ ID NO: 12929	RTT
12930	SEQ ID NO: 12930	RTT
12931	SEQ ID NO: 12931	RTT
12932	SEQ ID NO: 12932	RTT
12933	SEQ ID NO: 12933	RTT
12934	SEQ ID NO: 12934	RTT
12935	SEQ ID NO: 12935	RTT
12936	SEQ ID NO: 12936	RTT
12937	SEQ ID NO: 12937	RTT
12938	SEQ ID NO: 12938	RTT
12939	SEQ ID NO: 12939	RTT
12940	SEQ ID NO: 12940	RTT
12941	SEQ ID NO: 12941	RTT
12942	SEQ ID NO: 12942	RTT
12943	SEQ ID NO: 12943	RTT
12944	SEQ ID NO: 12944	RTT
12945	SEQ ID NO: 12945	RTT
12946	SEQ ID NO: 12946	RTT
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)

Sequence Number	Sequence	Description
3295	SEQ ID NO: 3295	PE3 ngRNA spacer (GG PAM)
3270	SEQ ID NO: 3270	PE3 ngRNA spacer (GG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
3266	SEQ ID NO: 3266	PE3 ngRNA spacer (TG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
3268	SEQ ID NO: 3268	PE3 ngRNA spacer (AG PAM)
3282	SEQ ID NO: 3282	PE3 ngRNA spacer (AG PAM)
3283	SEQ ID NO: 3283	PE3 ngRNA spacer (GG PAM)
1998	SEQ ID NO: 1998	PE3b ngRNA spacer (GG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
3285	SEQ ID NO: 3285	PE3 ngRNA spacer (GG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
2003	SEQ ID NO: 2003	PE3b ngRNA spacer (TG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
3279	SEQ ID NO: 3279	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
3280	SEQ ID NO: 3280	PE3 ngRNA spacer (TG PAM)
3260	SEQ ID NO: 3260	PE3 ngRNA spacer (AG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
3263	SEQ ID NO: 3263	PE3 ngRNA spacer (AG PAM)
3269	SEQ ID NO: 3269	PE3 ngRNA spacer (CG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
4091	SEQ ID NO: 4091	ngRNA (AG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
4110	SEQ ID NO: 4110	ngRNA (TG PAM)
4106	SEQ ID NO: 4106	ngRNA (CG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
4105	SEQ ID NO: 4105	ngRNA (AG PAM)
2011	SEQ ID NO: 2011	ngRNA (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
4124	SEQ ID NO: 4124	ngRNA (AG PAM)

Table 73

Sequence Number	Sequence	Description
12947	SEQ ID NO: 12947	PEgRNA spacer (AG PAM)
12948	SEQ ID NO: 12948	PEgRNA spacer (AG PAM)
12949	SEQ ID NO: 12949	PEgRNA spacer (AG PAM)
12950	SEQ ID NO: 12950	PEgRNA spacer (AG PAM)
12951	SEQ ID NO: 12951	PEgRNA spacer (AG PAM)
12952	SEQ ID NO: 12952	PEgRNA spacer (AG PAM)
12953	SEQ ID NO: 12953	PEgRNA spacer (AG PAM)
4135	ACA	PBS
7126	ACAC	PBS
12954	ACACT	PBS
12955	ACACTT	PBS
12956	ACACTTG	PBS
12957	ACACTTGG	PBS

Sequence Number	Sequence	Description
12958	ACACTT GGC	PBS
12959	SEQ ID NO: 12959	PBS
12960	SEQ ID NO: 12960	PBS
12961	SEQ ID NO: 12961	PBS
12962	SEQ ID NO: 12962	PBS
12963	SEQ ID NO: 12963	PBS
12964	SEQ ID NO: 12964	PBS
12965	SEQ ID NO: 12965	PBS
12966	SEQ ID NO: 12966	PBS
12967	SEQ ID NO: 12967	PBS
12968	SEQ ID NO: 12968	PBS
12969	SEQ ID NO: 12969	RTT*56 (PAM silencing)
12970	SEQ ID NO: 12970	RTT
12971	SEQ ID NO: 12971	RTT*55 (PAM silencing)
12972	SEQ ID NO: 12972	RTT*56 (PAM silencing)
12973	SEQ ID NO: 12973	RTT
12974	SEQ ID NO: 12974	RTT*55 (PAM silencing)
12975	SEQ ID NO: 12975	RTT*56 (PAM silencing)
12976	SEQ ID NO: 12976	RTT*55 (PAM silencing)
12977	SEQ ID NO: 12977	RTT
12978	SEQ ID NO: 12978	RTT*55 (PAM silencing)
12979	SEQ ID NO: 12979	RTT*56 (PAM silencing)
12980	SEQ ID NO: 12980	RTT
12981	SEQ ID NO: 12981	RTT
12982	SEQ ID NO: 12982	RTT*55 (PAM silencing)
12983	SEQ ID NO: 12983	RTT*56 (PAM silencing)
12984	SEQ ID NO: 12984	RTT
12985	SEQ ID NO: 12985	RTT*55 (PAM silencing)
12986	SEQ ID NO: 12986	RTT*56 (PAM silencing)
12987	SEQ ID NO: 12987	RTT*56 (PAM silencing)
12988	SEQ ID NO: 12988	RTT
12989	SEQ ID NO: 12989	RTT*55 (PAM silencing)
12990	SEQ ID NO: 12990	RTT*55 (PAM silencing)
12991	SEQ ID NO: 12991	RTT
12992	SEQ ID NO: 12992	RTT*56 (PAM silencing)
12993	SEQ ID NO: 12993	RTT*55 (PAM silencing)
12994	SEQ ID NO: 12994	RTT
12995	SEQ ID NO: 12995	RTT*56 (PAM silencing)
12996	SEQ ID NO: 12996	RTT*55 (PAM silencing)
12997	SEQ ID NO: 12997	RTT*56 (PAM silencing)
12998	SEQ ID NO: 12998	RTT
12999	SEQ ID NO: 12999	RTT
13000	SEQ ID NO: 13000	RTT*55 (PAM silencing)
13001	SEQ ID NO: 13001	RTT*56 (PAM silencing)
13002	SEQ ID NO: 13002	RTT*56 (PAM silencing)
13003	SEQ ID NO: 13003	RTT
13004	SEQ ID NO: 13004	RTT*55 (PAM silencing)
13005	SEQ ID NO: 13005	RTT
13006	SEQ ID NO: 13006	RTT*56 (PAM silencing)
13007	SEQ ID NO: 13007	RTT*55 (PAM silencing)
13008	SEQ ID NO: 13008	RTT*55 (PAM silencing)
13009	SEQ ID NO: 13009	RTT
13010	SEQ ID NO: 13010	RTT*56 (PAM silencing)
13011	SEQ ID NO: 13011	RTT*55 (PAM silencing)
13012	SEQ ID NO: 13012	RTT*56 (PAM silencing)
13013	SEQ ID NO: 13013	RTT
13014	SEQ ID NO: 13014	RTT
13015	SEQ ID NO: 13015	RTT*56 (PAM silencing)
13016	SEQ ID NO: 13016	RTT*55 (PAM silencing)
13017	SEQ ID NO: 13017	RTT*56 (PAM silencing)
13018	SEQ ID NO: 13018	RTT
13019	SEQ ID NO: 13019	RTT*55 (PAM silencing)
13020	SEQ ID NO: 13020	RTT*56 (PAM silencing)
13021	SEQ ID NO: 13021	RTT*55 (PAM silencing)
13022	SEQ ID NO: 13022	RTT
13023	SEQ ID NO: 13023	RTT
13024	SEQ ID NO: 13024	RTT*55 (PAM silencing)
13025	SEQ ID NO: 13025	RTT*56 (PAM silencing)
13026	SEQ ID NO: 13026	RTT
13027	SEQ ID NO: 13027	RTT*55 (PAM silencing)
13028	SEQ ID NO: 13028	RTT*56 (PAM silencing)
13029	SEQ ID NO: 13029	RTT
13030	SEQ ID NO: 13030	RTT*56 (PAM silencing)
13031	SEQ ID NO: 13031	RTT*55 (PAM silencing)
13032	SEQ ID NO: 13032	RTT*55 (PAM silencing)
13033	SEQ ID NO: 13033	RTT
13034	SEQ ID NO: 13034	RTT*56 (PAM silencing)
13035	SEQ ID NO: 13035	RTT*55 (PAM silencing)

Sequence Number	Sequence	Description
13036	SEQ ID NO: 13036	RTT*56 (PAM silencing)
13037	SEQ ID NO: 13037	RTT
13038	SEQ ID NO: 13038	RTT*55 (PAM silencing)
13039	SEQ ID NO: 13039	RTT*56 (PAM silencing)
13040	SEQ ID NO: 13040	RTT
13041	SEQ ID NO: 13041	RTT
13042	SEQ ID NO: 13042	RTT*55 (PAM silencing)
13043	SEQ ID NO: 13043	RTT*56 (PAM silencing)
13044	SEQ ID NO: 13044	RTT*55 (PAM silencing)
13045	SEQ ID NO: 13045	RTT
13046	SEQ ID NO: 13046	RTT*56 (PAM silencing)
13047	SEQ ID NO: 13047	RTT
13048	SEQ ID NO: 13048	RTT*56 (PAM silencing)
13049	SEQ ID NO: 13049	RTT*55 (PAM silencing)
13050	SEQ ID NO: 13050	RTT*55 (PAM silencing)
13051	SEQ ID NO: 13051	RTT*56 (PAM silencing)
13052	SEQ ID NO: 13052	RTT
13053	SEQ ID NO: 13053	RTT
13054	SEQ ID NO: 13054	RTT*56 (PAM silencing)
13055	SEQ ID NO: 13055	RTT*55 (PAM silencing)
13056	SEQ ID NO: 13056	RTT
13057	SEQ ID NO: 13057	RTT*56 (PAM silencing)
13058	SEQ ID NO: 13058	RTT*55 (PAM silencing)
13059	SEQ ID NO: 13059	RTT*56 (PAM silencing)
13060	SEQ ID NO: 13060	RTT

Sequence Number	Sequence	Description
13061	SEQ ID NO: 13061	RTT*55 (PAM silencing)
13062	SEQ ID NO: 13062	RTT*55 (PAM silencing)
13063	SEQ ID NO: 13063	RTT
13064	SEQ ID NO: 13064	RTT*56 (PAM silencing)
13065	SEQ ID NO: 13065	RTT*56 (PAM silencing)
13066	SEQ ID NO: 13066	RTT
13067	SEQ ID NO: 13067	RTT*55 (PAM silencing)
13068	SEQ ID NO: 13068	RTT*56 (PAM silencing)
13069	SEQ ID NO: 13069	RTT
13070	SEQ ID NO: 13070	RTT*55 (PAM silencing)
13071	SEQ ID NO: 13071	RTT
13072	SEQ ID NO: 13072	RTT*56 (PAM silencing)
13073	SEQ ID NO: 13073	RTT*55 (PAM silencing)
13074	SEQ ID NO: 13074	RTT*56 (PAM silencing)
13075	SEQ ID NO: 13075	RTT*55 (PAM silencing)
13076	SEQ ID NO: 13076	RTT
13077	SEQ ID NO: 13077	RTT
13078	SEQ ID NO: 13078	RTT*56 (PAM silencing)
13079	SEQ ID NO: 13079	RTT*55 (PAM silencing)
13080	SEQ ID NO: 13080	RTT*55 (PAM silencing)
13081	SEQ ID NO: 13081	RTT
13082	SEQ ID NO: 13082	RTT*56 (PAM silencing)
13083	SEQ ID NO: 13083	RTT*56 (PAM silencing)
13084	SEQ ID NO: 13084	RTT*55 (PAM silencing)
13085	SEQ ID NO: 13085	RTT

Sequence Number	Sequence	Description
13086	SEQ ID NO: 13086	RTT*56 (PAM silencing)
13087	SEQ ID NO: 13087	RTT*55 (PAM silencing)
13088	SEQ ID NO: 13088	RTT
13089	SEQ ID NO: 13089	RTT*56 (PAM silencing)
13090	SEQ ID NO: 13090	RTT
13091	SEQ ID NO: 13091	RTT*55 (PAM silencing)
13092	SEQ ID NO: 13092	RTT*56 (PAM silencing)
13093	SEQ ID NO: 13093	RTT
13094	SEQ ID NO: 13094	RTT*55 (PAM silencing)
13095	SEQ ID NO: 13095	RTT*55 (PAM silencing)
13096	SEQ ID NO: 13096	RTT*56 (PAM silencing)
13097	SEQ ID NO: 13097	RTT
13098	SEQ ID NO: 13098	RTT*55 (PAM silencing)
13099	SEQ ID NO: 13099	RTT*56 (PAM silencing)
13100	SEQ ID NO: 13100	RTT
13101	SEQ ID NO: 13101	RTT
13102	SEQ ID NO: 13102	RTT*55 (PAM silencing)
13103	SEQ ID NO: 13103	RTT*56 (PAM silencing)
13104	SEQ ID NO: 13104	RTT*56 (PAM silencing)
13105	SEQ ID NO: 13105	RTT
13106	SEQ ID NO: 13106	RTT*55 (PAM silencing)
13107	SEQ ID NO: 13107	RTT*55 (PAM silencing)
13108	SEQ ID NO: 13108	RTT*56 (PAM silencing)
13109	SEQ ID NO: 13109	RTT
13110	SEQ ID NO: 13110	RTT

Sequence Number	Sequence	Description
13111	SEQ ID NO: 13111	RTT*56 (PAM silencing)
13112	SEQ ID NO: 13112	RTT*55 (PAM silencing)
13113	SEQ ID NO: 13113	RTT*56 (PAM silencing)
13114	SEQ ID NO: 13114	RTT*55 (PAM silencing)
13115	SEQ ID NO: 13115	RTT
13116	SEQ ID NO: 13116	RTT*55 (PAM silencing)
13117	SEQ ID NO: 13117	RTT*56 (PAM silencing)
13118	SEQ ID NO: 13118	RTT
13119	SEQ ID NO: 13119	RTT*55 (PAM silencing)
13120	SEQ ID NO: 13120	RTT*56 (PAM silencing)
13121	SEQ ID NO: 13121	RTT
13122	SEQ ID NO: 13122	RTT
13123	SEQ ID NO: 13123	RTT*56 (PAM silencing)
13124	SEQ ID NO: 13124	RTT*55 (PAM silencing)
13125	SEQ ID NO: 13125	RTT*55 (PAM silencing)
13126	SEQ ID NO: 13126	RTT
13127	SEQ ID NO: 13127	RTT*56 (PAM silencing)
13128	SEQ ID NO: 13128	RTT*56 (PAM silencing)
13129	SEQ ID NO: 13129	RTT
13130	SEQ ID NO: 13130	RTT*55 (PAM silencing)
13131	SEQ ID NO: 13131	RTT
13132	SEQ ID NO: 13132	RTT*56 (PAM silencing)
13133	SEQ ID NO: 13133	RTT*55 (PAM silencing)
13134	SEQ ID NO: 13134	RTT
13135	SEQ ID NO: 13135	RTT*55 (PAM silencing)

Sequence Number	Sequence	Description
13136	SEQ ID NO: 13136	RTT*56 (PAM silencing)
13137	SEQ ID NO: 13137	RTT*56 (PAM silencing)
13138	SEQ ID NO: 13138	RTT*55 (PAM silencing)
13139	SEQ ID NO: 13139	RTT
13140	SEQ ID NO: 13140	RTT*55 (PAM silencing)
13141	SEQ ID NO: 13141	RTT*56 (PAM silencing)
13142	SEQ ID NO: 13142	RTT
13143	SEQ ID NO: 13143	RTT*56 (PAM silencing)
13144	SEQ ID NO: 13144	RTT
13145	SEQ ID NO: 13145	RTT*55 (PAM silencing)
13146	SEQ ID NO: 13146	RTT*56 (PAM silencing)
13147	SEQ ID NO: 13147	RTT
13148	SEQ ID NO: 13148	RTT*55 (PAM silencing)
13149	SEQ ID NO: 13149	RTT*56 (PAM silencing)
13150	SEQ ID NO: 13150	RTT
13151	SEQ ID NO: 13151	RTT*55 (PAM silencing)
13152	SEQ ID NO: 13152	RTT*55 (PAM silencing)
13153	SEQ ID NO: 13153	RTT
13154	SEQ ID NO: 13154	RTT*56 (PAM silencing)
13155	SEQ ID NO: 13155	RTT
13156	SEQ ID NO: 13156	RTT*55 (PAM silencing)
13157	SEQ ID NO: 13157	RTT*56 (PAM silencing)
13158	SEQ ID NO: 13158	RTT
13159	SEQ ID NO: 13159	RTT*56 (PAM silencing)
13160	SEQ ID NO: 13160	RTT*55 (PAM silencing)

Sequence Number	Sequence	Description
13161	SEQ ID NO: 13161	RTT
13162	SEQ ID NO: 13162	RTT*55 (PAM silencing)
13163	SEQ ID NO: 13163	RTT*56 (PAM silencing)
13164	SEQ ID NO: 13164	RTT
13165	SEQ ID NO: 13165	RTT*55 (PAM silencing)
13166	SEQ ID NO: 13166	RTT*56 (PAM silencing)
13167	SEQ ID NO: 13167	RTT
13168	SEQ ID NO: 13168	RTT*56 (PAM silencing)
13169	SEQ ID NO: 13169	RTT*55 (PAM silencing)
13170	SEQ ID NO: 13170	RTT
13171	SEQ ID NO: 13171	RTT*55 (PAM silencing)
13172	SEQ ID NO: 13172	RTT*56 (PAM silencing)
13173	SEQ ID NO: 13173	RTT*55 (PAM silencing)
13174	SEQ ID NO: 13174	RTT*56 (PAM silencing)
13175	SEQ ID NO: 13175	RTT
13176	SEQ ID NO: 13176	RTT*56 (PAM silencing)
13177	SEQ ID NO: 13177	RTT*55 (PAM silencing)
13178	SEQ ID NO: 13178	RTT
13179	SEQ ID NO: 13179	RTT*55 (PAM silencing)
13180	SEQ ID NO: 13180	RTT
13181	SEQ ID NO: 13181	RTT*56 (PAM silencing)
13182	SEQ ID NO: 13182	RTT*55 (PAM silencing)
13183	SEQ ID NO: 13183	RTT*56 (PAM silencing)
13184	SEQ ID NO: 13184	RTT
13185	SEQ ID NO: 13185	RTT

Sequence Number	Sequence	Description
13186	SEQ ID NO: 13186	RTT*56 (PAM silencing)
13187	SEQ ID NO: 13187	RTT*55 (PAM silencing)
13188	SEQ ID NO: 13188	RTT
13189	SEQ ID NO: 13189	RTT*56 (PAM silencing)
13190	SEQ ID NO: 13190	RTT*55 (PAM silencing)
13191	SEQ ID NO: 13191	RTT*55 (PAM silencing)
13192	SEQ ID NO: 13192	RTT
13193	SEQ ID NO: 13193	RTT*56 (PAM silencing)
13194	SEQ ID NO: 13194	RTT
13195	SEQ ID NO: 13195	RTT*56 (PAM silencing)
13196	SEQ ID NO: 13196	RTT*55 (PAM silencing)
13197	SEQ ID NO: 13197	RTT*55 (PAM silencing)
13198	SEQ ID NO: 13198	RTT
13199	SEQ ID NO: 13199	RTT*56 (PAM silencing)
13200	SEQ ID NO: 13200	RTT
13201	SEQ ID NO: 13201	RTT*55 (PAM silencing)
13202	SEQ ID NO: 13202	RTT*56 (PAM silencing)
13203	SEQ ID NO: 13203	RTT*55 (PAM silencing)
13204	SEQ ID NO: 13204	RTT
13205	SEQ ID NO: 13205	RTT*56 (PAM silencing)
13206	SEQ ID NO: 13206	RTT*55 (PAM silencing)
13207	SEQ ID NO: 13207	RTT
13208	SEQ ID NO: 13208	RTT*56 (PAM silencing)
13209	SEQ ID NO: 13209	RTT*55 (PAM silencing)
13210	SEQ ID NO: 13210	RTT

Sequence Number	Sequence	Description
13211	SEQ ID NO: 13211	RTT*56 (PAM silencing)
13212	SEQ ID NO: 13212	RTT*55 (PAM silencing)
13213	SEQ ID NO: 13213	RTT
13214	SEQ ID NO: 13214	RTT*56 (PAM silencing)
13215	SEQ ID NO: 13215	RTT*55 (PAM silencing)
13216	SEQ ID NO: 13216	RTT*56 (PAM silencing)
13217	SEQ ID NO: 13217	RTT
13218	SEQ ID NO: 13218	RTT
13219	SEQ ID NO: 13219	RTT*56 (PAM silencing)
13220	SEQ ID NO: 13220	RTT*55 (PAM silencing)
13221	SEQ ID NO: 13221	RTT
13222	SEQ ID NO: 13222	RTT*55 (PAM silencing)
13223	SEQ ID NO: 13223	RTT*56 (PAM silencing)
13224	SEQ ID NO: 13224	RTT*55 (PAM silencing)
13225	SEQ ID NO: 13225	RTT
13226	SEQ ID NO: 13226	RTT*56 (PAM silencing)
13227	SEQ ID NO: 13227	RTT*55 (PAM silencing)
13228	SEQ ID NO: 13228	RTT*56 (PAM silencing)
13229	SEQ ID NO: 13229	RTT
13230	SEQ ID NO: 13230	RTT*55 (PAM silencing)
13231	SEQ ID NO: 13231	RTT
13232	SEQ ID NO: 13232	RTT*56 (PAM silencing)
13233	SEQ ID NO: 13233	RTT
13234	SEQ ID NO: 13234	RTT*55 (PAM silencing)
13235	SEQ ID NO: 13235	RTT*56 (PAM silencing)

Sequence Number	Sequence	Description
13236	SEQ ID NO: 13236	RTT*56 (PAM silencing)
13237	SEQ ID NO: 13237	RTT
13238	SEQ ID NO: 13238	RTT*55 (PAM silencing)
13239	SEQ ID NO: 13239	RTT*56 (PAM silencing)
13240	SEQ ID NO: 13240	RTT
13241	SEQ ID NO: 13241	RTT*55 (PAM silencing)
3293	SEQ ID NO: 3293	PE3 ngRNA spacer (GG PAM)
3273	SEQ ID NO: 3273	PE3 ngRNA spacer (TG PAM)
3260	SEQ ID NO: 3260	PE3 ngRNA spacer (AG PAM)
13242	SEQ ID NO: 13242	PE3b*55 ngRNA spacer (TG PAM)
3244	SEQ ID NO: 3244	PE3 ngRNA spacer (TG PAM)
3266	SEQ ID NO: 3266	PE3 ngRNA spacer (TG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
3295	SEQ ID NO: 3295	PE3 ngRNA spacer (GG PAM)
3285	SEQ ID NO: 3285	PE3 ngRNA spacer (GG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
3279	SEQ ID NO: 3279	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (TG PAM)
3270	SEQ ID NO: 3270	PE3 ngRNA spacer (GG PAM)
3269	SEQ ID NO: 3269	PE3 ngRNA spacer (CG PAM)
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
13243	SEQ ID NO: 13243	PE3b*55 ngRNA spacer (AG;GG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
3268	SEQ ID NO: 3268	PE3 ngRNA spacer (AG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
3282	SEQ ID NO: 3282	PE3 ngRNA spacer (AG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
3263	SEQ ID NO: 3263	PE3 ngRNA spacer (AG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA

Sequence Number	Sequence	Description
		spacer (TG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
3283	SEQ ID NO: 3283	PE3 ngRNA spacer (GG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)
2005	SEQ ID NO: 2005	PE3b ngRNA spacer (GG PAM)
3280	SEQ ID NO: 3280	PE3 ngRNA spacer (TG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
4091	SEQ ID NO: 4091	ngRNA (AG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
4110	SEQ ID NO: 4110	ngRNA (TG PAM)
4106	SEQ ID NO: 4106	ngRNA (CG PAM)
4105	SEQ ID NO: 4105	ngRNA (AG PAM)
4087	SEQ ID NO: 4087	ngRNA (TG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
4115	SEQ ID NO: 4115	ngRNA (TG PAM)
4124	SEQ ID NO: 4124	ngRNA (AG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)

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Sequence Number	Sequence	Description
13244	SEQ ID NO: 13244	PEgRNA spacer (GG PAM)
13245	SEQ ID NO: 13245	PEgRNA spacer (GG PAM)
13246	SEQ ID NO: 13246	PEgRNA spacer (GG PAM)
13247	SEQ ID NO: 13247	PEgRNA spacer (GG PAM)
13248	SEQ ID NO: 13248	PEgRNA spacer (GG PAM)
13249	SEQ ID NO: 13249	PEgRNA spacer (GG PAM)
13250	SEQ ID NO: 13250	PEgRNA spacer (GG PAM)
5632	GGC	PBS
5633	GGCT	PBS
13251	GGCTG	PBS
13252	GGCTGG	PBS
13253	GGCTGG A	PBS
13254	GGCTGG AA	PBS
13255	GGCTGG AAC	PBS
13256	SEQ ID NO: 13256	PBS
13257	SEQ ID NO: 13257	PBS
13258	SEQ ID NO: 13258	PBS
13259	SEQ ID NO: 13259	PBS
13260	SEQ ID NO: 13260	PBS
13261	SEQ ID NO: 13261	PBS
13262	SEQ ID NO: 13262	PBS
13263	SEQ ID NO: 13263	PBS
13264	SEQ ID NO: 13264	PBS
13265	SEQ ID NO: 13265	PBS
13266	SEQ ID NO: 13266	RTT*99 (PAM silencing)
13267	SEQ ID NO: 13267	RTT*101 (PAM silencing)
13268	SEQ ID NO: 13268	RTT

Sequence Number	Sequence	Description
13269	SEQ ID NO: 13269	RTT*100 (PAM silencing)
13270	SEQ ID NO: 13270	RTT*100 (PAM silencing)
13271	SEQ ID NO: 13271	RTT*101 (PAM silencing)
13272	SEQ ID NO: 13272	RTT
13273	SEQ ID NO: 13273	RTT*99 (PAM silencing)
13274	SEQ ID NO: 13274	RTT*101 (PAM silencing)
13275	SEQ ID NO: 13275	RTT
13276	SEQ ID NO: 13276	RTT*99 (PAM silencing)
13277	SEQ ID NO: 13277	RTT*100 (PAM silencing)
13278	SEQ ID NO: 13278	RTT*101 (PAM silencing)
13279	SEQ ID NO: 13279	RTT*99 (PAM silencing)
13280	SEQ ID NO: 13280	RTT*100 (PAM silencing)
13281	SEQ ID NO: 13281	RTT
13282	SEQ ID NO: 13282	RTT*99 (PAM silencing)
13283	SEQ ID NO: 13283	RTT*100 (PAM silencing)
13284	SEQ ID NO: 13284	RTT
13285	SEQ ID NO: 13285	RTT*101 (PAM silencing)
13286	SEQ ID NO: 13286	RTT*100 (PAM silencing)
13287	SEQ ID NO: 13287	RTT*99 (PAM silencing)
13288	SEQ ID NO: 13288	RTT*101 (PAM silencing)
13289	SEQ ID NO: 13289	RTT
13290	SEQ ID NO: 13290	RTT*99 (PAM silencing)
13291	SEQ ID NO: 13291	RTT*100 (PAM silencing)
13292	SEQ ID NO: 13292	RTT
13293	SEQ ID NO: 13293	RTT*101 (PAM silencing)
13294	SEQ ID NO: 13294	RTT
13295	SEQ ID NO: 13295	RTT*99 (PAM silencing)
13296	SEQ ID NO: 13296	RTT*101 (PAM silencing)
13297	SEQ ID NO: 13297	RTT*100 (PAM silencing)
13298	SEQ ID NO: 13298	RTT*101 (PAM silencing)
13299	SEQ ID NO: 13299	RTT*100 (PAM silencing)
13300	SEQ ID NO: 13300	RTT*99 (PAM silencing)
13301	SEQ ID NO: 13301	RTT
13302	SEQ ID NO: 13302	RTT*101 (PAM silencing)
13303	SEQ ID NO: 13303	RTT
13304	SEQ ID NO: 13304	RTT*100 (PAM silencing)
13305	SEQ ID NO: 13305	RTT*99 (PAM silencing)
13306	SEQ ID NO: 13306	RTT*101 (PAM silencing)
13307	SEQ ID NO: 13307	RTT*99 (PAM silencing)
13308	SEQ ID NO: 13308	RTT
13309	SEQ ID NO: 13309	RTT*100 (PAM silencing)
13310	SEQ ID NO: 13310	RTT*99 (PAM silencing)
13311	SEQ ID NO: 13311	RTT
13312	SEQ ID NO: 13312	RTT*100 (PAM silencing)
13313	SEQ ID NO: 13313	RTT*101 (PAM silencing)
13314	SEQ ID NO: 13314	RTT*101 (PAM silencing)
13315	SEQ ID NO: 13315	RTT
13316	SEQ ID NO: 13316	RTT*100 (PAM silencing)
13317	SEQ ID NO: 13317	RTT*99 (PAM silencing)
13318	SEQ ID NO: 13318	RTT*101 (PAM silencing)
13319	SEQ ID NO: 13319	RTT*99 (PAM silencing)
13320	SEQ ID NO: 13320	RTT*100 (PAM silencing)
13321	SEQ ID NO: 13321	RTT
13322	SEQ ID NO: 13322	RTT
13323	SEQ ID NO: 13323	RTT*101 (PAM silencing)
13324	SEQ ID NO: 13324	RTT*100 (PAM silencing)
13325	SEQ ID NO: 13325	RTT*99 (PAM silencing)
13326	SEQ ID NO: 13326	RTT*101 (PAM silencing)
13327	SEQ ID NO: 13327	RTT*100 (PAM silencing)
13328	SEQ ID NO: 13328	RTT
13329	SEQ ID NO: 13329	RTT*99 (PAM silencing)
13330	SEQ ID NO: 13330	RTT*101 (PAM silencing)
13331	SEQ ID NO: 13331	RTT*100 (PAM silencing)
13332	SEQ ID NO: 13332	RTT*99 (PAM silencing)
13333	SEQ ID NO: 13333	RTT
13334	SEQ ID NO: 13334	RTT*100 (PAM silencing)
13335	SEQ ID NO: 13335	RTT*101 (PAM silencing)
13336	SEQ ID NO: 13336	RTT
13337	SEQ ID NO: 13337	RTT*99 (PAM silencing)
13338	SEQ ID NO: 13338	RTT
13339	SEQ ID NO: 13339	RTT*99 (PAM silencing)
13340	SEQ ID NO: 13340	RTT*101 (PAM silencing)

Sequence Number	Sequence	Description
13341	SEQ ID NO: 13341	RTT*100 (PAM silencing)
13342	SEQ ID NO: 13342	RTT*99 (PAM silencing)
13343	SEQ ID NO: 13343	RTT*100 (PAM silencing)
13344	SEQ ID NO: 13344	RTT*101 (PAM silencing)
13345	SEQ ID NO: 13345	RTT
13346	SEQ ID NO: 13346	RTT
13347	SEQ ID NO: 13347	RTT*99 (PAM silencing)
13348	SEQ ID NO: 13348	RTT*101 (PAM silencing)
13349	SEQ ID NO: 13349	RTT*100 (PAM silencing)
13350	SEQ ID NO: 13350	RTT*101 (PAM silencing)
13351	SEQ ID NO: 13351	RTT*100 (PAM silencing)
13352	SEQ ID NO: 13352	RTT*99 (PAM silencing)
13353	SEQ ID NO: 13353	RTT
13354	SEQ ID NO: 13354	RTT
13355	SEQ ID NO: 13355	RTT*99 (PAM silencing)
13356	SEQ ID NO: 13356	RTT*101 (PAM silencing)
13357	SEQ ID NO: 13357	RTT*100 (PAM silencing)
13358	SEQ ID NO: 13358	RTT*99 (PAM silencing)
13359	SEQ ID NO: 13359	RTT*101 (PAM silencing)
13360	SEQ ID NO: 13360	RTT
13361	SEQ ID NO: 13361	RTT*100 (PAM silencing)
13362	SEQ ID NO: 13362	RTT*101 (PAM silencing)
13363	SEQ ID NO: 13363	RTT*99 (PAM silencing)
13364	SEQ ID NO: 13364	RTT
13365	SEQ ID NO: 13365	RTT*100 (PAM silencing)
13366	SEQ ID NO: 13366	RTT*100 (PAM silencing)
13367	SEQ ID NO: 13367	RTT*101 (PAM silencing)
13368	SEQ ID NO: 13368	RTT
13369	SEQ ID NO: 13369	RTT*99 (PAM silencing)
13370	SEQ ID NO: 13370	RTT
13371	SEQ ID NO: 13371	RTT*101 (PAM silencing)
13372	SEQ ID NO: 13372	RTT*100 (PAM silencing)
13373	SEQ ID NO: 13373	RTT*99 (PAM silencing)
13374	SEQ ID NO: 13374	RTT*101 (PAM silencing)
13375	SEQ ID NO: 13375	RTT*100 (PAM silencing)
13376	SEQ ID NO: 13376	RTT
13377	SEQ ID NO: 13377	RTT*99 (PAM silencing)
13378	SEQ ID NO: 13378	RTT*99 (PAM silencing)
13379	SEQ ID NO: 13379	RTT*100 (PAM silencing)
13380	SEQ ID NO: 13380	RTT
13381	SEQ ID NO: 13381	RTT*101 (PAM silencing)
13382	SEQ ID NO: 13382	RTT
13383	SEQ ID NO: 13383	RTT*100 (PAM silencing)
13384	SEQ ID NO: 13384	RTT*99 (PAM silencing)
13385	SEQ ID NO: 13385	RTT*101 (PAM silencing)
13386	SEQ ID NO: 13386	RTT*99 (PAM silencing)
13387	SEQ ID NO: 13387	RTT
13388	SEQ ID NO: 13388	RTT*101 (PAM silencing)
13389	SEQ ID NO: 13389	RTT*100 (PAM silencing)
13390	SEQ ID NO: 13390	RTT*101 (PAM silencing)
13391	SEQ ID NO: 13391	RTT*99 (PAM silencing)
13392	SEQ ID NO: 13392	RTT*100 (PAM silencing)
13393	SEQ ID NO: 13393	RTT
13394	SEQ ID NO: 13394	RTT*99 (PAM silencing)
13395	SEQ ID NO: 13395	RTT
13396	SEQ ID NO: 13396	RTT*101 (PAM silencing)
13397	SEQ ID NO: 13397	RTT*100 (PAM silencing)
13398	SEQ ID NO: 13398	RTT*99 (PAM silencing)
13399	SEQ ID NO: 13399	RTT
13400	SEQ ID NO: 13400	RTT*101 (PAM silencing)
13401	SEQ ID NO: 13401	RTT*100 (PAM silencing)
13402	SEQ ID NO: 13402	RTT*101 (PAM silencing)
13403	SEQ ID NO: 13403	RTT
13404	SEQ ID NO: 13404	RTT*99 (PAM silencing)
13405	SEQ ID NO: 13405	RTT*100 (PAM silencing)
13406	SEQ ID NO: 13406	RTT*100 (PAM silencing)
13407	SEQ ID NO: 13407	RTT*101 (PAM silencing)
13408	SEQ ID NO: 13408	RTT
13409	SEQ ID NO: 13409	RTT*99 (PAM silencing)
13410	SEQ ID NO: 13410	RTT*101 (PAM silencing)
13411	SEQ ID NO: 13411	RTT*100 (PAM silencing)
13412	SEQ ID NO: 13412	RTT

Sequence Number	Sequence	Description
13413	SEQ ID NO: 13413	RTT*99 (PAM silencing)
13414	SEQ ID NO: 13414	RTT*101 (PAM silencing)
13415	SEQ ID NO: 13415	RTT*100 (PAM silencing)
13416	SEQ ID NO: 13416	RTT
13417	SEQ ID NO: 13417	RTT*99 (PAM silencing)
13418	SEQ ID NO: 13418	RTT*99 (PAM silencing)
13419	SEQ ID NO: 13419	RTT*101 (PAM silencing)
13420	SEQ ID NO: 13420	RTT
13421	SEQ ID NO: 13421	RTT*100 (PAM silencing)
13422	SEQ ID NO: 13422	RTT
13423	SEQ ID NO: 13423	RTT*99 (PAM silencing)
13424	SEQ ID NO: 13424	RTT*101 (PAM silencing)
13425	SEQ ID NO: 13425	RTT*100 (PAM silencing)
13426	SEQ ID NO: 13426	RTT*99 (PAM silencing)
13427	SEQ ID NO: 13427	RTT*101 (PAM silencing)
13428	SEQ ID NO: 13428	RTT
13429	SEQ ID NO: 13429	RTT*100 (PAM silencing)
13430	SEQ ID NO: 13430	RTT
13431	SEQ ID NO: 13431	RTT*100 (PAM silencing)
13432	SEQ ID NO: 13432	RTT*101 (PAM silencing)
13433	SEQ ID NO: 13433	RTT*99 (PAM silencing)
13434	SEQ ID NO: 13434	RTT*99 (PAM silencing)
13435	SEQ ID NO: 13435	RTT
13436	SEQ ID NO: 13436	RTT*101 (PAM silencing)
13437	SEQ ID NO: 13437	RTT*100 (PAM silencing)
13438	SEQ ID NO: 13438	RTT*100 (PAM silencing)
13439	SEQ ID NO: 13439	RTT*101 (PAM silencing)
13440	SEQ ID NO: 13440	RTT*99 (PAM silencing)
13441	SEQ ID NO: 13441	RTT
13442	SEQ ID NO: 13442	RTT*99 (PAM silencing)
13443	SEQ ID NO: 13443	RTT
13444	SEQ ID NO: 13444	RTT*100 (PAM silencing)
13445	SEQ ID NO: 13445	RTT*101 (PAM silencing)
13446	SEQ ID NO: 13446	RTT*101 (PAM silencing)
13447	SEQ ID NO: 13447	RTT
13448	SEQ ID NO: 13448	RTT*99 (PAM silencing)
13449	SEQ ID NO: 13449	RTT*100 (PAM silencing)
13450	SEQ ID NO: 13450	RTT*101 (PAM silencing)
13451	SEQ ID NO: 13451	RTT*100 (PAM silencing)
13452	SEQ ID NO: 13452	RTT*99 (PAM silencing)
13453	SEQ ID NO: 13453	RTT
13454	SEQ ID NO: 13454	RTT*100 (PAM silencing)
13455	SEQ ID NO: 13455	RTT*101 (PAM silencing)
13456	SEQ ID NO: 13456	RTT
13457	SEQ ID NO: 13457	RTT*99 (PAM silencing)
13458	SEQ ID NO: 13458	RTT*101 (PAM silencing)
13459	SEQ ID NO: 13459	RTT*100 (PAM silencing)
13460	SEQ ID NO: 13460	RTT*99 (PAM silencing)
13461	SEQ ID NO: 13461	RTT
13462	SEQ ID NO: 13462	RTT
13463	SEQ ID NO: 13463	RTT*99 (PAM silencing)
13464	SEQ ID NO: 13464	RTT*101 (PAM silencing)
13465	SEQ ID NO: 13465	RTT*100 (PAM silencing)
13466	SEQ ID NO: 13466	RTT*99 (PAM silencing)
13467	SEQ ID NO: 13467	RTT
13468	SEQ ID NO: 13468	RTT*101 (PAM silencing)
13469	SEQ ID NO: 13469	RTT*100 (PAM silencing)
13470	SEQ ID NO: 13470	RTT*100 (PAM silencing)
13471	SEQ ID NO: 13471	RTT*99 (PAM silencing)
13472	SEQ ID NO: 13472	RTT
13473	SEQ ID NO: 13473	RTT*101 (PAM silencing)
13474	SEQ ID NO: 13474	RTT
13475	SEQ ID NO: 13475	RTT*101 (PAM silencing)
13476	SEQ ID NO: 13476	RTT*100 (PAM silencing)
13477	SEQ ID NO: 13477	RTT*99 (PAM silencing)
13478	SEQ ID NO: 13478	RTT*99 (PAM silencing)
13479	SEQ ID NO: 13479	RTT*100 (PAM silencing)
13480	SEQ ID NO: 13480	RTT
13481	SEQ ID NO: 13481	RTT*101 (PAM silencing)
13482	SEQ ID NO: 13482	RTT*100 (PAM silencing)
13483	SEQ ID NO: 13483	RTT
13484	SEQ ID NO: 13484	RTT*99 (PAM silencing)

Sequence Number	Sequence	Description
13485	SEQ ID NO: 13485	RTT*101 (PAM silencing)
13486	SEQ ID NO: 13486	RTT
13487	SEQ ID NO: 13487	RTT*99 (PAM silencing)
13488	SEQ ID NO: 13488	RTT*101 (PAM silencing)
13489	SEQ ID NO: 13489	RTT*100 (PAM silencing)
13490	SEQ ID NO: 13490	RTT*100 (PAM silencing)
13491	SEQ ID NO: 13491	RTT*101 (PAM silencing)
13492	SEQ ID NO: 13492	RTT
13493	SEQ ID NO: 13493	RTT*99 (PAM silencing)
13494	SEQ ID NO: 13494	RTT
13495	SEQ ID NO: 13495	RTT*99 (PAM silencing)
13496	SEQ ID NO: 13496	RTT*101 (PAM silencing)
13497	SEQ ID NO: 13497	RTT*100 (PAM silencing)
13498	SEQ ID NO: 13498	RTT*99 (PAM silencing)
13499	SEQ ID NO: 13499	RTT*101 (PAM silencing)
13500	SEQ ID NO: 13500	RTT
13501	SEQ ID NO: 13501	RTT*100 (PAM silencing)
13502	SEQ ID NO: 13502	RTT*101 (PAM silencing)
13503	SEQ ID NO: 13503	RTT*100 (PAM silencing)
13504	SEQ ID NO: 13504	RTT
13505	SEQ ID NO: 13505	RTT*99 (PAM silencing)
13506	SEQ ID NO: 13506	RTT*101 (PAM silencing)
13507	SEQ ID NO: 13507	RTT
13508	SEQ ID NO: 13508	RTT*99 (PAM silencing)
13509	SEQ ID NO: 13509	RTT*100 (PAM silencing)
13510	SEQ ID NO: 13510	RTT*99 (PAM silencing)
13511	SEQ ID NO: 13511	RTT*101 (PAM silencing)
13512	SEQ ID NO: 13512	RTT*100 (PAM silencing)
13513	SEQ ID NO: 13513	RTT
13514	SEQ ID NO: 13514	RTT*100 (PAM silencing)
13515	SEQ ID NO: 13515	RTT
13516	SEQ ID NO: 13516	RTT*101 (PAM silencing)
13517	SEQ ID NO: 13517	RTT*99 (PAM silencing)
13518	SEQ ID NO: 13518	RTT*100 (PAM silencing)
13519	SEQ ID NO: 13519	RTT*99 (PAM silencing)
13520	SEQ ID NO: 13520	RTT
13521	SEQ ID NO: 13521	RTT*101 (PAM silencing)
13522	SEQ ID NO: 13522	RTT
13523	SEQ ID NO: 13523	RTT*100 (PAM silencing)
13524	SEQ ID NO: 13524	RTT*101 (PAM silencing)
13525	SEQ ID NO: 13525	RTT*99 (PAM silencing)
13526	SEQ ID NO: 13526	RTT*101 (PAM silencing)
13527	SEQ ID NO: 13527	RTT
13528	SEQ ID NO: 13528	RTT*100 (PAM silencing)
13529	SEQ ID NO: 13529	RTT*99 (PAM silencing)
13530	SEQ ID NO: 13530	RTT*101 (PAM silencing)
13531	SEQ ID NO: 13531	RTT*100 (PAM silencing)
13532	SEQ ID NO: 13532	RTT*99 (PAM silencing)
13533	SEQ ID NO: 13533	RTT
13534	SEQ ID NO: 13534	RTT
13535	SEQ ID NO: 13535	RTT*99 (PAM silencing)
13536	SEQ ID NO: 13536	RTT*101 (PAM silencing)
13537	SEQ ID NO: 13537	RTT*100 (PAM silencing)
13538	SEQ ID NO: 13538	RTT*100 (PAM silencing)
13539	SEQ ID NO: 13539	RTT
13540	SEQ ID NO: 13540	RTT*99 (PAM silencing)
13541	SEQ ID NO: 13541	RTT*101 (PAM silencing)
13542	SEQ ID NO: 13542	RTT*99 (PAM silencing)
13543	SEQ ID NO: 13543	RTT
13544	SEQ ID NO: 13544	RTT*100 (PAM silencing)
13545	SEQ ID NO: 13545	RTT*101 (PAM silencing)
13546	SEQ ID NO: 13546	RTT*99 (PAM silencing)
13547	SEQ ID NO: 13547	RTT*100 (PAM silencing)
13548	SEQ ID NO: 13548	RTT
13549	SEQ ID NO: 13549	RTT*101 (PAM silencing)
13550	SEQ ID NO: 13550	RTT*101 (PAM silencing)
13551	SEQ ID NO: 13551	RTT*99 (PAM silencing)
13552	SEQ ID NO: 13552	RTT*100 (PAM silencing)
13553	SEQ ID NO: 13553	RTT
13554	SEQ ID NO: 13554	RTT*99 (PAM silencing)
13555	SEQ ID NO: 13555	RTT*100 (PAM silencing)
13556	SEQ ID NO: 13556	RTT*101 (PAM silencing)

Sequence Number	Sequence	Description
13557	SEQ ID NO: 13557	RTT
13558	SEQ ID NO: 13558	RTT*101 (PAM silencing)
13559	SEQ ID NO: 13559	RTT
13560	SEQ ID NO: 13560	RTT*100 (PAM silencing)
13561	SEQ ID NO: 13561	RTT*99 (PAM silencing)
13562	SEQ ID NO: 13562	RTT*100 (PAM silencing)
13563	SEQ ID NO: 13563	RTT
13564	SEQ ID NO: 13564	RTT*101 (PAM silencing)
13565	SEQ ID NO: 13565	RTT*99 (PAM silencing)
13566	SEQ ID NO: 13566	RTT*101 (PAM silencing)
13567	SEQ ID NO: 13567	RTT
13568	SEQ ID NO: 13568	RTT*100 (PAM silencing)
13569	SEQ ID NO: 13569	RTT*99 (PAM silencing)
13570	SEQ ID NO: 13570	RTT*99 (PAM silencing)
13571	SEQ ID NO: 13571	RTT*100 (PAM silencing)
13572	SEQ ID NO: 13572	RTT
13573	SEQ ID NO: 13573	RTT*101 (PAM silencing)
13574	SEQ ID NO: 13574	RTT
13575	SEQ ID NO: 13575	RTT*99 (PAM silencing)
13576	SEQ ID NO: 13576	RTT*101 (PAM silencing)
13577	SEQ ID NO: 13577	RTT*100 (PAM silencing)
13578	SEQ ID NO: 13578	RTT*101 (PAM silencing)
13579	SEQ ID NO: 13579	RTT*100 (PAM silencing)
13580	SEQ ID NO: 13580	RTT*99 (PAM silencing)
13581	SEQ ID NO: 13581	RTT
13582	SEQ ID NO: 13582	RTT*99 (PAM silencing)
13583	SEQ ID NO: 13583	RTT*101 (PAM silencing)
13584	SEQ ID NO: 13584	RTT
13585	SEQ ID NO: 13585	RTT*100 (PAM silencing)
13586	SEQ ID NO: 13586	RTT
13587	SEQ ID NO: 13587	RTT*100 (PAM silencing)
13588	SEQ ID NO: 13588	RTT*99 (PAM silencing)
13589	SEQ ID NO: 13589	RTT*101 (PAM silencing)
13590	SEQ ID NO: 13590	RTT*100 (PAM silencing)
13591	SEQ ID NO: 13591	RTT
13592	SEQ ID NO: 13592	RTT*99 (PAM silencing)
13593	SEQ ID NO: 13593	RTT*101 (PAM silencing)
13594	SEQ ID NO: 13594	RTT*101 (PAM silencing)
13595	SEQ ID NO: 13595	RTT*100 (PAM silencing)
13596	SEQ ID NO: 13596	RTT*99 (PAM silencing)
13597	SEQ ID NO: 13597	RTT
13598	SEQ ID NO: 13598	RTT*101 (PAM silencing)
13599	SEQ ID NO: 13599	RTT
13600	SEQ ID NO: 13600	RTT*99 (PAM silencing)
13601	SEQ ID NO: 13601	RTT*100 (PAM silencing)
13602	SEQ ID NO: 13602	RTT*100 (PAM silencing)
13603	SEQ ID NO: 13603	RTT*99 (PAM silencing)
13604	SEQ ID NO: 13604	RTT
13605	SEQ ID NO: 13605	RTT*101 (PAM silencing)
13606	SEQ ID NO: 13606	RTT*99 (PAM silencing)
13607	SEQ ID NO: 13607	RTT*100 (PAM silencing)
13608	SEQ ID NO: 13608	RTT
13609	SEQ ID NO: 13609	RTT*101 (PAM silencing)
13610	SEQ ID NO: 13610	RTT*101 (PAM silencing)
13611	SEQ ID NO: 13611	RTT*99 (PAM silencing)
13612	SEQ ID NO: 13612	RTT*100 (PAM silencing)
13613	SEQ ID NO: 13613	RTT
13614	SEQ ID NO: 13614	RTT*101 (PAM silencing)
13615	SEQ ID NO: 13615	RTT*100 (PAM silencing)
13616	SEQ ID NO: 13616	RTT*99 (PAM silencing)
13617	SEQ ID NO: 13617	RTT
13618	SEQ ID NO: 13618	RTT
13619	SEQ ID NO: 13619	RTT*100 (PAM silencing)
13620	SEQ ID NO: 13620	RTT*101 (PAM silencing)
13621	SEQ ID NO: 13621	RTT*99 (PAM silencing)
13622	SEQ ID NO: 13622	RTT*99 (PAM silencing)
13623	SEQ ID NO: 13623	RTT*101 (PAM silencing)
13624	SEQ ID NO: 13624	RTT*100 (PAM silencing)
13625	SEQ ID NO: 13625	RTT
13626	SEQ ID NO: 13626	RTT
13627	SEQ ID NO: 13627	RTT*100 (PAM silencing)
13628	SEQ ID NO: 13628	RTT*99 (PAM silencing)

Sequence Number	Sequence	Description
13629	SEQ ID NO: 13629	RTT*101 (PAM silencing)
3271	SEQ ID NO: 3271	PE3b*99 ngRNA spacer (TG PAM)
3293	SEQ ID NO: 3293	PE3 ngRNA spacer (GG PAM)
3278	SEQ ID NO: 3278	PE3 ngRNA spacer (GG PAM)
3268	SEQ ID NO: 3268	PE3 ngRNA spacer (AG PAM)
3295	SEQ ID NO: 3295	PE3 ngRNA spacer (GG PAM)
13630	SEQ ID NO: 13630	PE3b*99 ngRNA spacer (GG PAM)
2004	SEQ ID NO: 2004	PE3b ngRNA spacer (GG PAM)
3248	SEQ ID NO: 3248	PE3 ngRNA spacer (CG PAM)
3280	SEQ ID NO: 3280	PE3 ngRNA spacer (TG PAM)
2127	SEQ ID NO: 2127	PE3 ngRNA spacer (TG PAM)
2059	SEQ ID NO: 2059	PE3 ngRNA spacer (GG PAM)
3297	SEQ ID NO: 3297	PE3b*101 ngRNA spacer (TG PAM)
3266	SEQ ID NO: 3266	PE3 ngRNA spacer (TG PAM)
1994	SEQ ID NO: 1994	PE3b ngRNA spacer (TG PAM)
3264	SEQ ID NO: 3264	PE3b*100 ngRNA spacer (TG PAM)
3279	SEQ ID NO: 3279	PE3 ngRNA spacer (TG PAM)
3275	SEQ ID NO: 3275	PE3 ngRNA spacer (TG PAM)
13631	SEQ ID NO: 13631	PE3b*101 ngRNA spacer (GG PAM)
3269	SEQ ID NO: 3269	PE3 ngRNA spacer (CG PAM)
3262	SEQ ID NO: 3262	PE3 ngRNA spacer (CG PAM)
3283	SEQ ID NO: 3283	PE3 ngRNA spacer (GG PAM)
13632	SEQ ID NO: 13632	PE3b*101 ngRNA spacer (GG PAM)
3273	SEQ ID NO: 3273	PE3 ngRNA spacer (TG PAM)
3272	SEQ ID NO: 3272	PE3b*99 ngRNA spacer (TG PAM)
3282	SEQ ID NO: 3282	PE3 ngRNA spacer (AG PAM)
3285	SEQ ID NO: 3285	PE3 ngRNA spacer (GG PAM)
13633	SEQ ID NO: 13633	PE3b*100 ngRNA spacer (GG PAM)
3263	SEQ ID NO: 3263	PE3 ngRNA spacer (AG PAM)
2057	SEQ ID NO: 2057	PE3 ngRNA spacer (GG PAM)
2058	SEQ ID NO: 2058	PE3 ngRNA spacer (TG PAM)
3244	SEQ ID NO: 3244	PE3 ngRNA spacer (TG PAM)
2056	SEQ ID NO: 2056	PE3 ngRNA spacer (TG PAM)
3270	SEQ ID NO: 3270	PE3 ngRNA spacer (GG PAM)
3291	SEQ ID NO: 3291	PE3 ngRNA spacer (TG PAM)
2125	SEQ ID NO: 2125	PE3 ngRNA spacer (TG PAM)
2006	SEQ ID NO: 2006	PE3 ngRNA spacer (TG PAM)
3260	SEQ ID NO: 3260	PE3 ngRNA spacer (AG PAM)
2000	SEQ ID NO: 2000	PE3b ngRNA spacer (TG PAM)
2126	SEQ ID NO: 2126	PE3 ngRNA spacer (TG PAM)
13634	SEQ ID NO: 13634	PE3b*99 ngRNA spacer (GG PAM)
3299	SEQ ID NO: 3299	PE3b*100 ngRNA spacer (TG PAM)
3277	SEQ ID NO: 3277	PE3 ngRNA spacer (TG PAM)
13635	SEQ ID NO: 13635	PE3b*100 ngRNA spacer (GG PAM)
3247	SEQ ID NO: 3247	PE3b*101 ngRNA spacer (TG PAM)
3287	SEQ ID NO: 3287	PE3 ngRNA spacer (AG PAM)

Sequence Number	Sequence	Description
4106	SEQ ID NO: 4106	ngRNA (CG PAM)
4105	SEQ ID NO: 4105	ngRNA (AG PAM)
2061	SEQ ID NO: 2061	ngRNA (TG PAM)
4087	SEQ ID NO: 4087	ngRNA (TG PAM)
4108	SEQ ID NO: 4108	ngRNA (TG PAM)
4110	SEQ ID NO: 4110	ngRNA (TG PAM)
4099	SEQ ID NO: 4099	ngRNA (TG PAM)
4091	SEQ ID NO: 4091	ngRNA (AG PAM)
4086	SEQ ID NO: 4086	ngRNA (TG PAM)
4090	SEQ ID NO: 4090	ngRNA (TG PAM)
4085	SEQ ID NO: 4085	ngRNA (TG PAM)
2012	SEQ ID NO: 2012	ngRNA (TG PAM)
4101	SEQ ID NO: 4101	ngRNA (TG PAM)
2013	SEQ ID NO: 2013	ngRNA (TG PAM)
4100	SEQ ID NO: 4100	ngRNA (TG PAM)
2060	SEQ ID NO: 2060	ngRNA (GG PAM)
4120	SEQ ID NO: 4120	ngRNA (TG PAM)
4113	SEQ ID NO: 4113	ngRNA (TG PAM)
2015	SEQ ID NO: 2015	ngRNA (TG PAM)
4117	SEQ ID NO: 4117	ngRNA (TG PAM)
4123	SEQ ID NO: 4123	ngRNA (TG PAM)
4122	SEQ ID NO: 4122	ngRNA (TG PAM)
4124	SEQ ID NO: 4124	ngRNA (AG PAM)
4118	SEQ ID NO: 4118	ngRNA (TG PAM)
4125	SEQ ID NO: 4125	ngRNA (TG PAM)
4115	SEQ ID NO: 4115	ngRNA (TG PAM)
2016	SEQ ID NO: 2016	ngRNA (TG PAM)
2062	SEQ ID NO: 2062	ngRNA (GG PAM)

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Sequence Number	Sequence	Description
13636	SEQ ID NO: 13636	PEgRNA spacer
		(CTGG PAM)
13637	SEQ ID NO: 13637	PEgRNA spacer (CTGG PAM)
13638	SEQ ID NO: 13638	PEgRNA spacer (CTGG PAM)
13639	SEQ ID NO: 13639	PEgRNA spacer (CTGG PAM)
13640	SEQ ID NO: 13640	PEgRNA spacer (CTGG PAM)
13641	SEQ ID NO: 13641	PEgRNA spacer (CTGG PAM)
13642	SEQ ID NO: 13642	PEgRNA spacer (CTGG PAM)
13643	GAC	PBS
13644	GACC	PBS
13645	GACCA	PBS
13646	GACCAG	PBS
13647	GACCAGA	PBS
13648	GACCAGAG	PBS
13649	GACCAGAGA	PBS
13650	SEQ ID NO: 13650	PBS
13651	SEQ ID NO: 13651	PBS
13652	SEQ ID NO: 13652	PBS
13653	SEQ ID NO: 13653	PBS
13654	SEQ ID NO: 13654	PBS
13655	SEQ ID NO: 13655	PBS
13656	SEQ ID NO: 13656	PBS
13657	SEQ ID NO: 13657	PBS
13658	SEQ ID NO: 13658	PBS
13659	SEQ ID NO: 13659	PBS
13660	SEQ ID NO: 13660	RTT*81 (PAM silencing)
13661	SEQ ID NO: 13661	RTT*83 (PAM silencing)
13662	SEQ ID NO: 13662	RTT*80 (PAM silencing)
13663	SEQ ID NO: 13663	RTT
13664	SEQ ID NO: 13664	RTT*82 (PAM silencing)
13665	SEQ ID NO: 13665	RTT
13666	SEQ ID NO: 13666	RTT*83 (PAM silencing)
13667	SEQ ID NO: 13667	RTT*80 (PAM silencing)
13668	SEQ ID NO: 13668	RTT*81 (PAM silencing)
13669	SEQ ID NO: 13669	RTT*82 (PAM silencing)
13670	SEQ ID NO: 13670	RTT*80 (PAM silencing)
13671	SEQ ID NO: 13671	RTT*82 (PAM silencing)
13672	SEQ ID NO: 13672	RTT
13673	SEQ ID NO: 13673	RTT*81 (PAM silencing)
13674	SEQ ID NO: 13674	RTT*83 (PAM silencing)
13675	SEQ ID NO: 13675	RTT*80 (PAM silencing)
13676	SEQ ID NO: 13676	RTT*83 (PAM silencing)
13677	SEQ ID NO: 13677	RTT*82 (PAM silencing)
13678	SEQ ID NO: 13678	RTT*81 (PAM silencing)
13679	SEQ ID NO: 13679	RTT
13680	SEQ ID NO: 13680	RTT*80 (PAM silencing)
13681	SEQ ID NO: 13681	RTT*81 (PAM silencing)
13682	SEQ ID NO: 13682	RTT*83 (PAM silencing)
13683	SEQ ID NO: 13683	RTT
13684	SEQ ID NO: 13684	RTT*82 (PAM silencing)
13685	SEQ ID NO: 13685	RTT*81 (PAM silencing)
13686	SEQ ID NO: 13686	RTT*83 (PAM silencing)

Sequence Number	Sequence	Description
13687	SEQ ID NO: 13687	RTT*82 (PAM silencing)
13688	SEQ ID NO: 13688	RTT*80 (PAM silencing)
13689	SEQ ID NO: 13689	RTT
98	SEQ ID NO: 98	PE3 ngRNA spacer (GGGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TGGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GGGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AGGG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAGG PAM)
6536	SEQ ID NO: 6536	PE3 ngRNA spacer (ATGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AGGG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GGGG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAGG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAGG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAGG PAM)
109	SEQ ID NO: 109	ngRNA (GGGG PAM)
101	SEQ ID NO: 101	ngRNA (TGGG PAM)
102	SEQ ID NO: 102	ngRNA (AGGG PAM)
105	SEQ ID NO: 105	ngRNA (GGGG PAM)
100	SEQ ID NO: 100	ngRNA (GGGG PAM)
104	SEQ ID NO: 104	ngRNA (AGGG PAM)
112	SEQ ID NO: 112	ngRNA (GGGG PAM)
117	SEQ ID NO: 117	ngRNA (AGGG PAM)
113	SEQ ID NO: 113	ngRNA (GGGG PAM)

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Sequence Number	Sequence	Description
13690	SEQ ID NO: 13690	PEgRNA spacer (GTGG PAM)
13691	SEQ ID NO: 13691	PEgRNA spacer (GTGG PAM)
13692	SEQ ID NO: 13692	PEgRNA spacer (GTGG PAM)
13693	SEQ ID NO: 13693	PEgRNA spacer (GTGG PAM)
13694	SEQ ID NO: 13694	PEgRNA spacer (GTGG PAM)
13695	SEQ ID NO: 13695	PEgRNA spacer (GTGG PAM)
13696	SEQ ID NO: 13696	PEgRNA spacer (GTGG PAM)
13697	GAT	PBS
13698	GATG	PBS
13699	GATGA	PBS
13700	GATGAC	PBS
13701	GATGAC C	PBS
13702	GATGAC CA	PBS
13703	GATGAC CAG	PBS
13704	SEQ ID NO: 13704	PBS
13705	SEQ ID NO: 13705	PBS
13706	SEQ ID NO: 13706	PBS
13707	SEQ ID NO: 13707	PBS
13708	SEQ ID NO: 13708	PBS
13709	SEQ ID NO: 13709	PBS
13710	SEQ ID NO: 13710	PBS
13711	SEQ ID NO: 13711	PBS
13712	SEQ ID NO: 13712	PBS
13713	SEQ ID NO: 13713	PBS
13714	SEQ ID NO: 13714	RTT*102 (PAM silencing)
13715	SEQ ID NO: 13715	RTT*104 (PAM silencing)
13716	SEQ ID NO: 13716	RTT
13717	SEQ ID NO: 13717	RTT*103 (PAM silencing)
13718	SEQ ID NO: 13718	RTT
13719	SEQ ID NO: 13719	RTT*103 (PAM silencing)
13720	SEQ ID NO: 13720	RTT*104 (PAM silencing)
13721	SEQ ID NO: 13721	RTT*102 (PAM silencing)
13722	SEQ ID NO: 13722	RTT*102 (PAM silencing)
13723	SEQ ID NO: 13723	RTT*103 (PAM silencing)
13724	SEQ ID NO: 13724	RTT
13725	SEQ ID NO: 13725	RTT*104 (PAM silencing)
13726	SEQ ID NO: 13726	RTT*103 (PAM silencing)
13727	SEQ ID NO: 13727	RTT
13728	SEQ ID NO: 13728	RTT*104 (PAM silencing)
13729	SEQ ID NO: 13729	RTT*102 (PAM silencing)
13730	SEQ ID NO: 13730	RTT*103 (PAM silencing)

Sequence Number	Sequence	Description
13731	SEQ ID NO: 13731	RTT*104 (PAM silencing)
13732	SEQ ID NO: 13732	RTT
13733	SEQ ID NO: 13733	RTT*102 (PAM silencing)
13734	SEQ ID NO: 13734	RTT*104 (PAM silencing)
13735	SEQ ID NO: 13735	RTT*102 (PAM silencing)
13736	SEQ ID NO: 13736	RTT
13737	SEQ ID NO: 13737	RTT*103 (PAM silencing)
13738	SEQ ID NO: 13738	RTT*104 (PAM silencing)
13739	SEQ ID NO: 13739	RTT*102 (PAM silencing)
13740	SEQ ID NO: 13740	RTT
13741	SEQ ID NO: 13741	RTT*103 (PAM silencing)
13742	SEQ ID NO: 13742	RTT*102 (PAM silencing)
13743	SEQ ID NO: 13743	RTT
13744	SEQ ID NO: 13744	RTT*103 (PAM silencing)
13745	SEQ ID NO: 13745	RTT*104 (PAM silencing)
13746	SEQ ID NO: 13746	RTT*103 (PAM silencing)
13747	SEQ ID NO: 13747	RTT*104 (PAM silencing)
13748	SEQ ID NO: 13748	RTT*102 (PAM silencing)
13749	SEQ ID NO: 13749	RTT
76	SEQ ID NO: 76	PE3 ngRNA spacer (GGGG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAGG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAGG PAM)
9861	SEQ ID NO: 9861	PE3b*104 ngRNA spacer (CAGG PAM)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAGG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAGG PAM)
13750	SEQ ID NO: 13750	PE3b*102 ngRNA spacer (CAGG PAM)
9862	SEQ ID NO: 9862	PE3b*103 ngRNA spacer (CAGG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GGGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AGGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TGGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AGGG PAM)
6536	SEQ ID NO: 6536	PE3 ngRNA spacer (ATGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GGGG PAM)
104	SEQ ID NO: 104	ngRNA (AGGG PAM)
105	SEQ ID NO: 105	ngRNA (GGGG PAM)
109	SEQ ID NO: 109	ngRNA (GGGG PAM)
102	SEQ ID NO: 102	ngRNA (AGGG PAM)
101	SEQ ID NO: 101	ngRNA (TGGG PAM)
100	SEQ ID NO: 100	ngRNA (GGGG PAM)
117	SEQ ID NO: 117	ngRNA (AGGG PAM)
112	SEQ ID NO: 112	ngRNA (GGGG PAM)
113	SEQ ID NO: 113	ngRNA (GGGG PAM)

Table 77

Sequence Number	Sequence	Description
13751	SEQ ID NO: 13751	PEgRNA spacer (GTGG PAM)
13752	SEQ ID NO: 13752	PEgRNA spacer (GTGG PAM)
13753	SEQ ID NO: 13753	PEgRNA spacer (GTGG PAM)
13754	SEQ ID NO: 13754	PEgRNA spacer (GTGG PAM)
13755	SEQ ID NO: 13755	PEgRNA spacer (GTGG PAM)
13756	SEQ ID NO: 13756	PEgRNA spacer (GTGG PAM)
13757	SEQ ID NO: 13757	PEgRNA spacer (GTGG PAM)
2024	AAC	PBS
13758	AACC	PBS
13759	AACCA	PBS
13760	AACCAC	PBS
13761	AACCACC	PBS
13762	AACCACCA	PBS
13763	AACCACCAG	PBS
13764	SEQ ID NO: 13764	PBS
13765	SEQ ID NO: 13765	PBS
13766	SEQ ID NO: 13766	PBS
13767	SEQ ID NO: 13767	PBS
13768	SEQ ID NO: 13768	PBS

Sequence Number	Sequence	Description
13769	SEQ ID NO: 13769	PBS
13770	SEQ ID NO: 13770	PBS
13771	SEQ ID NO: 13771	PBS
13772	SEQ ID NO: 13772	PBS
13773	SEQ ID NO: 13773	PBS
13774	SEQ ID NO: 13774	RTT*102 (PAM silencing)
13775	SEQ ID NO: 13775	RTT*103 (PAM silencing)
13776	SEQ ID NO: 13776	RTT*104 (PAM silencing)
13777	SEQ ID NO: 13777	RTT
13778	SEQ ID NO: 13778	RTT*103 (PAM silencing)
13779	SEQ ID NO: 13779	RTT*104 (PAM silencing)
13780	SEQ ID NO: 13780	RTT
13781	SEQ ID NO: 13781	RTT*102 (PAM silencing)
13782	SEQ ID NO: 13782	RTT*103 (PAM silencing)
13783	SEQ ID NO: 13783	RTT*102 (PAM silencing)
13784	SEQ ID NO: 13784	RTT*104 (PAM silencing)
13785	SEQ ID NO: 13785	RTT
13786	SEQ ID NO: 13786	RTT*103 (PAM silencing)
13787	SEQ ID NO: 13787	RTT
13788	SEQ ID NO: 13788	RTT*104 (PAM silencing)
13789	SEQ ID NO: 13789	RTT*102 (PAM silencing)
13790	SEQ ID NO: 13790	RTT*104 (PAM silencing)
13791	SEQ ID NO: 13791	RTT*103 (PAM silencing)
13792	SEQ ID NO: 13792	RTT*102 (PAM silencing)
13793	SEQ ID NO: 13793	RTT
13794	SEQ ID NO: 13794	RTT*104 (PAM silencing)
13795	SEQ ID NO: 13795	RTT*103 (PAM silencing)
13796	SEQ ID NO: 13796	RTT
13797	SEQ ID NO: 13797	RTT*102 (PAM silencing)
13798	SEQ ID NO: 13798	RTT*104 (PAM silencing)
13799	SEQ ID NO: 13799	RTT*102 (PAM silencing)
13800	SEQ ID NO: 13800	RTT
13801	SEQ ID NO: 13801	RTT*103 (PAM silencing)
13802	SEQ ID NO: 13802	RTT*104 (PAM silencing)
13803	SEQ ID NO: 13803	RTT*102 (PAM silencing)
13804	SEQ ID NO: 13804	RTT*103 (PAM silencing)
13805	SEQ ID NO: 13805	RTT
13806	SEQ ID NO: 13806	RTT*102 (PAM silencing)
13807	SEQ ID NO: 13807	RTT
13808	SEQ ID NO: 13808	RTT*103 (PAM silencing)
13809	SEQ ID NO: 13809	RTT*104 (PAM silencing)
13810	SEQ ID NO: 13810	RTT*102 (PAM silencing)
13811	SEQ ID NO: 13811	RTT*104 (PAM silencing)
13812	SEQ ID NO: 13812	RTT*103 (PAM silencing)
13813	SEQ ID NO: 13813	RTT
13814	SEQ ID NO: 13814	RTT*103 (PAM silencing)
13815	SEQ ID NO: 13815	RTT*104 (PAM silencing)
13816	SEQ ID NO: 13816	RTT*102 (PAM silencing)
13817	SEQ ID NO: 13817	RTT
13818	SEQ ID NO: 13818	RTT*102 (PAM silencing)
13819	SEQ ID NO: 13819	RTT*104 (PAM silencing)
13820	SEQ ID NO: 13820	RTT
13821	SEQ ID NO: 13821	RTT*103 (PAM silencing)
13822	SEQ ID NO: 13822	RTT*103 (PAM silencing)
13823	SEQ ID NO: 13823	RTT*102 (PAM silencing)
13824	SEQ ID NO: 13824	RTT
13825	SEQ ID NO: 13825	RTT*104 (PAM silencing)
13826	SEQ ID NO: 13826	RTT*102 (PAM silencing)
13827	SEQ ID NO: 13827	RTT*104 (PAM silencing)
13828	SEQ ID NO: 13828	RTT
13829	SEQ ID NO: 13829	RTT*103 (PAM silencing)
13830	SEQ ID NO: 13830	RTT
13831	SEQ ID NO: 13831	RTT*102 (PAM silencing)
13832	SEQ ID NO: 13832	RTT*103 (PAM silencing)
13833	SEQ ID NO: 13833	RTT*104 (PAM silencing)
13834	SEQ ID NO: 13834	RTT*102 (PAM silencing)
13835	SEQ ID NO: 13835	RTT*103 (PAM silencing)
13836	SEQ ID NO: 13836	RTT
13837	SEQ ID NO: 13837	RTT*104 (PAM silencing)
13838	SEQ ID NO: 13838	RTT*104 (PAM silencing)
13839	SEQ ID NO: 13839	RTT*102 (PAM silencing)
13840	SEQ ID NO: 13840	RTT
13841	SEQ ID NO: 13841	RTT*103 (PAM silencing)

Sequence Number	Sequence	Description
13842	SEQ ID NO: 13842	RTT*103 (PAM silencing)
13843	SEQ ID NO: 13843	RTT*102 (PAM silencing)
13844	SEQ ID NO: 13844	RTT*104 (PAM silencing)
13845	SEQ ID NO: 13845	RTT
6536	SEQ ID NO: 6536	PE3 ngRNA spacer (ATGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AGGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TGGG PAM)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GGGG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAGG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAGG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GGGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AGGG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GGGG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAGG PAM)
109	SEQ ID NO: 109	ngRNA (GGGG PAM)
105	SEQ ID NO: 105	ngRNA (GGGG PAM)
102	SEQ ID NO: 102	ngRNA (AGGG PAM)
101	SEQ ID NO: 101	ngRNA (TGGG PAM)
104	SEQ ID NO: 104	ngRNA (AGGG PAM)
100	SEQ ID NO: 100	ngRNA (GGGG PAM)
113	SEQ ID NO: 113	ngRNA (GGGG PAM)
117	SEQ ID NO: 117	ngRNA (AGGG PAM)
112	SEQ ID NO: 112	ngRNA (GGGG PAM)

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Sequence Number	Sequence	Description
13846	SEQ ID NO: 13846	PEgRNA spacer (GCGG PAM)
13847	SEQ ID NO: 13847	PEgRNA spacer (GCGG PAM)
13848	SEQ ID NO: 13848	PEgRNA spacer (GCGG PAM)
13849	SEQ ID NO: 13849	PEgRNA spacer (GCGG PAM)
13850	SEQ ID NO: 13850	PEgRNA spacer (GCGG PAM)
13851	SEQ ID NO: 13851	PEgRNA spacer (GCGG PAM)
13852	SEQ ID NO: 13852	PEgRNA spacer (GCGG PAM)
10073	CTC	PBS
12110	CTCA	PBS
13853	CTCAG	PBS
13854	CTCAGC	PBS
13855	CTCAGC C	PBS
13856	CTCAGC CA	PBS
13857	CTCAGC CAC	PBS
13858	SEQ ID NO: 13858	PBS
13859	SEQ ID NO: 13859	PBS
13860	SEQ ID NO: 13860	PBS
13861	SEQ ID NO: 13861	PBS
13862	SEQ ID NO: 13862	PBS
13863	SEQ ID NO: 13863	PBS
13864	SEQ ID NO: 13864	PBS
13865	SEQ ID NO: 13865	PBS
13866	SEQ ID NO: 13866	PBS
13867	SEQ ID NO: 13867	PBS
13868	SEQ ID NO: 13868	RTT*94 (PAM silencing)
13869	SEQ ID NO: 13869	RTT*95 (PAM silencing)
13870	SEQ ID NO: 13870	RTT
13871	SEQ ID NO: 13871	RTT*96 (PAM silencing)
13872	SEQ ID NO: 13872	RTT*94 (PAM silencing)
13873	SEQ ID NO: 13873	RTT*96 (PAM silencing)
13874	SEQ ID NO: 13874	RTT
13875	SEQ ID NO: 13875	RTT*95 (PAM silencing)
13876	SEQ ID NO: 13876	RTT*94 (PAM silencing)
13877	SEQ ID NO: 13877	RTT
13878	SEQ ID NO: 13878	RTT*96 (PAM silencing)
13879	SEQ ID NO: 13879	RTT*95 (PAM silencing)
13880	SEQ ID NO: 13880	RTT*95 (PAM silencing)
13881	SEQ ID NO: 13881	RTT*96 (PAM silencing)
13882	SEQ ID NO: 13882	RTT*94 (PAM silencing)
13883	SEQ ID NO: 13883	RTT
13884	SEQ ID NO: 13884	RTT*94 (PAM silencing)
13885	SEQ ID NO: 13885	RTT*95 (PAM silencing)

Sequence Number	Sequence	Description
13886	SEQ ID NO: 13886	RTT*96 (PAM silencing)
13887	SEQ ID NO: 13887	RTT
13888	SEQ ID NO: 13888	RTT
13889	SEQ ID NO: 13889	RTT*95 (PAM silencing)
13890	SEQ ID NO: 13890	RTT*96 (PAM silencing)
13891	SEQ ID NO: 13891	RTT*94 (PAM silencing)
13892	SEQ ID NO: 13892	RTT
13893	SEQ ID NO: 13893	RTT*94 (PAM silencing)
13894	SEQ ID NO: 13894	RTT*95 (PAM silencing)
13895	SEQ ID NO: 13895	RTT*96 (PAM silencing)
13896	SEQ ID NO: 13896	RTT*96 (PAM silencing)
13897	SEQ ID NO: 13897	RTT*95 (PAM silencing)
13898	SEQ ID NO: 13898	RTT
13899	SEQ ID NO: 13899	RTT*94 (PAM silencing)
13900	SEQ ID NO: 13900	RTT*96 (PAM silencing)
13901	SEQ ID NO: 13901	RTT*95 (PAM silencing)
13902	SEQ ID NO: 13902	RTT*94 (PAM silencing)
13903	SEQ ID NO: 13903	RTT
13904	SEQ ID NO: 13904	RTT*95 (PAM silencing)
13905	SEQ ID NO: 13905	RTT*94 (PAM silencing)
13906	SEQ ID NO: 13906	RTT
13907	SEQ ID NO: 13907	RTT*96 (PAM silencing)
13908	SEQ ID NO: 13908	RTT
13909	SEQ ID NO: 13909	RTT*94 (PAM silencing)
13910	SEQ ID NO: 13910	RTT*95 (PAM silencing)
13911	SEQ ID NO: 13911	RTT*96 (PAM silencing)
13912	SEQ ID NO: 13912	RTT
13913	SEQ ID NO: 13913	RTT*94 (PAM silencing)
13914	SEQ ID NO: 13914	RTT*96 (PAM silencing)
13915	SEQ ID NO: 13915	RTT*95 (PAM silencing)
13916	SEQ ID NO: 13916	RTT*94 (PAM silencing)
13917	SEQ ID NO: 13917	RTT*96 (PAM silencing)
13918	SEQ ID NO: 13918	RTT
13919	SEQ ID NO: 13919	RTT*95 (PAM silencing)
13920	SEQ ID NO: 13920	RTT*94 (PAM silencing)
13921	SEQ ID NO: 13921	RTT*95 (PAM silencing)
13922	SEQ ID NO: 13922	RTT
13923	SEQ ID NO: 13923	RTT*96 (PAM silencing)
13924	SEQ ID NO: 13924	RTT
13925	SEQ ID NO: 13925	RTT*94 (PAM silencing)
13926	SEQ ID NO: 13926	RTT*95 (PAM silencing)
13927	SEQ ID NO: 13927	RTT*96 (PAM silencing)
13928	SEQ ID NO: 13928	RTT*95 (PAM silencing)
13929	SEQ ID NO: 13929	RTT*96 (PAM silencing)
13930	SEQ ID NO: 13930	RTT
13931	SEQ ID NO: 13931	RTT*94 (PAM silencing)
13932	SEQ ID NO: 13932	RTT*96 (PAM silencing)
13933	SEQ ID NO: 13933	RTT*94 (PAM silencing)
13934	SEQ ID NO: 13934	RTT*95 (PAM silencing)
13935	SEQ ID NO: 13935	RTT
13936	SEQ ID NO: 13936	RTT*94 (PAM silencing)
13937	SEQ ID NO: 13937	RTT*96 (PAM silencing)
13938	SEQ ID NO: 13938	RTT
13939	SEQ ID NO: 13939	RTT*95 (PAM silencing)
13940	SEQ ID NO: 13940	RTT*96 (PAM silencing)
13941	SEQ ID NO: 13941	RTT
13942	SEQ ID NO: 13942	RTT*95 (PAM silencing)
13943	SEQ ID NO: 13943	RTT*94 (PAM silencing)
13944	SEQ ID NO: 13944	RTT*94 (PAM silencing)
13945	SEQ ID NO: 13945	RTT*95 (PAM silencing)
13946	SEQ ID NO: 13946	RTT
13947	SEQ ID NO: 13947	RTT*96 (PAM silencing)
13948	SEQ ID NO: 13948	RTT*96 (PAM silencing)
13949	SEQ ID NO: 13949	RTT*95 (PAM silencing)
13950	SEQ ID NO: 13950	RTT*94 (PAM silencing)
13951	SEQ ID NO: 13951	RTT
13952	SEQ ID NO: 13952	RTT*94 (PAM silencing)
13953	SEQ ID NO: 13953	RTT
13954	SEQ ID NO: 13954	RTT*95 (PAM silencing)
13955	SEQ ID NO: 13955	RTT*96 (PAM silencing)
13956	SEQ ID NO: 13956	RTT
13957	SEQ ID NO: 13957	RTT*94 (PAM silencing)

Sequence Number	Sequence	Description
13958	SEQ ID NO: 13958	RTT*95 (PAM silencing)
13959	SEQ ID NO: 13959	RTT*96 (PAM silencing)
13960	SEQ ID NO: 13960	RTT*94 (PAM silencing)
13961	SEQ ID NO: 13961	RTT*95 (PAM silencing)
13962	SEQ ID NO: 13962	RTT
13963	SEQ ID NO: 13963	RTT*96 (PAM silencing)
13964	SEQ ID NO: 13964	RTT*94 (PAM silencing)
13965	SEQ ID NO: 13965	RTT*96 (PAM silencing)
13966	SEQ ID NO: 13966	RTT*95 (PAM silencing)
13967	SEQ ID NO: 13967	RTT
13968	SEQ ID NO: 13968	RTT*96 (PAM silencing)
13969	SEQ ID NO: 13969	RTT*95 (PAM silencing)
13970	SEQ ID NO: 13970	RTT*94 (PAM silencing)
13971	SEQ ID NO: 13971	RTT
13972	SEQ ID NO: 13972	RTT*94 (PAM silencing)
13973	SEQ ID NO: 13973	RTT*95 (PAM silencing)
13974	SEQ ID NO: 13974	RTT*96 (PAM silencing)
13975	SEQ ID NO: 13975	RTT
13976	SEQ ID NO: 13976	RTT*96 (PAM silencing)
13977	SEQ ID NO: 13977	RTT*95 (PAM silencing)
13978	SEQ ID NO: 13978	RTT
13979	SEQ ID NO: 13979	RTT*94 (PAM silencing)
13980	SEQ ID NO: 13980	RTT
13981	SEQ ID NO: 13981	RTT*95 (PAM silencing)
13982	SEQ ID NO: 13982	RTT*94 (PAM silencing)
13983	SEQ ID NO: 13983	RTT*96 (PAM silencing)
13984	SEQ ID NO: 13984	RTT*95 (PAM silencing)
13985	SEQ ID NO: 13985	RTT
13986	SEQ ID NO: 13986	RTT*96 (PAM silencing)
13987	SEQ ID NO: 13987	RTT*94 (PAM silencing)
95	SEQ ID NO: 95	PE3 ngRNA spacer (GGGG PAM)
68	SEQ ID NO: 68	PE3 ngRNA spacer (TGGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AGGG PAM)
98	SEQ ID NO: 98	PE3 ngRNA spacer (GGGG PAM)
6449	SEQ ID NO: 6449	PE3 ngRNA spacer (CAGG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAGG PAM)
6536	SEQ ID NO: 6536	PE3 ngRNA spacer (ATGG PAM)
76	SEQ ID NO: 76	PE3 ngRNA spacer (GGGG PAM)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAGG PAM)
96	SEQ ID NO: 96	PE3 ngRNA spacer (AGGG PAM)
104	SEQ ID NO: 104	ngRNA (AGGG PAM)
102	SEQ ID NO: 102	ngRNA (AGGG PAM)
100	SEQ ID NO: 100	ngRNA (GGGG PAM)
109	SEQ ID NO: 109	ngRNA (GGGG PAM)
101	SEQ ID NO: 101	ngRNA (TGGG PAM)
105	SEQ ID NO: 105	ngRNA (GGGG PAM)
113	SEQ ID NO: 113	ngRNA (GGGG PAM)
117	SEQ ID NO: 117	ngRNA (AGGG PAM)
112	SEQ ID NO: 112	ngRNA (GGGG PAM)

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Sequence Number	Sequence	Description
13988	SEQ ID NO: 13988	PEgRNA spacer (CTGG PAM)
13989	SEQ ID NO: 13989	PEgRNA spacer (CTGG PAM)
13990	SEQ ID NO: 13990	PEgRNA spacer (CTGG PAM)
13991	SEQ ID NO: 13991	PEgRNA spacer (CTGG PAM)
13992	SEQ ID NO: 13992	PEgRNA spacer (CTGG PAM)
13993	SEQ ID NO: 13993	PEgRNA spacer (CTGG PAM)
13994	SEQ ID NO: 13994	PEgRNA spacer (CTGG PAM)
5849	AAT	PBS
5850	AATG	PBS
13995	AATGA	PBS
13996	AATGAA	PBS
13997	AATGAAC	PBS
13998	AATGAACA	PBS

Sequence Number	Sequence	Description
13999	AATGAA CAC	PBS
14000	SEQ ID NO: 14000	PBS
14001	SEQ ID NO: 14001	PBS
14002	SEQ ID NO: 14002	PBS
14003	SEQ ID NO: 14003	PBS
14004	SEQ ID NO: 14004	PBS
14005	SEQ ID NO: 14005	PBS
14006	SEQ ID NO: 14006	PBS
14007	SEQ ID NO: 14007	PBS
14008	SEQ ID NO: 14008	PBS
14009	SEQ ID NO: 14009	PBS
14010	SEQ ID NO: 14010	RTT
14011	SEQ ID NO: 14011	RTT*82 (PAM silencing)
14012	SEQ ID NO: 14012	RTT*83 (PAM silencing)
14013	SEQ ID NO: 14013	RTT*81 (PAM silencing)
14014	SEQ ID NO: 14014	RTT*80 (PAM silencing)
14015	SEQ ID NO: 14015	RTT*82 (PAM silencing)
14016	SEQ ID NO: 14016	RTT
14017	SEQ ID NO: 14017	RTT*81 (PAM silencing)
14018	SEQ ID NO: 14018	RTT*80 (PAM silencing)
14019	SEQ ID NO: 14019	RTT*83 (PAM silencing)
14020	SEQ ID NO: 14020	RTT*83 (PAM silencing)
14021	SEQ ID NO: 14021	RTT*82 (PAM silencing)
14022	SEQ ID NO: 14022	RTT*81 (PAM silencing)
14023	SEQ ID NO: 14023	RTT*80 (PAM silencing)
14024	SEQ ID NO: 14024	RTT
14025	SEQ ID NO: 14025	RTT*80 (PAM silencing)
14026	SEQ ID NO: 14026	RTT
14027	SEQ ID NO: 14027	RTT*82 (PAM silencing)
14028	SEQ ID NO: 14028	RTT*83 (PAM silencing)
14029	SEQ ID NO: 14029	RTT*81 (PAM silencing)
14030	SEQ ID NO: 14030	RTT
14031	SEQ ID NO: 14031	RTT*83 (PAM silencing)
14032	SEQ ID NO: 14032	RTT*82 (PAM silencing)
14033	SEQ ID NO: 14033	RTT*80 (PAM silencing)
14034	SEQ ID NO: 14034	RTT*81 (PAM silencing)
14035	SEQ ID NO: 14035	RTT*83 (PAM silencing)
14036	SEQ ID NO: 14036	RTT*80 (PAM silencing)
14037	SEQ ID NO: 14037	RTT*81 (PAM silencing)
14038	SEQ ID NO: 14038	RTT
14039	SEQ ID NO: 14039	RTT*82 (PAM silencing)
14040	SEQ ID NO: 14040	RTT*83 (PAM silencing)
14041	SEQ ID NO: 14041	RTT
14042	SEQ ID NO: 14042	RTT*80 (PAM silencing)
14043	SEQ ID NO: 14043	RTT*82 (PAM silencing)
14044	SEQ ID NO: 14044	RTT*81 (PAM silencing)
14045	SEQ ID NO: 14045	RTT*80 (PAM silencing)
14046	SEQ ID NO: 14046	RTT
14047	SEQ ID NO: 14047	RTT*82 (PAM silencing)
14048	SEQ ID NO: 14048	RTT*81 (PAM silencing)
14049	SEQ ID NO: 14049	RTT*83 (PAM silencing)
14050	SEQ ID NO: 14050	RTT*82 (PAM silencing)
14051	SEQ ID NO: 14051	RTT
14052	SEQ ID NO: 14052	RTT*81 (PAM silencing)
14053	SEQ ID NO: 14053	RTT*80 (PAM silencing)
14054	SEQ ID NO: 14054	RTT*83 (PAM silencing)
14055	SEQ ID NO: 14055	RTT*81 (PAM silencing)
14056	SEQ ID NO: 14056	RTT*80 (PAM silencing)
14057	SEQ ID NO: 14057	RTT*83 (PAM silencing)
14058	SEQ ID NO: 14058	RTT*82 (PAM silencing)
14059	SEQ ID NO: 14059	RTT
14060	SEQ ID NO: 14060	RTT*80 (PAM silencing)
14061	SEQ ID NO: 14061	RTT*82 (PAM silencing)
14062	SEQ ID NO: 14062	RTT
14063	SEQ ID NO: 14063	RTT*83 (PAM silencing)
14064	SEQ ID NO: 14064	RTT*81 (PAM silencing)
14065	SEQ ID NO: 14065	RTT
14066	SEQ ID NO: 14066	RTT*83 (PAM silencing)
14067	SEQ ID NO: 14067	RTT*82 (PAM silencing)
14068	SEQ ID NO: 14068	RTT*80 (PAM silencing)
14069	SEQ ID NO: 14069	RTT*81 (PAM silencing)
14070	SEQ ID NO: 14070	RTT*82 (PAM silencing)
14071	SEQ ID NO: 14071	RTT*80 (PAM silencing)
14072	SEQ ID NO: 14072	RTT*81 (PAM silencing)

Sequence Number	Sequence	Description
14073	SEQ ID NO: 14073	RTT*83 (PAM silencing)
14074	SEQ ID NO: 14074	RTT
14075	SEQ ID NO: 14075	RTT*80 (PAM silencing)
14076	SEQ ID NO: 14076	RTT*83 (PAM silencing)
14077	SEQ ID NO: 14077	RTT*82 (PAM silencing)
14078	SEQ ID NO: 14078	RTT*81 (PAM silencing)
14079	SEQ ID NO: 14079	RTT
14080	SEQ ID NO: 14080	RTT*81 (PAM silencing)
14081	SEQ ID NO: 14081	RTT*82 (PAM silencing)
14082	SEQ ID NO: 14082	RTT*83 (PAM silencing)
14083	SEQ ID NO: 14083	RTT
14084	SEQ ID NO: 14084	RTT*80 (PAM silencing)
14085	SEQ ID NO: 14085	RTT*82 (PAM silencing)
14086	SEQ ID NO: 14086	RTT*80 (PAM silencing)
14087	SEQ ID NO: 14087	RTT
14088	SEQ ID NO: 14088	RTT*81 (PAM silencing)
14089	SEQ ID NO: 14089	RTT*83 (PAM silencing)
14090	SEQ ID NO: 14090	RTT
14091	SEQ ID NO: 14091	RTT*83 (PAM silencing)
14092	SEQ ID NO: 14092	RTT*80 (PAM silencing)
14093	SEQ ID NO: 14093	RTT*82 (PAM silencing)
14094	SEQ ID NO: 14094	RTT*81 (PAM silencing)
14095	SEQ ID NO: 14095	RTT*80 (PAM silencing)
14096	SEQ ID NO: 14096	RTT
14097	SEQ ID NO: 14097	RTT*83 (PAM silencing)
14098	SEQ ID NO: 14098	RTT*82 (PAM silencing)
14099	SEQ ID NO: 14099	RTT*81 (PAM silencing)
14100	SEQ ID NO: 14100	RTT
14101	SEQ ID NO: 14101	RTT*82 (PAM silencing)
14102	SEQ ID NO: 14102	RTT*81 (PAM silencing)
14103	SEQ ID NO: 14103	RTT*80 (PAM silencing)
14104	SEQ ID NO: 14104	RTT*83 (PAM silencing)
14105	SEQ ID NO: 14105	RTT*80 (PAM silencing)
14106	SEQ ID NO: 14106	RTT*82 (PAM silencing)
14107	SEQ ID NO: 14107	RTT*81 (PAM silencing)
14108	SEQ ID NO: 14108	RTT*83 (PAM silencing)
14109	SEQ ID NO: 14109	RTT
14110	SEQ ID NO: 14110	RTT*83 (PAM silencing)
14111	SEQ ID NO: 14111	RTT*82 (PAM silencing)
14112	SEQ ID NO: 14112	RTT*80 (PAM silencing)
14113	SEQ ID NO: 14113	RTT*81 (PAM silencing)
14114	SEQ ID NO: 14114	RTT
14115	SEQ ID NO: 14115	RTT
14116	SEQ ID NO: 14116	RTT*80 (PAM silencing)
14117	SEQ ID NO: 14117	RTT*81 (PAM silencing)
14118	SEQ ID NO: 14118	RTT*82 (PAM silencing)
14119	SEQ ID NO: 14119	RTT*83 (PAM silencing)
14120	SEQ ID NO: 14120	RTT*81 (PAM silencing)
14121	SEQ ID NO: 14121	RTT
14122	SEQ ID NO: 14122	RTT*83 (PAM silencing)
14123	SEQ ID NO: 14123	RTT*80 (PAM silencing)
14124	SEQ ID NO: 14124	RTT*82 (PAM silencing)
14125	SEQ ID NO: 14125	RTT*83 (PAM silencing)
14126	SEQ ID NO: 14126	RTT
14127	SEQ ID NO: 14127	RTT*80 (PAM silencing)
14128	SEQ ID NO: 14128	RTT*81 (PAM silencing)
14129	SEQ ID NO: 14129	RTT*82 (PAM silencing)
14130	SEQ ID NO: 14130	RTT*81 (PAM silencing)
14131	SEQ ID NO: 14131	RTT*83 (PAM silencing)
14132	SEQ ID NO: 14132	RTT*80 (PAM silencing)
14133	SEQ ID NO: 14133	RTT
14134	SEQ ID NO: 14134	RTT*82 (PAM silencing)
14135	SEQ ID NO: 14135	RTT*82 (PAM silencing)
14136	SEQ ID NO: 14136	RTT*81 (PAM silencing)
14137	SEQ ID NO: 14137	RTT*83 (PAM silencing)
14138	SEQ ID NO: 14138	RTT*80 (PAM silencing)
14139	SEQ ID NO: 14139	RTT
14140	SEQ ID NO: 14140	RTT*81 (PAM silencing)
14141	SEQ ID NO: 14141	RTT
14142	SEQ ID NO: 14142	RTT*83 (PAM silencing)
14143	SEQ ID NO: 14143	RTT*80 (PAM silencing)

Sequence Number	Sequence	Description
14144	SEQ ID NO: 14144	RTT*82 (PAM silencing)
14145	SEQ ID NO: 14145	RTT*80 (PAM silencing)
14146	SEQ ID NO: 14146	RTT*82 (PAM silencing)
14147	SEQ ID NO: 14147	RTT*81 (PAM silencing)
14148	SEQ ID NO: 14148	RTT
14149	SEQ ID NO: 14149	RTT*83 (PAM silencing)
14150	SEQ ID NO: 14150	RTT*81 (PAM silencing)
14151	SEQ ID NO: 14151	RTT*80 (PAM silencing)
14152	SEQ ID NO: 14152	RTT*82 (PAM silencing)
14153	SEQ ID NO: 14153	RTT
14154	SEQ ID NO: 14154	RTT*83 (PAM silencing)
14155	SEQ ID NO: 14155	RTT*81 (PAM silencing)
14156	SEQ ID NO: 14156	RTT*80 (PAM silencing)
14157	SEQ ID NO: 14157	RTT*82 (PAM silencing)
14158	SEQ ID NO: 14158	RTT
14159	SEQ ID NO: 14159	RTT*83 (PAM silencing)
14160	SEQ ID NO: 14160	RTT*83 (PAM silencing)
14161	SEQ ID NO: 14161	RTT*81 (PAM silencing)
14162	SEQ ID NO: 14162	RTT
14163	SEQ ID NO: 14163	RTT*82 (PAM silencing)
14164	SEQ ID NO: 14164	RTT*80 (PAM silencing)
14165	SEQ ID NO: 14165	RTT*80 (PAM silencing)
14166	SEQ ID NO: 14166	RTT*82 (PAM silencing)
14167	SEQ ID NO: 14167	RTT*81 (PAM silencing)
14168	SEQ ID NO: 14168	RTT*83 (PAM silencing)
14169	SEQ ID NO: 14169	RTT
14170	SEQ ID NO: 14170	RTT*80 (PAM silencing)
14171	SEQ ID NO: 14171	RTT*83 (PAM silencing)
14172	SEQ ID NO: 14172	RTT
14173	SEQ ID NO: 14173	RTT*82 (PAM silencing)
14174	SEQ ID NO: 14174	RTT*81 (PAM silencing)
14175	SEQ ID NO: 14175	RTT
14176	SEQ ID NO: 14176	RTT*81 (PAM silencing)
14177	SEQ ID NO: 14177	RTT*80 (PAM silencing)
14178	SEQ ID NO: 14178	RTT*82 (PAM silencing)
14179	SEQ ID NO: 14179	RTT*83 (PAM silencing)
14180	SEQ ID NO: 14180	RTT*81 (PAM silencing)
14181	SEQ ID NO: 14181	RTT*82 (PAM silencing)
14182	SEQ ID NO: 14182	RTT*80 (PAM silencing)
14183	SEQ ID NO: 14183	RTT*83 (PAM silencing)
14184	SEQ ID NO: 14184	RTT
14185	SEQ ID NO: 14185	RTT*82 (PAM silencing)
14186	SEQ ID NO: 14186	RTT*81 (PAM silencing)
14187	SEQ ID NO: 14187	RTT*80 (PAM silencing)
14188	SEQ ID NO: 14188	RTT
14189	SEQ ID NO: 14189	RTT*83 (PAM silencing)
14190	SEQ ID NO: 14190	RTT
14191	SEQ ID NO: 14191	RTT*83 (PAM silencing)
14192	SEQ ID NO: 14192	RTT*80 (PAM silencing)
14193	SEQ ID NO: 14193	RTT*82 (PAM silencing)
14194	SEQ ID NO: 14194	RTT*81 (PAM silencing)
14195	SEQ ID NO: 14195	RTT*83 (PAM silencing)
14196	SEQ ID NO: 14196	RTT*80 (PAM silencing)
14197	SEQ ID NO: 14197	RTT
14198	SEQ ID NO: 14198	RTT*82 (PAM silencing)
14199	SEQ ID NO: 14199	RTT*81 (PAM silencing)
14200	SEQ ID NO: 14200	RTT*81 (PAM silencing)
14201	SEQ ID NO: 14201	RTT*80 (PAM silencing)
14202	SEQ ID NO: 14202	RTT
14203	SEQ ID NO: 14203	RTT*82 (PAM silencing)
14204	SEQ ID NO: 14204	RTT*83 (PAM silencing)
14205	SEQ ID NO: 14205	RTT
14206	SEQ ID NO: 14206	RTT*81 (PAM silencing)
14207	SEQ ID NO: 14207	RTT*80 (PAM silencing)
14208	SEQ ID NO: 14208	RTT*82 (PAM silencing)
14209	SEQ ID NO: 14209	RTT*83 (PAM silencing)
14210	SEQ ID NO: 14210	RTT*83 (PAM silencing)
14211	SEQ ID NO: 14211	RTT*80 (PAM silencing)
14212	SEQ ID NO: 14212	RTT
14213	SEQ ID NO: 14213	RTT*81 (PAM silencing)

Sequence Number	Sequence	Description
14214	SEQ ID NO: 14214	RTT*82 (PAM silencing)
14215	SEQ ID NO: 14215	RTT*81 (PAM silencing)
14216	SEQ ID NO: 14216	RTT*82 (PAM silencing)
14217	SEQ ID NO: 14217	RTT
14218	SEQ ID NO: 14218	RTT*80 (PAM silencing)
14219	SEQ ID NO: 14219	RTT*83 (PAM silencing)
14220	SEQ ID NO: 14220	RTT*80 (PAM silencing)
14221	SEQ ID NO: 14221	RTT*81 (PAM silencing)
14222	SEQ ID NO: 14222	RTT*83 (PAM silencing)
14223	SEQ ID NO: 14223	RTT*82 (PAM silencing)
14224	SEQ ID NO: 14224	RTT
14225	SEQ ID NO: 14225	RTT*82 (PAM silencing)
14226	SEQ ID NO: 14226	RTT*80 (PAM silencing)
14227	SEQ ID NO: 14227	RTT*81 (PAM silencing)
14228	SEQ ID NO: 14228	RTT*83 (PAM silencing)
14229	SEQ ID NO: 14229	RTT
14230	SEQ ID NO: 14230	RTT*81 (PAM silencing)
14231	SEQ ID NO: 14231	RTT*82 (PAM silencing)
14232	SEQ ID NO: 14232	RTT*80 (PAM silencing)
14233	SEQ ID NO: 14233	RTT
14234	SEQ ID NO: 14234	RTT*83 (PAM silencing)
14235	SEQ ID NO: 14235	RTT*83 (PAM silencing)
14236	SEQ ID NO: 14236	RTT
14237	SEQ ID NO: 14237	RTT*80 (PAM silencing)
14238	SEQ ID NO: 14238	RTT*82 (PAM silencing)
14239	SEQ ID NO: 14239	RTT*81 (PAM silencing)
14240	SEQ ID NO: 14240	RTT*80 (PAM silencing)
14241	SEQ ID NO: 14241	RTT*81 (PAM silencing)
14242	SEQ ID NO: 14242	RTT*82 (PAM silencing)
14243	SEQ ID NO: 14243	RTT
14244	SEQ ID NO: 14244	RTT*83 (PAM silencing)
14245	SEQ ID NO: 14245	RTT*81 (PAM silencing)
14246	SEQ ID NO: 14246	RTT*82 (PAM silencing)
14247	SEQ ID NO: 14247	RTT*83 (PAM silencing)
14248	SEQ ID NO: 14248	RTT
14249	SEQ ID NO: 14249	RTT*80 (PAM silencing)
14250	SEQ ID NO: 14250	RTT*81 (PAM silencing)
14251	SEQ ID NO: 14251	RTT*80 (PAM silencing)
14252	SEQ ID NO: 14252	RTT*82 (PAM silencing)
14253	SEQ ID NO: 14253	RTT*83 (PAM silencing)
14254	SEQ ID NO: 14254	RTT
14255	SEQ ID NO: 14255	RTT*82 (PAM silencing)
14256	SEQ ID NO: 14256	RTT*80 (PAM silencing)
14257	SEQ ID NO: 14257	RTT*83 (PAM silencing)
14258	SEQ ID NO: 14258	RTT*81 (PAM silencing)
14259	SEQ ID NO: 14259	RTT
14260	SEQ ID NO: 14260	RTT
14261	SEQ ID NO: 14261	RTT*80 (PAM silencing)
14262	SEQ ID NO: 14262	RTT*82 (PAM silencing)
14263	SEQ ID NO: 14263	RTT*83 (PAM silencing)
14264	SEQ ID NO: 14264	RTT*81 (PAM silencing)
14265	SEQ ID NO: 14265	RTT*81 (PAM silencing)
14266	SEQ ID NO: 14266	RTT*83 (PAM silencing)
14267	SEQ ID NO: 14267	RTT
14268	SEQ ID NO: 14268	RTT*80 (PAM silencing)
14269	SEQ ID NO: 14269	RTT*82 (PAM silencing)
14270	SEQ ID NO: 14270	RTT*81 (PAM silencing)
14271	SEQ ID NO: 14271	RTT*82 (PAM silencing)
14272	SEQ ID NO: 14272	RTT
14273	SEQ ID NO: 14273	RTT*83 (PAM silencing)
14274	SEQ ID NO: 14274	RTT*80 (PAM silencing)
14275	SEQ ID NO: 14275	RTT*80 (PAM silencing)
14276	SEQ ID NO: 14276	RTT*82 (PAM silencing)
14277	SEQ ID NO: 14277	RTT
14278	SEQ ID NO: 14278	RTT*81 (PAM silencing)
14279	SEQ ID NO: 14279	RTT*83 (PAM silencing)
14280	SEQ ID NO: 14280	RTT
14281	SEQ ID NO: 14281	RTT*82 (PAM silencing)
14282	SEQ ID NO: 14282	RTT*83 (PAM silencing)
14283	SEQ ID NO: 14283	RTT*80 (PAM silencing)
14284	SEQ ID NO: 14284	RTT*81 (PAM silencing)

Sequence Number	Sequence	Description
14285	SEQ ID NO: 14285	RTT*82 (PAM silencing)
14286	SEQ ID NO: 14286	RTT*80 (PAM silencing)
14287	SEQ ID NO: 14287	RTT*83 (PAM silencing)
14288	SEQ ID NO: 14288	RTT*81 (PAM silencing)
14289	SEQ ID NO: 14289	RTT
14290	SEQ ID NO: 14290	RTT*83 (PAM silencing)
14291	SEQ ID NO: 14291	RTT*82 (PAM silencing)
14292	SEQ ID NO: 14292	RTT*80 (PAM silencing)
14293	SEQ ID NO: 14293	RTT*81 (PAM silencing)
14294	SEQ ID NO: 14294	RTT
14295	SEQ ID NO: 14295	RTT
14296	SEQ ID NO: 14296	RTT*82 (PAM silencing)
14297	SEQ ID NO: 14297	RTT*81 (PAM silencing)
14298	SEQ ID NO: 14298	RTT*83 (PAM silencing)
14299	SEQ ID NO: 14299	RTT*80 (PAM silencing)
14300	SEQ ID NO: 14300	RTT*80 (PAM silencing)
14301	SEQ ID NO: 14301	RTT*81 (PAM silencing)
14302	SEQ ID NO: 14302	RTT*82 (PAM silencing)
14303	SEQ ID NO: 14303	RTT
14304	SEQ ID NO: 14304	RTT*83 (PAM silencing)
14305	SEQ ID NO: 14305	RTT*82 (PAM silencing)
14306	SEQ ID NO: 14306	RTT*80 (PAM silencing)
14307	SEQ ID NO: 14307	RTT*83 (PAM silencing)
14308	SEQ ID NO: 14308	RTT*81 (PAM silencing)
14309	SEQ ID NO: 14309	RTT
14310	SEQ ID NO: 14310	RTT*83 (PAM silencing)
14311	SEQ ID NO: 14311	RTT*82 (PAM silencing)
14312	SEQ ID NO: 14312	RTT*80 (PAM silencing)
14313	SEQ ID NO: 14313	RTT*81 (PAM silencing)
14314	SEQ ID NO: 14314	RTT
14315	SEQ ID NO: 14315	RTT*81 (PAM silencing)
14316	SEQ ID NO: 14316	RTT*80 (PAM silencing)
14317	SEQ ID NO: 14317	RTT*83 (PAM silencing)
14318	SEQ ID NO: 14318	RTT
14319	SEQ ID NO: 14319	RTT*82 (PAM silencing)
14320	SEQ ID NO: 14320	RTT*83 (PAM silencing)
14321	SEQ ID NO: 14321	RTT
14322	SEQ ID NO: 14322	RTT*82 (PAM silencing)
14323	SEQ ID NO: 14323	RTT*80 (PAM silencing)
14324	SEQ ID NO: 14324	RTT*81 (PAM silencing)
14325	SEQ ID NO: 14325	RTT*81 (PAM silencing)
14326	SEQ ID NO: 14326	RTT
14327	SEQ ID NO: 14327	RTT*80 (PAM silencing)
14328	SEQ ID NO: 14328	RTT*83 (PAM silencing)
14329	SEQ ID NO: 14329	RTT*82 (PAM silencing)
14330	SEQ ID NO: 14330	RTT*80 (PAM silencing)
14331	SEQ ID NO: 14331	RTT
14332	SEQ ID NO: 14332	RTT*81 (PAM silencing)
14333	SEQ ID NO: 14333	RTT*83 (PAM silencing)
14334	SEQ ID NO: 14334	RTT*82 (PAM silencing)
14335	SEQ ID NO: 14335	RTT
14336	SEQ ID NO: 14336	RTT*82 (PAM silencing)
14337	SEQ ID NO: 14337	RTT*81 (PAM silencing)
14338	SEQ ID NO: 14338	RTT*80 (PAM silencing)
14339	SEQ ID NO: 14339	RTT*83 (PAM silencing)
14340	SEQ ID NO: 14340	RTT*83 (PAM silencing)
14341	SEQ ID NO: 14341	RTT*81 (PAM silencing)
14342	SEQ ID NO: 14342	RTT*82 (PAM silencing)
14343	SEQ ID NO: 14343	RTT
14344	SEQ ID NO: 14344	RTT*80 (PAM silencing)
14345	SEQ ID NO: 14345	RTT
14346	SEQ ID NO: 14346	RTT*83 (PAM silencing)
14347	SEQ ID NO: 14347	RTT*81 (PAM silencing)
14348	SEQ ID NO: 14348	RTT*82 (PAM silencing)
14349	SEQ ID NO: 14349	RTT*80 (PAM silencing)
14350	SEQ ID NO: 14350	RTT*83 (PAM silencing)
14351	SEQ ID NO: 14351	RTT*80 (PAM silencing)
14352	SEQ ID NO: 14352	RTT*81 (PAM silencing)
14353	SEQ ID NO: 14353	RTT*82 (PAM silencing)
14354	SEQ ID NO: 14354	RTT

Sequence Number	Sequence	Description
14355	SEQ ID NO: 14355	RTT*83 (PAM silencing)
14356	SEQ ID NO: 14356	RTT
14357	SEQ ID NO: 14357	RTT*81 (PAM silencing)
14358	SEQ ID NO: 14358	RTT*80 (PAM silencing)
14359	SEQ ID NO: 14359	RTT*82 (PAM silencing)
14360	SEQ ID NO: 14360	RTT*80 (PAM silencing)
14361	SEQ ID NO: 14361	RTT*81 (PAM silencing)
14362	SEQ ID NO: 14362	RTT*83 (PAM silencing)
14363	SEQ ID NO: 14363	RTT
14364	SEQ ID NO: 14364	RTT*82 (PAM silencing)
14365	SEQ ID NO: 14365	RTT*80 (PAM silencing)
14366	SEQ ID NO: 14366	RTT
14367	SEQ ID NO: 14367	RTT*82 (PAM silencing)
14368	SEQ ID NO: 14368	RTT*83 (PAM silencing)
14369	SEQ ID NO: 14369	RTT*81 (PAM silencing)
14370	SEQ ID NO: 14370	RTT*83 (PAM silencing)
14371	SEQ ID NO: 14371	RTT*80 (PAM silencing)
14372	SEQ ID NO: 14372	RTT*82 (PAM silencing)
14373	SEQ ID NO: 14373	RTT
14374	SEQ ID NO: 14374	RTT*81 (PAM silencing)
14375	SEQ ID NO: 14375	RTT*83 (PAM silencing)
14376	SEQ ID NO: 14376	RTT
14377	SEQ ID NO: 14377	RTT*80 (PAM silencing)
14378	SEQ ID NO: 14378	RTT*82 (PAM silencing)
14379	SEQ ID NO: 14379	RTT*81 (PAM silencing)
14380	SEQ ID NO: 14380	RTT*82 (PAM silencing)
14381	SEQ ID NO: 14381	RTT*83 (PAM silencing)
14382	SEQ ID NO: 14382	RTT*81 (PAM silencing)
14383	SEQ ID NO: 14383	RTT
14384	SEQ ID NO: 14384	RTT*80 (PAM silencing)
14385	SEQ ID NO: 14385	RTT*80 (PAM silencing)
14386	SEQ ID NO: 14386	RTT*83 (PAM silencing)
14387	SEQ ID NO: 14387	RTT*82 (PAM silencing)
14388	SEQ ID NO: 14388	RTT
14389	SEQ ID NO: 14389	RTT*81 (PAM silencing)
14390	SEQ ID NO: 14390	RTT*82 (PAM silencing)
14391	SEQ ID NO: 14391	RTT*80 (PAM silencing)
14392	SEQ ID NO: 14392	RTT
14393	SEQ ID NO: 14393	RTT*81 (PAM silencing)
14394	SEQ ID NO: 14394	RTT*83 (PAM silencing)
14395	SEQ ID NO: 14395	RTT*82 (PAM silencing)
14396	SEQ ID NO: 14396	RTT*83 (PAM silencing)
14397	SEQ ID NO: 14397	RTT*81 (PAM silencing)
14398	SEQ ID NO: 14398	RTT
14399	SEQ ID NO: 14399	RTT*80 (PAM silencing)
14400	SEQ ID NO: 14400	RTT*82 (PAM silencing)
14401	SEQ ID NO: 14401	RTT*81 (PAM silencing)
14402	SEQ ID NO: 14402	RTT*83 (PAM silencing)
14403	SEQ ID NO: 14403	RTT
14404	SEQ ID NO: 14404	RTT*80 (PAM silencing)
14405	SEQ ID NO: 14405	RTT*80 (PAM silencing)
14406	SEQ ID NO: 14406	RTT*82 (PAM silencing)
14407	SEQ ID NO: 14407	RTT
14408	SEQ ID NO: 14408	RTT*81 (PAM silencing)
14409	SEQ ID NO: 14409	RTT*83 (PAM silencing)
14410	SEQ ID NO: 14410	RTT*80 (PAM silencing)
14411	SEQ ID NO: 14411	RTT*81 (PAM silencing)
14412	SEQ ID NO: 14412	RTT
14413	SEQ ID NO: 14413	RTT*83 (PAM silencing)
14414	SEQ ID NO: 14414	RTT*82 (PAM silencing)
14415	SEQ ID NO: 14415	RTT*82 (PAM silencing)
14416	SEQ ID NO: 14416	RTT*83 (PAM silencing)
14417	SEQ ID NO: 14417	RTT
14418	SEQ ID NO: 14418	RTT*81 (PAM silencing)
14419	SEQ ID NO: 14419	RTT*80 (PAM silencing)
14420	SEQ ID NO: 14420	RTT*80 (PAM silencing)
14421	SEQ ID NO: 14421	RTT*83 (PAM silencing)
14422	SEQ ID NO: 14422	RTT*81 (PAM silencing)
14423	SEQ ID NO: 14423	RTT*82 (PAM silencing)
14424	SEQ ID NO: 14424	RTT
14425	SEQ ID NO: 14425	RTT*83 (PAM silencing)

Sequence Number	Sequence	Description
14426	SEQ ID NO: 14426	RTT*80 (PAM silencing)
14427	SEQ ID NO: 14427	RTT*82 (PAM silencing)
14428	SEQ ID NO: 14428	RTT*81 (PAM silencing)
14429	SEQ ID NO: 14429	RTT
14430	SEQ ID NO: 14430	RTT*80 (PAM silencing)
14431	SEQ ID NO: 14431	RTT
14432	SEQ ID NO: 14432	RTT*82 (PAM silencing)
14433	SEQ ID NO: 14433	RTT*83 (PAM silencing)
14434	SEQ ID NO: 14434	RTT*81 (PAM silencing)
14435	SEQ ID NO: 14435	RTT*81 (PAM silencing)
14436	SEQ ID NO: 14436	RTT
14437	SEQ ID NO: 14437	RTT*80 (PAM silencing)
14438	SEQ ID NO: 14438	RTT*83 (PAM silencing)
14439	SEQ ID NO: 14439	RTT*82 (PAM silencing)
14440	SEQ ID NO: 14440	RTT*82 (PAM silencing)
14441	SEQ ID NO: 14441	RTT*80 (PAM silencing)
14442	SEQ ID NO: 14442	RTT
14443	SEQ ID NO: 14443	RTT*83 (PAM silencing)
14444	SEQ ID NO: 14444	RTT*81 (PAM silencing)
14445	SEQ ID NO: 14445	RTT*81 (PAM silencing)
14446	SEQ ID NO: 14446	RTT
14447	SEQ ID NO: 14447	RTT*82 (PAM silencing)
14448	SEQ ID NO: 14448	RTT*80 (PAM silencing)
14449	SEQ ID NO: 14449	RTT*83 (PAM silencing)
14450	SEQ ID NO: 14450	RTT*80 (PAM silencing)
14451	SEQ ID NO: 14451	RTT*82 (PAM silencing)
14452	SEQ ID NO: 14452	RTT*81 (PAM silencing)
14453	SEQ ID NO: 14453	RTT
14454	SEQ ID NO: 14454	RTT*83 (PAM silencing)
14455	SEQ ID NO: 14455	RTT*80 (PAM silencing)
14456	SEQ ID NO: 14456	RTT*82 (PAM silencing)
14457	SEQ ID NO: 14457	RTT*81 (PAM silencing)
14458	SEQ ID NO: 14458	RTT
14459	SEQ ID NO: 14459	RTT*83 (PAM silencing)
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAGG PAM)
1226	SEQ ID NO: 1226	PE3b*83 ngRNA spacer (AAGG;AGGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer (AGGG PAM)
1216	SEQ ID NO: 1216	PE3 ngRNA spacer (GAGG PAM)
1236	SEQ ID NO: 1236	PE3b*81 ngRNA spacer (AGGG PAM)
1225	SEQ ID NO: 1225	PE3b*82 ngRNA spacer (AGGG PAM)
1244	SEQ ID NO: 1244	PE3 ngRNA spacer (AAGG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer
		(CAGG PAM)
104	SEQ ID NO: 104	ngRNA (AGGG PAM)
117	SEQ ID NO: 117	ngRNA (AGGG PAM)

Table 80

Sequence Number	Sequence	Description
14460	SEQ ID NO: 14460	PEgRNA spacer (GTGG PAM)
14461	SEQ ID NO: 14461	PEgRNA spacer (GTGG PAM)
14462	SEQ ID NO: 14462	PEgRNA spacer (GTGG PAM)
14463	SEQ ID NO: 14463	PEgRNA spacer (GTGG PAM)
14464	SEQ ID NO: 14464	PEgRNA spacer (GTGG PAM)
14465	SEQ ID NO: 14465	PEgRNA spacer (GTGG PAM)
14466	SEQ ID NO: 14466	PEgRNA spacer (GTGG PAM)
14467	CCC	PBS
14468	CCCA	PBS
14469	CCCAG	PBS
14470	CCCAGG	PBS
14471	CCCAGGG	PBS
14472	CCCAGGGC	PBS
14473	CCCAGGGCA	PBS
14474	SEQ ID NO: 14474	PBS
14475	SEQ ID NO: 14475	PBS
14476	SEQ ID NO: 14476	PBS
14477	SEQ ID NO: 14477	PBS
14478	SEQ ID NO: 14478	PBS
14479	SEQ ID NO: 14479	PBS
14480	SEQ ID NO: 14480	PBS
14481	SEQ ID NO: 14481	PBS

Sequence Number	Sequence	Description
14482	SEQ ID NO: 14482	PBS
14483	SEQ ID NO: 14483	PBS
14484	SEQ ID NO: 14484	RTT
14485	SEQ ID NO: 14485	RTT
14486	SEQ ID NO: 14486	RTT
14487	SEQ ID NO: 14487	RTT
14488	SEQ ID NO: 14488	RTT
14489	SEQ ID NO: 14489	RTT
14490	SEQ ID NO: 14490	RTT
14491	SEQ ID NO: 14491	RTT
14492	SEQ ID NO: 14492	RTT
14493	SEQ ID NO: 14493	RTT
14494	SEQ ID NO: 14494	RTT
14495	SEQ ID NO: 14495	RTT
14496	SEQ ID NO: 14496	RTT
14497	SEQ ID NO: 14497	RTT
14498	SEQ ID NO: 14498	RTT
14499	SEQ ID NO: 14499	RTT
14500	SEQ ID NO: 14500	RTT
14501	SEQ ID NO: 14501	RTT
14502	SEQ ID NO: 14502	RTT
14503	SEQ ID NO: 14503	RTT
14504	SEQ ID NO: 14504	RTT
14505	SEQ ID NO: 14505	RTT
14506	SEQ ID NO: 14506	RTT
14507	SEQ ID NO: 14507	RTT
14508	SEQ ID NO: 14508	RTT
14509	SEQ ID NO: 14509	RTT
14510	SEQ ID NO: 14510	RTT
14511	SEQ ID NO: 14511	RTT
14512	SEQ ID NO: 14512	RTT
14513	SEQ ID NO: 14513	RTT
14514	SEQ ID NO: 14514	RTT

Sequence Number	Sequence	Description
14515	SEQ ID NO: 14515	RTT
14516	SEQ ID NO: 14516	RTT
14517	SEQ ID NO: 14517	RTT
14518	SEQ ID NO: 14518	RTT
14519	SEQ ID NO: 14519	RTT
14520	SEQ ID NO: 14520	RTT
14521	SEQ ID NO: 14521	RTT
14522	SEQ ID NO: 14522	RTT
14523	SEQ ID NO: 14523	RTT
14524	SEQ ID NO: 14524	RTT
14525	SEQ ID NO: 14525	RTT
14526	SEQ ID NO: 14526	RTT
14527	SEQ ID NO: 14527	RTT
14528	SEQ ID NO: 14528	RTT
14529	SEQ ID NO: 14529	RTT
14530	SEQ ID NO: 14530	RTT
14531	SEQ ID NO: 14531	RTT
14532	SEQ ID NO: 14532	RTT
14533	SEQ ID NO: 14533	RTT
14534	SEQ ID NO: 14534	RTT
14535	SEQ ID NO: 14535	RTT
14536	SEQ ID NO: 14536	RTT
14537	SEQ ID NO: 14537	RTT
14538	SEQ ID NO: 14538	RTT
14539	SEQ ID NO: 14539	RTT
14540	SEQ ID NO: 14540	RTT
14541	SEQ ID NO: 14541	RTT
14542	SEQ ID NO: 14542	RTT
14543	SEQ ID NO: 14543	RTT
14544	SEQ ID NO: 14544	RTT
14545	SEQ ID NO: 14545	RTT
14546	SEQ ID NO: 14546	RTT
14547	SEQ ID NO: 14547	RTT

Sequence Number	Sequence	Description
14548	SEQ ID NO: 14548	RTT
14549	SEQ ID NO: 14549	RTT
14550	SEQ ID NO: 14550	RTT
14551	SEQ ID NO: 14551	RTT
14552	SEQ ID NO: 14552	RTT
14553	SEQ ID NO: 14553	RTT
14554	SEQ ID NO: 14554	RTT
14555	SEQ ID NO: 14555	RTT
14556	SEQ ID NO: 14556	RTT
14557	SEQ ID NO: 14557	RTT
14558	SEQ ID NO: 14558	RTT
14559	SEQ ID NO: 14559	RTT
14560	SEQ ID NO: 14560	RTT
14561	SEQ ID NO: 14561	RTT
14562	SEQ ID NO: 14562	RTT
14563	SEQ ID NO: 14563	RTT
14564	SEQ ID NO: 14564	RTT
14565	SEQ ID NO: 14565	RTT
14566	SEQ ID NO: 14566	RTT
14567	SEQ ID NO: 14567	RTT
14568	SEQ ID NO: 14568	RTT
14569	SEQ ID NO: 14569	RTT
14570	SEQ ID NO: 14570	RTT
14571	SEQ ID NO: 14571	RTT
14572	SEQ ID NO: 14572	RTT
14573	SEQ ID NO: 14573	RTT
14574	SEQ ID NO: 14574	RTT
1224	SEQ ID NO: 1224	PE3b ngRNA spacer (CAGG PAM)
1216	SEQ ID NO: 1216	PE3 ngRNA spacer (GAGG PAM)
93	SEQ ID NO: 93	PE3b ngRNA spacer

Sequence Number	Sequence	Description
		(AGGG PAM)
1227	SEQ ID NO: 1227	PE3 ngRNA spacer (CAGG PAM)
1244	SEQ ID NO: 1244	PE3 ngRNA spacer (AAGG PAM)
14575	SEQ ID NO: 14575	PE3 ngRNA spacer (ATGG PAM)
104	SEQ ID NO: 104	ngRNA (AGGG PAM)
117	SEQ ID NO: 117	ngRNA (AGGG PAM)

Table 81

Sequence Number	Sequence	Description
14576	SEQ ID NO: 14576	PEgRNA spacer (ATGG PAM)
14577	SEQ ID NO: 14577	PEgRNA spacer (ATGG PAM)
14578	SEQ ID NO: 14578	PEgRNA spacer (ATGG PAM)
14579	SEQ ID NO: 14579	PEgRNA spacer (ATGG PAM)
14580	SEQ ID NO: 14580	PEgRNA spacer (ATGG PAM)
14581	SEQ ID NO: 14581	PEgRNA spacer (ATGG PAM)
14582	SEQ ID NO: 14582	PEgRNA spacer (ATGG PAM)
14583	TAG	PBS
14584	TAGA	PBS
14585	TAGAA	PBS
14586	TAGAAT	PBS
14587	TAGAAT T	PBS
14588	TAGAAT TA	PBS
14589	TAGAAT TAC	PBS
14590	SEQ ID NO: 14590	PBS
14591	SEQ ID NO: 14591	PBS
14592	SEQ ID NO: 14592	PBS
14593	SEQ ID NO: 14593	PBS
14594	SEQ ID NO: 14594	PBS
14595	SEQ ID NO: 14595	PBS
14596	SEQ ID NO: 14596	PBS
14597	SEQ ID NO: 14597	PBS
14598	SEQ ID NO: 14598	PBS
14599	SEQ ID NO: 14599	PBS
14600	SEQ ID NO: 14600	RTT
14601	SEQ ID NO: 14601	RTT
14602	SEQ ID NO: 14602	RTT
14603	SEQ ID NO: 14603	RTT
7159	SEQ ID NO: 7159	PE3b ngRNA spacer (TTGG PAM)
7112	SEQ ID NO: 7112	PE3b ngRNA spacer (AAGG PAM)
7117	SEQ ID NO: 7117	PE3 ngRNA spacer (CAGG PAM)
7157	SEQ ID NO: 7157	PE3b ngRNA spacer (CTGG PAM)
7156	SEQ ID NO: 7156	PE3b ngRNA spacer (GTGG PAM)

Table 82

Sequence Number	Sequence	Description
14604	SEQ ID NO: 14604	PEgRNA spacer (CCTGGT PAM)
14605	SEQ ID NO: 14605	PEgRNA spacer (CCTGGT PAM)
14606	SEQ ID NO: 14606	PEgRNA spacer (CCTGGT PAM)
14607	SEQ ID NO: 14607	PEgRNA spacer (CCTGGT PAM)
14608	SEQ ID NO: 14608	PEgRNA spacer (CCTGGT PAM)
14609	SEQ ID NO: 14609	PEgRNA spacer (CCTGGT PAM)
14610	SEQ ID NO: 14610	PEgRNA spacer (CCTGGT PAM)
7082	ACC	PBS
7083	ACCA	PBS
9905	ACCAG	PBS
14611	ACCAGA	PBS
14612	ACCAGA G	PBS
14613	ACCAGA GA	PBS
14614	ACCAGA GAA	PBS
14615	SEQ ID NO: 14615	PBS
14616	SEQ ID NO: 14616	PBS
14617	SEQ ID NO: 14617	PBS
14618	SEQ ID NO: 14618	PBS
14619	SEQ ID NO: 14619	PBS
14620	SEQ ID NO: 14620	PBS
14621	SEQ ID NO: 14621	PBS
14622	SEQ ID NO: 14622	PBS
14623	SEQ ID NO: 14623	PBS
14624	SEQ ID NO: 14624	PBS
14625	SEQ ID NO: 14625	RTT*69 (PAM silencing)
14626	SEQ ID NO: 14626	RTT
14627	SEQ ID NO: 14627	RTT*68 (PAM silencing)
14628	SEQ ID NO: 14628	RTT*68 (PAM silencing)
14629	SEQ ID NO: 14629	RTT*69 (PAM silencing)
14630	SEQ ID NO: 14630	RTT
14631	SEQ ID NO: 14631	RTT
14632	SEQ ID NO: 14632	RTT*68 (PAM silencing)

Sequence Number	Sequence	Description
14633	SEQ ID NO: 14633	RTT*69 (PAM silencing)
14634	SEQ ID NO: 14634	RTT*69 (PAM silencing)
14635	SEQ ID NO: 14635	RTT*68 (PAM silencing)
14636	SEQ ID NO: 14636	RTT
14637	SEQ ID NO: 14637	RTT
14638	SEQ ID NO: 14638	RTT*68 (PAM silencing)
14639	SEQ ID NO: 14639	RTT*69 (PAM silencing)
6455	SEQ ID NO: 6455	PE3 ngRNA spacer (CAGGAT PAM)
6453	SEQ ID NO: 6453	PE3 ngRNA spacer (AAGAA T PAM)
70	SEQ ID NO: 70	PE3b ngRNA spacer (GGCAAT PAM)

Table 83

Sequence Number	Sequence	Description
14640	SEQ ID NO: 14640	PEgRNA spacer (CATGGT PAM)
14641	SEQ ID NO: 14641	PEgRNA spacer (CATGGT PAM)
14642	SEQ ID NO: 14642	PEgRNA spacer (CATGGT PAM)
14643	SEQ ID NO: 14643	PEgRNA spacer (CATGGT PAM)
14644	SEQ ID NO: 14644	PEgRNA spacer (CATGGT PAM)
14645	SEQ ID NO: 14645	PEgRNA spacer (CATGGT PAM)
14646	SEQ ID NO: 14646	PEgRNA spacer (CATGGT PAM)
10833	AGA	PBS
14647	AGAA	PBS
14648	AGAAT	PBS
14649	AGAATT	PBS
14650	AGAATT A	PBS
14651	AGAATT AC	PBS
14652	AGAATT ACT	PBS
14653	SEQ ID NO: 14653	PBS
14654	SEQ ID NO: 14654	PBS
14655	SEQ ID NO: 14655	PBS
14656	SEQ ID NO: 14656	PBS
14657	SEQ ID NO: 14657	PBS
14658	SEQ ID NO: 14658	PBS
14659	SEQ ID NO: 14659	PBS
14660	SEQ ID NO: 14660	PBS
14661	SEQ ID NO: 14661	PBS
14662	SEQ ID NO: 14662	PBS
14663	SEQ ID NO: 14663	RTT
14664	SEQ ID NO: 14664	RTT
14665	SEQ ID NO: 14665	RTT
6000	SEQ ID NO: 6000	PE3 ngRNA spacer (ACAAAT PAM)
6001	SEQ ID NO: 6001	PE3 ngRNA spacer (TTCAGT PAM)
6454	SEQ ID NO: 6454	PE3 ngRNA spacer (TAGAAT PAM)
6002	SEQ ID NO: 6002	PE3 ngRNA spacer (TCAGGT PAM)
5999	SEQ ID NO: 5999	PE3b ngRNA spacer (AAAGG T PAM)

Table 84

Sequence Number	Sequence	Description
14666	SEQ ID NO: 14666	PEgRNA spacer (CCAAGT PAM)
14667	SEQ ID NO: 14667	PEgRNA spacer (CCAAGT PAM)
14668	SEQ ID NO: 14668	PEgRNA spacer (CCAAGT PAM)
14669	SEQ ID NO: 14669	PEgRNA spacer (CCAAGT PAM)
14670	SEQ ID NO: 14670	PEgRNA spacer (CCAAGT PAM)
14671	SEQ ID NO: 14671	PEgRNA spacer (CCAAGT PAM)
14672	SEQ ID NO: 14672	PEgRNA spacer (CCAAGT PAM)
9870	AGG	PBS
14673	AGGT	PBS
14674	AGGTA	PBS
14675	AGGTAA	PBS
14676	AGGTAA C	PBS
14677	AGGTAA CA	PBS
14678	AGGTAA CAG	PBS
14679	SEQ ID NO: 14679	PBS
14680	SEQ ID NO: 14680	PBS
14681	SEQ ID NO: 14681	PBS
14682	SEQ ID NO: 14682	PBS
14683	SEQ ID NO: 14683	PBS
14684	SEQ ID NO: 14684	PBS
14685	SEQ ID NO: 14685	PBS
14686	SEQ ID NO: 14686	PBS
14687	SEQ ID NO: 14687	PBS
14688	SEQ ID NO: 14688	PBS
14689	SEQ ID NO: 14689	RTT
14690	SEQ ID NO: 14690	RTT
14691	SEQ ID NO: 14691	RTT
14692	SEQ ID NO: 14692	RTT
14693	SEQ ID NO: 14693	RTT

Sequence Number	Sequence	Description
14694	SEQ ID NO: 14694	RTT
14695	SEQ ID NO: 14695	RTT
14696	SEQ ID NO: 14696	RTT
14697	SEQ ID NO: 14697	RTT
14698	SEQ ID NO: 14698	RTT
14699	SEQ ID NO: 14699	RTT
14700	SEQ ID NO: 14700	RTT
14701	SEQ ID NO: 14701	RTT
14702	SEQ ID NO: 14702	RTT
14703	SEQ ID NO: 14703	RTT
14704	SEQ ID NO: 14704	RTT
14705	SEQ ID NO: 14705	RTT
14706	SEQ ID NO: 14706	RTT
14707	SEQ ID NO: 14707	RTT
14708	SEQ ID NO: 14708	RTT
14709	SEQ ID NO: 14709	RTT
14710	SEQ ID NO: 14710	RTT
14711	SEQ ID NO: 14711	RTT
14712	SEQ ID NO: 14712	RTT
14713	SEQ ID NO: 14713	RTT
14714	SEQ ID NO: 14714	RTT
14715	SEQ ID NO: 14715	RTT
14716	SEQ ID NO: 14716	RTT
14717	SEQ ID NO: 14717	RTT
14718	SEQ ID NO: 14718	RTT
14719	SEQ ID NO: 14719	RTT
14720	SEQ ID NO: 14720	RTT
14721	SEQ ID NO: 14721	RTT
14722	SEQ ID NO: 14722	RTT
14723	SEQ ID NO: 14723	RTT
14724	SEQ ID NO: 14724	RTT
14725	SEQ ID NO: 14725	RTT
14726	SEQ ID NO: 14726	RTT

Sequence Number	Sequence	Description
14727	SEQ ID NO: 14727	RTT
14728	SEQ ID NO: 14728	RTT
14729	SEQ ID NO: 14729	RTT
14730	SEQ ID NO: 14730	RTT
14731	SEQ ID NO: 14731	RTT
14732	SEQ ID NO: 14732	RTT
14733	SEQ ID NO: 14733	RTT
14734	SEQ ID NO: 14734	RTT
14735	SEQ ID NO: 14735	RTT
14736	SEQ ID NO: 14736	RTT
14737	SEQ ID NO: 14737	RTT
14738	SEQ ID NO: 14738	RTT
14739	SEQ ID NO: 14739	RTT
14740	SEQ ID NO: 14740	RTT
14741	SEQ ID NO: 14741	RTT
14742	SEQ ID NO: 14742	RTT
14743	SEQ ID NO: 14743	RTT
14744	SEQ ID NO: 14744	RTT
14745	SEQ ID NO: 14745	RTT
14746	SEQ ID NO: 14746	RTT
14747	SEQ ID NO: 14747	RTT
14748	SEQ ID NO: 14748	RTT
14749	SEQ ID NO: 14749	RTT
14750	SEQ ID NO: 14750	RTT
14751	SEQ ID NO: 14751	RTT
14752	SEQ ID NO: 14752	RTT
14753	SEQ ID NO: 14753	RTT
14754	SEQ ID NO: 14754	RTT
14755	SEQ ID NO: 14755	RTT
14756	SEQ ID NO: 14756	RTT
14757	SEQ ID NO: 14757	RTT
14758	SEQ ID NO: 14758	RTT
14759	SEQ ID NO: 14759	RTT

Sequence Number	Sequence	Description
14760	SEQ ID NO: 14760	RTT
14761	SEQ ID NO: 14761	RTT
14762	SEQ ID NO: 14762	RTT
14763	SEQ ID NO: 14763	RTT
14764	SEQ ID NO: 14764	RTT
14765	SEQ ID NO: 14765	RTT
14766	SEQ ID NO: 14766	RTT
14767	SEQ ID NO: 14767	RTT
14768	SEQ ID NO: 14768	RTT
5999	SEQ ID NO: 5999	PE3b ngRNA spacer (AAAGG T PAM)

Table 85: Description of Legends present in Tables 1-84

Symbol	Explanation
*1	RTT encodes AAGG-to-AAAG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*2	RTT encodes AGAGG-to-AAAGG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*3	RTT encodes AGAGG-to-AACGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*4	RTT encodes AGAGG-to-AACGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*5	RTT encodes AGAGG-to-AACGG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*6	RTT encodes AGAGG-to-AACGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*7	RTT encodes AGAGG-to-AGCGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*8	RTT encodes AGAGG-to-AGCGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*9	RTT encodes AGAGG-to-AGCGG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*10	RTT encodes AGAGG-to-AGCGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*11	RTT encodes AGA-to-AAA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*12	RTT encodes AGC-to-TCA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*13	RTT encodes AGC-to-TCC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*14	RTT encodes AGC-to-TCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*15	RTT encodes AGC-to-TCT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*16	RTT encodes AGGAGC-to-AGAAGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*17	RTT encodes AGGAGC-to-AGATCA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*18	RTT encodes AGGAGC-to-AGATCC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*19	RTT encodes AGGAGC-to-AGATCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.

*20	RTT encodes AGGAGC-to-AGATCT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*21	RTT encodes AGGAGC-to-AGGTCA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*22	RTT encodes AGGAGC-to-AGGTCC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*23	RTT encodes AGGAGC-to-AGGTCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*24	RTT encodes AGGAGC-to-AGGTCT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*25	RTT encodes AGGAGC-to-CGAAGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*26	RTT encodes AGGAGC-to-CGATCA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*27	RTT encodes AGGAGC-to-CGATCC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*28	RTT encodes AGGAGC-to-CGATCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*29	RTT encodes AGGAGC-to-CGATCT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*30	RTT encodes AGGAGC-to-CGCAGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*31	RTT encodes AGGAGC-to-CGCTCA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*32	RTT encodes AGGAGC-to-CGCTCC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*33	RTT encodes AGGAGC-to-CGCTCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*34	RTT encodes AGGAGC-to-CGCTCT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*35	RTT encodes AGGAGC-to-CGTAGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*36	RTT encodes AGGAGC-to-CGTTCA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*37	RTT encodes AGGAGC-to-CGTTCC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*38	RTT encodes AGGAGC-to-CGTTCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*39	RTT encodes AGGAGC-to-CGTTCT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*40	RTT encodes AGG-to-AAG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*41	RTT encodes AGG-to-AGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.

*42	RTT encodes AGG-to-CGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*43	RTT encodes AGG-to-CGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*44	RTT encodes AGG-to-CGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*45	RTT encodes AG-to-AA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*46	RTT encodes CAAG-to-AAGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*47	RTT encodes CAAG-to-AAGG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*48	RTT encodes CAAG-to-CAAA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*49	RTT encodes CAAG-to-CAGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*50	RTT encodes CAAG-to-CAGG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*51	RTT encodes CAAG-to-GAGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*52	RTT encodes CAAG-to-GAGG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*53	RTT encodes CAAG-to-TAGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*54	RTT encodes CAAG-to-TAGG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*55	RTT encodes CAG-to-CAA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*56	RTT encodes CAG-to-TAA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*57	RTT encodes CCGG-to-CCGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*58	RTT encodes CCGG-to-CCGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*59	RTT encodes CCGG-to-CCGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*60	RTT encodes CCGG-to-CCTA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*61	RTT encodes CCGG-to-CCTC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*62	RTT encodes CCGG-to-CCTG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*63	RTT encodes CCGG-to-CCTT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.

*64	RTT encodes CCGG-to-TCTA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*65	RTT encodes CCGG-to-TCTC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*66	RTT encodes CCGG-to-TCTG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*67	RTT encodes CCGG-to-TCTT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*68	RTT encodes CCTGGT-to-CCTCGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*69	RTT encodes CCTGGT-to-CCTTGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*70	RTT encodes CGG-to-AGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*71	RTT encodes CGG-to-CAG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*72	RTT encodes CGG-to-CCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*73	RTT encodes CGG-to-CGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*74	RTT encodes CGG-to-CGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*75	RTT encodes CGG-to-CGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*76	RTT encodes CGG-to-CTG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*77	RTT encodes CG-to-CA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*78	RTT encodes CG-to-CC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*79	RTT encodes CG-to-CT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*80	RTT encodes CTGG-to-CTAG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*81	RTT encodes CTGG-to-CTCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*82	RTT encodes CTGG-to-CTTG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*83	RTT encodes CTGG-to-TTAG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*84	RTT encodes GAGC-to-GTCA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*85	RTT encodes GAGC-to-GTCC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.

*86	RTT encodes GAGC-to-GTCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*87	RTT encodes GAGC-to-GTCT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*88	RTT encodes GAGG-to-GAGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*89	RTT encodes GAGG-to-GCGA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*90	RTT encodes GAGG-to-GCGC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*91	RTT encodes GAGG-to-GCGG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*92	RTT encodes GAGG-to-GCGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*93	RTT encodes GAG-to-GAA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*94	RTT encodes GCGG-to-GCAG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*95	RTT encodes GCGG-to-GCCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*96	RTT encodes GCGG-to-GCTG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*97	RTT encodes GGTGGT-to-GGTCGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*98	RTT encodes GGTGGT-to-GGTTGT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*99	RTT encodes GG-to-GA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*100	RTT encodes GG-to-GC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*101	RTT encodes GG-to-GT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*102	RTT encodes GTGG-to-GTAG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*103	RTT encodes GTGG-to-GTCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*104	RTT encodes GTGG-to-GTTG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*105	RTT encodes TGA-to-TAA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*106	RTT encodes TGA-to-TCA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*107	RTT encodes TGA-to-TTA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.

*108	RTT encodes TGG-to-TAG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*109	RTT encodes TGG-to-TCG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*110	RTT encodes TGG-to-TTG silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*111	RTT encodes TG-to-TA silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*112	RTT encodes TG-to-TC silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
*113	RTT encodes TG-to-TT silent edit(s); ngRNA spacer has 100% complementarity with strand edited by corresponding RTT.
PE3b*X ngRNA spacer have 100% complementarity to an edited strand incorporating a polynucleotide encoded by a corresponding RTT*X wherein X is the same integer. In some embodiments X may be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 21, 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, 80, 81, 82, 83, 84, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, or 113	

[262] In some embodiments, the ng search target sequence is located on the non-target strand, within 10 base pairs to 100 base pairs of an intended nucleotide edit incorporated by the PEgRNA on the edit strand. In some embodiments, the ng target search target sequence is within 10 bp, 20 bp, 30 bp, 40 bp, 50 bp, 60 bp, 70 bp, 80 bp, 90 bp, 91 bp, 92 bp, 93 bp, 94 bp, 95 bp, 96 bp, 97 bp, 98 bp, 99 bp, or 100 bp of an intended nucleotide edit incorporated by the PEgRNA on the edit strand. In some embodiments, the 5' ends of the ng search target sequence and the PEgRNA search target sequence are within 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 bp apart from each other. In some embodiments, the 5' ends of the ng search target sequence and the PEgRNA search target sequence are within 10 bp, 20 bp, 30 bp, 40 bp, 50 bp, 60 bp, 70 bp, 80 bp, 90 bp, 91 bp, 92 bp, 93 bp, 94 bp, 95 bp, 96 bp, 97 bp, 98 bp, 99 bp, or 100 bp apart from each other.

[263] In some embodiments, an ng spacer sequence is complementary to, and may hybridize with the second search target sequence only after an intended nucleotide edit has been incorporated on the edit strand, by the editing template of a PEgRNA. Such a prime editing system maybe referred to as a "PE3b" prime editing system or composition. In some embodiments, the ngRNA comprises a spacer sequence that matches only the edit strand after incorporation of the nucleotide edits, but not the endogenous target gene sequence on the edit strand. Accordingly, in some embodiments, an intended nucleotide edit is incorporated within the ng search target sequence. In some embodiments, the intended nucleotide edit is incorporated within about 1-10 nucleotides of the position corresponding to the PAM of the ng search target sequence. Exemplary combinations of PEgRNA components, e.g., spacer, PBS, and edit template/RTT, as well as combinations of each PEgRNA and corresponding ngRNA(s) are provided in Tables 1-84. Tables 1-84 each contain three columns. The left column is the sequence number. The

middle column provides the sequence of the component as actual sequence or by reference to a SEQ ID NO. Although all the sequences provided in Tables 1-84 are RNA sequences, "T" is used instead of a "U" in the sequences for consistency with the ST.26 standard used in the accompanying sequence listing. The right column contains a description of the sequence.

[264] The PEgRNAs exemplified in Tables 1-84 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to a listed **PEgRNA spacer** sequence; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template comprising at its 3' end any **RTT** sequence from the same table as the PEgRNA spacer, and (ii) a prime binding site (PBS) comprising at its 5' end any **PBS** sequence from the same table as the PEgRNA spacer. The PEgRNA spacer can be, for example, 16-22 nucleotides in length. The PEgRNA spacers in Tables 1-84 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The one or more synonymous mutations can be PAM silencing mutations. Editing templates/RTTs in Tables 1-84 that include PAM silencing mutations are annotated with a * followed by a number code. The explanation of the number code can be found in Table 85. The PBS can be, for example, 3 to 19 nucleotides in length. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[265] The PEgRNA provided in Tables 1-84 can comprise, from 5' to 3', the spacer, the gRNA core, the edit template, and the PBS. The 3' end of the edit template can be contiguous with the 5' end of the PBS. The PEgRNA can comprise multiple RNA molecules (e.g., a crRNA containing the PEgRNA spacer and a tracrRNA containing the extension arm) or can be a single gRNA molecule. Any PEgRNA exemplified in Tables 1-84 may comprise, or further comprise, a 3' motif at the 3' end of the extension arm, for example, a hairpin-forming motif or a series of 1, 2, 3, 4, 5, 6, 7 or more U nucleotides. In some embodiments, the PEgRNA comprises 4 U nucleotides at its 3' end. Without being bound by theory, such 3' motifs are believed to increase PEgRNA stability. The PEgRNA may alternatively or additionally comprise one or more chemical modifications, such as phosphorothioate (PS) bond(s), 2'-O-methylated (2'-Ome) nucleotides, or a combination thereof. In some embodiments, the PEgRNA comprise 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates the presence of a phosphorothioate bond. PEgRNA sequences exemplified in Tables 1-84 may alternatively be adapted for expression from a DNA template, for example, by including a 5' terminal G if the spacer of the PEgRNA begins with another nucleotide, by including 6 or 7 U nucleotides at the 3' end of the extension arm, or both. Such expression-adapted sequences may further comprise a hairpin-forming motif between the PBS and the 3' terminal U series.

[266] Any of the PEgRNAs of Tables 1-84 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in the same table as the PEgRNA spacer

and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of the listed spacer. In some embodiments, the spacer of the ngRNA is the complete sequence of an ngRNA spacer listed in the same table as the PEgRNA spacer. The ngRNA spacers in Tables 1-84 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select an ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor with the PEgRNA, thus avoiding the need to use two different Cas9 proteins. The ngRNA can comprise multiple RNA molecules (e.g., a crRNA containing the ngRNA spacer and a tracrRNA) or can be a single gRNA molecule. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). The particular PAM silencing synonymous mutation corresponding to a given number code can be found in Table 85.

[267] Any ngRNA sequence provided in Tables 1-84 may comprise, or further comprise, a 3' motif at their 3' end, for example, a series of 1, 2, 3, 4, 5, 6, 7 or more U nucleotides. In some embodiments, the ngRNA comprises 4 U nucleotides at its 3' end. Without being bound by theory, such 3' motifs are believed to increase ngRNA stability. The ngRNA may alternatively or additionally comprise one or more chemical modifications, such as phosphorothioate (PS) bond(s), 2'-O-methylated (2'-Ome) nucleotides, or a combination thereof. In some embodiments, the ngRNA comprise 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates the presence of a phosphorothioate bond. NgRNA sequences may alternatively be adapted for expression from a DNA template, for example, by including a 5' terminal G if the spacer of the ngRNA begins with another nucleotide, by including 6 or 7 U nucleotides at the 3' end of the ngRNA, or both.

[268] In some embodiments, the gRNA core for the PEgRNA and/or the ngRNA comprises a sequence selected from SEQ ID Nos 14894-14896.

[269] Table 1 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGG PAM sequence. The PEgRNAs of Table 1 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[270] The PEgRNAs exemplified in Table 1 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 1; (b) a gRNA core capable of complexing with a Cas9 protein, and

(c) an extension arm comprising: (i) an editing template at least 94 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 25-29, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 8. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to sequence number 1-7. In some embodiments, the PEgRNA spacer comprises sequence number 5. The PEgRNA spacers in Table 1 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 25, 33, 36, 42, 49, 53, or 55. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 26, 27, 28, 29, 30, 31, 32, 34, 35, 37, 38, 39, 40, 41, 43, 44, 45, 46, 47, 48, 50, 51, 52, 54, 56, 57, 58, or 59. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 8-24. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[271] Any of the PEgRNAs of Table 1 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 1 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60-99. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 1. The ngRNA spacers in Table 1 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 1 can comprise a sequence corresponding to sequence number 100-118.

[272] Table 2 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGG PAM sequence. The PEgRNAs of Table

2 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[273] The PEgRNAs exemplified in Table 2 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 119; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 91 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 143-146, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 126. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to sequence number 119-125. In some embodiments, the PEgRNA spacer comprises sequence number 123. The PEgRNA spacers in Table 2 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 145, 149, 152, 155, 161, 166, 170, 172, 176, or 182. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 143, 144, 146, 147, 148, 150, 151, 153, 154, 156, 157, 158, 159, 160, 162, 163, 164, 165, 167, 168, 169, 171, 173, 174, 175, 177, 178, 179, 180, or 181. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 126-142. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[274] Any of the PEgRNAs of Table 2 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 2 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 63, 64, 65, 67, 68, 69, 70, 71, 72, 75, 76, 77, 78, 79, 81, 84, 85, 88, 90, 91, 92, 93, 95, 96, 97, 98, 99, 183, 184, 185, 186, 187, 188, 189, 190, 191, or 192. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 2. The ngRNA spacers in Table 2 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by

more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 2 can comprise a sequence corresponding to any one of sequence numbers 100-118.

[275] Table 3 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGG PAM sequence. The PEgRNAs of Table 3 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[276] The PEgRNAs exemplified in Table 3 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 193; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 82 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 217-220, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 200. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 193-199. In some embodiments, the PEgRNA spacer comprises sequence number 197. The PEgRNA spacers in Table 3 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 220, 222, 228, 232, 236, 240, 241, 247, 251, 253, 257, 262, 268, 269, 276, 280, 284, 287, or 289. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 217, 218, 219, 221, 223, 224, 225, 226, 227, 229, 230, 231, 233, 234, 235, 237, 238, 239, 242, 243, 244, 245, 246, 248, 249, 250, 252, 254, 255, 256, 258, 259, 260, 261, 263, 264, 265, 266, 267, 270, 271, 272, 273, 274, 275, 277, 278, 279, 281, 282, 283, 285, 286, 288, 290, 291, or 292. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 200-216. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[277] Any of the PEgRNAs of Table 3 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 3 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 63, 64, 65, 68, 69, 70, 72, 76, 77, 78, 79, 81, 84, 85, 88, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 295, 296, or 297. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 3. The ngRNA spacers in Table 3 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9

protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 3 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 115, 116, 117, or 118.

[278] Table 4 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGG PAM sequence. The PEgRNAs of Table 4 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[279] The PEgRNAs exemplified in Table 4 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 298; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 73 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 322-323, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 305. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 298-304. In some embodiments, the PEgRNA spacer comprises sequence number 302. The PEgRNA spacers in Table 4 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 322, 324, 326, 329, 330, 333, 334, 337, 338, 340, 342, 344, 347, 349, 350, 352, 355, 356, 359, 361, 363, 364, 366, 368, 370, 373, 374, or 377. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 323, 325, 327, 328, 331, 332, 335, 336, 339, 341, 343, 345, 346, 348, 351, 353, 354, 357, 358, 360, 362, 365, 367, 369, 371, 372, 375, or 376. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 305-321. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[280] Any of the PEgRNAs of Table 4 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 4 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 63, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 88, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, or 379. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 4. The ngRNA spacers in Table 4 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 4 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 115, 116, 117, or 118.

[281] Table 5 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CG or CGG PAM sequence. The PEgRNAs of Table 5 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[282] The PEgRNAs exemplified in Table 5 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 380; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 70 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 404-407, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 387. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 380-386. In some embodiments, the PEgRNA spacer comprises sequence number 384. The PEgRNA spacers in Table 5 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 407, 409, 413, 419, 423, 427, 429, 432, 438, 442, 447, 450, 452, 457, 462, 467, 470, 473, 476, 482, 486, 491, 492,

497, 501, 506, 508, 514, 519, 521, or 524. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 404, 405, 406, 408, 410, 411, 412, 414, 415, 416, 417, 418, 420, 421, 422, 424, 425, 426, 428, 430, 431, 433, 434, 435, 436, 437, 439, 440, 441, 443, 444, 445, 446, 448, 449, 451, 453, 454, 455, 456, 458, 459, 460, 461, 463, 464, 465, 466, 468, 469, 471, 472, 474, 475, 477, 478, 479, 480, 481, 483, 484, 485, 487, 488, 489, 490, 493, 494, 495, 496, 498, 499, 500, 502, 503, 504, 505, 507, 509, 510, 511, 512, 513, 515, 516, 517, 518, 520, 522, 523, 525, 526, or 527. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 387-403. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[283] Any of the PEgRNAs of Table 5 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 5 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 61, 62, 63, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 88, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, or 378. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 5. The ngRNA spacers in Table 5 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 5 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 115, 116, 117, or 118.

[284] Table 6 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGG PAM sequence. The PEgRNAs of Table 6 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[285] The PEgRNAs exemplified in Table 6 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 528; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 65 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 552-556, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 535. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 528-534. In some embodiments, the PEgRNA spacer comprises sequence number 532. The PEgRNA spacers in Table 6 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 556, 558, 565, 569, 576, 579, 583, 590, 594, 597, 603, 608, 614, 619, 622, 628, 633, 640, 643, 648, 654, 660, 662, 671, 674, 678, 682, 690, 694, 697, 703, 708, 712, 720, 722, or 728. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 552, 553, 554, 555, 557, 559, 560, 561, 562, 563, 564, 566, 567, 568, 570, 571, 572, 573, 574, 575, 577, 578, 580, 581, 582, 584, 585, 586, 587, 588, 589, 591, 592, 593, 595, 596, 598, 599, 600, 601, 602, 604, 605, 606, 607, 609, 610, 611, 612, 613, 615, 616, 617, 618, 620, 621, 623, 624, 625, 626, 627, 629, 630, 631, 632, 634, 635, 636, 637, 638, 639, 641, 642, 644, 645, 646, 647, 649, 650, 651, 652, 653, 655, 656, 657, 658, 659, 661, 663, 664, 665, 666, 667, 668, 669, 670, 672, 673, 675, 676, 677, 679, 680, 681, 683, 684, 685, 686, 687, 688, 689, 691, 692, 693, 695, 696, 698, 699, 700, 701, 702, 704, 705, 706, 707, 709, 710, 711, 713, 714, 715, 716, 717, 718, 719, 721, 723, 724, 725, 726, 727, 729, 730, or 731. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 535-551. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[286] Any of the PEgRNAs of Table 6 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 6 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 61, 62, 63, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 88, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, 732, or 733. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 6. The ngRNA spacers in Table 6 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a

complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 6 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 115, 116, 117, or 118.

[287] Table 7 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG, TGG, or TGGG PAM sequence. The PEgRNAs of Table 7 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[288] The PEgRNAs exemplified in Table 7 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 734; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 757-761, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 200. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 734-740. In some embodiments, the PEgRNA spacer comprises sequence number 738. The PEgRNA spacers in Table 7 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 759, 764, 767, 774, 777, 785, 788, 796, 797, 802, 809, 812, 821, 823, 829, 833, 840, 845, 848, 854, 857, 862, 870, 874, 881, 886, 890, 896, 900, 903, 910, 914, 917, 924, 928, 936, 937, 946, 950, 956, 957, 963, 967, 972, 981, 985, 987, 993, 1000, 1006, 1009, 1014, 1018, 1023, 1027, 1032, 1038, 1043, 1048, 1052, 1058, 1063, 1067, 1076, 1080, 1085, 1088, 1096, 1099, 1104, 1107, 1113, 1117, 1124, 1128, 1133, 1140, 1146, 1151, 1155, 1161, 1162, 1167, 1175, 1181, 1186, 1189, 1193, 1199, 1205, or 1207. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 757, 758, 760, 761, 762, 763, 765, 766, 768, 769, 770, 771, 772, 773, 775, 776, 778, 779, 780, 781, 782, 783, 784, 786, 787, 789, 790, 791, 792, 793, 794, 795, 798, 799, 800, 801, 803, 804, 805, 806, 807, 808, 810, 811, 813, 814, 815, 816, 817, 818, 819, 820, 822, 824, 825, 826, 827, 828, 830, 831, 832, 834, 835, 836, 837, 838, 839, 841,

842, 843, 844, 846, 847, 849, 850, 851, 852, 853, 855, 856, 858, 859, 860, 861, 863, 864, 865, 866, 867, 868, 869, 871, 872, 873, 875, 876, 877, 878, 879, 880, 882, 883, 884, 885, 887, 888, 889, 891, 892, 893, 894, 895, 897, 898, 899, 901, 902, 904, 905, 906, 907, 908, 909, 911, 912, 913, 915, 916, 918, 919, 920, 921, 922, 923, 925, 926, 927, 929, 930, 931, 932, 933, 934, 935, 938, 939, 940, 941, 942, 943, 944, 945, 947, 948, 949, 951, 952, 953, 954, 955, 958, 959, 960, 961, 962, 964, 965, 966, 968, 969, 970, 971, 973, 974, 975, 976, 977, 978, 979, 980, 982, 983, 984, 986, 988, 989, 990, 991, 992, 994, 995, 996, 997, 998, 999, 1001, 1002, 1003, 1004, 1005, 1007, 1008, 1010, 1011, 1012, 1013, 1015, 1016, 1017, 1019, 1020, 1021, 1022, 1024, 1025, 1026, 1028, 1029, 1030, 1031, 1033, 1034, 1035, 1036, 1037, 1039, 1040, 1041, 1042, 1044, 1045, 1046, 1047, 1049, 1050, 1051, 1053, 1054, 1055, 1056, 1057, 1059, 1060, 1061, 1062, 1064, 1065, 1066, 1068, 1069, 1070, 1071, 1072, 1073, 1074, 1075, 1077, 1078, 1079, 1081, 1082, 1083, 1084, 1086, 1087, 1089, 1090, 1091, 1092, 1093, 1094, 1095, 1097, 1098, 1100, 1101, 1102, 1103, 1105, 1106, 1108, 1109, 1110, 1111, 1112, 1114, 1115, 1116, 1118, 1119, 1120, 1121, 1122, 1123, 1125, 1126, 1127, 1129, 1130, 1131, 1132, 1134, 1135, 1136, 1137, 1138, 1139, 1141, 1142, 1143, 1144, 1145, 1147, 1148, 1149, 1150, 1152, 1153, 1154, 1156, 1157, 1158, 1159, 1160, 1163, 1164, 1165, 1166, 1168, 1169, 1170, 1171, 1172, 1173, 1174, 1176, 1177, 1178, 1179, 1180, 1182, 1183, 1184, 1185, 1187, 1188, 1190, 1191, 1192, 1194, 1195, 1196, 1197, 1198, 1200, 1201, 1202, 1203, 1204, 1206, 1208, 1209, 1210, or 1211. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 200, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, or 756. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[289] The PEgRNA can comprise, from 5' to 3', the spacer, the gRNA core, the edit template, and the PBS. The 3' end of the edit template can be contiguous with the 5' end of the PBS. The PEgRNA can comprise multiple RNA molecules or can be a single RNA molecule. Exemplary PEgRNAs provided in Table 7 can comprise a sequence corresponding to any one of sequence numbers 1245-1524. Any PEgRNA exemplified in Table 7 may comprise, or further comprise, a 3' motif at the 3' end of the extension arm, for example, a hairpin-forming motif or a series of 1, 2, 3, 4, 5, 6, 7 or more U nucleotides. In some embodiments, the PEgRNA comprises 4 U nucleotides at its 3' end. Without being bound by theory, such 3' motifs are believed to increase PEgRNA stability. The PEgRNA may alternatively or additionally comprise one or more chemical modifications, such as phosphorothioate (PS) bond(s), 2'-O-methylated (2'-Ome) nucleotides, or a combination thereof. In some embodiments, the PEgRNA comprise 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates the presence of a phosphorothioate bond. PEgRNA sequences exemplified in Table 7 may alternatively be adapted for expression from a DNA template, for example, by including a 5' terminal G if the spacer of the PEgRNA begins with another nucleotide, by including 6 or 7 U nucleotides at the 3' end of the extension arm, or both. Such expression-adapted sequences may further comprise a hairpin-forming motif between the PBS and the 3' terminal U series.

[290] Any of the PEgRNAs of Table 7 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 7 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 63, 70, 79, 84, 88, 92, 93, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1215, 1216, 1217, 1218, 1219, 1220, 1221, 1222, 1223, 1224, 1225, 1226, 1227, 1228, 1229, 1230, 1231, 1232, 1233, 1234, 1235, 1236, 1237, 1238, 1239, 1240, 1241, 1242, 1243, or 1244. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 7. The ngRNA spacers in Table 7 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 7 can comprise a sequence corresponding to sequence number 103, 104, 107, 114, 115, 116, 117, 1525, 1526, 1527, or 1528.

[291] Table 8 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG or GGG PAM sequence. The PEgRNAs of Table 8 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[292] The PEgRNAs exemplified in Table 8 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 1529; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 1553, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 1536. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 1529-1535. In some embodiments, the PEgRNA spacer comprises sequence number 1533. The PEgRNA spacers in Table 8 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers

1553-1643. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 1536-1552. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[293] The PEgRNA can comprise, from 5' to 3', the spacer, the gRNA core, the edit template, and the PBS. The 3' end of the edit template can be contiguous with the 5' end of the PBS. The PEgRNA can comprise multiple RNA molecules or can be a single RNA molecule. Exemplary PEgRNAs provided in Table 8 can comprise a sequence corresponding to any one of sequence numbers 1644-1727. Any PEgRNA exemplified in Table 8 may comprise, or further comprise, a 3' motif at the 3' end of the extension arm, for example, a hairpin-forming motif or a series of 1, 2, 3, 4, 5, 6, 7 or more U nucleotides. In some embodiments, the PEgRNA comprises 4 U nucleotides at its 3' end. Without being bound by theory, such 3' motifs are believed to increase PEgRNA stability. The PEgRNA may alternatively or additionally comprise one or more chemical modifications, such as phosphorothioate (PS) bond(s), 2'-O-methylated (2'-Ome) nucleotides, or a combination thereof. In some embodiments, the PEgRNA comprise 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates the presence of a phosphorothioate bond. PEgRNA sequences exemplified in Table 8 may alternatively be adapted for expression from a DNA template, for example, by including a 5' terminal G if the spacer of the PEgRNA begins with another nucleotide, by including 6 or 7 U nucleotides at the 3' end of the extension arm, or both. Such expression-adapted sequences may further comprise a hairpin-forming motif between the PBS and the 3' terminal U series.

[294] Any of the PEgRNAs of Table 8 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 8 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 63, 70, 84, 88, 92, 93, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1217, 1220, 1222, 1223, 1228, 1229, 1233, 1234, 1238, 1239, 1240, or 1243. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 8. The ngRNA spacers in Table 8 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous

mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 8 can comprise a sequence corresponding to sequence number 103, 104, 107, 114, 115, 116, 117, 1525, 1526, 1527, or 1528.

[295] Table 9 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGG PAM sequence. The PEgRNAs of Table 9 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[296] The PEgRNAs exemplified in Table 9 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 1728; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 1752, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 1735. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 1728-1734. In some embodiments, the PEgRNA spacer comprises sequence number 1732. The PEgRNA spacers in Table 9 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 1752-1842. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 1735-1751. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[297] The PEgRNA can comprise, from 5' to 3', the spacer, the gRNA core, the edit template, and the PBS. The 3' end of the edit template can be contiguous with the 5' end of the PBS. The PEgRNA can comprise multiple RNA molecules or can be a single RNA molecule. Exemplary PEgRNAs provided in Table 9 can comprise a sequence corresponding to any one of sequence numbers 1846-1957. Any PEgRNA exemplified in Table 9 may comprise, or further comprise, a 3' motif at the 3' end of the extension arm, for example, a hairpin-forming motif or a series of 1, 2, 3, 4, 5, 6, 7 or more U nucleotides. In some embodiments, the PEgRNA comprises 4 U nucleotides at its 3' end. Without being bound by theory, such 3' motifs are believed to increase PEgRNA stability. The PEgRNA may alternatively or additionally comprise one or more chemical modifications, such as phosphorothioate (PS) bond(s), 2'-O-methylated (2'-Ome) nucleotides, or a combination thereof. In some embodiments, the PEgRNA comprise 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates the presence of a phosphorothioate bond. PEgRNA sequences exemplified in Table 9 may alternatively be adapted for expression from a

DNA template, for example, by including a 5' terminal G if the spacer of the PEgRNA begins with another nucleotide, by including 6 or 7 U nucleotides at the 3' end of the extension arm, or both. Such expression-adapted sequences may further comprise a hairpin-forming motif between the PBS and the 3' terminal U series.

[298] Any of the PEgRNAs of Table 9 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 9 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 63, 84, 88, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1217, 1220, 1222, 1223, 1228, 1229, 1233, 1234, 1238, 1239, 1240, 1243, 1843, 1844, or 1845. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 9. The ngRNA spacers in Table 9 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 9 can comprise a sequence corresponding to sequence number 107, 114, 115, 116, 1525, 1526, 1527, 1528, 1958, or 1959.

[299] Table 10 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGG PAM sequence. The PEgRNAs of Table 10 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[300] The PEgRNAs exemplified in Table 10 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 1960; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 96 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 1984, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 1967. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 1960-1966. In some embodiments, the PEgRNA spacer comprises sequence number 1964. The PEgRNA spacers in Table 10 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription

template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 1984-1988. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 1967-1983. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[301] Any of the PEgRNAs of Table 10 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 10 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 63, 88, 1989, 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, or 2009. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 10. The ngRNA spacers in Table 10 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 10 can comprise a sequence corresponding to sequence number 115, 116, 2010, 2011, 2012, 2013, 2014, 2015, or 2016.

[302] Table 11 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGG PAM sequence. The PEgRNAs of Table 11 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[303] The PEgRNAs exemplified in Table 11 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 2017; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 86 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 2041, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 2024. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 2017-2023. In some embodiments, the PEgRNA spacer comprises sequence

number 2021. The PEgRNA spacers in Table 11 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 2041-2055. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 2024-2040. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[304] Any of the PEgRNAs of Table 11 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 11 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 63, 88, 1989, 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, or 2059. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 11. The ngRNA spacers in Table 11 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 11 can comprise a sequence corresponding to sequence number 115, 116, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[305] Table 12 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGG PAM sequence. The PEgRNAs of Table 12 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[306] The PEgRNAs exemplified in Table 12 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 2063; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 63 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 2087, and (ii) a prime binding site

(PBS) comprising at its 5' end a sequence corresponding to sequence number 2070. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 2063-2069. In some embodiments, the PEgRNA spacer comprises sequence number 2067. The PEgRNA spacers in Table 12 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 2087-2124. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 2070-2086. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[307] Any of the PEgRNAs of Table 12 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 12 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 63, 88, 1989, 1990, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, or 2127. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 12. The ngRNA spacers in Table 12 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 12 can comprise a sequence corresponding to sequence number 115, 116, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[308] Table 13 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGG PAM sequence. The PEgRNAs of Table 13 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[309] The PEgRNAs exemplified in Table 13 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 2128; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 2152-2163, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 2135. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 2128-2134. In some embodiments, the PEgRNA spacer comprises sequence number 2132. The PEgRNA spacers in Table 13 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 2162, 2175, 2180, 2191, 2209, 2223, 2226, 2238, 2256, 2263, 2279, 2295, 2307, 2313, 2324, 2338, 2348, 2360, 2372, 2380, 2394, 2406, 2423, 2436, 2447, 2454, 2469, 2487, 2494, 2503, 2522, 2533, 2546, 2559, 2567, 2576, 2587, 2601, 2619, 2620, 2638, 2652, 2665, 2671, 2682, 2701, 2712, 2724, 2732, 2747, 2758, 2765, 2785, 2798, 2804, 2814, 2825, 2839, 2858, 2865, 2875, 2887, 2906, 2913, 2927, 2941, 2944, 2956, 2968, 2982, 2996, 3012, 3019, 3038, 3047, 3061, 3073, 3084, 3092, 3102, 3114, 3125, 3145, 3159, 3165, 3180, 3184, 3206, 3214, 3227, or 3242. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 2152, 2153, 2154, 2155, 2156, 2157, 2158, 2159, 2160, 2161, 2163, 2164, 2165, 2166, 2167, 2168, 2169, 2170, 2171, 2172, 2173, 2174, 2176, 2177, 2178, 2179, 2181, 2182, 2183, 2184, 2185, 2186, 2187, 2188, 2189, 2190, 2192, 2193, 2194, 2195, 2196, 2197, 2198, 2199, 2200, 2201, 2202, 2203, 2204, 2205, 2206, 2207, 2208, 2210, 2211, 2212, 2213, 2214, 2215, 2216, 2217, 2218, 2219, 2220, 2221, 2222, 2224, 2225, 2227, 2228, 2229, 2230, 2231, 2232, 2233, 2234, 2235, 2236, 2237, 2239, 2240, 2241, 2242, 2243, 2244, 2245, 2246, 2247, 2248, 2249, 2250, 2251, 2252, 2253, 2254, 2255, 2257, 2258, 2259, 2260, 2261, 2262, 2264, 2265, 2266, 2267, 2268, 2269, 2270, 2271, 2272, 2273, 2274, 2275, 2276, 2277, 2278, 2280, 2281, 2282, 2283, 2284, 2285, 2286, 2287, 2288, 2289, 2290, 2291, 2292, 2293, 2294, 2296, 2297, 2298, 2299, 2300, 2301, 2302, 2303, 2304, 2305, 2306, 2308, 2309, 2310, 2311, 2312, 2314, 2315, 2316, 2317, 2318, 2319, 2320, 2321, 2322, 2323, 2325, 2326, 2327, 2328, 2329, 2330, 2331, 2332, 2333, 2334, 2335, 2336, 2337, 2339, 2340, 2341, 2342, 2343, 2344, 2345, 2346, 2347, 2349, 2350, 2351, 2352, 2353, 2354, 2355, 2356, 2357, 2358, 2359, 2361, 2362, 2363, 2364, 2365, 2366, 2367, 2368, 2369, 2370, 2371, 2373, 2374, 2375, 2376, 2377, 2378, 2379, 2381, 2382, 2383, 2384, 2385, 2386, 2387, 2388, 2389, 2390, 2391, 2392, 2393, 2395, 2396, 2397, 2398, 2399, 2400, 2401, 2402, 2403, 2404, 2405, 2407, 2408, 2409, 2410, 2411, 2412, 2413, 2414, 2415, 2416, 2417, 2418, 2419, 2420, 2421, 2422, 2424, 2425, 2426, 2427, 2428, 2429, 2430, 2431, 2432, 2433, 2434, 2435, 2437, 2438, 2439, 2440, 2441, 2442, 2443, 2444, 2445, 2446, 2448, 2449, 2450, 2451, 2452, 2453, 2455, 2456, 2457, 2458, 2459, 2460, 2461, 2462, 2463, 2464, 2465, 2466, 2467, 2468, 2470, 2471, 2472, 2473, 2474, 2475,

2476, 2477, 2478, 2479, 2480, 2481, 2482, 2483, 2484, 2485, 2486, 2488, 2489, 2490, 2491, 2492, 2493, 2495, 2496, 2497, 2498, 2499, 2500, 2501, 2502, 2504, 2505, 2506, 2507, 2508, 2509, 2510, 2511, 2512, 2513, 2514, 2515, 2516, 2517, 2518, 2519, 2520, 2521, 2523, 2524, 2525, 2526, 2527, 2528, 2529, 2530, 2531, 2532, 2534, 2535, 2536, 2537, 2538, 2539, 2540, 2541, 2542, 2543, 2544, 2545, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2602, 2603, 2604, 2605, 2606, 2607, 2608, 2609, 2610, 2611, 2612, 2613, 2614, 2615, 2616, 2617, 2618, 2621, 2622, 2623, 2624, 2625, 2626, 2627, 2628, 2629, 2630, 2631, 2632, 2633, 2634, 2635, 2636, 2637, 2639, 2640, 2641, 2642, 2643, 2644, 2645, 2646, 2647, 2648, 2649, 2650, 2651, 2653, 2654, 2655, 2656, 2657, 2658, 2659, 2660, 2661, 2662, 2663, 2664, 2666, 2667, 2668, 2669, 2670, 2672, 2673, 2674, 2675, 2676, 2677, 2678, 2679, 2680, 2681, 2683, 2684, 2685, 2686, 2687, 2688, 2689, 2690, 2691, 2692, 2693, 2694, 2695, 2696, 2697, 2698, 2699, 2700, 2702, 2703, 2704, 2705, 2706, 2707, 2708, 2709, 2710, 2711, 2713, 2714, 2715, 2716, 2717, 2718, 2719, 2720, 2721, 2722, 2723, 2725, 2726, 2727, 2728, 2729, 2730, 2731, 2733, 2734, 2735, 2736, 2737, 2738, 2739, 2740, 2741, 2742, 2743, 2744, 2745, 2746, 2748, 2749, 2750, 2751, 2752, 2753, 2754, 2755, 2756, 2757, 2759, 2760, 2761, 2762, 2763, 2764, 2766, 2767, 2768, 2769, 2770, 2771, 2772, 2773, 2774, 2775, 2776, 2777, 2778, 2779, 2780, 2781, 2782, 2783, 2784, 2786, 2787, 2788, 2789, 2790, 2791, 2792, 2793, 2794, 2795, 2796, 2797, 2799, 2800, 2801, 2802, 2803, 2805, 2806, 2807, 2808, 2809, 2810, 2811, 2812, 2813, 2815, 2816, 2817, 2818, 2819, 2820, 2821, 2822, 2823, 2824, 2826, 2827, 2828, 2829, 2830, 2831, 2832, 2833, 2834, 2835, 2836, 2837, 2838, 2840, 2841, 2842, 2843, 2844, 2845, 2846, 2847, 2848, 2849, 2850, 2851, 2852, 2853, 2854, 2855, 2856, 2857, 2859, 2860, 2861, 2862, 2863, 2864, 2866, 2867, 2868, 2869, 2870, 2871, 2872, 2873, 2874, 2876, 2877, 2878, 2879, 2880, 2881, 2882, 2883, 2884, 2885, 2886, 2888, 2889, 2890, 2891, 2892, 2893, 2894, 2895, 2896, 2897, 2898, 2899, 2900, 2901, 2902, 2903, 2904, 2905, 2907, 2908, 2909, 2910, 2911, 2912, 2914, 2915, 2916, 2917, 2918, 2919, 2920, 2921, 2922, 2923, 2924, 2925, 2926, 2928, 2929, 2930, 2931, 2932, 2933, 2934, 2935, 2936, 2937, 2938, 2939, 2940, 2942, 2943, 2945, 2946, 2947, 2948, 2949, 2950, 2951, 2952, 2953, 2954, 2955, 2957, 2958, 2959, 2960, 2961, 2962, 2963, 2964, 2965, 2966, 2967, 2969, 2970, 2971, 2972, 2973, 2974, 2975, 2976, 2977, 2978, 2979, 2980, 2981, 2983, 2984, 2985, 2986, 2987, 2988, 2989, 2990, 2991, 2992, 2993, 2994, 2995, 2997, 2998, 2999, 3000, 3001, 3002, 3003, 3004, 3005, 3006, 3007, 3008, 3009, 3010, 3011, 3013, 3014, 3015, 3016, 3017, 3018, 3020, 3021, 3022, 3023, 3024, 3025, 3026, 3027, 3028, 3029, 3030, 3031, 3032, 3033, 3034, 3035, 3036, 3037, 3039, 3040, 3041, 3042, 3043, 3044, 3045, 3046, 3048, 3049, 3050, 3051, 3052, 3053, 3054, 3055, 3056, 3057, 3058, 3059, 3060, 3062, 3063, 3064, 3065, 3066, 3067, 3068, 3069, 3070, 3071, 3072, 3074, 3075, 3076, 3077, 3078, 3079, 3080, 3081, 3082, 3083, 3085, 3086, 3087, 3088, 3089, 3090, 3091, 3093, 3094, 3095, 3096, 3097, 3098, 3099, 3100, 3101, 3103, 3104, 3105, 3106, 3107, 3108, 3109, 3110, 3111, 3112, 3113, 3115, 3116, 3117, 3118, 3119, 3120, 3121, 3122, 3123, 3124, 3126, 3127, 3128, 3129, 3130, 3131, 3132, 3133, 3134, 3135, 3136, 3137, 3138, 3139, 3140, 3141, 3142, 3143, 3144, 3146, 3147, 3148, 3149, 3150, 3151, 3152, 3153, 3154, 3155, 3156, 3157, 3158, 3160, 3161,

3162, 3163, 3164, 3166, 3167, 3168, 3169, 3170, 3171, 3172, 3173, 3174, 3175, 3176, 3177, 3178, 3179, 3181, 3182, 3183, 3185, 3186, 3187, 3188, 3189, 3190, 3191, 3192, 3193, 3194, 3195, 3196, 3197, 3198, 3199, 3200, 3201, 3202, 3203, 3204, 3205, 3207, 3208, 3209, 3210, 3211, 3212, 3213, 3215, 3216, 3217, 3218, 3219, 3220, 3221, 3222, 3223, 3224, 3225, 3226, 3228, 3229, 3230, 3231, 3232, 3233, 3234, 3235, 3236, 3237, 3238, 3239, 3240, 3241, or 3243. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 2135-2151. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[310] The PEgRNA can comprise, from 5' to 3', the spacer, the gRNA core, the edit template, and the PBS. The 3' end of the edit template can be contiguous with the 5' end of the PBS. The PEgRNA can comprise multiple RNA molecules or can be a single RNA molecule. Exemplary PEgRNAs provided in Table 13 can comprise a sequence corresponding to any one of sequence numbers 3300-4083. Any PEgRNA exemplified in Table 13 may comprise, or further comprise, a 3' motif at the 3' end of the extension arm, for example, a hairpin-forming motif or a series of 1, 2, 3, 4, 5, 6, 7 or more U nucleotides. In some embodiments, the PEgRNA comprises 4 U nucleotides at its 3' end. Without being bound by theory, such 3' motifs are believed to increase PEgRNA stability. The PEgRNA may alternatively or additionally comprise one or more chemical modifications, such as phosphorothioate (PS) bond(s), 2'-O-methylated (2'-Ome) nucleotides, or a combination thereof. In some embodiments, the PEgRNA comprise 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates the presence of a phosphorothioate bond. PEgRNA sequences exemplified in Table 13 may alternatively be adapted for expression from a DNA template, for example, by including a 5' terminal G if the spacer of the PEgRNA begins with another nucleotide, by including 6 or 7 U nucleotides at the 3' end of the extension arm, or both. Such expression-adapted sequences may further comprise a hairpin-forming motif between the PBS and the 3' terminal U series.

[311] Any of the PEgRNAs of Table 13 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 13 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 63, 88, 1994, 2000, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3245, 3246, 3247, 3248, 3249, 3250, 3251, 3252, 3253, 3254, 3255, 3256, 3257, 3258, 3259, 3260, 3261, 3262, 3263, 3264, 3265, 3266, 3267, 3268, 3269, 3270, 3271, 3272, 3273, 3274, 3275, 3276, 3277, 3278, 3279, 3280, 3281, 3282, 3283, 3284, 3285, 3286, 3287, 3288, 3289, 3290, 3291, 3292, 3293, 3294, 3295, 3296, 3297, 3298, or 3299. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 13. The ngRNA spacers in Table 13 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of

directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 13 can comprise a sequence corresponding to sequence number 115, 116, 2012, 2013, 2015, 2016, 2060, 2061, 2062, 4084, 4085, 4086, 4087, 4088, 4089, 4090, 4091, 4092, 4093, 4094, 4095, 4096, 4097, 4098, 4099, 4100, 4101, 4102, 4103, 4104, 4105, 4106, 4107, 4108, 4109, 4110, 4111, 4112, 4113, 4114, 4115, 4116, 4117, 4118, 4119, 4120, 4121, 4122, 4123, 4124, 4125, 4126, or 4127.

[312] Exemplary PEgRNA and ngRNA from Table 13 are further excerpted in Table 107 below. All these sequences contained in Table 107 are RNA sequences; however, the Us are presented as Ts to be consistent with ST.26 convention

Table 107: Exemplary PEgRNA and ngRNA from Table 13

Description	Sequence
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGAAGGTGGCTGGAAC TTTT (SEQ ID NO: 14769) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGAAGGTG (SEQ ID NO: 2237; Length: 17; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAAC (Sequence number: 2140; Length: 8)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCGCCCTGGGAAGGTGGCTGGAACACT TTT (SEQ ID NO: 14770) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: GCCCTGGGAAGGTG (SEQ ID NO: 2205; Length: 14; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTGCCCTGGGACGGTGGCTGGAACAC TTTT (SEQ ID NO: 14771) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TGCCCTGGGACGGTG (SEQ ID NO: 2218; Length: 15; Encodes CGG-to-CGT PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTGCCCTGGGAAGGTGGCTGGAACAC TTTT (SEQ ID NO: 14772) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TGCCCTGGGAAGGTG (SEQ ID NO: 2212; Length: 15; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTGCCCTGGGGCGGTGGCTGGAACA CTTTT (SEQ ID NO: 14773) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTGCCCTGGGGCGGTG (SEQ ID NO: 2235; Length: 16; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTGCCCTGGGACGGTGGCTGGAACA CTTTT (SEQ ID NO: 14774) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTGCCCTGGGACGGTG (SEQ ID NO: 2232; Length: 16; Encodes CGG-to-CGT PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)

PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTGCCCTGGGGAGGTGGCTGGAACA CTTTT (SEQ ID NO: 14775) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTGCCCTGGGGAGGTG (SEQ ID NO: 2229; Length: 16; Encodes CGG-to-CTC PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTGCCCTGGGAAGGTGGCTGGAACA CTTTT (SEQ ID NO: 14776) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTGCCCTGGGAAGGTG (SEQ ID NO: 2233; Length: 16; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGTCGGTGGCTGGAACA CTTTT (SEQ ID NO: 14777) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGTCGGTG (SEQ ID NO: 2245; Length: 17; Encodes CGG-to-CGA PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGGCGGTGGCTGGAAC ACTTTT (SEQ ID NO: 14778) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGGCGGTG (SEQ ID NO: 2240; Length: 17; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGACGGTGGCTGGAAC ACTTTT (SEQ ID NO: 14779) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGACGGTG (SEQ ID NO: 2242; Length: 17; Encodes CGG-to-CGT PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGTAGGTGGCTGGAAC ACTTTT (SEQ ID NO: 14780) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGTAGGTG (SEQ ID NO: 2243; Length: 17; Encodes CGG-to-CTA PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)

PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGGAGGTGGCTGGAAC ACTTTT (SEQ ID NO: 14781) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGGAGGTG (SEQ ID NO: 2236; Length: 17; Encodes CGG-to-CTC PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGCAGGTGGCTGGAAC ACTTTT (SEQ ID NO: 14782) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGCAGGTG (SEQ ID NO: 2244; Length: 17; Encodes CGG-to-CTG PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGAAGGTGGCTGGAAC ACTTTT (SEQ ID NO: 14783) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGAAGGTG (SEQ ID NO: 2237; Length: 17; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTCATTGCCCTGGGGCGGTGGCTGGAA CACTTTT (SEQ ID NO: 14784) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TCATTGCCCTGGGGCGGTG (SEQ ID NO: 2269; Length: 19; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTCATTGCCCTGGGACGGTGGCTGGAA CACTTTT (SEQ ID NO: 14785) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TCATTGCCCTGGGACGGTG (SEQ ID NO: 2271; Length: 19; Encodes CGG-to-CGT PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTCATTGCCCTGGGGAGGTGGCTGGA ACACTTTT (SEQ ID NO: 14786) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TCATTGCCCTGGGGAGGTG (SEQ ID NO: 2264; Length: 19; Encodes CGG-to-CTC PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)

PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTCATTGCCCTGGGCAGGTGGCTGGA ACACTTTT (SEQ ID NO: 14787) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTCATTGCCCTGGGCAGGTG (SEQ ID NO: 2272; Length: 20; Encodes CGG-to-CTG PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCGCCCTGGGAAGGTGGCTGGAACACT TTTTT (SEQ ID NO: 14788) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: GCCCTGGGAAGGTG (SEQ ID NO: 2205; Length: 14; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAACACTT (SEQ ID NO: 2144; Length: 12)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTGCCCTGGGAAGGTGGCTGGAACA CTTTTTT (SEQ ID NO: 14789) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTGCCCTGGGAAGGTG (SEQ ID NO: 2233; Length: 16; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAACACTT (SEQ ID NO: 2144; Length: 12)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGGCGGTGGCTGGAAC ACTTTTTT (SEQ ID NO: 14790) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGGCGGTG (SEQ ID NO: 2240; Length: 17; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACACTT (SEQ ID NO: 2144; Length: 12)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGGCGGTGGCTGGAAC ACTTGGTTTT (SEQ ID NO: 14791) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGGCGGTG (SEQ ID NO: 2240; Length: 17; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACACTTGG (SEQ ID NO: 2146; Length: 14)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGGCGGTGGCTGGAAC ACTTGTTTT (SEQ ID NO: 14792) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGGCGGTG (SEQ ID NO: 2240; Length: 17; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACACTTG (SEQ ID NO: 2145; Length: 13)

PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCGCCCTGGGAAGGTGGCTGGAACTTTT (SEQ ID NO: 14793) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: GCCCTGGGAAGGTG (SEQ ID NO: 2205; Length: 14; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAAC (SEQ ID NO: 2140; Length: 8)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGTCGGTGGCTGGAACA CTTTTTT (SEQ ID NO: 14794) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGTCGGTG (SEQ ID NO: 2245; Length: 17; Encodes CGG-to-CGA PAM silencing synonymous mutation) PBS: GCTGGAACACTT (SEQ ID NO: 2144; Length: 12)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCATTGCCCTGGGGCGGTGGCTGGAAC ACTTTTTT (SEQ ID NO: 14790) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: ATTGCCCTGGGGCGGTG (SEQ ID NO: 2240; Length: 17; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACACTT (SEQ ID NO: 2144; Length: 12)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTCATTGCCCTGGGGCGGTGGCTGGA ACACTTGGTTTT (SEQ ID NO: 14796) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTCATTGCCCTGGGGCGGTG (SEQ ID NO: 2277; Length: 20; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACACTTGG (SEQ ID NO: 2146; Length: 14)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTCATTGCCCTGGGTAGGTGGCTGGA ACACTTTTTT (SEQ ID NO: 14797) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTCATTGCCCTGGGTAGGTG (SEQ ID NO: 2281; Length: 20; Encodes CGG-to-CTA PAM silencing synonymous mutation) PBS: GCTGGAACACTT (SEQ ID NO: 2144; Length: 12)
PEgRNA:	TTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTCATTGCCCTGGGAAGGTGGCTGGA ACACTTTTTT (SEQ ID NO: 14798) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TTCATTGCCCTGGGAAGGTG (SEQ ID NO: 2274; Length: 20; Encodes CGG-to-CTT PAM silencing synonymous mutation) PBS: GCTGGAACACTT (SEQ ID NO: 2144; Length: 12)

PEgRNA:	GTTGCCAAGTGTTCCAGCCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTC CGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTCATTGCCCTGGGGCGGTGGCTGGA ACACTTTT (SEQ ID NO: 14799) Spacer: TTGCCAAGTGTTCCAGCCAC (SEQ ID NO: 2132; Length: 20) RTT: TCATTGCCCTGGGGCGGTG (SEQ ID NO: 2269; Length: 19; Encodes CGG-to-CGC PAM silencing synonymous mutation) PBS: GCTGGAACAC (SEQ ID NO: 2142; Length: 10)
PE3 ngRNA:	GGTTGCTGTGGCTGAGAAGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTC CGTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14800) Spacer: GGTTGCTGTGGCTGAGAAGG (SEQ ID NO: 3269)
PE3 ngRNA:	GGTCATCCTGGTGGTTGCTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14801) Spacer: GGTCATCCTGGTGGTTGCTG (SEQ ID NO: 3279)
PE3b ngRNA:	TGTTCATTGCCCTGGGCCGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14802) Spacer: TGTTCATTGCCCTGGGCCGG (SEQ ID NO: 1994)
PE3b* ngRNA:	TGTTCATTGCCCTGGGACGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14803) Spacer: TGTTCATTGCCCTGGGACGG (SEQ ID NO: 3247; Complementary to edited strand containing a CGG-to-CGT synonymous PAM silencing mutation)
PE3b* ngRNA:	TGTTCATTGCCCTGGGGAGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14804) Spacer: TGTTCATTGCCCTGGGGAGG (SEQ ID NO: 3249; Complementary to edited strand containing a CGG-to-CTC synonymous PAM silencing mutation)
PE3b* ngRNA:	TGTTCATTGCCCTGGGAAGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14805) Spacer: TGTTCATTGCCCTGGGAAGG (SEQ ID NO: 3267; Complementary to edited strand containing a CGG-to-CTT synonymous PAM silencing mutation)
PE3b* ngRNA:	TGTTCATTGCCCTGGGCAGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14806) Spacer: TGTTCATTGCCCTGGGCAGG (SEQ ID NO: 3288; Complementary to edited strand containing a CGG-to-CTG synonymous PAM silencing mutation)
PE3b* ngRNA:	TGTTCATTGCCCTGGGGCGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14807) Spacer: TGTTCATTGCCCTGGGGCGG (SEQ ID NO: 3299; Complementary to edited strand containing a CGG-to-CGC synonymous PAM silencing mutation)
PE3b* ngRNA:	TGTTCATTGCCCTGGGTCGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14808) Spacer: TGTTCATTGCCCTGGGTCGG (SEQ ID NO: 3272; Complementary to edited strand containing a CGG-to-CGA synonymous PAM silencing mutation)

PE3b*	TGTTCATTGCCCTGGGTAGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGGCTAGTCC
ngRNA:	GTTATCAACTTGAAAAAGTGGCACCGAGTCGGTGCTTTT (SEQ ID NO: 14809)
	Spacer: TGTTCATTGCCCTGGGTAGG (SEQ ID NO: 3258; Complementary to edited strand containing a CGG-to-CTA synonymous PAM silencing mutation)

[313] 14 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGA PAM sequence. The PEgRNAs of Table 14 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[314] The PEgRNAs exemplified in Table 14 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 4128; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 78 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 4152, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4135. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4128-4134. In some embodiments, the PEgRNA spacer comprises sequence number 4132. The PEgRNA spacers in Table 14 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 4152-4174. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4135-4151. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[315] Any of the PEgRNAs of Table 14 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 14 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 64, 65, 68, 69, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 14. The ngRNA spacers in Table 14 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect

complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 14 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[316] Table 15 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGA PAM sequence. The PEgRNAs of Table 15 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[317] The PEgRNAs exemplified in Table 15 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 4176; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 76 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 4200-4201, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4183. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4176-4182. In some embodiments, the PEgRNA spacer comprises sequence number 4180. The PEgRNA spacers in Table 15 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 4200, 4203, 4204, 4207, 4209, 4210, 4213, 4215, 4216, 4218, 4221, 4223, 4225, 4226, 4228, 4231, 4232, 4235, 4236, 4239, 4241, 4243, 4244, 4247, or 4248. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 4201, 4202, 4205, 4206, 4208, 4211, 4212, 4214, 4217, 4219, 4220, 4222, 4224, 4227, 4229, 4230, 4233, 4234, 4237, 4238, 4240, 4242, 4245, 4246, or 4249. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4183-4199. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[318] Any of the PEgRNAs of Table 15 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 15 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, 4175, or 4250. In some

embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 15. The ngRNA spacers in Table 15 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 15 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[319] Table 16 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG or GGA PAM sequence. The PEgRNAs of Table 16 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[320] The PEgRNAs exemplified in Table 16 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 4251; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 69 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 4275, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4258. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4251-4257. In some embodiments, the PEgRNA spacer comprises sequence number 4255. The PEgRNA spacers in Table 16 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 4275-4306. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4258-4274. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[321] Any of the PEgRNAs of Table 16 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 16 and a gRNA core capable of

complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 61, 62, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, 733, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 16. The ngRNA spacers in Table 16 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 16 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[322] Table 17 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGA PAM sequence. The PEgRNAs of Table 17 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[323] The PEgRNAs exemplified in Table 17 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 4307; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 67 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 4331-4340, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4314. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4307-4313. In some embodiments, the PEgRNA spacer comprises sequence number 4311. The PEgRNA spacers in Table 17 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 4336, 4348, 4356, 4368, 4373, 4383, 4398, 4405, 4411, 4428, 4437, 4442, 4456, 4461, 4479, 4490, 4496, 4502, 4514, 4527, 4531, 4544, 4551, 4569, 4572, 4585, 4599, 4604, 4611, 4622, 4636, 4642, 4657, or 4662. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous

mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 4331, 4332, 4333, 4334, 4335, 4337, 4338, 4339, 4340, 4341, 4342, 4343, 4344, 4345, 4346, 4347, 4349, 4350, 4351, 4352, 4353, 4354, 4355, 4357, 4358, 4359, 4360, 4361, 4362, 4363, 4364, 4365, 4366, 4367, 4369, 4370, 4371, 4372, 4374, 4375, 4376, 4377, 4378, 4379, 4380, 4381, 4382, 4384, 4385, 4386, 4387, 4388, 4389, 4390, 4391, 4392, 4393, 4394, 4395, 4396, 4397, 4399, 4400, 4401, 4402, 4403, 4404, 4406, 4407, 4408, 4409, 4410, 4412, 4413, 4414, 4415, 4416, 4417, 4418, 4419, 4420, 4421, 4422, 4423, 4424, 4425, 4426, 4427, 4429, 4430, 4431, 4432, 4433, 4434, 4435, 4436, 4438, 4439, 4440, 4441, 4443, 4444, 4445, 4446, 4447, 4448, 4449, 4450, 4451, 4452, 4453, 4454, 4455, 4457, 4458, 4459, 4460, 4462, 4463, 4464, 4465, 4466, 4467, 4468, 4469, 4470, 4471, 4472, 4473, 4474, 4475, 4476, 4477, 4478, 4480, 4481, 4482, 4483, 4484, 4485, 4486, 4487, 4488, 4489, 4491, 4492, 4493, 4494, 4495, 4497, 4498, 4499, 4500, 4501, 4503, 4504, 4505, 4506, 4507, 4508, 4509, 4510, 4511, 4512, 4513, 4515, 4516, 4517, 4518, 4519, 4520, 4521, 4522, 4523, 4524, 4525, 4526, 4528, 4529, 4530, 4532, 4533, 4534, 4535, 4536, 4537, 4538, 4539, 4540, 4541, 4542, 4543, 4545, 4546, 4547, 4548, 4549, 4550, 4552, 4553, 4554, 4555, 4556, 4557, 4558, 4559, 4560, 4561, 4562, 4563, 4564, 4565, 4566, 4567, 4568, 4570, 4571, 4573, 4574, 4575, 4576, 4577, 4578, 4579, 4580, 4581, 4582, 4583, 4584, 4586, 4587, 4588, 4589, 4590, 4591, 4592, 4593, 4594, 4595, 4596, 4597, 4598, 4600, 4601, 4602, 4603, 4605, 4606, 4607, 4608, 4609, 4610, 4612, 4613, 4614, 4615, 4616, 4617, 4618, 4619, 4620, 4621, 4623, 4624, 4625, 4626, 4627, 4628, 4629, 4630, 4631, 4632, 4633, 4634, 4635, 4637, 4638, 4639, 4640, 4641, 4643, 4644, 4645, 4646, 4647, 4648, 4649, 4650, 4651, 4652, 4653, 4654, 4655, 4656, 4658, 4659, 4660, 4661, 4663, 4664, 4665, 4666, 4667, 4668, 4669, or 4670. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4314-4330. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[324] Any of the PEgRNAs of Table 17 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 17 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 61, 62, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, 733, 4175, or 4671. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 17. The ngRNA spacers in Table 17 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template

encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 17 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[325] Table 18 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG or GGA PAM sequence. The PEgRNAs of Table 18 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[326] The PEgRNAs exemplified in Table 18 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 4672; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 64 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 4696-4720, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4679. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4672-4678. In some embodiments, the PEgRNA spacer comprises sequence number 4676. The PEgRNA spacers in Table 18 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 4698, 4728, 4762, 4775, 4799, 4827, 4851, 4879, 4901, 4933, 4949, 4982, 5004, 5042, 5056, 5077, 5100, 5134, 5155, 5180, 5199, 5228, 5262, 5275, 5302, 5321, 5365, 5382, 5415, 5430, 5456, 5486, 5500, 5529, 5557, 5586, or 5609. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 4696, 4697, 4699, 4700, 4701, 4702, 4703, 4704, 4705, 4706, 4707, 4708, 4709, 4710, 4711, 4712, 4713, 4714, 4715, 4716, 4717, 4718, 4719, 4720, 4721, 4722, 4723, 4724, 4725, 4726, 4727, 4729, 4730, 4731, 4732, 4733, 4734, 4735, 4736, 4737, 4738, 4739, 4740, 4741, 4742, 4743, 4744, 4745, 4746, 4747, 4748, 4749, 4750, 4751, 4752, 4753, 4754, 4755, 4756, 4757, 4758, 4759, 4760, 4761, 4763, 4764, 4765, 4766, 4767, 4768, 4769, 4770, 4771, 4772, 4773, 4774, 4776, 4777, 4778, 4779, 4780, 4781, 4782, 4783, 4784, 4785, 4786, 4787, 4788, 4789, 4790, 4791, 4792, 4793, 4794, 4795, 4796, 4797, 4798, 4800, 4801, 4802, 4803, 4804, 4805, 4806, 4807, 4808, 4809, 4810, 4811, 4812, 4813, 4814, 4815, 4816, 4817, 4818, 4819, 4820, 4821, 4822, 4823, 4824, 4825, 4826, 4828, 4829, 4830, 4831, 4832, 4833, 4834, 4835, 4836, 4837, 4838, 4839, 4840, 4841, 4842, 4843, 4844, 4845, 4846, 4847, 4848, 4849, 4850, 4852, 4853, 4854, 4855, 4856, 4857, 4858, 4859, 4860, 4861, 4862, 4863, 4864, 4865, 4866, 4867, 4868, 4869, 4870, 4871, 4872, 4873, 4874, 4875, 4876, 4877, 4878, 4880, 4881, 4882,

4883, 4884, 4885, 4886, 4887, 4888, 4889, 4890, 4891, 4892, 4893, 4894, 4895, 4896, 4897, 4898, 4899, 4900, 4902, 4903, 4904, 4905, 4906, 4907, 4908, 4909, 4910, 4911, 4912, 4913, 4914, 4915, 4916, 4917, 4918, 4919, 4920, 4921, 4922, 4923, 4924, 4925, 4926, 4927, 4928, 4929, 4930, 4931, 4932, 4934, 4935, 4936, 4937, 4938, 4939, 4940, 4941, 4942, 4943, 4944, 4945, 4946, 4947, 4948, 4950, 4951, 4952, 4953, 4954, 4955, 4956, 4957, 4958, 4959, 4960, 4961, 4962, 4963, 4964, 4965, 4966, 4967, 4968, 4969, 4970, 4971, 4972, 4973, 4974, 4975, 4976, 4977, 4978, 4979, 4980, 4981, 4983, 4984, 4985, 4986, 4987, 4988, 4989, 4990, 4991, 4992, 4993, 4994, 4995, 4996, 4997, 4998, 4999, 5000, 5001, 5002, 5003, 5005, 5006, 5007, 5008, 5009, 5010, 5011, 5012, 5013, 5014, 5015, 5016, 5017, 5018, 5019, 5020, 5021, 5022, 5023, 5024, 5025, 5026, 5027, 5028, 5029, 5030, 5031, 5032, 5033, 5034, 5035, 5036, 5037, 5038, 5039, 5040, 5041, 5043, 5044, 5045, 5046, 5047, 5048, 5049, 5050, 5051, 5052, 5053, 5054, 5055, 5057, 5058, 5059, 5060, 5061, 5062, 5063, 5064, 5065, 5066, 5067, 5068, 5069, 5070, 5071, 5072, 5073, 5074, 5075, 5076, 5078, 5079, 5080, 5081, 5082, 5083, 5084, 5085, 5086, 5087, 5088, 5089, 5090, 5091, 5092, 5093, 5094, 5095, 5096, 5097, 5098, 5099, 5101, 5102, 5103, 5104, 5105, 5106, 5107, 5108, 5109, 5110, 5111, 5112, 5113, 5114, 5115, 5116, 5117, 5118, 5119, 5120, 5121, 5122, 5123, 5124, 5125, 5126, 5127, 5128, 5129, 5130, 5131, 5132, 5133, 5135, 5136, 5137, 5138, 5139, 5140, 5141, 5142, 5143, 5144, 5145, 5146, 5147, 5148, 5149, 5150, 5151, 5152, 5153, 5154, 5156, 5157, 5158, 5159, 5160, 5161, 5162, 5163, 5164, 5165, 5166, 5167, 5168, 5169, 5170, 5171, 5172, 5173, 5174, 5175, 5176, 5177, 5178, 5179, 5181, 5182, 5183, 5184, 5185, 5186, 5187, 5188, 5189, 5190, 5191, 5192, 5193, 5194, 5195, 5196, 5197, 5198, 5200, 5201, 5202, 5203, 5204, 5205, 5206, 5207, 5208, 5209, 5210, 5211, 5212, 5213, 5214, 5215, 5216, 5217, 5218, 5219, 5220, 5221, 5222, 5223, 5224, 5225, 5226, 5227, 5229, 5230, 5231, 5232, 5233, 5234, 5235, 5236, 5237, 5238, 5239, 5240, 5241, 5242, 5243, 5244, 5245, 5246, 5247, 5248, 5249, 5250, 5251, 5252, 5253, 5254, 5255, 5256, 5257, 5258, 5259, 5260, 5261, 5263, 5264, 5265, 5266, 5267, 5268, 5269, 5270, 5271, 5272, 5273, 5274, 5276, 5277, 5278, 5279, 5280, 5281, 5282, 5283, 5284, 5285, 5286, 5287, 5288, 5289, 5290, 5291, 5292, 5293, 5294, 5295, 5296, 5297, 5298, 5299, 5300, 5301, 5303, 5304, 5305, 5306, 5307, 5308, 5309, 5310, 5311, 5312, 5313, 5314, 5315, 5316, 5317, 5318, 5319, 5320, 5322, 5323, 5324, 5325, 5326, 5327, 5328, 5329, 5330, 5331, 5332, 5333, 5334, 5335, 5336, 5337, 5338, 5339, 5340, 5341, 5342, 5343, 5344, 5345, 5346, 5347, 5348, 5349, 5350, 5351, 5352, 5353, 5354, 5355, 5356, 5357, 5358, 5359, 5360, 5361, 5362, 5363, 5364, 5366, 5367, 5368, 5369, 5370, 5371, 5372, 5373, 5374, 5375, 5376, 5377, 5378, 5379, 5380, 5381, 5383, 5384, 5385, 5386, 5387, 5388, 5389, 5390, 5391, 5392, 5393, 5394, 5395, 5396, 5397, 5398, 5399, 5400, 5401, 5402, 5403, 5404, 5405, 5406, 5407, 5408, 5409, 5410, 5411, 5412, 5413, 5414, 5416, 5417, 5418, 5419, 5420, 5421, 5422, 5423, 5424, 5425, 5426, 5427, 5428, 5429, 5431, 5432, 5433, 5434, 5435, 5436, 5437, 5438, 5439, 5440, 5441, 5442, 5443, 5444, 5445, 5446, 5447, 5448, 5449, 5450, 5451, 5452, 5453, 5454, 5455, 5457, 5458, 5459, 5460, 5461, 5462, 5463, 5464, 5465, 5466, 5467, 5468, 5469, 5470, 5471, 5472, 5473, 5474, 5475, 5476, 5477, 5478, 5479, 5480, 5481, 5482, 5483, 5484, 5485, 5487, 5488, 5489, 5490, 5491, 5492, 5493, 5494, 5495, 5496, 5497, 5498, 5499, 5501, 5502, 5503, 5504, 5505, 5506, 5507, 5508, 5509, 5510, 5511, 5512, 5513, 5514, 5515, 5516, 5517, 5518, 5519, 5520, 5521, 5522, 5523, 5524, 5525, 5526, 5527, 5528, 5530, 5531, 5532, 5533, 5534, 5535, 5536, 5537,

5538, 5539, 5540, 5541, 5542, 5543, 5544, 5545, 5546, 5547, 5548, 5549, 5550, 5551, 5552, 5553, 5554, 5555, 5556, 5558, 5559, 5560, 5561, 5562, 5563, 5564, 5565, 5566, 5567, 5568, 5569, 5570, 5571, 5572, 5573, 5574, 5575, 5576, 5577, 5578, 5579, 5580, 5581, 5582, 5583, 5584, 5585, 5587, 5588, 5589, 5590, 5591, 5592, 5593, 5594, 5595, 5596, 5597, 5598, 5599, 5600, 5601, 5602, 5603, 5604, 5605, 5606, 5607, 5608, 5610, 5611, 5612, 5613, 5614, 5615, 5616, 5617, 5618, 5619, or 5620. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 4679-4695. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[327] Any of the PEgRNAs of Table 18 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 18 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 61, 62, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, 732, 733, 4175, 5621, 5622, 5623, or 5624. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 18. The ngRNA spacers in Table 18 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 18 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[328] Table 19 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGA PAM sequence. The PEgRNAs of Table 19 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[329] The PEgRNAs exemplified in Table 19 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 5625; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 55 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 5649-5652, and (ii) a

prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5632. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 5625-5631. In some embodiments, the PEgRNA spacer comprises sequence number 5629. The PEgRNA spacers in Table 19 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 5650, 5655, 5657, 5664, 5667, 5669, 5676, 5679, 5682, 5687, 5692, 5695, 5700, 5703, 5707, 5711, 5716, 5717, 5721, 5728, 5730, 5734, 5737, 5741, 5747, 5751, 5756, 5757, 5763, 5768, 5771, 5776, 5777, 5783, 5785, 5790, 5793, 5800, 5802, 5807, 5809, 5815, 5818, 5823, 5827, or 5830. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 5649, 5651, 5652, 5653, 5654, 5656, 5658, 5659, 5660, 5661, 5662, 5663, 5665, 5666, 5668, 5670, 5671, 5672, 5673, 5674, 5675, 5677, 5678, 5680, 5681, 5683, 5684, 5685, 5686, 5688, 5689, 5690, 5691, 5693, 5694, 5696, 5697, 5698, 5699, 5701, 5702, 5704, 5705, 5706, 5708, 5709, 5710, 5712, 5713, 5714, 5715, 5718, 5719, 5720, 5722, 5723, 5724, 5725, 5726, 5727, 5729, 5731, 5732, 5733, 5735, 5736, 5738, 5739, 5740, 5742, 5743, 5744, 5745, 5746, 5748, 5749, 5750, 5752, 5753, 5754, 5755, 5758, 5759, 5760, 5761, 5762, 5764, 5765, 5766, 5767, 5769, 5770, 5772, 5773, 5774, 5775, 5778, 5779, 5780, 5781, 5782, 5784, 5786, 5787, 5788, 5789, 5791, 5792, 5794, 5795, 5796, 5797, 5798, 5799, 5801, 5803, 5804, 5805, 5806, 5808, 5810, 5811, 5812, 5813, 5814, 5816, 5817, 5819, 5820, 5821, 5822, 5824, 5825, 5826, 5828, 5829, 5831, or 5832. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 5632-5648. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[330] Any of the PEgRNAs of Table 19 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 19 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 61, 62, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, 732, 733, 1213, 1229, 4175, 5833, 5834, 5835, 5836, 5837, 5838, 5839, 5840, or 5841. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 19. The ngRNA spacers in Table 19 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect

complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 19 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[331] Table 20 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CG or CGA PAM sequence. The PEgRNAs of Table 20 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[332] The PEgRNAs exemplified in Table 20 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 5842; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 45 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 5866, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5849. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 5842-5848. In some embodiments, the PEgRNA spacer comprises sequence number 5846. The PEgRNA spacers in Table 20 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 5866-5921. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 5849-5865. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[333] Any of the PEgRNAs of Table 20 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 20 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 64, 65, 68, 70, 72, 76, 78, 79, 81, 84, 85, 91, 92, 93, 95, 97, 98, 99, 189, 293, 294, 378, 732, 733, 1213, 1228, 1229, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 20. The ngRNA spacers in Table 20 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA

is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 20 can comprise a sequence corresponding to sequence number 100, 101, 103, 104, 105, 107, 109, 110, 112, 113, 114, 117, or 118.

[334] Table 21 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGA PAM sequence. The PEgRNAs of Table 21 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[335] The PEgRNAs exemplified in Table 21 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 5922; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 88 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 5946, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5929. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 5922-5928. In some embodiments, the PEgRNA spacer comprises sequence number 5926. The PEgRNA spacers in Table 21 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 5946-5958. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 5929-5945. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[336] Any of the PEgRNAs of Table 21 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 21 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2059, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 21. The ngRNA

spacers in Table 21 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 21 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[337] Table 22 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG, GGA, or GGAAGT PAM sequence. The PEgRNAs of Table 22 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[338] The PEgRNAs exemplified in Table 22 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 5959; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 85 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 5983, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5966. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 5959-5965. In some embodiments, the PEgRNA spacer comprises sequence number 5963. The PEgRNA spacers in Table 22 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 5983-5998. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 5966-5982. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[339] Any of the PEgRNAs of Table 22 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 22 and a gRNA core capable of

complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 4175, 5999, 6000, 6001, or 6002. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 22. The ngRNA spacers in Table 22 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 22 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[340] Table 23 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG, TGA, or TGAGAT PAM sequence. The PEgRNAs of Table 23 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[341] The PEgRNAs exemplified in Table 23 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6003; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 80 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 6026, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4314. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6003-6009. In some embodiments, the PEgRNA spacer comprises sequence number 6007. The PEgRNA spacers in Table 23 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 6026-6046. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 4314, 6010, 6011, 6012, 6013, 6014, 6015, 6016, 6017,

6018, 6019, 6020, 6021, 6022, 6023, 6024, or 6025. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[342] Any of the PEgRNAs of Table 23 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 23 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 4175, 5999, 6000, 6001, or 6002. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 23. The ngRNA spacers in Table 23 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 23 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[343] Table 24 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG or AGA PAM sequence. The PEgRNAs of Table 24 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[344] The PEgRNAs exemplified in Table 24 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6047; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 78 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 6070, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4258. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6047-6053. In some embodiments, the PEgRNA spacer comprises sequence number 6051. The PEgRNA spacers in Table 24 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the

editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 6070-6092. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 4258, 6054, 6055, 6056, 6057, 6058, 6059, 6060, 6061, 6062, 6063, 6064, 6065, 6066, 6067, 6068, or 6069. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[345] Any of the PEgRNAs of Table 24 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 24 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 24. The ngRNA spacers in Table 24 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 24 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[346] Table 25 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGA PAM sequence. The PEgRNAs of Table 25 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[347] The PEgRNAs exemplified in Table 25 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6093; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 66 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 6115, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 2024. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one

of sequence numbers 6093-6099. In some embodiments, the PEgRNA spacer comprises sequence number 6097. The PEgRNA spacers in Table 25 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 6115-6149. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 2024, 2025, 6100, 6101, 6102, 6103, 6104, 6105, 6106, 6107, 6108, 6109, 6110, 6111, 6112, 6113, or 6114. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[348] Any of the PEgRNAs of Table 25 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 25 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 25. The ngRNA spacers in Table 25 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 25 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[349] Table 26 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG or GGA PAM sequence. The PEgRNAs of Table 26 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[350] The PEgRNAs exemplified in Table 26 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6150; (b) a gRNA core capable of complexing with a Cas9

protein, and (c) an extension arm comprising: (i) an editing template at least 62 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 6174, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6157. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6150-6156. In some embodiments, the PEgRNA spacer comprises sequence number 6154. The PEgRNA spacers in Table 26 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 6174-6212. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6157-6173. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[351] Any of the PEgRNAs of Table 26 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 26 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 26. The ngRNA spacers in Table 26 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 26 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[352] Table 27 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGA PAM sequence. The PEgRNAs of

Table 27 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[353] The PEgRNAs exemplified in Table 27 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6213; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 47 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 6237, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6220. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6213-6219. In some embodiments, the PEgRNA spacer comprises sequence number 6217. The PEgRNA spacers in Table 27 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 6237-6290. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6220-6236. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[354] Any of the PEgRNAs of Table 27 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 27 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3248, 3262, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 27. The ngRNA spacers in Table 27 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA

provided in Table 27 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[355] Table 28 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG or TGA PAM sequence. The PEgRNAs of Table 28 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[356] The PEgRNAs exemplified in Table 28 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6291; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 41 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 6315, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6298. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6291-6297. In some embodiments, the PEgRNA spacer comprises sequence number 6295. The PEgRNA spacers in Table 28 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 6315-6374. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6298-6314. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[357] Any of the PEgRNAs of Table 28 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 28 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1994, 1995, 1997, 1998, 2000, 2001, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3248, 3262, 3277, 3291, or 4175. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 28. The ngRNA spacers in Table 28 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by

more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 28 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[358] Table 29 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GAG PAM sequence. The PEgRNAs of Table 29 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[359] The PEgRNAs exemplified in Table 29 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6375; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 77 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 6398-6399, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5929. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6375-6381. In some embodiments, the PEgRNA spacer comprises sequence number 6379. The PEgRNA spacers in Table 29 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 6399, 6401, 6403, 6404, 6407, 6408, 6410, 6412, 6415, 6417, 6419, 6421, 6423, 6425, 6427, 6428, 6431, 6433, 6435, 6437, 6438, 6441, 6442, or 6444. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 6398, 6400, 6402, 6405, 6406, 6409, 6411, 6413, 6414, 6416, 6418, 6420, 6422, 6424, 6426, 6429, 6430, 6432, 6434, 6436, 6439, 6440, 6443, or 6445. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 5929, 6382, 6383, 6384, 6385, 6386, 6387, 6388, 6389, 6390, 6391, 6392, 6393, 6394, 6395, 6396, or 6397. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[360] Any of the PEgRNAs of Table 29 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 29 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1224, 1227, 6446, 6447, 6448, 6449, 6450, 6451, 6452, 6453, 6454, 6455, 6456, or 6457. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 29. The ngRNA spacers in Table 29 are annotated with their PAM

sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[361] Table 30 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AAG or AAGG PAM sequence. The PEgRNAs of Table 30 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[362] The PEgRNAs exemplified in Table 30 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6458; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 74 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 6482-6483, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6465. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6458-6464. In some embodiments, the PEgRNA spacer comprises sequence number 6462. The PEgRNA spacers in Table 30 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 6482, 6484, 6486, 6489, 6490, 6493, 6495, 6497, 6498, 6500, 6502, 6504, 6507, 6508, 6511, 6512, 6515, 6517, 6518, 6521, 6523, 6524, 6526, 6528, 6530, 6532, or 6535. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 6483, 6485, 6487, 6488, 6491, 6492, 6494, 6496, 6499, 6501, 6503, 6505, 6506, 6509, 6510, 6513, 6514, 6516, 6519, 6520, 6522, 6525, 6527, 6529, 6531, 6533, or 6534. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6465-6481. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[363] Any of the PEgRNAs of Table 30 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 30 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 68, 76, 93, 95, 96, 98, 1224, 1227, 6446, 6448, 6449, 6450, 6453, 6454, 6455, 6456, 6457, 6536, or 6537. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 30. The ngRNA spacers in Table 30 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 30 can comprise a sequence corresponding to sequence number 100, 101, 102, 104, 105, 109, 112, 113, or 117.

[364] Table 31 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GAG PAM sequence. The PEgRNAs of Table 31 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[365] The PEgRNAs exemplified in Table 31 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6538; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 68 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 6562-6563, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6545. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6538-6544. In some embodiments, the PEgRNA spacer comprises sequence number 6542. The PEgRNA spacers in Table 31 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 6563, 6565, 6566, 6568, 6571, 6573, 6574, 6577, 6579, 6581, 6582, 6585, 6587, 6588, 6590, 6593, 6595, 6597, 6599, 6600, 6603, 6605, 6607, 6609, 6610, 6612, 6615, 6616, 6618, 6621, 6623,

6624, or 6626. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 6562, 6564, 6567, 6569, 6570, 6572, 6575, 6576, 6578, 6580, 6583, 6584, 6586, 6589, 6591, 6592, 6594, 6596, 6598, 6601, 6602, 6604, 6606, 6608, 6611, 6613, 6614, 6617, 6619, 6620, 6622, 6625, or 6627. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6545-6561. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[366] Any of the PEgRNAs of Table 31 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 31 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1224, 1227, 6446, 6448, 6449, 6453, 6454, 6455, 6456, or 6457. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 31. The ngRNA spacers in Table 31 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[367] Table 32 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GAG or GAGG PAM sequence. The PEgRNAs of Table 32 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[368] The PEgRNAs exemplified in Table 32 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6628; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 66 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 6651-6656, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 1735. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence

corresponding to any one of sequence numbers 6628-6634. In some embodiments, the PEgRNA spacer comprises sequence number 6632. The PEgRNA spacers in Table 32 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 6651, 6657, 6663, 6674, 6676, 6681, 6692, 6695, 6703, 6710, 6713, 6720, 6727, 6731, 6738, 6744, 6750, 6758, 6762, 6767, 6773, 6779, 6787, 6793, 6800, 6806, 6810, 6814, 6820, 6827, 6832, 6838, 6843, 6849, or 6857. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 6652, 6653, 6654, 6655, 6656, 6658, 6659, 6660, 6661, 6662, 6664, 6665, 6666, 6667, 6668, 6669, 6670, 6671, 6672, 6673, 6675, 6677, 6678, 6679, 6680, 6682, 6683, 6684, 6685, 6686, 6687, 6688, 6689, 6690, 6691, 6693, 6694, 6696, 6697, 6698, 6699, 6700, 6701, 6702, 6704, 6705, 6706, 6707, 6708, 6709, 6711, 6712, 6714, 6715, 6716, 6717, 6718, 6719, 6721, 6722, 6723, 6724, 6725, 6726, 6728, 6729, 6730, 6732, 6733, 6734, 6735, 6736, 6737, 6739, 6740, 6741, 6742, 6743, 6745, 6746, 6747, 6748, 6749, 6751, 6752, 6753, 6754, 6755, 6756, 6757, 6759, 6760, 6761, 6763, 6764, 6765, 6766, 6768, 6769, 6770, 6771, 6772, 6774, 6775, 6776, 6777, 6778, 6780, 6781, 6782, 6783, 6784, 6785, 6786, 6788, 6789, 6790, 6791, 6792, 6794, 6795, 6796, 6797, 6798, 6799, 6801, 6802, 6803, 6804, 6805, 6807, 6808, 6809, 6811, 6812, 6813, 6815, 6816, 6817, 6818, 6819, 6821, 6822, 6823, 6824, 6825, 6826, 6828, 6829, 6830, 6831, 6833, 6834, 6835, 6836, 6837, 6839, 6840, 6841, 6842, 6844, 6845, 6846, 6847, 6848, 6850, 6851, 6852, 6853, 6854, 6855, 6856, 6858, 6859, or 6860. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 1735, 6635, 6636, 6637, 6638, 6639, 6640, 6641, 6642, 6643, 6644, 6645, 6646, 6647, 6648, 6649, or 6650. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[369] Any of the PEgRNAs of Table 32 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 32 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 68, 76, 93, 95, 96, 98, 1224, 1227, 6446, 6448, 6449, 6453, 6454, 6455, 6456, 6457, or 6536. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 32. The ngRNA spacers in Table 32 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect

complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 32 can comprise a sequence corresponding to sequence number 100, 101, 102, 104, 105, 109, 112, 113, or 117.

[370] Table 33 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GAG PAM sequence. The PEgRNAs of Table 33 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[371] The PEgRNAs exemplified in Table 33 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 6861; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 63 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 6885-6889, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6868. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 6861-6867. In some embodiments, the PEgRNA spacer comprises sequence number 6865. The PEgRNA spacers in Table 33 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 6886, 6892, 6899, 6903, 6907, 6913, 6919, 6922, 6928, 6932, 6936, 6940, 6947, 6950, 6958, 6964, 6966, 6973, 6979, 6980, 6987, 6990, 6999, 7003, 7009, 7014, 7017, 7021, 7027, 7030, 7036, 7043, 7047, 7050, 7058, 7063, 7067, or 7070. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 6885, 6887, 6888, 6889, 6890, 6891, 6893, 6894, 6895, 6896, 6897, 6898, 6900, 6901, 6902, 6904, 6905, 6906, 6908, 6909, 6910, 6911, 6912, 6914, 6915, 6916, 6917, 6918, 6920, 6921, 6923, 6924, 6925, 6926, 6927, 6929, 6930, 6931, 6933, 6934, 6935, 6937, 6938, 6939, 6941, 6942, 6943, 6944, 6945, 6946, 6948, 6949, 6951, 6952, 6953, 6954, 6955, 6956, 6957, 6959, 6960, 6961, 6962, 6963, 6965, 6967, 6968, 6969, 6970, 6971, 6972, 6974, 6975, 6976, 6977, 6978, 6981, 6982, 6983, 6984, 6985, 6986, 6988, 6989, 6991, 6992, 6993, 6994, 6995, 6996, 6997, 6998, 7000, 7001, 7002, 7004, 7005, 7006, 7007, 7008, 7010, 7011, 7012, 7013, 7015, 7016, 7018, 7019, 7020, 7022, 7023, 7024, 7025, 7026, 7028, 7029, 7031, 7032, 7033, 7034, 7035, 7037, 7038, 7039, 7040, 7041, 7042, 7044, 7045, 7046, 7048, 7049, 7051, 7052, 7053, 7054, 7055, 7056, 7057, 7059, 7060, 7061, 7062, 7064, 7065, 7066, 7068, 7069, 7071, 7072, 7073, or 7074. The PBS can be, for example, 3 to 19 nucleotides in length

and can comprise the sequence corresponding to any one of sequence numbers 6868-6884. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[372] Any of the PEgRNAs of Table 33 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 33 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1224, 1227, 6446, 6448, 6449, 6453, 6454, 6455, 6456, or 6457. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 33. The ngRNA spacers in Table 33 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[373] Table 34 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CAG PAM sequence. The PEgRNAs of Table 34 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[374] The PEgRNAs exemplified in Table 34 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7075; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 89 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 7099, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7082. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7075-7081. In some embodiments, the PEgRNA spacer comprises sequence number 7079. The PEgRNA spacers in Table 34 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 7099-7110. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise

the sequence corresponding to any one of sequence numbers 7082-7098. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[375] Any of the PEgRNAs of Table 34 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 34 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 6454, 6455, 7111, 7112, 7113, 7114, 7115, 7116, 7117, or 7118. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 34. The ngRNA spacers in Table 34 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[376] Table 35 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GAG or GAGG PAM sequence. The PEgRNAs of Table 35 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[377] The PEgRNAs exemplified in Table 35 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7119; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 87 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 7142, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4135. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7119-7125. In some embodiments, the PEgRNA spacer comprises sequence number 7123. The PEgRNA spacers in Table 35 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 7142-7155. Alternatively, the editing template can encode one or more synonymous mutations relative to

the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 4135, 7126, 7127, 7128, 7129, 7130, 7131, 7132, 7133, 7134, 7135, 7136, 7137, 7138, 7139, 7140, or 7141. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[378] Any of the PEgRNAs of Table 35 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 35 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 2056, 6454, 6455, 7111, 7112, 7113, 7114, 7115, 7116, 7117, 7118, 7156, 7157, 7158, or 7159. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 35. The ngRNA spacers in Table 35 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 35 can comprise a sequence corresponding to sequence number 2061.

[379] Table 36 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AAG PAM sequence. The PEgRNAs of Table 36 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[380] The PEgRNAs exemplified in Table 36 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7160; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 83 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 7184, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7167. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7160-7166. In some embodiments, the PEgRNA spacer comprises sequence number 7164. The PEgRNA spacers in Table 36 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription

template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 7184-7201. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7167-7183. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[381] Any of the PEgRNAs of Table 36 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 36 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 6454, 6455, 7111, 7112, 7113, 7114, 7115, 7116, 7117, or 7118. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 36. The ngRNA spacers in Table 36 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[382] Table 37 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GAG PAM sequence. The PEgRNAs of Table 37 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[383] The PEgRNAs exemplified in Table 37 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7202; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 79 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 7225, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6868. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7202-7208. In some embodiments, the PEgRNA spacer comprises sequence number 7206. The PEgRNA spacers in Table 37 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription

template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 7225-7246. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 6868, 7209, 7210, 7211, 7212, 7213, 7214, 7215, 7216, 7217, 7218, 7219, 7220, 7221, 7222, 7223, or 7224. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[384] Any of the PEgRNAs of Table 37 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 37 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 6454, 6455, 7111, 7112, 7113, 7114, 7115, 7116, 7117, or 7118. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 37. The ngRNA spacers in Table 37 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[385] Table 38 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AAG or AAGG PAM sequence. The PEgRNAs of Table 38 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[386] The PEgRNAs exemplified in Table 38 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7247; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 64 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 7271, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7254. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7247-7253. In some embodiments, the PEgRNA spacer comprises sequence

number 7251. The PEgRNA spacers in Table 38 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 7271-7307. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7254-7270. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[387] Any of the PEgRNAs of Table 38 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 38 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 2056, 6454, 6455, 7111, 7112, 7113, 7114, 7115, 7116, 7117, 7118, 7156, 7157, 7158, or 7159. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 38. The ngRNA spacers in Table 38 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 38 can comprise a sequence corresponding to sequence number 2061.

[388] Table 39 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GAG PAM sequence. The PEgRNAs of Table 39 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[389] The PEgRNAs exemplified in Table 39 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7308; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 61 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 7331, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 305. The PEgRNA spacer

can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7308-7314. In some embodiments, the PEgRNA spacer comprises sequence number 7312. The PEgRNA spacers in Table 39 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 7331-7370. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 305, 7315, 7316, 7317, 7318, 7319, 7320, 7321, 7322, 7323, 7324, 7325, 7326, 7327, 7328, 7329, or 7330. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[390] Any of the PEgRNAs of Table 39 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 39 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 6454, 6455, 7111, 7112, 7113, 7114, 7115, 7116, 7117, or 7118. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 39. The ngRNA spacers in Table 39 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[391] Table 40 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CAG PAM sequence. The PEgRNAs of Table 40 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[392] The PEgRNAs exemplified in Table 40 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7371; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 58 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 7393, and (ii) a prime binding site

(PBS) comprising at its 5' end a sequence corresponding to sequence number 6545. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7371-7377. In some embodiments, the PEgRNA spacer comprises sequence number 7375. The PEgRNA spacers in Table 40 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 7393-7435. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 6545, 6546, 7378, 7379, 7380, 7381, 7382, 7383, 7384, 7385, 7386, 7387, 7388, 7389, 7390, 7391, or 7392. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[393] Any of the PEgRNAs of Table 40 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 40 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 6454, 6455, 7111, 7112, 7113, 7114, 7115, 7116, 7117, or 7118. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 40. The ngRNA spacers in Table 40 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[394] Table 41 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AAG PAM sequence. The PEgRNAs of Table 41 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[395] The PEgRNAs exemplified in Table 41 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7436; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 39 nucleotides in length and

comprising at its 3' end a sequence corresponding to sequence number 7460, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7443. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7436-7442. In some embodiments, the PEgRNA spacer comprises sequence number 7440. The PEgRNA spacers in Table 41 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 7460-7521. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7443-7459. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[396] Any of the PEgRNAs of Table 41 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 41 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 6454, 6455, 7112, 7113, 7115, 7116, or 7117. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 41. The ngRNA spacers in Table 41 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[397] Table 42 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AAG PAM sequence. The PEgRNAs of Table 42 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[398] The PEgRNAs exemplified in Table 42 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 7522; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 19 nucleotides in length and

comprising at its 3' end a sequence corresponding to any one of sequence numbers 7546-7555, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7529. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7522-7528. In some embodiments, the PEgRNA spacer comprises sequence number 7526. The PEgRNA spacers in Table 42 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 7547, 7558, 7574, 7585, 7594, 7605, 7607, 7620, 7632, 7644, 7653, 7659, 7671, 7681, 7686, 7696, 7708, 7716, 7735, 7737, 7754, 7760, 7771, 7778, 7788, 7801, 7806, 7822, 7829, 7840, 7848, 7861, 7875, 7877, 7889, 7900, 7915, 7922, 7932, 7942, 7950, 7962, 7968, 7979, 7987, 7997, 8014, 8022, 8031, 8036, 8050, 8062, 8071, 8078, 8086, 8103, 8106, 8119, 8127, 8139, 8146, 8162, 8171, 8178, 8193, 8201, 8206, 8216, 8233, 8238, 8246, 8262, 8271, 8283, 8294, 8305, 8306, 8321, 8335, 8340, 8353, or 8362. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 7546, 7548, 7549, 7550, 7551, 7552, 7553, 7554, 7555, 7556, 7557, 7559, 7560, 7561, 7562, 7563, 7564, 7565, 7566, 7567, 7568, 7569, 7570, 7571, 7572, 7573, 7575, 7576, 7577, 7578, 7579, 7580, 7581, 7582, 7583, 7584, 7586, 7587, 7588, 7589, 7590, 7591, 7592, 7593, 7595, 7596, 7597, 7598, 7599, 7600, 7601, 7602, 7603, 7604, 7606, 7608, 7609, 7610, 7611, 7612, 7613, 7614, 7615, 7616, 7617, 7618, 7619, 7621, 7622, 7623, 7624, 7625, 7626, 7627, 7628, 7629, 7630, 7631, 7633, 7634, 7635, 7636, 7637, 7638, 7639, 7640, 7641, 7642, 7643, 7645, 7646, 7647, 7648, 7649, 7650, 7651, 7652, 7654, 7655, 7656, 7657, 7658, 7660, 7661, 7662, 7663, 7664, 7665, 7666, 7667, 7668, 7669, 7670, 7672, 7673, 7674, 7675, 7676, 7677, 7678, 7679, 7680, 7682, 7683, 7684, 7685, 7687, 7688, 7689, 7690, 7691, 7692, 7693, 7694, 7695, 7697, 7698, 7699, 7700, 7701, 7702, 7703, 7704, 7705, 7706, 7707, 7709, 7710, 7711, 7712, 7713, 7714, 7715, 7717, 7718, 7719, 7720, 7721, 7722, 7723, 7724, 7725, 7726, 7727, 7728, 7729, 7730, 7731, 7732, 7733, 7734, 7736, 7738, 7739, 7740, 7741, 7742, 7743, 7744, 7745, 7746, 7747, 7748, 7749, 7750, 7751, 7752, 7753, 7755, 7756, 7757, 7758, 7759, 7761, 7762, 7763, 7764, 7765, 7766, 7767, 7768, 7769, 7770, 7772, 7773, 7774, 7775, 7776, 7777, 7779, 7780, 7781, 7782, 7783, 7784, 7785, 7786, 7787, 7789, 7790, 7791, 7792, 7793, 7794, 7795, 7796, 7797, 7798, 7799, 7800, 7802, 7803, 7804, 7805, 7807, 7808, 7809, 7810, 7811, 7812, 7813, 7814, 7815, 7816, 7817, 7818, 7819, 7820, 7821, 7823, 7824, 7825, 7826, 7827, 7828, 7830, 7831, 7832, 7833, 7834, 7835, 7836, 7837, 7838, 7839, 7841, 7842, 7843, 7844, 7845, 7846, 7847, 7849, 7850, 7851, 7852, 7853, 7854, 7855, 7856, 7857, 7858, 7859, 7860, 7862, 7863, 7864, 7865, 7866, 7867, 7868, 7869, 7870, 7871, 7872, 7873, 7874, 7876, 7878, 7879, 7880, 7881, 7882, 7883, 7884, 7885, 7886, 7887, 7888, 7890, 7891, 7892, 7893, 7894, 7895, 7896, 7897, 7898, 7899, 7901, 7902, 7903, 7904, 7905, 7906, 7907, 7908, 7909, 7910, 7911, 7912, 7913, 7914, 7916, 7917, 7918, 7919, 7920, 7921, 7923, 7924, 7925, 7926, 7927, 7928, 7929, 7930, 7931, 7933, 7934, 7935, 7936, 7937, 7938, 7939, 7940, 7941,

7943, 7944, 7945, 7946, 7947, 7948, 7949, 7951, 7952, 7953, 7954, 7955, 7956, 7957, 7958, 7959, 7960, 7961, 7963, 7964, 7965, 7966, 7967, 7969, 7970, 7971, 7972, 7973, 7974, 7975, 7976, 7977, 7978, 7980, 7981, 7982, 7983, 7984, 7985, 7986, 7988, 7989, 7990, 7991, 7992, 7993, 7994, 7995, 7996, 7998, 7999, 8000, 8001, 8002, 8003, 8004, 8005, 8006, 8007, 8008, 8009, 8010, 8011, 8012, 8013, 8015, 8016, 8017, 8018, 8019, 8020, 8021, 8023, 8024, 8025, 8026, 8027, 8028, 8029, 8030, 8032, 8033, 8034, 8035, 8037, 8038, 8039, 8040, 8041, 8042, 8043, 8044, 8045, 8046, 8047, 8048, 8049, 8051, 8052, 8053, 8054, 8055, 8056, 8057, 8058, 8059, 8060, 8061, 8063, 8064, 8065, 8066, 8067, 8068, 8069, 8070, 8072, 8073, 8074, 8075, 8076, 8077, 8079, 8080, 8081, 8082, 8083, 8084, 8085, 8087, 8088, 8089, 8090, 8091, 8092, 8093, 8094, 8095, 8096, 8097, 8098, 8099, 8100, 8101, 8102, 8104, 8105, 8107, 8108, 8109, 8110, 8111, 8112, 8113, 8114, 8115, 8116, 8117, 8118, 8120, 8121, 8122, 8123, 8124, 8125, 8126, 8128, 8129, 8130, 8131, 8132, 8133, 8134, 8135, 8136, 8137, 8138, 8140, 8141, 8142, 8143, 8144, 8145, 8147, 8148, 8149, 8150, 8151, 8152, 8153, 8154, 8155, 8156, 8157, 8158, 8159, 8160, 8161, 8163, 8164, 8165, 8166, 8167, 8168, 8169, 8170, 8172, 8173, 8174, 8175, 8176, 8177, 8179, 8180, 8181, 8182, 8183, 8184, 8185, 8186, 8187, 8188, 8189, 8190, 8191, 8192, 8194, 8195, 8196, 8197, 8198, 8199, 8200, 8202, 8203, 8204, 8205, 8207, 8208, 8209, 8210, 8211, 8212, 8213, 8214, 8215, 8217, 8218, 8219, 8220, 8221, 8222, 8223, 8224, 8225, 8226, 8227, 8228, 8229, 8230, 8231, 8232, 8234, 8235, 8236, 8237, 8239, 8240, 8241, 8242, 8243, 8244, 8245, 8247, 8248, 8249, 8250, 8251, 8252, 8253, 8254, 8255, 8256, 8257, 8258, 8259, 8260, 8261, 8263, 8264, 8265, 8266, 8267, 8268, 8269, 8270, 8272, 8273, 8274, 8275, 8276, 8277, 8278, 8279, 8280, 8281, 8282, 8284, 8285, 8286, 8287, 8288, 8289, 8290, 8291, 8292, 8293, 8295, 8296, 8297, 8298, 8299, 8300, 8301, 8302, 8303, 8304, 8307, 8308, 8309, 8310, 8311, 8312, 8313, 8314, 8315, 8316, 8317, 8318, 8319, 8320, 8322, 8323, 8324, 8325, 8326, 8327, 8328, 8329, 8330, 8331, 8332, 8333, 8334, 8336, 8337, 8338, 8339, 8341, 8342, 8343, 8344, 8345, 8346, 8347, 8348, 8349, 8350, 8351, 8352, 8354, 8355, 8356, 8357, 8358, 8359, 8360, 8361, 8363, 8364, or 8365. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 7529-7545. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[399] Any of the PEgRNAs of Table 42 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 42 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 6454, 6455, 7112, 8366, 8367, 8368, 8369, 8370, 8371, 8372, 8373, 8374, 8375, 8376, 8377, 8378, 8379, 8380, or 8381. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 42. The ngRNA spacers in Table 42 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the

non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[400] Table 43 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CAG PAM sequence. The PEgRNAs of Table 43 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[401] The PEgRNAs exemplified in Table 43 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 8382; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 11 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 8405-8407, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5929. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 8382-8388. In some embodiments, the PEgRNA spacer comprises sequence number 8386. The PEgRNA spacers in Table 43 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 8406, 8409, 8412, 8416, 8417, 8421, 8425, 8427, 8430, 8432, 8436, 8438, 8441, 8445, 8449, 8452, 8455, 8457, 8460, 8464, 8465, 8469, 8473, 8475, 8479, 8482, 8485, 8487, 8491, 8494, 8496, 8499, 8502, 8506, 8509, 8510, 8514, 8517, 8520, 8522, 8527, 8530, 8533, 8536, 8538, 8541, 8544, 8547, 8550, 8553, 8555, 8559, 8563, 8564, 8567, 8571, 8575, 8576, 8580, 8583, 8585, 8590, 8592, 8596, 8597, 8602, 8605, 8606, 8611, 8613, 8617, 8619, 8621, 8626, 8627, 8630, 8635, 8637, 8639, 8643, 8646, 8649, 8651, 8655, 8657, 8661, 8664, 8668, 8669, or 8672. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 8405, 8407, 8408, 8410, 8411, 8413, 8414, 8415, 8418, 8419, 8420, 8422, 8423, 8424, 8426, 8428, 8429, 8431, 8433, 8434, 8435, 8437, 8439, 8440, 8442, 8443, 8444, 8446, 8447, 8448, 8450, 8451, 8453, 8454, 8456, 8458, 8459, 8461, 8462, 8463, 8466, 8467, 8468, 8470, 8471, 8472, 8474, 8476, 8477, 8478, 8480, 8481, 8483, 8484, 8486, 8488, 8489, 8490, 8492, 8493, 8495, 8497, 8498, 8500, 8501, 8503, 8504, 8505, 8507, 8508, 8511, 8512, 8513, 8515, 8516, 8518, 8519, 8521, 8523, 8524, 8525, 8526, 8528, 8529, 8531, 8532, 8534, 8535, 8537, 8539, 8540, 8542, 8543, 8545, 8546, 8548, 8549, 8551, 8552, 8554, 8556, 8557, 8558, 8560, 8561, 8562, 8565, 8566, 8568, 8569, 8570,

8572, 8573, 8574, 8577, 8578, 8579, 8581, 8582, 8584, 8586, 8587, 8588, 8589, 8591, 8593, 8594, 8595, 8598, 8599, 8600, 8601, 8603, 8604, 8607, 8608, 8609, 8610, 8612, 8614, 8615, 8616, 8618, 8620, 8622, 8623, 8624, 8625, 8628, 8629, 8631, 8632, 8633, 8634, 8636, 8638, 8640, 8641, 8642, 8644, 8645, 8647, 8648, 8650, 8652, 8653, 8654, 8656, 8658, 8659, 8660, 8662, 8663, 8665, 8666, 8667, 8670, 8671, 8673, or 8674. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 5929, 8389, 8390, 8391, 8392, 8393, 8394, 8395, 8396, 8397, 8398, 8399, 8400, 8401, 8402, 8403, or 8404. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[402] Any of the PEgRNAs of Table 43 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 43 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 6454, 6455, 8373, 8374, 8376, 8377, 8380, or 8675. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 43. The ngRNA spacers in Table 43 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[403] Table 44 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CAG or CAGG PAM sequence. The PEgRNAs of Table 44 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[404] The PEgRNAs exemplified in Table 44 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 8676; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 8699-8710, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7167. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence

corresponding to any one of sequence numbers 8676-8682. In some embodiments, the PEgRNA spacer comprises sequence number 8680. The PEgRNA spacers in Table 44 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 8710, 8718, 8730, 8743, 8752, 8764, 8780, 8794, 8796, 8815, 8828, 8840, 8850, 8857, 8874, 8883, 8893, 8910, 8918, 8935, 8946, 8958, 8964, 8979, 8993, 9007, 9015, 9033, 9045, 9048, 9060, 9073, 9092, 9095, 9108, 9124, 9136, 9144, 9163, 9177, 9183, 9198, 9207, 9223, 9233, 9249, 9252, 9267, 9282, 9289, 9299, 9314, 9325, 9342, 9357, 9369, 9380, 9383, 9403, 9409, 9420, 9435, 9443, 9460, 9467, 9485, 9496, 9506, 9519, 9538, 9546, 9562, 9563, 9576, 9593, 9604, 9611, 9632, 9643, 9657, 9665, 9676, 9687, 9702, 9709, 9730, 9740, 9748, 9763, 9768, or 9779. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 8699, 8700, 8701, 8702, 8703, 8704, 8705, 8706, 8707, 8708, 8709, 8711, 8712, 8713, 8714, 8715, 8716, 8717, 8719, 8720, 8721, 8722, 8723, 8724, 8725, 8726, 8727, 8728, 8729, 8731, 8732, 8733, 8734, 8735, 8736, 8737, 8738, 8739, 8740, 8741, 8742, 8744, 8745, 8746, 8747, 8748, 8749, 8750, 8751, 8753, 8754, 8755, 8756, 8757, 8758, 8759, 8760, 8761, 8762, 8763, 8765, 8766, 8767, 8768, 8769, 8770, 8771, 8772, 8773, 8774, 8775, 8776, 8777, 8778, 8779, 8781, 8782, 8783, 8784, 8785, 8786, 8787, 8788, 8789, 8790, 8791, 8792, 8793, 8795, 8797, 8798, 8799, 8800, 8801, 8802, 8803, 8804, 8805, 8806, 8807, 8808, 8809, 8810, 8811, 8812, 8813, 8814, 8816, 8817, 8818, 8819, 8820, 8821, 8822, 8823, 8824, 8825, 8826, 8827, 8829, 8830, 8831, 8832, 8833, 8834, 8835, 8836, 8837, 8838, 8839, 8841, 8842, 8843, 8844, 8845, 8846, 8847, 8848, 8849, 8851, 8852, 8853, 8854, 8855, 8856, 8858, 8859, 8860, 8861, 8862, 8863, 8864, 8865, 8866, 8867, 8868, 8869, 8870, 8871, 8872, 8873, 8875, 8876, 8877, 8878, 8879, 8880, 8881, 8882, 8884, 8885, 8886, 8887, 8888, 8889, 8890, 8891, 8892, 8894, 8895, 8896, 8897, 8898, 8899, 8900, 8901, 8902, 8903, 8904, 8905, 8906, 8907, 8908, 8909, 8911, 8912, 8913, 8914, 8915, 8916, 8917, 8919, 8920, 8921, 8922, 8923, 8924, 8925, 8926, 8927, 8928, 8929, 8930, 8931, 8932, 8933, 8934, 8936, 8937, 8938, 8939, 8940, 8941, 8942, 8943, 8944, 8945, 8947, 8948, 8949, 8950, 8951, 8952, 8953, 8954, 8955, 8956, 8957, 8959, 8960, 8961, 8962, 8963, 8965, 8966, 8967, 8968, 8969, 8970, 8971, 8972, 8973, 8974, 8975, 8976, 8977, 8978, 8980, 8981, 8982, 8983, 8984, 8985, 8986, 8987, 8988, 8989, 8990, 8991, 8992, 8994, 8995, 8996, 8997, 8998, 8999, 9000, 9001, 9002, 9003, 9004, 9005, 9006, 9008, 9009, 9010, 9011, 9012, 9013, 9014, 9016, 9017, 9018, 9019, 9020, 9021, 9022, 9023, 9024, 9025, 9026, 9027, 9028, 9029, 9030, 9031, 9032, 9034, 9035, 9036, 9037, 9038, 9039, 9040, 9041, 9042, 9043, 9044, 9046, 9047, 9049, 9050, 9051, 9052, 9053, 9054, 9055, 9056, 9057, 9058, 9059, 9061, 9062, 9063, 9064, 9065, 9066, 9067, 9068, 9069, 9070, 9071, 9072, 9074, 9075, 9076, 9077, 9078, 9079, 9080, 9081, 9082, 9083, 9084, 9085, 9086, 9087, 9088, 9089, 9090, 9091, 9093, 9094, 9096, 9097, 9098, 9099, 9100, 9101, 9102, 9103, 9104, 9105, 9106, 9107, 9109, 9110, 9111, 9112, 9113, 9114, 9115, 9116, 9117, 9118, 9119, 9120, 9121, 9122, 9123, 9125, 9126, 9127, 9128, 9129, 9130, 9131, 9132, 9133,

9134, 9135, 9137, 9138, 9139, 9140, 9141, 9142, 9143, 9145, 9146, 9147, 9148, 9149, 9150, 9151, 9152, 9153, 9154, 9155, 9156, 9157, 9158, 9159, 9160, 9161, 9162, 9164, 9165, 9166, 9167, 9168, 9169, 9170, 9171, 9172, 9173, 9174, 9175, 9176, 9178, 9179, 9180, 9181, 9182, 9184, 9185, 9186, 9187, 9188, 9189, 9190, 9191, 9192, 9193, 9194, 9195, 9196, 9197, 9199, 9200, 9201, 9202, 9203, 9204, 9205, 9206, 9208, 9209, 9210, 9211, 9212, 9213, 9214, 9215, 9216, 9217, 9218, 9219, 9220, 9221, 9222, 9224, 9225, 9226, 9227, 9228, 9229, 9230, 9231, 9232, 9234, 9235, 9236, 9237, 9238, 9239, 9240, 9241, 9242, 9243, 9244, 9245, 9246, 9247, 9248, 9250, 9251, 9253, 9254, 9255, 9256, 9257, 9258, 9259, 9260, 9261, 9262, 9263, 9264, 9265, 9266, 9268, 9269, 9270, 9271, 9272, 9273, 9274, 9275, 9276, 9277, 9278, 9279, 9280, 9281, 9283, 9284, 9285, 9286, 9287, 9288, 9290, 9291, 9292, 9293, 9294, 9295, 9296, 9297, 9298, 9300, 9301, 9302, 9303, 9304, 9305, 9306, 9307, 9308, 9309, 9310, 9311, 9312, 9313, 9315, 9316, 9317, 9318, 9319, 9320, 9321, 9322, 9323, 9324, 9326, 9327, 9328, 9329, 9330, 9331, 9332, 9333, 9334, 9335, 9336, 9337, 9338, 9339, 9340, 9341, 9343, 9344, 9345, 9346, 9347, 9348, 9349, 9350, 9351, 9352, 9353, 9354, 9355, 9356, 9358, 9359, 9360, 9361, 9362, 9363, 9364, 9365, 9366, 9367, 9368, 9370, 9371, 9372, 9373, 9374, 9375, 9376, 9377, 9378, 9379, 9381, 9382, 9384, 9385, 9386, 9387, 9388, 9389, 9390, 9391, 9392, 9393, 9394, 9395, 9396, 9397, 9398, 9399, 9400, 9401, 9402, 9404, 9405, 9406, 9407, 9408, 9410, 9411, 9412, 9413, 9414, 9415, 9416, 9417, 9418, 9419, 9421, 9422, 9423, 9424, 9425, 9426, 9427, 9428, 9429, 9430, 9431, 9432, 9433, 9434, 9436, 9437, 9438, 9439, 9440, 9441, 9442, 9444, 9445, 9446, 9447, 9448, 9449, 9450, 9451, 9452, 9453, 9454, 9455, 9456, 9457, 9458, 9459, 9461, 9462, 9463, 9464, 9465, 9466, 9468, 9469, 9470, 9471, 9472, 9473, 9474, 9475, 9476, 9477, 9478, 9479, 9480, 9481, 9482, 9483, 9484, 9486, 9487, 9488, 9489, 9490, 9491, 9492, 9493, 9494, 9495, 9497, 9498, 9499, 9500, 9501, 9502, 9503, 9504, 9505, 9507, 9508, 9509, 9510, 9511, 9512, 9513, 9514, 9515, 9516, 9517, 9518, 9520, 9521, 9522, 9523, 9524, 9525, 9526, 9527, 9528, 9529, 9530, 9531, 9532, 9533, 9534, 9535, 9536, 9537, 9539, 9540, 9541, 9542, 9543, 9544, 9545, 9547, 9548, 9549, 9550, 9551, 9552, 9553, 9554, 9555, 9556, 9557, 9558, 9559, 9560, 9561, 9564, 9565, 9566, 9567, 9568, 9569, 9570, 9571, 9572, 9573, 9574, 9575, 9577, 9578, 9579, 9580, 9581, 9582, 9583, 9584, 9585, 9586, 9587, 9588, 9589, 9590, 9591, 9592, 9594, 9595, 9596, 9597, 9598, 9599, 9600, 9601, 9602, 9603, 9605, 9606, 9607, 9608, 9609, 9610, 9612, 9613, 9614, 9615, 9616, 9617, 9618, 9619, 9620, 9621, 9622, 9623, 9624, 9625, 9626, 9627, 9628, 9629, 9630, 9631, 9633, 9634, 9635, 9636, 9637, 9638, 9639, 9640, 9641, 9642, 9644, 9645, 9646, 9647, 9648, 9649, 9650, 9651, 9652, 9653, 9654, 9655, 9656, 9658, 9659, 9660, 9661, 9662, 9663, 9664, 9666, 9667, 9668, 9669, 9670, 9671, 9672, 9673, 9674, 9675, 9677, 9678, 9679, 9680, 9681, 9682, 9683, 9684, 9685, 9686, 9688, 9689, 9690, 9691, 9692, 9693, 9694, 9695, 9696, 9697, 9698, 9699, 9700, 9701, 9703, 9704, 9705, 9706, 9707, 9708, 9710, 9711, 9712, 9713, 9714, 9715, 9716, 9717, 9718, 9719, 9720, 9721, 9722, 9723, 9724, 9725, 9726, 9727, 9728, 9729, 9731, 9732, 9733, 9734, 9735, 9736, 9737, 9738, 9739, 9741, 9742, 9743, 9744, 9745, 9746, 9747, 9749, 9750, 9751, 9752, 9753, 9754, 9755, 9756, 9757, 9758, 9759, 9760, 9761, 9762, 9764, 9765, 9766, 9767, 9769, 9770, 9771, 9772, 9773, 9774, 9775, 9776, 9777, 9778, 9780, 9781, 9782, 9783, 9784, 9785, 9786, 9787, 9788, 9789, or 9790. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 7167, 8683, 8684, 8685, 8686, 8687,

8688, 8689, 8690, 8691, 8692, 8693, 8694, 8695, 8696, 8697, or 8698. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[405] Any of the PEgRNAs of Table 44 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 44 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 2056, 6454, 6455, 7156, 7157, 7158, 8373, 8374, 8376, 8377, 8380, 9791, 9792, 9793, 9794, 9795, 9796, 9797, 9798, 9799, 9800, 9801, 9802, 9803, 9804, 9805, 9806, 9807, 9808, 9809, 9810, 9811, or 9812. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 44. The ngRNA spacers in Table 44 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 44 can comprise a sequence corresponding to sequence number 2061.

[406] Table 45 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG or GGTGGT PAM sequence. The PEgRNAs of Table 45 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[407] The PEgRNAs exemplified in Table 45 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 9813; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 93 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 9837-9839, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 9820. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 9813-9819. In some embodiments, the PEgRNA spacer comprises sequence number 9817. The PEgRNA spacers in Table 45 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred

to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 9839, 9840, 9843, 9846, 9850, 9852, 9857, or 9859. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 9837, 9838, 9841, 9842, 9844, 9845, 9847, 9848, 9849, 9851, 9853, 9854, 9855, 9856, 9858, or 9860. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 9820-9836. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[408] Any of the PEgRNAs of Table 45 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 45 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 64, 65, 67, 68, 69, 70, 71, 72, 75, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 6453, 6455, 9861, or 9862. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 45. The ngRNA spacers in Table 45 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 45 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 117, or 118.

[409] Table 46 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG PAM sequence. The PEgRNAs of Table 46 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[410] The PEgRNAs exemplified in Table 46 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 9863; (b) a gRNA core capable of complexing with a Cas9

protein, and (c) an extension arm comprising: (i) an editing template at least 90 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 9887, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 9870. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 9863-9869. In some embodiments, the PEgRNA spacer comprises sequence number 9867. The PEgRNA spacers in Table 46 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 9887-9897. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 9870-9886. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[411] Any of the PEgRNAs of Table 46 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 46 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 64, 65, 67, 68, 69, 70, 71, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, or 189. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 46. The ngRNA spacers in Table 46 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 46 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 117, or 118.

[412] Table 47 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 47

can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[413] The PEgRNAs exemplified in Table 47 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 9898; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 87 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 9920, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7082. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 9898-9904. In some embodiments, the PEgRNA spacer comprises sequence number 9902. The PEgRNA spacers in Table 47 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 9920-9933. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 7082, 7083, 9905, 9906, 9907, 9908, 9909, 9910, 9911, 9912, 9913, 9914, 9915, 9916, 9917, 9918, or 9919. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[414] Any of the PEgRNAs of Table 47 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 47 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 64, 65, 67, 68, 69, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, or 189. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 47. The ngRNA spacers in Table 47 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the

asterisk (*). Exemplary ngRNA provided in Table 47 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 117, or 118.

[415] Table 48 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 48 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[416] The PEgRNAs exemplified in Table 48 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 9934; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 84 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 9956, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7082. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 9934-9940. In some embodiments, the PEgRNA spacer comprises sequence number 9938. The PEgRNA spacers in Table 48 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 9956-9972. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 7082, 7083, 9941, 9942, 9943, 9944, 9945, 9946, 9947, 9948, 9949, 9950, 9951, 9952, 9953, 9954, or 9955. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[417] Any of the PEgRNAs of Table 48 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 48 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 64, 65, 68, 69, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, or 294. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 48. The ngRNA spacers in Table 48 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation.

Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 48 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[418] Table 49 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG PAM sequence. The PEgRNAs of Table 49 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[419] The PEgRNAs exemplified in Table 49 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 9973; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 81 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 9995, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 1536. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 9973-9979. In some embodiments, the PEgRNA spacer comprises sequence number 9977. The PEgRNA spacers in Table 49 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 9995-10014. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 1536, 1537, 9980, 9981, 9982, 9983, 9984, 9985, 9986, 9987, 9988, 9989, 9990, 9991, 9992, 9993, or 9994. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[420] Any of the PEgRNAs of Table 49 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 49 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 64, 65, 68, 69, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, or 294. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 49. The ngRNA spacers in Table 49 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3

ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 49 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[421] Table 50 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG PAM sequence. The PEgRNAs of Table 50 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[422] The PEgRNAs exemplified in Table 50 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 10015; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 72 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 10037, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6298. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10015-10021. In some embodiments, the PEgRNA spacer comprises sequence number 10019. The PEgRNA spacers in Table 50 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 10037-10065. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 6298, 6299, 10022, 10023, 10024, 10025, 10026, 10027, 10028, 10029, 10030, 10031, 10032, 10033, 10034, 10035, or 10036. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[423] Any of the PEgRNAs of Table 50 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 50 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 60, 61, 62, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, or 378. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 50. The ngRNA spacers in Table 50 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select

a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 50 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[424] Table 51 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG PAM sequence. The PEgRNAs of Table 51 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[425] The PEgRNAs exemplified in Table 51 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 10066; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 62 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 10090-10094, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 10073. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10066-10072. In some embodiments, the PEgRNA spacer comprises sequence number 10070. The PEgRNA spacers in Table 51 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 10092, 10098, 10100, 10109, 10111, 10119, 10120, 10126, 10131, 10138, 10144, 10145, 10151, 10159, 10162, 10166, 10170, 10178, 10181, 10186, 10190, 10199, 10204, 10206, 10210, 10218, 10223, 10226, 10233, 10235, 10242, 10249, 10251, 10256, 10264, 10266, 10274, 10275, or 10281. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 10090, 10091, 10093, 10094, 10095, 10096, 10097, 10099, 10101, 10102, 10103, 10104, 10105, 10106, 10107, 10108, 10110, 10112, 10113, 10114, 10115, 10116, 10117, 10118, 10121, 10122, 10123, 10124, 10125, 10127, 10128, 10129, 10130, 10132, 10133, 10134, 10135, 10136, 10137, 10139, 10140, 10141,

10142, 10143, 10146, 10147, 10148, 10149, 10150, 10152, 10153, 10154, 10155, 10156, 10157, 10158, 10160, 10161, 10163, 10164, 10165, 10167, 10168, 10169, 10171, 10172, 10173, 10174, 10175, 10176, 10177, 10179, 10180, 10182, 10183, 10184, 10185, 10187, 10188, 10189, 10191, 10192, 10193, 10194, 10195, 10196, 10197, 10198, 10200, 10201, 10202, 10203, 10205, 10207, 10208, 10209, 10211, 10212, 10213, 10214, 10215, 10216, 10217, 10219, 10220, 10221, 10222, 10224, 10225, 10227, 10228, 10229, 10230, 10231, 10232, 10234, 10236, 10237, 10238, 10239, 10240, 10241, 10243, 10244, 10245, 10246, 10247, 10248, 10250, 10252, 10253, 10254, 10255, 10257, 10258, 10259, 10260, 10261, 10262, 10263, 10265, 10267, 10268, 10269, 10270, 10271, 10272, 10273, 10276, 10277, 10278, 10279, 10280, 10282, 10283, or 10284. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10073-10089. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[426] Any of the PEgRNAs of Table 51 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 51 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 61, 62, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 90, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, 732, 733, 1213, 10285, 10286, 10287, or 10288. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 51. The ngRNA spacers in Table 51 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 51 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[427] Table 52 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 52 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[428] The PEgRNAs exemplified in Table 52 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 10289; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 57 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 10311, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 10073. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10289-10295. In some embodiments, the PEgRNA spacer comprises sequence number 10293. The PEgRNA spacers in Table 52 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 10311-10354. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 10073, 10074, 10296, 10297, 10298, 10299, 10300, 10301, 10302, 10303, 10304, 10305, 10306, 10307, 10308, 10309, or 10310. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[429] Any of the PEgRNAs of Table 52 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 52 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 61, 62, 64, 65, 68, 70, 72, 76, 77, 78, 79, 81, 84, 85, 91, 92, 93, 95, 96, 97, 98, 99, 189, 293, 294, 378, 732, 733, 1213, or 1229. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 52. The ngRNA spacers in Table 52 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 52 can comprise a sequence corresponding to sequence number 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 112, 113, 114, 117, or 118.

[430] Table 53 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CG PAM sequence. The PEgRNAs of Table 53 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[431] The PEgRNAs exemplified in Table 53 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 10355; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 40 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 10379-10382, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 10362. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10355-10361. In some embodiments, the PEgRNA spacer comprises sequence number 10359. The PEgRNA spacers in Table 53 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 10382, 10384, 10388, 10392, 10396, 10399, 10403, 10408, 10412, 10418, 10420, 10424, 10428, 10431, 10438, 10441, 10445, 10448, 10452, 10455, 10459, 10466, 10468, 10473, 10476, 10480, 10486, 10488, 10493, 10497, 10500, 10504, 10508, 10512, 10517, 10521, 10525, 10529, 10533, 10537, 10541, 10546, 10548, 10553, 10558, 10562, 10565, 10567, 10572, 10578, 10581, 10586, 10588, 10591, 10596, 10601, 10605, 10609, 10614, 10616, or 10620. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 10379, 10380, 10381, 10383, 10385, 10386, 10387, 10389, 10390, 10391, 10393, 10394, 10395, 10397, 10398, 10400, 10401, 10402, 10404, 10405, 10406, 10407, 10409, 10410, 10411, 10413, 10414, 10415, 10416, 10417, 10419, 10421, 10422, 10423, 10425, 10426, 10427, 10429, 10430, 10432, 10433, 10434, 10435, 10436, 10437, 10439, 10440, 10442, 10443, 10444, 10446, 10447, 10449, 10450, 10451, 10453, 10454, 10456, 10457, 10458, 10460, 10461, 10462, 10463, 10464, 10465, 10467, 10469, 10470, 10471, 10472, 10474, 10475, 10477, 10478, 10479, 10481, 10482, 10483, 10484, 10485, 10487, 10489, 10490, 10491, 10492, 10494, 10495, 10496, 10498, 10499, 10501, 10502, 10503, 10505, 10506, 10507, 10509, 10510, 10511, 10513, 10514, 10515, 10516, 10518, 10519, 10520, 10522, 10523, 10524, 10526, 10527, 10528, 10530, 10531, 10532, 10534, 10535, 10536, 10538, 10539, 10540, 10542, 10543, 10544, 10545, 10547, 10549, 10550, 10551, 10552, 10554, 10555, 10556, 10557, 10559, 10560, 10561, 10563, 10564, 10566, 10568, 10569, 10570, 10571, 10573, 10574, 10575, 10576, 10577, 10579, 10580, 10582, 10583, 10584, 10585, 10587, 10589, 10590, 10592, 10593, 10594, 10595, 10597, 10598, 10599, 10600, 10602, 10603, 10604, 10606, 10607, 10608, 10610, 10611, 10612, 10613, 10615, 10617, 10618, 10619, 10621, or 10622. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers

10362-10378. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[432] Any of the PEgRNAs of Table 53 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 53 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 64, 68, 70, 72, 76, 78, 79, 81, 84, 85, 91, 92, 93, 95, 97, 98, 99, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1228, 1229, 10623, 10624, 10625, 10626, 10627, 10628, 10629, 10630, or 10631. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 53. The ngRNA spacers in Table 53 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 53 can comprise a sequence corresponding to sequence number 100, 101, 103, 104, 105, 107, 109, 110, 112, 113, 114, 117, or 118.

[433] Table 54 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 54 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[434] The PEgRNAs exemplified in Table 54 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 10632; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 31 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 10656, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 10639. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10632-10638. In some embodiments, the PEgRNA spacer comprises sequence number 10636. The PEgRNA spacers in Table 54 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For

example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 10656-10725. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10639-10655. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[435] Any of the PEgRNAs of Table 54 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 54 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 68, 70, 72, 76, 79, 84, 85, 91, 92, 93, 95, 97, 98, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1223, 1228, 1229, 1233, or 1234. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 54. The ngRNA spacers in Table 54 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 54 can comprise a sequence corresponding to sequence number 100, 101, 103, 104, 105, 107, 109, 110, 112, 113, 114, 117, 118, 1526, or 1527.

[436] Table 55 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 55 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[437] The PEgRNAs exemplified in Table 55 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 10726; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 24 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 10749, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6465. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10726-10732. In some embodiments, the PEgRNA spacer comprises

sequence number 10730. The PEgRNA spacers in Table 55 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 10749-10825. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 6465, 10733, 10734, 10735, 10736, 10737, 10738, 10739, 10740, 10741, 10742, 10743, 10744, 10745, 10746, 10747, or 10748. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[438] Any of the PEgRNAs of Table 55 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 55 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 70, 79, 84, 91, 92, 93, 97, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1217, 1223, 1228, 1229, 1233, or 1234. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 55. The ngRNA spacers in Table 55 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 55 can comprise a sequence corresponding to sequence number 103, 104, 107, 114, 117, 1526, or 1527.

[439] Table 56 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 56 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[440] The PEgRNAs exemplified in Table 56 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 10826; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 22 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 10850-10853, and (ii)

a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 10833. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10826-10832. In some embodiments, the PEgRNA spacer comprises sequence number 10830. The PEgRNA spacers in Table 56 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 10852, 10856, 10860, 10865, 10866, 10870, 10877, 10881, 10883, 10888, 10892, 10894, 10898, 10904, 10907, 10911, 10916, 10919, 10922, 10927, 10933, 10937, 10938, 10943, 10949, 10950, 10955, 10958, 10964, 10967, 10973, 10975, 10981, 10984, 10987, 10992, 10995, 10998, 11003, 11007, 11013, 11017, 11019, 11025, 11028, 11033, 11035, 11038, 11044, 11046, 11053, 11056, 11060, 11063, 11066, 11072, 11074, 11081, 11082, 11088, 11090, 11097, 11098, 11105, 11108, 11112, 11114, 11119, 11122, 11129, 11132, 11136, 11138, 11142, 11149, 11150, 11157, 11158, or 11165. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 10850, 10851, 10853, 10854, 10855, 10857, 10858, 10859, 10861, 10862, 10863, 10864, 10867, 10868, 10869, 10871, 10872, 10873, 10874, 10875, 10876, 10878, 10879, 10880, 10882, 10884, 10885, 10886, 10887, 10889, 10890, 10891, 10893, 10895, 10896, 10897, 10899, 10900, 10901, 10902, 10903, 10905, 10906, 10908, 10909, 10910, 10912, 10913, 10914, 10915, 10917, 10918, 10920, 10921, 10923, 10924, 10925, 10926, 10928, 10929, 10930, 10931, 10932, 10934, 10935, 10936, 10939, 10940, 10941, 10942, 10944, 10945, 10946, 10947, 10948, 10951, 10952, 10953, 10954, 10956, 10957, 10959, 10960, 10961, 10962, 10963, 10965, 10966, 10968, 10969, 10970, 10971, 10972, 10974, 10976, 10977, 10978, 10979, 10980, 10982, 10983, 10985, 10986, 10988, 10989, 10990, 10991, 10993, 10994, 10996, 10997, 10999, 11000, 11001, 11002, 11004, 11005, 11006, 11008, 11009, 11010, 11011, 11012, 11014, 11015, 11016, 11018, 11020, 11021, 11022, 11023, 11024, 11026, 11027, 11029, 11030, 11031, 11032, 11034, 11036, 11037, 11039, 11040, 11041, 11042, 11043, 11045, 11047, 11048, 11049, 11050, 11051, 11052, 11054, 11055, 11057, 11058, 11059, 11061, 11062, 11064, 11065, 11067, 11068, 11069, 11070, 11071, 11073, 11075, 11076, 11077, 11078, 11079, 11080, 11083, 11084, 11085, 11086, 11087, 11089, 11091, 11092, 11093, 11094, 11095, 11096, 11099, 11100, 11101, 11102, 11103, 11104, 11106, 11107, 11109, 11110, 11111, 11113, 11115, 11116, 11117, 11118, 11120, 11121, 11123, 11124, 11125, 11126, 11127, 11128, 11130, 11131, 11133, 11134, 11135, 11137, 11139, 11140, 11141, 11143, 11144, 11145, 11146, 11147, 11148, 11151, 11152, 11153, 11154, 11155, 11156, 11159, 11160, 11161, 11162, 11163, or 11164. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 10833-10849. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[441] Any of the PEgRNAs of Table 56 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 56 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 70, 79, 84, 91, 92, 93, 97, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1217, 1223, 1228, 1229, 1233, 1234, 1240, 11166, 11167, 11168, 11169, 11170, or 11171. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 56. The ngRNA spacers in Table 56 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 56 can comprise a sequence corresponding to sequence number 103, 104, 107, 114, 117, 1526, or 1527.

[442] Table 57 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 57 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[443] The PEgRNAs exemplified in Table 57 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 11172; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 15 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 11193, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 2024. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 11172-11178. In some embodiments, the PEgRNA spacer comprises sequence number 11176. The PEgRNA spacers in Table 57 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 11193-11278. Alternatively, the editing template can encode one or more synonymous

mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 2024, 2025, 2026, 11179, 11180, 11181, 11182, 11183, 11184, 11185, 11186, 11187, 11188, 11189, 11190, 11191, or 11192. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[444] Any of the PEgRNAs of Table 57 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 57 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 70, 79, 84, 92, 93, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1217, 1220, 1222, 1223, 1228, 1229, 1233, 1234, 1239, 1240, or 1243. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 57. The ngRNA spacers in Table 57 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 57 can comprise a sequence corresponding to sequence number 103, 104, 107, 114, 117, 1525, 1526, 1527, or 1528.

[445] Table 58 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG PAM sequence. The PEgRNAs of Table 58 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[446] The PEgRNAs exemplified in Table 58 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 11279; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 11302, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5632. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 11279-11285. In some embodiments, the PEgRNA spacer comprises sequence number 11283. The PEgRNA spacers in Table 58 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse

transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 11302-11392. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 5632, 11286, 11287, 11288, 11289, 11290, 11291, 11292, 11293, 11294, 11295, 11296, 11297, 11298, 11299, 11300, or 11301. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[447] Any of the PEgRNAs of Table 58 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 58 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 70, 84, 92, 93, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1217, 1220, 1222, 1223, 1228, 1229, 1233, 1234, 1238, 1239, 1240, 1243, or 1843. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 58. The ngRNA spacers in Table 58 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 58 can comprise a sequence corresponding to sequence number 103, 104, 107, 114, 117, 1525, 1526, 1527, or 1528.

[448] Table 59 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 59 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[449] The PEgRNAs exemplified in Table 59 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 11393; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 11416-11420, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4183. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence

corresponding to any one of sequence numbers 11393-11399. In some embodiments, the PEgRNA spacer comprises sequence number 11397. The PEgRNA spacers in Table 59 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 11418, 11422, 11427, 11435, 11440, 11443, 11447, 11454, 11457, 11465, 11469, 11471, 11477, 11484, 11488, 11491, 11498, 11503, 11508, 11514, 11516, 11521, 11526, 11535, 11536, 11545, 11546, 11554, 11558, 11565, 11568, 11571, 11577, 11583, 11590, 11595, 11598, 11602, 11606, 11615, 11619, 11625, 11626, 11634, 11638, 11644, 11649, 11651, 11660, 11661, 11669, 11673, 11677, 11684, 11689, 11691, 11699, 11705, 11706, 11714, 11719, 11721, 11727, 11735, 11740, 11741, 11748, 11752, 11760, 11765, 11766, 11771, 11777, 11783, 11790, 11793, 11799, 11804, 11807, 11812, 11816, 11821, 11830, 11835, 11836, 11843, 11849, 11852, 11858, 11865, or 11867. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 11416, 11417, 11419, 11420, 11421, 11423, 11424, 11425, 11426, 11428, 11429, 11430, 11431, 11432, 11433, 11434, 11436, 11437, 11438, 11439, 11441, 11442, 11444, 11445, 11446, 11448, 11449, 11450, 11451, 11452, 11453, 11455, 11456, 11458, 11459, 11460, 11461, 11462, 11463, 11464, 11466, 11467, 11468, 11470, 11472, 11473, 11474, 11475, 11476, 11478, 11479, 11480, 11481, 11482, 11483, 11485, 11486, 11487, 11489, 11490, 11492, 11493, 11494, 11495, 11496, 11497, 11499, 11500, 11501, 11502, 11504, 11505, 11506, 11507, 11509, 11510, 11511, 11512, 11513, 11515, 11517, 11518, 11519, 11520, 11522, 11523, 11524, 11525, 11527, 11528, 11529, 11530, 11531, 11532, 11533, 11534, 11537, 11538, 11539, 11540, 11541, 11542, 11543, 11544, 11547, 11548, 11549, 11550, 11551, 11552, 11553, 11555, 11556, 11557, 11559, 11560, 11561, 11562, 11563, 11564, 11566, 11567, 11569, 11570, 11572, 11573, 11574, 11575, 11576, 11578, 11579, 11580, 11581, 11582, 11584, 11585, 11586, 11587, 11588, 11589, 11591, 11592, 11593, 11594, 11596, 11597, 11599, 11600, 11601, 11603, 11604, 11605, 11607, 11608, 11609, 11610, 11611, 11612, 11613, 11614, 11616, 11617, 11618, 11620, 11621, 11622, 11623, 11624, 11627, 11628, 11629, 11630, 11631, 11632, 11633, 11635, 11636, 11637, 11639, 11640, 11641, 11642, 11643, 11645, 11646, 11647, 11648, 11650, 11652, 11653, 11654, 11655, 11656, 11657, 11658, 11659, 11662, 11663, 11664, 11665, 11666, 11667, 11668, 11670, 11671, 11672, 11674, 11675, 11676, 11678, 11679, 11680, 11681, 11682, 11683, 11685, 11686, 11687, 11688, 11690, 11692, 11693, 11694, 11695, 11696, 11697, 11698, 11700, 11701, 11702, 11703, 11704, 11707, 11708, 11709, 11710, 11711, 11712, 11713, 11715, 11716, 11717, 11718, 11720, 11722, 11723, 11724, 11725, 11726, 11728, 11729, 11730, 11731, 11732, 11733, 11734, 11736, 11737, 11738, 11739, 11742, 11743, 11744, 11745, 11746, 11747, 11749, 11750, 11751, 11753, 11754, 11755, 11756, 11757, 11758, 11759, 11761, 11762, 11763, 11764, 11767, 11768, 11769, 11770, 11772, 11773, 11774, 11775, 11776, 11778, 11779, 11780, 11781, 11782, 11784, 11785, 11786, 11787, 11788, 11789, 11791, 11792, 11794, 11795, 11796, 11797, 11798, 11800, 11801, 11802, 11803, 11805,

11806, 11808, 11809, 11810, 11811, 11813, 11814, 11815, 11817, 11818, 11819, 11820, 11822, 11823, 11824, 11825, 11826, 11827, 11828, 11829, 11831, 11832, 11833, 11834, 11837, 11838, 11839, 11840, 11841, 11842, 11844, 11845, 11846, 11847, 11848, 11850, 11851, 11853, 11854, 11855, 11856, 11857, 11859, 11860, 11861, 11862, 11863, 11864, 11866, 11868, 11869, or 11870. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 4183, 11400, 11401, 11402, 11403, 11404, 11405, 11406, 11407, 11408, 11409, 11410, 11411, 11412, 11413, 11414, or 11415. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[450] Any of the PEgRNAs of Table 59 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 59 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 84, 92, 93, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1217, 1220, 1222, 1223, 1228, 1229, 1233, 1234, 1238, 1239, 1240, 1243, 1843, 1844, 1845, 11871, 11872, 11873, 11874, 11875, 11876, 11877, 11878, 11879, 11880, 11881, 11882, 11883, or 11884. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 59. The ngRNA spacers in Table 59 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 59 can comprise a sequence corresponding to sequence number 103, 104, 107, 114, 117, 1525, 1526, 1527, 1528, 1958, or 1959.

[451] Table 60 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG PAM sequence. The PEgRNAs of Table 60 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[452] The PEgRNAs exemplified in Table 60 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 11885; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and

comprising at its 3' end a sequence corresponding to sequence number 11908, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5632. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 11885-11891. In some embodiments, the PEgRNA spacer comprises sequence number 11889. The PEgRNA spacers in Table 60 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 11908-11998. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 5632, 11892, 11893, 11894, 11895, 11896, 11897, 11898, 11899, 11900, 11901, 11902, 11903, 11904, 11905, 11906, or 11907. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[453] Any of the PEgRNAs of Table 60 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 60 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 62, 84, 189, 293, 294, 378, 732, 733, 1212, 1213, 1214, 1217, 1220, 1222, 1223, 1228, 1229, 1233, 1234, 1238, 1239, 1240, 1243, 1843, 1844, or 1845. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 60. The ngRNA spacers in Table 60 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 60 can comprise a sequence corresponding to sequence number 107, 114, 1525, 1526, 1527, 1528, 1958, or 1959.

[454] Table 61 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG PAM sequence. The PEgRNAs of Table

61 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[455] The PEgRNAs exemplified in Table 61 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 11999; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 95 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12023, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 12006. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 11999-12005. In some embodiments, the PEgRNA spacer comprises sequence number 12003. The PEgRNA spacers in Table 61 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12023-12028. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12006-12022. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[456] Any of the PEgRNAs of Table 61 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 61 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of any one of sequence numbers 1989-2009. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 61. The ngRNA spacers in Table 61 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 61 can comprise a sequence corresponding to any one of sequence numbers 2010-2016.

[457] Table 62 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 62 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[458] The PEgRNAs exemplified in Table 62 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12029; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 93 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12053, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 12036. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12029-12035. In some embodiments, the PEgRNA spacer comprises sequence number 12033. The PEgRNA spacers in Table 62 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12053-12060. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12036-12052. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[459] Any of the PEgRNAs of Table 62 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 62 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, or 2059. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 62. The ngRNA spacers in Table 62 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are

coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 62 can comprise a sequence corresponding to any one of sequence numbers 2010-2016.

[460] Table 63 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG PAM sequence. The PEgRNAs of Table 63 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[461] The PEgRNAs exemplified in Table 63 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12061; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 82 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12084, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 387. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12061-12067. In some embodiments, the PEgRNA spacer comprises sequence number 12065. The PEgRNA spacers in Table 63 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12084-12102. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 387, 12068, 12069, 12070, 12071, 12072, 12073, 12074, 12075, 12076, 12077, 12078, 12079, 12080, 12081, 12082, or 12083. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[462] Any of the PEgRNAs of Table 63 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 63 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, or 2059. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 63. The ngRNA spacers in Table 63 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template

encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 63 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[463] Table 64 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 64 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[464] The PEgRNAs exemplified in Table 64 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12103; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 73 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12126, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 10073. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12103-12109. In some embodiments, the PEgRNA spacer comprises sequence number 12107. The PEgRNA spacers in Table 64 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12126-12153. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 10073, 12110, 12111, 12112, 12113, 12114, 12115, 12116, 12117, 12118, 12119, 12120, 12121, 12122, 12123, 12124, or 12125. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[465] Any of the PEgRNAs of Table 64 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 64 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, or 2126. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 64. The ngRNA spacers in Table 64 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the

ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 64 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[466] Table 65 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG PAM sequence. The PEgRNAs of Table 65 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[467] The PEgRNAs exemplified in Table 65 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12154; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 60 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12176, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6298. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12154-12160. In some embodiments, the PEgRNA spacer comprises sequence number 12158. The PEgRNA spacers in Table 65 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 12176-12216. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 6298, 6299, 12161, 12162, 12163, 12164, 12165, 12166, 12167, 12168, 12169, 12170, 12171, 12172, 12173, 12174, or 12175. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[468] Any of the PEgRNAs of Table 65 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 65 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, or 3262. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table

65. The ngRNA spacers in Table 65 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 65 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[469] Table 66 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG PAM sequence. The PEgRNAs of Table 66 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[470] The PEgRNAs exemplified in Table 66 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12217; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 57 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12238, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4314. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12217-12223. In some embodiments, the PEgRNA spacer comprises sequence number 12221. The PEgRNA spacers in Table 66 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12238-12281. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 4314, 4315, 4316, 12224, 12225, 12226, 12227, 12228, 12229, 12230, 12231, 12232, 12233, 12234, 12235, 12236, or 12237. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[471] Any of the PEgRNAs of Table 66 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 66 and a gRNA core capable of

complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, or 3262. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 66. The ngRNA spacers in Table 66 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 66 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[472] Table 67 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG PAM sequence. The PEgRNAs of Table 67 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[473] The PEgRNAs exemplified in Table 67 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12282; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 38 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12306, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 12289. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12282-12288. In some embodiments, the PEgRNA spacer comprises sequence number 12286. The PEgRNA spacers in Table 67 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12306-12368. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12289-12305. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[474] Any of the PEgRNAs of Table 67 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 67 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1994, 1997, 1998, 2000, 2001, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3248, 3262, 3277, 3287, or 3291. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 67. The ngRNA spacers in Table 67 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 67 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, or 2062.

[475] Table 68 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 68 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[476] The PEgRNAs exemplified in Table 68 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12369; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 35 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12391, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 6298. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12369-12375. In some embodiments, the PEgRNA spacer comprises sequence number 12373. The PEgRNA spacers in Table 68 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12391-12456. Alternatively, the editing template can encode one or more synonymous

mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 6298, 6299, 12376, 12377, 12378, 12379, 12380, 12381, 12382, 12383, 12384, 12385, 12386, 12387, 12388, 12389, or 12390. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[477] Any of the PEgRNAs of Table 68 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 68 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1992, 1994, 1997, 1998, 2000, 2001, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3248, 3262, 3268, 3277, 3283, 3287, or 3291. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 68. The ngRNA spacers in Table 68 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 68 can comprise a sequence corresponding to sequence number 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, 2062, 4091, or 4124.

[478] Table 69 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 69 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[479] The PEgRNAs exemplified in Table 69 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12457; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 32 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12480, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 2135. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12457-12463. In some embodiments, the PEgRNA spacer comprises sequence number 12461. The PEgRNA spacers in Table 69 are annotated with their PAM sequence(s),

enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12480-12548. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 2135, 12464, 12465, 12466, 12467, 12468, 12469, 12470, 12471, 12472, 12473, 12474, 12475, 12476, 12477, 12478, or 12479. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[480] Any of the PEgRNAs of Table 69 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 69 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1989, 1990, 1994, 1998, 2000, 2001, 2003, 2004, 2005, 2006, 2008, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3248, 3262, 3268, 3277, 3282, 3283, 3285, 3287, or 3291. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 69. The ngRNA spacers in Table 69 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 69 can comprise a sequence corresponding to sequence number 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, 2062, 4091, or 4124.

[481] Table 70 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 70 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[482] The PEgRNAs exemplified in Table 70 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12549; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 23 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12571, and (ii) a prime binding

site (PBS) comprising at its 5' end a sequence corresponding to sequence number 2070. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12549-12555. In some embodiments, the PEgRNA spacer comprises sequence number 12553. The PEgRNA spacers in Table 70 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12571-12648. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 2070, 2071, 12556, 12557, 12558, 12559, 12560, 12561, 12562, 12563, 12564, 12565, 12566, 12567, 12568, 12569, or 12570. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[483] Any of the PEgRNAs of Table 70 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 70 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1990, 1994, 1998, 2000, 2001, 2003, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3248, 3260, 3262, 3263, 3266, 3268, 3269, 3270, 3277, 3282, 3283, 3285, 3287, or 3291. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 70. The ngRNA spacers in Table 70 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 70 can comprise a sequence corresponding to sequence number 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, 2062, 4091, 4105, 4106, or 4124.

[484] Table 71 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG PAM sequence. The PEgRNAs of Table 71 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[485] The PEgRNAs exemplified in Table 71 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12649; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 18 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 12672-12673, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 200. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12649-12655. In some embodiments, the PEgRNA spacer comprises sequence number 12653. The PEgRNA spacers in Table 71 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 12672, 12675, 12677, 12679, 12681, 12682, 12685, 12687, 12688, 12691, 12693, 12694, 12696, 12699, 12700, 12702, 12704, 12707, 12708, 12711, 12713, 12714, 12717, 12718, 12721, 12723, 12725, 12727, 12729, 12730, 12732, 12735, 12737, 12738, 12741, 12742, 12744, 12746, 12749, 12751, 12753, 12755, 12757, 12759, 12760, 12762, 12764, 12766, 12768, 12771, 12772, 12774, 12777, 12779, 12780, 12782, 12785, 12786, 12789, 12790, 12793, 12794, 12796, 12799, 12800, 12802, 12804, 12807, 12808, 12810, 12812, 12815, 12816, 12818, 12821, 12822, 12824, 12827, 12828, 12830, 12832, 12835, or 12837. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 12673, 12674, 12676, 12678, 12680, 12683, 12684, 12686, 12689, 12690, 12692, 12695, 12697, 12698, 12701, 12703, 12705, 12706, 12709, 12710, 12712, 12715, 12716, 12719, 12720, 12722, 12724, 12726, 12728, 12731, 12733, 12734, 12736, 12739, 12740, 12743, 12745, 12747, 12748, 12750, 12752, 12754, 12756, 12758, 12761, 12763, 12765, 12767, 12769, 12770, 12773, 12775, 12776, 12778, 12781, 12783, 12784, 12787, 12788, 12791, 12792, 12795, 12797, 12798, 12801, 12803, 12805, 12806, 12809, 12811, 12813, 12814, 12817, 12819, 12820, 12823, 12825, 12826, 12829, 12831, 12833, 12834, or 12836. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 200, 12656, 12657, 12658, 12659, 12660, 12661, 12662, 12663, 12664, 12665, 12666, 12667, 12668, 12669, 12670, or 12671. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[486] Any of the PEgRNAs of Table 71 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 71 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1990, 1994, 1998, 2000, 2003, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3248, 3260, 3262, 3263, 3266, 3268, 3269, 3270, 3277, 3279, 3282, 3283, 3285, 3287, 3291, 3295, 12838, 12839, or 12840. In some embodiments, the

spacer of the ngRNA is a ngRNA spacer listed in Table 71. The ngRNA spacers in Table 71 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 71 can comprise a sequence corresponding to sequence number 2011, 2012, 2013, 2014, 2015, 2016, 2060, 2061, 2062, 4091, 4105, 4106, 4110, or 4124.

[487] Table 72 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a TG PAM sequence. The PEgRNAs of Table 72 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[488] The PEgRNAs exemplified in Table 72 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12841; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 16 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 12862, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5632. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12841-12847. In some embodiments, the PEgRNA spacer comprises sequence number 12845. The PEgRNA spacers in Table 72 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 12862-12946. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 5632, 11286, 11287, 12848, 12849, 12850, 12851, 12852, 12853, 12854, 12855, 12856, 12857, 12858, 12859, 12860, or 12861. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[489] Any of the PEgRNAs of Table 72 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence

corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 72 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1994, 1998, 2000, 2003, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3248, 3260, 3262, 3263, 3266, 3268, 3269, 3270, 3277, 3279, 3280, 3282, 3283, 3285, 3287, 3291, or 3295. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 72. The ngRNA spacers in Table 72 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 72 can comprise a sequence corresponding to sequence number 2011, 2012, 2013, 2015, 2016, 2060, 2061, 2062, 4091, 4105, 4106, 4110, or 4124.

[490] Table 73 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a AG PAM sequence. The PEgRNAs of Table 73 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[491] The PEgRNAs exemplified in Table 73 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 12947; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 12969-12971, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 4135. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 12947-12953. In some embodiments, the PEgRNA spacer comprises sequence number 12951. The PEgRNA spacers in Table 73 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 12970, 12973, 12977, 12980, 12981, 12984, 12988, 12991, 12994, 12998, 12999, 13003, 13005, 13009, 13013, 13014, 13018, 13022, 13023, 13026, 13029, 13033, 13037, 13040, 13041, 13045, 13047, 13052, 13053, 13056, 13060, 13063, 13066, 13069, 13071, 13076, 13077, 13081, 13085,

13088, 13090, 13093, 13097, 13100, 13101, 13105, 13109, 13110, 13115, 13118, 13121, 13122, 13126, 13129, 13131, 13134, 13139, 13142, 13144, 13147, 13150, 13153, 13155, 13158, 13161, 13164, 13167, 13170, 13175, 13178, 13180, 13184, 13185, 13188, 13192, 13194, 13198, 13200, 13204, 13207, 13210, 13213, 13217, 13218, 13221, 13225, 13229, 13231, 13233, 13237, or 13240. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 12969, 12971, 12972, 12974, 12975, 12976, 12978, 12979, 12982, 12983, 12985, 12986, 12987, 12989, 12990, 12992, 12993, 12995, 12996, 12997, 13000, 13001, 13002, 13004, 13006, 13007, 13008, 13010, 13011, 13012, 13015, 13016, 13017, 13019, 13020, 13021, 13024, 13025, 13027, 13028, 13030, 13031, 13032, 13034, 13035, 13036, 13038, 13039, 13042, 13043, 13044, 13046, 13048, 13049, 13050, 13051, 13054, 13055, 13057, 13058, 13059, 13061, 13062, 13064, 13065, 13067, 13068, 13070, 13072, 13073, 13074, 13075, 13078, 13079, 13080, 13082, 13083, 13084, 13086, 13087, 13089, 13091, 13092, 13094, 13095, 13096, 13098, 13099, 13102, 13103, 13104, 13106, 13107, 13108, 13111, 13112, 13113, 13114, 13116, 13117, 13119, 13120, 13123, 13124, 13125, 13127, 13128, 13130, 13132, 13133, 13135, 13136, 13137, 13138, 13140, 13141, 13143, 13145, 13146, 13148, 13149, 13151, 13152, 13154, 13156, 13157, 13159, 13160, 13162, 13163, 13165, 13166, 13168, 13169, 13171, 13172, 13173, 13174, 13176, 13177, 13179, 13181, 13182, 13183, 13186, 13187, 13189, 13190, 13191, 13193, 13195, 13196, 13197, 13199, 13201, 13202, 13203, 13205, 13206, 13208, 13209, 13211, 13212, 13214, 13215, 13216, 13219, 13220, 13222, 13223, 13224, 13226, 13227, 13228, 13230, 13232, 13234, 13235, 13236, 13238, 13239, or 13241. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 4135, 7126, 12954, 12955, 12956, 12957, 12958, 12959, 12960, 12961, 12962, 12963, 12964, 12965, 12966, 12967, or 12968. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[492] Any of the PEgRNAs of Table 73 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 73 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1994, 2000, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3248, 3260, 3262, 3263, 3266, 3268, 3269, 3270, 3273, 3277, 3279, 3280, 3282, 3283, 3285, 3287, 3291, 3293, 3295, 13242, or 13243. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 73. The ngRNA spacers in Table 73 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A

PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 73 can comprise a sequence corresponding to sequence number 2012, 2013, 2015, 2016, 2060, 2061, 2062, 4087, 4091, 4105, 4106, 4110, 4115, or 4124.

[493] Table 74 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GG PAM sequence. The PEgRNAs of Table 74 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[494] The PEgRNAs exemplified in Table 74 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 13244; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 13266-13269, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5632. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 13244-13250. In some embodiments, the PEgRNA spacer comprises sequence number 13248. The PEgRNA spacers in Table 74 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 13268, 13272, 13275, 13281, 13284, 13289, 13292, 13294, 13301, 13303, 13308, 13311, 13315, 13321, 13322, 13328, 13333, 13336, 13338, 13345, 13346, 13353, 13354, 13360, 13364, 13368, 13370, 13376, 13380, 13382, 13387, 13393, 13395, 13399, 13403, 13408, 13412, 13416, 13420, 13422, 13428, 13430, 13435, 13441, 13443, 13447, 13453, 13456, 13461, 13462, 13467, 13472, 13474, 13480, 13483, 13486, 13492, 13494, 13500, 13504, 13507, 13513, 13515, 13520, 13522, 13527, 13533, 13534, 13539, 13543, 13548, 13553, 13557, 13559, 13563, 13567, 13572, 13574, 13581, 13584, 13586, 13591, 13597, 13599, 13604, 13608, 13613, 13617, 13618, 13625, or 13626. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 13266, 13267, 13269, 13270, 13271, 13273, 13274, 13276, 13277, 13278, 13279, 13280, 13282, 13283, 13285, 13286, 13287, 13288, 13290, 13291, 13293, 13295, 13296, 13297, 13298, 13299, 13300, 13302, 13304, 13305, 13306, 13307, 13309, 13310, 13312, 13313, 13314, 13316, 13317, 13318, 13319, 13320, 13323, 13324, 13325, 13326,

13327, 13329, 13330, 13331, 13332, 13334, 13335, 13337, 13339, 13340, 13341, 13342, 13343, 13344, 13347, 13348, 13349, 13350, 13351, 13352, 13355, 13356, 13357, 13358, 13359, 13361, 13362, 13363, 13365, 13366, 13367, 13369, 13371, 13372, 13373, 13374, 13375, 13377, 13378, 13379, 13381, 13383, 13384, 13385, 13386, 13388, 13389, 13390, 13391, 13392, 13394, 13396, 13397, 13398, 13400, 13401, 13402, 13404, 13405, 13406, 13407, 13409, 13410, 13411, 13413, 13414, 13415, 13417, 13418, 13419, 13421, 13423, 13424, 13425, 13426, 13427, 13429, 13431, 13432, 13433, 13434, 13436, 13437, 13438, 13439, 13440, 13442, 13444, 13445, 13446, 13448, 13449, 13450, 13451, 13452, 13454, 13455, 13457, 13458, 13459, 13460, 13463, 13464, 13465, 13466, 13468, 13469, 13470, 13471, 13473, 13475, 13476, 13477, 13478, 13479, 13481, 13482, 13484, 13485, 13487, 13488, 13489, 13490, 13491, 13493, 13495, 13496, 13497, 13498, 13499, 13501, 13502, 13503, 13505, 13506, 13508, 13509, 13510, 13511, 13512, 13514, 13516, 13517, 13518, 13519, 13521, 13523, 13524, 13525, 13526, 13528, 13529, 13530, 13531, 13532, 13535, 13536, 13537, 13538, 13540, 13541, 13542, 13544, 13545, 13546, 13547, 13549, 13550, 13551, 13552, 13554, 13555, 13556, 13558, 13560, 13561, 13562, 13564, 13565, 13566, 13568, 13569, 13570, 13571, 13573, 13575, 13576, 13577, 13578, 13579, 13580, 13582, 13583, 13585, 13587, 13588, 13589, 13590, 13592, 13593, 13594, 13595, 13596, 13598, 13600, 13601, 13602, 13603, 13605, 13606, 13607, 13609, 13610, 13611, 13612, 13614, 13615, 13616, 13619, 13620, 13621, 13622, 13623, 13624, 13627, 13628, or 13629. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 5632, 5633, 13251, 13252, 13253, 13254, 13255, 13256, 13257, 13258, 13259, 13260, 13261, 13262, 13263, 13264, or 13265. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[495] Any of the PEgRNAs of Table 74 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 74 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 1994, 2000, 2004, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3247, 3248, 3260, 3262, 3263, 3264, 3266, 3268, 3269, 3270, 3271, 3272, 3273, 3275, 3277, 3278, 3279, 3280, 3282, 3283, 3285, 3287, 3291, 3293, 3295, 3297, 3299, 13630, 13631, 13632, 13633, 13634, or 13635. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 74. The ngRNA spacers in Table 74 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation.

Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 74 can comprise a sequence corresponding to sequence number 2012, 2013, 2015, 2016, 2060, 2061, 2062, 4085, 4086, 4087, 4090, 4091, 4099, 4100, 4101, 4105, 4106, 4108, 4110, 4113, 4115, 4117, 4118, 4120, 4122, 4123, 4124, or 4125.

[496] Table 75 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CTGG PAM sequence. The PEgRNAs of Table 75 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[497] The PEgRNAs exemplified in Table 75 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 13636; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 95 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 13660-13664, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 13643. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 13636-13642. In some embodiments, the PEgRNA spacer comprises sequence number 13640. The PEgRNA spacers in Table 75 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 13663, 13665, 13672, 13679, 13683, or 13689. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 13660, 13661, 13662, 13664, 13666, 13667, 13668, 13669, 13670, 13671, 13673, 13674, 13675, 13676, 13677, 13678, 13680, 13681, 13682, 13684, 13685, 13686, 13687, or 13688. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 13643-13659. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[498] Any of the PEgRNAs of Table 75 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 75 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 68, 76, 93, 95, 96, 98, 1224, 1227, 6449, 6455, or 6536. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 75. The ngRNA spacers in Table 75 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence

compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 75 can comprise a sequence corresponding to sequence number 100, 101, 102, 104, 105, 109, 112, 113, or 117.

[499] Table 76 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GTGG PAM sequence. The PEgRNAs of Table 76 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[500] The PEgRNAs exemplified in Table 76 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 13690; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 92 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 13714-13717, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 13697. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 13690-13696. In some embodiments, the PEgRNA spacer comprises sequence number 13694. The PEgRNA spacers in Table 76 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 13716, 13718, 13724, 13727, 13732, 13736, 13740, 13743, or 13749. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 13714, 13715, 13717, 13719, 13720, 13721, 13722, 13723, 13725, 13726, 13728, 13729, 13730, 13731, 13733, 13734, 13735, 13737, 13738, 13739, 13741, 13742, 13744, 13745, 13746, 13747, or 13748. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 13697-13713. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[501] Any of the PEgRNAs of Table 76 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 76 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 68, 76, 93, 95, 96, 98, 1224, 1227, 6449, 6455, 6536, 9861, 9862, or 13750. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 76. The ngRNA spacers in Table 76 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 76 can comprise a sequence corresponding to sequence number 100, 101, 102, 104, 105, 109, 112, 113, or 117.

[502] Table 77 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GTGG PAM sequence. The PEgRNAs of Table 77 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[503] The PEgRNAs exemplified in Table 77 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 13751; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 83 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 13774-13777, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 2024. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 13751-13757. In some embodiments, the PEgRNA spacer comprises sequence number 13755. The PEgRNA spacers in Table 77 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 13777, 13780, 13785, 13787, 13793, 13796, 13800, 13805, 13807, 13813, 13817, 13820, 13824, 13828, 13830, 13836, 13840, or 13845. Alternatively, the editing template can encode one

or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 13774, 13775, 13776, 13778, 13779, 13781, 13782, 13783, 13784, 13786, 13788, 13789, 13790, 13791, 13792, 13794, 13795, 13797, 13798, 13799, 13801, 13802, 13803, 13804, 13806, 13808, 13809, 13810, 13811, 13812, 13814, 13815, 13816, 13818, 13819, 13821, 13822, 13823, 13825, 13826, 13827, 13829, 13831, 13832, 13833, 13834, 13835, 13837, 13838, 13839, 13841, 13842, 13843, or 13844. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 2024, 13758, 13759, 13760, 13761, 13762, 13763, 13764, 13765, 13766, 13767, 13768, 13769, 13770, 13771, 13772, or 13773. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[504] Any of the PEgRNAs of Table 77 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 77 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 68, 76, 93, 95, 96, 98, 1224, 1227, 6449, or 6536. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 77. The ngRNA spacers in Table 77 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 77 can comprise a sequence corresponding to sequence number 100, 101, 102, 104, 105, 109, 112, 113, or 117.

[505] Table 78 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GCGG PAM sequence. The PEgRNAs of Table 78 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[506] The PEgRNAs exemplified in Table 78 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 13846; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 71 nucleotides in length and

comprising at its 3' end a sequence corresponding to any one of sequence numbers 13868-13871, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 10073. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 13846-13852. In some embodiments, the PEgRNA spacer comprises sequence number 13850. The PEgRNA spacers in Table 78 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 13870, 13874, 13877, 13883, 13887, 13888, 13892, 13898, 13903, 13906, 13908, 13912, 13918, 13922, 13924, 13930, 13935, 13938, 13941, 13946, 13951, 13953, 13956, 13962, 13967, 13971, 13975, 13978, 13980, or 13985. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 13868, 13869, 13871, 13872, 13873, 13875, 13876, 13878, 13879, 13880, 13881, 13882, 13884, 13885, 13886, 13889, 13890, 13891, 13893, 13894, 13895, 13896, 13897, 13899, 13900, 13901, 13902, 13904, 13905, 13907, 13909, 13910, 13911, 13913, 13914, 13915, 13916, 13917, 13919, 13920, 13921, 13923, 13925, 13926, 13927, 13928, 13929, 13931, 13932, 13933, 13934, 13936, 13937, 13939, 13940, 13942, 13943, 13944, 13945, 13947, 13948, 13949, 13950, 13952, 13954, 13955, 13957, 13958, 13959, 13960, 13961, 13963, 13964, 13965, 13966, 13968, 13969, 13970, 13972, 13973, 13974, 13976, 13977, 13979, 13981, 13982, 13983, 13984, 13986, or 13987. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 10073, 12110, 13853, 13854, 13855, 13856, 13857, 13858, 13859, 13860, 13861, 13862, 13863, 13864, 13865, 13866, or 13867. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[507] Any of the PEgRNAs of Table 78 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 78 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 68, 76, 93, 95, 96, 98, 1224, 1227, 6449, or 6536. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 78. The ngRNA spacers in Table 78 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-

edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 78 can comprise a sequence corresponding to sequence number 100, 101, 102, 104, 105, 109, 112, 113, or 117.

[508] Table 79 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CTGG PAM sequence. The PEgRNAs of Table 79 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[509] The PEgRNAs exemplified in Table 79 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 13988; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 11 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 14010-14014, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 5849. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 13988-13994. In some embodiments, the PEgRNA spacer comprises sequence number 13992. The PEgRNA spacers in Table 79 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 14010, 14016, 14024, 14026, 14030, 14038, 14041, 14046, 14051, 14059, 14062, 14065, 14074, 14079, 14083, 14087, 14090, 14096, 14100, 14109, 14114, 14115, 14121, 14126, 14133, 14139, 14141, 14148, 14153, 14158, 14162, 14169, 14172, 14175, 14184, 14188, 14190, 14197, 14202, 14205, 14212, 14217, 14224, 14229, 14233, 14236, 14243, 14248, 14254, 14259, 14260, 14267, 14272, 14277, 14280, 14289, 14294, 14295, 14303, 14309, 14314, 14318, 14321, 14326, 14331, 14335, 14343, 14345, 14354, 14356, 14363, 14366, 14373, 14376, 14383, 14388, 14392, 14398, 14403, 14407, 14412, 14417, 14424, 14429, 14431, 14436, 14442, 14446, 14453, or 14458. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 14011, 14012, 14013, 14014, 14015, 14017, 14018, 14019, 14020, 14021, 14022, 14023, 14025, 14027, 14028, 14029, 14031, 14032, 14033, 14034, 14035, 14036, 14037, 14039, 14040, 14042, 14043, 14044, 14045, 14047, 14048, 14049, 14050, 14052, 14053, 14054, 14055, 14056, 14057, 14058, 14060, 14061, 14063, 14064, 14066, 14067, 14068, 14069, 14070, 14071, 14072, 14073, 14075, 14076, 14077, 14078, 14080, 14081, 14082, 14084, 14085, 14086, 14088, 14089, 14091, 14092, 14093, 14094, 14095, 14097, 14098, 14099, 14101, 14102,

14103, 14104, 14105, 14106, 14107, 14108, 14110, 14111, 14112, 14113, 14116, 14117, 14118, 14119, 14120, 14122, 14123, 14124, 14125, 14127, 14128, 14129, 14130, 14131, 14132, 14134, 14135, 14136, 14137, 14138, 14140, 14142, 14143, 14144, 14145, 14146, 14147, 14149, 14150, 14151, 14152, 14154, 14155, 14156, 14157, 14159, 14160, 14161, 14163, 14164, 14165, 14166, 14167, 14168, 14170, 14171, 14173, 14174, 14176, 14177, 14178, 14179, 14180, 14181, 14182, 14183, 14185, 14186, 14187, 14189, 14191, 14192, 14193, 14194, 14195, 14196, 14198, 14199, 14200, 14201, 14203, 14204, 14206, 14207, 14208, 14209, 14210, 14211, 14213, 14214, 14215, 14216, 14218, 14219, 14220, 14221, 14222, 14223, 14225, 14226, 14227, 14228, 14230, 14231, 14232, 14234, 14235, 14237, 14238, 14239, 14240, 14241, 14242, 14244, 14245, 14246, 14247, 14249, 14250, 14251, 14252, 14253, 14255, 14256, 14257, 14258, 14261, 14262, 14263, 14264, 14265, 14266, 14268, 14269, 14270, 14271, 14273, 14274, 14275, 14276, 14278, 14279, 14281, 14282, 14283, 14284, 14285, 14286, 14287, 14288, 14290, 14291, 14292, 14293, 14296, 14297, 14298, 14299, 14300, 14301, 14302, 14304, 14305, 14306, 14307, 14308, 14310, 14311, 14312, 14313, 14315, 14316, 14317, 14319, 14320, 14322, 14323, 14324, 14325, 14327, 14328, 14329, 14330, 14332, 14333, 14334, 14336, 14337, 14338, 14339, 14340, 14341, 14342, 14344, 14346, 14347, 14348, 14349, 14350, 14351, 14352, 14353, 14355, 14357, 14358, 14359, 14360, 14361, 14362, 14364, 14365, 14367, 14368, 14369, 14370, 14371, 14372, 14374, 14375, 14377, 14378, 14379, 14380, 14381, 14382, 14384, 14385, 14386, 14387, 14389, 14390, 14391, 14393, 14394, 14395, 14396, 14397, 14399, 14400, 14401, 14402, 14404, 14405, 14406, 14408, 14409, 14410, 14411, 14413, 14414, 14415, 14416, 14418, 14419, 14420, 14421, 14422, 14423, 14425, 14426, 14427, 14428, 14430, 14432, 14433, 14434, 14435, 14437, 14438, 14439, 14440, 14441, 14443, 14444, 14445, 14447, 14448, 14449, 14450, 14451, 14452, 14454, 14455, 14456, 14457, or 14459. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 5849, 5850, 13995, 13996, 13997, 13998, 13999, 14000, 14001, 14002, 14003, 14004, 14005, 14006, 14007, 14008, or 14009. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[510] Any of the PEgRNAs of Table 79 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 79 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 93, 1216, 1224, 1225, 1226, 1227, 1236, or 1244. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 79. The ngRNA spacers in Table 79 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-

edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 79 can comprise a sequence corresponding to sequence number 104 or 117.

[511] Table 80 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a GTGG PAM sequence. The PEgRNAs of Table 80 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[512] The PEgRNAs exemplified in Table 80 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 14460; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 10 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 14484, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 14467. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 14460-14466. In some embodiments, the PEgRNA spacer comprises sequence number 14464. The PEgRNA spacers in Table 80 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 14484-14574. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 14467-14483. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[513] Any of the PEgRNAs of Table 80 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 80 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 93, 1216, 1224, 1227, 1244, or 14575. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 80. The ngRNA spacers in Table 80 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-

edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*). Exemplary ngRNA provided in Table 80 can comprise a sequence corresponding to sequence number 104 or 117.

[514] Table 81 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a ATGG PAM sequence. The PEgRNAs of Table 81 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[515] The PEgRNAs exemplified in Table 81 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 14576; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 97 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 14600, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 14583. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 14576-14582. In some embodiments, the PEgRNA spacer comprises sequence number 14580. The PEgRNA spacers in Table 81 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 14600-14603. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 14583-14599. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[516] Any of the PEgRNAs of Table 81 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 81 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 7112, 7117, 7156, 7157, or 7159. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 81. The ngRNA spacers in Table 81 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the

non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[517] Table 82 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CCTGGT PAM sequence. The PEgRNAs of Table 82 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[518] The PEgRNAs exemplified in Table 82 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 14604; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 96 nucleotides in length and comprising at its 3' end a sequence corresponding to any one of sequence numbers 14625-14627, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 7082. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 14604-14610. In some embodiments, the PEgRNA spacer comprises sequence number 14608. The PEgRNA spacers in Table 82 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to sequence number 14626, 14630, 14631, 14636, or 14637. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The editing template can encode one or more synonymous mutations that are PAM silencing mutations and can comprise at its 3' end the sequence corresponding to sequence number 14625, 14627, 14628, 14629, 14632, 14633, 14634, 14635, 14638, or 14639. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 7082, 7083, 9905, 14611, 14612, 14613, 14614, 14615, 14616, 14617, 14618, 14619, 14620, 14621, 14622, 14623, or 14624. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[519] Any of the PEgRNAs of Table 82 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 82 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 70, 6453, or 6455. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 82. The ngRNA spacers in Table 82 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be

advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[520] Table 83 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CATGGT PAM sequence. The PEgRNAs of Table 83 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[521] The PEgRNAs exemplified in Table 83 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 14640; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 98 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 14663, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 10833. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 14640-14646. In some embodiments, the PEgRNA spacer comprises sequence number 14644. The PEgRNA spacers in Table 83 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 14663-14665. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 10833, 14647, 14648, 14649, 14650, 14651, 14652, 14653, 14654, 14655, 14656, 14657, 14658, 14659, 14660, 14661, or 14662. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[522] Any of the PEgRNAs of Table 83 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 83 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 5999, 6000, 6001, 6002, or 6454. In some embodiments, the spacer of the ngRNA is a ngRNA spacer listed in Table 83. The ngRNA spacers

in Table 83 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[523] Table 84 provides Prime Editing guide RNAs (PEgRNAs) that can be used with any Prime Editor containing a Cas9 protein capable of recognizing a CCAAGT PAM sequence. The PEgRNAs of Table 84 can also be used in Prime Editing systems further comprising a nick guide RNA (ngRNA). Such PEgRNAs and Prime Editing systems can be used, for example, to correct an R778L mutation in ATP7B.

[524] The PEgRNAs exemplified in Table 84 comprise: (a) a spacer comprising at its 3' end a sequence corresponding to sequence number 14666; (b) a gRNA core capable of complexing with a Cas9 protein, and (c) an extension arm comprising: (i) an editing template at least 21 nucleotides in length and comprising at its 3' end a sequence corresponding to sequence number 14689, and (ii) a prime binding site (PBS) comprising at its 5' end a sequence corresponding to sequence number 9870. The PEgRNA spacer can be, for example, 16-22 nucleotides in length and can comprise the sequence corresponding to any one of sequence numbers 14666-14672. In some embodiments, the PEgRNA spacer comprises sequence number 14670. The PEgRNA spacers in Table 84 are annotated with their PAM sequence(s), enabling the selection of an appropriate Cas9 protein. The editing template can be referred to as a reverse transcription template (RTT). The editing template can encode wildtype ATP7B gene sequence. For example, the editing template can comprise at its 3' end the sequence corresponding to any one of sequence numbers 14689-14768. Alternatively, the editing template can encode one or more synonymous mutations relative to the wildtype ATP7B gene. The PBS can be, for example, 3 to 19 nucleotides in length and can comprise the sequence corresponding to sequence number 9870, 14673, 14674, 14675, 14676, 14677, 14678, 14679, 14680, 14681, 14682, 14683, 14684, 14685, 14686, 14687, or 14688. In some cases, a PBS length of no more than 3 nucleotides less than the PEgRNA spacer length is chosen.

[525] Any of the PEgRNAs of Table 84 can be used in a Prime Editing system further comprising a nick guide RNA (ngRNA). Such ngRNA can comprise a spacer comprising at its 3' end a sequence corresponding to nucleotides 5-20 of any ngRNA spacer listed in Table 84 and a gRNA core capable of complexing with a Cas9 protein. For example, the sequence in the spacer of the ngRNA can comprise nucleotides 5-20, 4-20, 3-20, 2-20, or 1-20 of sequence number 5999. In some embodiments, the spacer

of the ngRNA is a ngRNA spacer listed in Table 84. The ngRNA spacers in Table 84 are annotated with their PAM sequences, enabling selection of an appropriate Cas9 protein. It can be advantageous to select a ngRNA spacer that has a PAM sequence compatible with the Cas9 protein used in the Prime Editor, thus avoiding the need to use two different Cas9 proteins. The ngRNA is capable of directing a complexed Cas9 protein to bind the edit strand of the ATP7B gene; thus, a complexed Cas9 nickase containing a nuclease inactivating mutation in the HNH domain will nick the non-edit strand. A PE3 ngRNA spacer has perfect complementarity to the edit strand both pre- and post-edit; a PE3b ngRNA spacer has perfect complementarity to the edit strand post-edit; and a PE3* spacer has perfect complementarity to the edit strand post-edit with a PEgRNA containing an edit template encoding a PAM silencing mutation. Because some PAMs can be silenced by more than 1 synonymous mutation, edit templates (RTTs) encoding a PAM silencing mutation and ngRNA spacers having 100% complementary with the portion of the edit strand containing the encoded PAM silencing mutation are coded with a number following the asterisk (*).

[526]

[527] In some embodiments, the PEgRNA and/or the ngRNA comprises a gRNA core, wherein the gRNA core comprises a sequence selected from SEQ ID Nos:14894-14896.

[528] In some embodiments, a PEgRNA (or ngRNA) comprises an additional secondary structure at the 5' end. In some embodiments, a PEgRNA (or ngRNA) comprises an additional secondary structure at the 3' end.

[529] In some embodiments, the secondary structure comprises a pseudoknot. In some embodiments, the secondary structure comprises a pseudoknot derived from a virus. In some embodiments, the secondary structure comprises a pseudoknot of a Moloney murine leukemia virus (M-MLV) genome (a mpknot). In some embodiments, the secondary structure comprises a nucleotide sequence selected from the group consisting of

GGGUCAGGAGCCCCCCCCCUGAACCCAGGAUAACCCUCAAAGUCGGGGGGCAACC (SEQ ID No: 14921),

GUCAGGGUCAGGAGCCCCCCCCCUGAACCCAGGAUAACCCUCAAAGUCGGGGGGCAACCC (SEQ ID No: 14922),

GGGUCAGGAGCCCCCCCCCUGAACCCAGGAAAACCCUCAAAGUCGGGGGGCAACCC (SEQ ID No: 14923),

GGGUCAGGAGCCCCCCCCCUGCACCCAGGAAAACCCUCAAAGUCGGGGGGCAACCC (SEQ ID No: 14924),

GGGUCAGGAGCCCCCCCCCUGCACCCAGGAUAACCCUCAAAGUCGGGGGGCAACCC (SEQ ID No: 14925),

GUCAGGGUCAGGAGCCCCCCCCCUGAACCCAGGAAAACCCUCAAAGUCGGGGGGCAACCC (SEQ ID No: 14926),

GUCAGGGUCAGGAGCCCCCCCCCUGCACCCAGGAAAACCCUCAAAGUCGGGGGGCAACCC

(SEQ ID No: 14927), and
GGGUCAGGAGCCCCCCCCCUGAACCCAGGAUAACCCUCAAAGUCGGGGGGC (SEQ ID No: 14928), or a nucleotide sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity therewith. In some embodiments, the secondary structure comprises a nucleotide sequence of GGGUCAGGAGCCCCCCCCCUGAACCCAGGAUAACCCUCAAAGUCGGGGGGC (SEQ ID No: 14928), or a nucleotide sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity therewith.

[530] In some embodiments, the secondary structure comprises a quadruplex. In some embodiments, the secondary structure comprises a G-quadruplex. In some embodiments, the secondary structure comprises a nucleotide sequence selected from the group consisting of gq2(UGGUGGUGGUGGU) (SEQ ID No: 14929), stk40(GGGACAGGGCAGGGACAGGG) (SEQ ID No: 14930), apc2(GGGUCCGGGUCUGGGUCUGGG) (SEQ ID No: 14931), stard3(GGGCAGGGUCUGGGCUGGG) (SEQ ID No: 14932), tns1(GGGCUGGGAUGGGAAAGGG) (SEQ ID No: 14933), ceacam4(GGGCUCUGGGUGGGCCGGG) (SEQ ID No: 14934), erc1(GGGCUGGGCUGGGCAGGG) (SEQ ID No: 14935), pitpnm3(GGGUGGGCUGGGAAGGG) (SEQ ID No: 14936), rlf(GGGAGGGAGGGCUAGGG) (SEQ ID No: 14937), ube3c(GGGCAGGGCUGGGAGGG) (SEQ ID No: 14938), taf15(GGGUGGGAGGGCUGGG) (SEQ ID No: 14939), and xrn1(GCGUAACCUCCAUCCGAGUUGCAAGAGAGGGAAACGCAGUCUC) (SEQ ID No: 14940), or a nucleotide sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity therewith.

[531] In some embodiments, the secondary structure comprises aP4-P6 domain of a Group I intron. In some embodiments, the secondary structure comprises the nucleotide sequence of GGAAUUGCGGGAAAGGGGUCAACAGCCGUUCAGUACCAAGUCUCAGGGGAAACUUUGAG AUGGCCUUGCAAAGGGUAUGGUAAUAAGCUGACGGACAUGGUCCUAACCACGCAGCCAA GUCCUAAGUCAACAGAUCUUCUGUUGAUAUGGAUGCAGUUCA (SEQ ID No: 14941), or a nucleotide sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity therewith.

[532] In some embodiments, the secondary structure comprises a riboswitch aptamer. In some embodiments, the secondary structure comprises a riboswitch aptamer derived from a prequeosine-1 riboswitch aptamer. In some embodiments, the secondary structure comprises a modified prequeosine-1 riboswitch aptamer. In some embodiments, the secondary structure comprises a nucleotide sequence selected from the group consisting of of
UUGACGCGGUUCUAUCUAGUUACGCGUUAAACCAACUAGAAA (SEQ ID No: 14942), UUGACGCGGUUCUAUCUACUUACGCGUUAAACCAACUAGAAA (SEQ ID No: 14943), CGCGAGUCUAGGGGAUAACGCGUUAAACUUCCUAGAAGGCGGUU (SEQ ID No: 14944), CGCGGAUCUAGAUUGUAACGCGUUAAACCAUCUAGAAGGCGGUU (SEQ ID No: 14945), CGCGUCGCUACCGCCCGGCGCGUUAAACACACUAGAAGGCGGUU (SEQ ID No: 14946), and

CGCGGUUCUAUCUAGUUACGCGUUAAACCAACUAGAA (SEQ ID No: 14947), or a nucleotide sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity therewith. In some embodiments, the secondary structure comprises a nucleotide sequence selected from the group consisting of UUGACGCGGUUCUAUCUAGUUACGCGUUAAACCAACUAGAAA (SEQ ID No: 14942), CGCGAGUCUAGGGGAUAACGCGUUAAACUUCCUAGAAGGCGGUU (SEQ ID No: 14944), CGCGGAUCUAGAUUGUAACGCGUUAAACCAUCUAGAAGGCGGUU (SEQ ID No: 14945), CGCGUCGCUACCGCCCGGCGCGUUAAACACACUAGAAGGCGGUU (SEQ ID No: 14946), and CGCGGUUCUAUCUAGUUACGCGUUAAACCAACUAGAA (SEQ ID No: 14947), or a nucleotide sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity therewith. In some embodiments, the secondary structure comprises a nucleotide sequence of and CGCGGUUCUAUCUAGUUACGCGUUAAACCAACUAGAA (SEQ ID No: 14947), or a nucleotide sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity therewith.

[533] In some embodiments, the secondary structure is linked to one or more other component of a PEgRNA via a linker. For example, in some embodiments, the secondary structure is at the 3' end of the PEgRNA and is linked to the 3' end of a PBS via a linker. In some embodiments, the secondary structure is at the 5' end of the PEgRNA and is linked to the 5' end of a spacer via a linker. In some embodiments, the linker is a nucleotide linker that is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 nucleotides in length. In some embodiments, the linker is 5 to 10 nucleotides in length. In some embodiments, the linker is 10 to 20 nucleotides in length. In some embodiments, the linker is 15 to 25 nucleotides in length. In some embodiments, the linker is 8 nucleotides in length.

[534] In some embodiments, the linker is designed to minimize base pairing between the linker and another component of the PEgRNA. In some embodiments, the linker is designed to minimize base pairing between the linker and the spacer. In some embodiments, the linker is designed to minimize base pairing between the linker and the PBS. In some embodiments, the linker is designed to minimize base pairing between the linker and the editing template. In some embodiments, the linker is designed to minimize base pairing between the linker and the sequence of the RNA secondary structure. In some embodiments, the linker is optimized to minimize base pairing between the linker and another component of the PEgRNA, in order of the following priority: spacer, PBS, editing template and then scaffold. In some embodiments, base paring probability is calculated using ViennaRNA 2.0 ,as described in Lorenz, R. *et al*. ViennaRNA package 2.0. Algorithms Mol. Biol. 6, incorporated by reference in its entirety herein, under standard parameters (37 °C, 1 M NaCl, 0.05 M MgCl2).

[535] In some embodiments, the PEgRNA comprises a RNA secondary structure and/or a linker disclosed in Nelson et al. Engineered pegRNAs improve prime editing efficiency. Nat Biotechnol. (2021), the entirety of which is incorporated herein by reference.

[536] In some embodiments, a PEgRNA is transcribed from a nucleotide encoding the PEgRNA, for example, a DNA plasmid encoding the PEgRNA. In some embodiments, the PEgRNA comprises a self-

cleaving element. In some embodiments, the self-cleaving element improves transcription and/or processing of the PEgRNA when transcribed form the nucleotide encoding the PEgRNA. In some embodiments, the PEgRNA comprises a hairpin or a RNA quadruplex. In some embodiments, the PEgRNA comprises a self-cleaving ribozyme element, for example, a hammerhead, a pistol, a hatchet, a hairpin, a VS, a twister, or a twister sister ribozyme. In some embodiments, the PEgRNA comprises a HDV ribozyme. In some embodiments, the PEgRNA comprises a hairpin recognized by Csy4. In some embodiments, the PEgRNA comprises an ENE motif. In some embodiments, the PEgRNA comprises an element for nuclear expression (ENE) from MALAT1 lnc RNA. In some embodiments, the PEgRNA comprises an ENE element from Kaposi's sarcoma-associated herpesvirus (KSHV). In some embodiments, the PEgRNA comprises a 3' box of a U1 snRNA. In some embodiments, the PEgRNA forms a circular RNA.

[537] In some embodiments, the PEgRNA comprises a RNA secondary structure or a motif that improves binding to the DNA-RNA duple or enhances PEgRNA activity. In some embodiments, the PEgRNA comprises a sequence derived from a native nucleotide element involved in reverse transcription, e.g., initiation of retroviral transcription. In some embodiments, the PEgRNA comprises a sequence of, or derived from, a primer binding site of a substrate of a reverse transcriptase, a polypurine tract (PPT), or a kissing loop. In some embodiments, the PEgRNA comprises a dimerization motif, a kissing loop, or a GNRA tetraloop – tetraloop receptor pair that results in circularization of the PEgRNA. In some embodiments, the PEgRNA comprises a RNA secondary structure of a motif that results in physical separation of the spacer and the PBS of the PEgRNA, thereby prevents occlusion of the spacer and improves PEgRNA activity. In some embodiments, the PEgRNA comprises a secondary structure or motif, e.g., a 5' or 3' extension in the spacer region that form a toehold or hairpin, wherein the secondary structure or motif competes favorably against annealing between the spacer and the PBS of the PEgRNA, thereby prevents occlusion of the spacer and improves PEgRNA activity.

[538] In some embodiments, a PEgRNA comprises the sequence *GGCCGGCAUGGUCCCAGCCUCCUCGCUGGCGCCGGCUGGGCAACAUGCUUCGGCAUGGCGA AUGGGAC* (SEQ ID No: 14948) at the 3' end. In some embodiments, a PEgRNA comprises the structure [spacer]-[gRNA core]-[editing template]-[PBS]-*GGCCGGCAUGGUCCCAGCCUCCUCGCUGGCGCCGGCUGGGCAACAUGCUUCGGCAUGGCGA AUGGGAC* (SEQ ID NO: 14948), or [spacer]-[gRNA core]-[editing template]-[PBS]-*GGCCGGCAUGGUCCCAGCCUCCUCGCUGGCGCCGGCUGGGCAACAUGCUUCGGCAUGGCGA AUGGGAC*-(U)n (SEQ ID NO: 14962), wherein n is an integer between 3 and 7. The structure derived from hepatitis D virus (HDV) is italicized.

[539] In some embodiments, the PEgRNA comprises the sequence *GGUGGGAGACGUCCCACC* (SEQ ID No: 14949) at the 5' end and/or the sequence *UGGGAGACGUCCCACC* (SEQ ID NO: 14963) at the 3' end. In some embodiments, the PEgRNA comprises the following structure (M-MLV kissing loop): *GGUGGGAGACGUCCCACC* (SEQ ID NO: 14949)-[spacer]-[gRNA core]-[editing template]-

[PBS]-*UGGGAGACGUCCCACC (SEQ ID NO:* 14963*)*, or *GGUGGGAGACGUCCCACC (SEQ ID NO:* 14949*)*-[spacer]-[gRNA core]-[editing template]-[PBS]-*UGGGAGACGUCCCACC*-(U)n (SEQ ID NO: 14964), wherein n is an integer between 3 and 7. The kissing loop structure is italicized.

[540] In some embodiments, the PEgRNA comprises the sequence *GAGCAGCAUGGCGUCGCUGCUCAC* (SEQ ID No: 14950) at the 5' end and/or the sequence *CCAUCAGUUGACACCCUGAGG* (SEQ ID No: 14951) at the 3' end. In some embodiments, the PEgRNA comprises the following structure (VS ribozyme kissing loop):

[541] *GAGCAGCAUGGCGUCGCUGCUCAC (*SEQ ID NO: 14950*)*-[spacer]-[gRNA core]-[editing template]-[PBS]- *CCAUCAGUUGACACCCUGAGG* (SEQ ID NO: 14951*)*, or *GAGCAGCAUGGCGUCGCUGCUCAC* (SEQ ID NO: 14950)-[spacer]-[gRNA core]-[editing template]-[PBS]- *CCAUCAGUUGACACCCUGAGG*-(U)n (SEQ ID NO: 14965), wherein n is an integer between 3 and 7. (VS ribozyme kissing loop)

[542] In some embodiments, the PEgRNA comprises the sequence *GCAGACCUAAGUGGUGACAUAUGGUCUG* (SEQ ID No: 14952) at the 5' end and/or the sequence *CAUGCGAUUAGAAAUAAUCGCAUG* (SEQ ID No: 14953) at the 3' end. In some embodiments, the PEgRNA comprises the following structure (tetraloop and receptor): *GCAGACCUAAGUGGUGACAUAUGGUCUG* (SEQ ID NO: 14952)-[spacer]-[gRNA core]-[editing template]-[PBS]- *CAUGCGAUUAGAAAUAAUCGCAUG* (SEQ ID NO: 14953), or *GCAGACCUAAGUGGUGACAUAUGGUCUG* (SEQ ID NO: 14952)-[spacer]-[gRNA core]-[editing template]-[PBS]- *CAUGCGAUUAGAAAUAAUCGCAUG*-(U)n (SEQ ID NO: 14966), wherein n is an integer between 3 and 7. The tetraloop/tetraloop receptor structure is italicized.

[543] In some embodiments, the PEgRNA comprises the sequence GGCCGGCAUGGUCCCAGCCUCCUCGCUGGCGCCGGCUGGGCAACAUGCUUCGGCAUGGCGAAUGGGAC (SEQ ID No: 14948) or UCUGCCAUCAAAGCUGCGACCGUGCUCAGUCUGGUGGGAGACGUCCCACCGGCCGGCAUGGUCCCAGCCUCCUCGCUGGCGCCGGCUGGGCAACAUGCUUCGGCAUGGCGAAUGGGAC (SEQ ID No: 14954).

[544] In some embodiments, a PEgRNA comprises a gRNA core that comprises a modified direct repeat compared to the sequence of a naturally occurring CRISPR-Cas guide RNA scaffold, for example, a Cas9 gRNA scaffold. In some embodiments, the PEgRNA comprises a "flip and extension (F+E)" gRNA core, wherein one or more base pairs in a direct repeat is modified. In some embodiments, the PEgRNA comprises a first direct repeat (the first paring element or the lower stem), wherein a Uracil is changed to a Adenine (such that in the stem region, a U-A base pair is changed to a A-U base pair). In some embodiments, the PEgRNA comprises a first direct repeat wherein the fourth U-A base pair in the stem is changed to a A-U base pair. In some embodiments, the PEgRNA comprises a first direct repeat wherein one or more U-A base pair is changed to a G-C or C-G base pair. For example, in some embodiments, the PEgRNA comprises a first direct repeat comprising a modification to a GUUUU-

AAAAC pairing element, wherein one or more of the U-A base pairs is changed to a A-U base pair, a G-C base pair, or a C-G base pair. In some embodiments, the PEgRNA comprises an extended first direct repeat.

[545] In some embodiments, a PEgRNA comprises a gRNA core comprises the sequence GUUUUAGAGCUAUACGUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUUACGAAG UGGCACCGAGUCGGUGC (SEQ ID No: 14955) **or** GUUUUAGAGCUAUACGUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAACUUUACGAAG UGGGACCGAGUCGGUCC (SEQ ID No: 14956).

[546] In some embodiments, a PEgRNA comprises a gRNA core comprising the sequence GUUUUAGAGCUAGCUCAUGAAAAUGAGCUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUC AACUUGAAAAAGUGGGACCGAGUCGGUCC (SEQ ID No: 14957).

[547] In some embodiments, a PEgRNA comprises a gRNA core comprising the sequence GUUUGAGAGCUAGAAAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAG UGGGACCGAGUCGGUCC (SEQ ID No: 14906).

[548] In some embodiments, a PEgRNA comprises a gRNA core comprising the sequence GUUUAAGAGCUAGAAAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAACUUGAAAAAG UGGCACCGAGUCGGUGC (SEQ ID No: 14958). In some embodiments, a PEgRNA comprise a gRNA core comprising the sequence GUUUUAGAGCUAUGCUGGAAACAGCAUAGCAAGUUAAAAUAAGGCUAGUCCGUUAUCAA CUUGAAAAAGUGGCACCGAGUCGGUGC (SEQ ID No: 14959).

[549] In some embodiments, a PEgRNA comprise a gRNA core comprising the sequence GUUUAAGAGCUAUGCUGGAAACAGCAUAGCAAGUUUAAAUAAGGCUAGUCCGUUAUCAA CUUGAAAAAGUGGCACCG AGU CGGUGC (SEQ ID No: 14907).

[550] A PEgRNA and/or an ngRNA of this disclosure, in some embodiments, may include modified nucleotides, *e.g.*, chemically modified DNA or RNA nucleobases, and may include one or more nucleobase analogs (*e.g.*, modifications which might add functionality, such as temperature resilience). In some embodiments, PEgRNAs and/or ngRNAs as described herein may be chemically modified. The phrase "chemical modifications," as used herein, can include modifications which introduce chemistries which differ from those seen in naturally occurring DNA or RNAs, for example, covalent modifications such as the introduction of modified nucleotides, (*e.g.*, nucleotide analogs, or the inclusion of pendant groups which are not naturally found in DNA or RNA molecules).

[551] In some embodiments, the PEgRNAs provided in the disclosure may further comprise nucleotides added to the 5' of the PEgRNAs. In some embodiments, the PEgRNA further comprises 1, 2, or 3 additional nucleotides added to the 5' end. The additional nucleotides can be guanine, cytosine, adenine, or uracil. In some embodiments, the additional nucleotide at the 5' end of the PEgRNA is a guanine or cytosine. In some embodiments, the additional nucleotides can be chemically or biologically modified.

[552] In some embodiments, the PEgRNAs provided in the disclosure may further comprise nucleotides to the 3' of the PEgRNAs. In some embodiments, the PEgRNA further comprises 1, 2, or 3 additional nucleotides to the 3' end. The additional nucleotides can be guanine, cytosine, adenine, or uracil. In some embodiments, the additional nucleotides at the 3' end of the PEgRNA is a polynucleotide comprising at least 1 uracil. In some embodiments, the additional nucleotides can be chemically or biologically modified.

[553] In some embodiments, a PEgRNA or ngRNA is produced by transcription from a template nucleotide, for example, a template plasmid. In some embodiments, a polynucleotide encoding the PEgRNA or ngRNA is appended with one or more additional nucleotides that improves PEgRNA or ngRNA function or expression, e.g., expression from a plasmid that encodes the PEgRNA or ngRNA. In some embodiments, a polynucleotide encoding a PEgRNA or ngRNA is appended with one or more additional nucleotides at the 5' end or at the 3' end. In some embodiments, the polynucleotide encoding the PEgRNA or ngRNA is appended with a guanine at the 5' end, for example, if the first nucleotide at the 5' end of the spacer is not a guanine. In some embodiments, a polynucleotide encoding the PEgRNA or ngRNA is appended with nucleotide sequence CACC at the 5' end. In some embodiments, the polynucleotide encoding the PEgRNA or ngRNA is appended with an additional nucleotide adenine at the 3' end, for example, if the last nucleotide at the 3' end of the PBS is a Thymine. In some embodiments, the polynucleotide encoding the PEgRNA or ngRNA is appended with additional nucleotide sequence TTTTTT, TTTTTTT, TTTTT, or TTTT at the 3' end. In some embodiments, the PEgRNA or ngRNA comprises the appended nucleotides from the transcription template. In some embodiments, the PEgRNA or ngRNA further comprises one or more nucleotides at the 5' end or the 3' end in addition to spacer, PBS, and RTT sequences. in some embodiments, the PEgRNA or ngRNA further comprises a guanine at the 5' end, for example, when the first nucleotide at the 5' end of the spacer is not a guanine. In some embodiments, the PEgRNA or ngRNA further comprises nucleotide sequence CACC at the 5' end. In some embodiments, the PEgRNA or ngRNA further comprises an adenine at the 3' end, for example, if the last nucleotide at the 3' end of the PBS is a thymine. In some embodiments, the PEgRNA or ngRNA further comprises nucleotide sequence UUUUUUU, UUUUUU, UUUUU, or UUUU at the 3' end.

[554] In some embodiments, the PEgRNAs and/or ngRNAs provided in this disclosure may have undergone a chemical or biological modifications. Modifications may be made at any position within a PEgRNA or ngRNA, and may include modification to a nucleobase or to a phosphate backbone of the PEgRNA or ngRNA. In some embodiments, chemical modifications can be a structure guided modifications. In some embodiments, a chemical modification is at the 5' end and/or the 3' end of a PEgRNA. In some embodiments, a chemical modification is at the 5' end and/or the 3' end of a ngRNA. In some embodiments, a chemical modification may be within the spacer sequence, the extension arm, the editing template sequence, or the primer binding site of a PEgRNA. In some embodiments, a chemical modification may be within the spacer sequence or the gRNA core of a PEgRNA or a ngRNA.

In some embodiments, a chemical modification may be within the 3' most nucleotides of a PEgRNA or ngRNA. In some embodiments, a chemical modification may be within the 3' most end of a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more chemically modified nucleotides at the 3′ end. In some embodiments, a PEgRNA or ngRNA comprises 3 contiguous chemically modified nucleotides at the 3′ end. In some embodiments, a chemical modification may be within the 5' most end of a PEgRNA or ngRNA. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more chemically modified nucleotides at the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more chemically modified nucleotides at the 5' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, or 5 or more chemically modified nucleotides at the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, or 5 more chemically modified nucleotides at the 5' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, or 3 or more chemically modified nucleotides at the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, or 3 more chemically modified nucleotides at the 5' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more contiguous chemically modified nucleotides at the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more contiguous chemically modified nucleotides at the 5' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, or 5 contiguous chemically modified nucleotides at the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, or 5 contiguous chemically modified nucleotides at the 5' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, or 3 contiguous chemically modified nucleotides at the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, or 3 contiguous chemically modified nucleotides at the 5' end. In some embodiments, a PEgRNA or ngRNA comprises 3 contiguous chemically modified nucleotides at the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, or more chemically modified nucleotides near the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 3 contiguous chemically modified nucleotides at the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 3 contiguous chemically modified nucleotides at the 5' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, or more chemically modified nucleotides near the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, or more contiguous chemically modified nucleotides near the 3' end. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, or more chemically modified nucleotides near the 3' end, where the 3' most nucleotide is not modified, and the 1, 2, 3, 4, 5, or more chemically modified nucleotides precede the 3' most nucleotide in a 5'-to-3' order. In some embodiments, a PEgRNA or ngRNA comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or more chemically modified nucleotides near the 3' end, where the 3' most nucleotide is not modified, and the 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 or more chemically modified nucleotides precede the 3' most nucleotide in a 5'-to-3' order.

[555] In some embodiments, a PEgRNA or ngRNA comprises one or more chemical modified nucleotides in the gRNA core. The gRNA core of a PEgRNA may comprise one or more regions of a

base paired lower stem, a base paired upper stem, where the lower stem and upper stem may be connected by a bulge comprising unpaired RNAs. The gRNA core may further comprise a nexus distal from the spacer sequence. In some embodiments, the gRNA core comprises one or more chemically modified nucleotides in the lower stem, upper stem, and/or the hairpin regions. In some embodiments, all of the nucleotides in the lower stem, upper stem, and/or the hairpin regions are chemically modified.

[556] A chemical modification to a PEgRNA or ngRNA can comprise a 2′-O-thionocarbamate-protected nucleoside phosphoramidite, a 2′-O-methyl (M), a 2′-O-methyl 3′phosphorothioate (MS), or a 2′-O-methyl 3′thioPACE (MSP), or any combination thereof. In some embodiments, a chemically modified PEgRNA and/or ngRNA can comprise a '-O-methyl (M) RNA, a 2′-O-methyl 3′phosphorothioate (MS) RNA, a 2′-O-methyl 3′thioPACE (MSP) RNA, a 2'-F RNA, a phosphorothioate bond modification, any other chemical modifications known in the art, or any combination thereof. A chemical modification may also include, for example, the incorporation of non-nucleotide linkages or modified nucleotides into the PEgRNA and/or ngRNA (*e.g.*, modifications to one or both of the 3' and 5' ends of a guide RNA molecule). Such modifications can include the addition of bases to an RNA sequence, complexing the RNA with an agent (*e.g.*, a protein or a complementary nucleic acid molecule), and inclusion of elements which change the structure of an RNA molecule (*e.g.*, which form secondary structures).

Prime Editing Compositions

[557] Disclosed herein, in some embodiments, are compositions, systems, and methods using a prime editing composition. The term "prime editing composition" or "prime editing system" refers to compositions involved in the method of prime editing as described herein. A prime editing composition may include a prime editor, *e.g.*, a prime editor fusion protein, and a PEgRNA. A prime editing composition may further comprise additional elements, such as second strand nicking ngRNAs. Components of a prime editing composition may be combined to form a complex for prime editing, or may be kept separately, *e.g.*, for administration purposes. In some embodiments, a prime editing composition comprises a prime editor fusion protein complexed with a PEgRNA and optionally complexed with a ngRNA. In some embodiments, the prime editing composition comprises a prime editor comprising a DNA binding domain and a DNA polymerase domain associated with each other through a PEgRNA. For example, the prime editing composition may comprise a prime editor comprising a DNA binding domain and a DNA polymerase domain linked to each other by an RNA-protein recruitment aptamer RNA sequence, which is linked to a PEgRNA. In some embodiments, a prime editing composition comprises a PEgRNA and a polynucleotide, a polynucleotide construct, or a vector that encodes a prime editor fusion protein. In some embodiments, a prime editing composition comprises a PEgRNA, a ngRNA, and a polynucleotide, a polynucleotide construct, or a vector that encodes a prime editor fusion protein. In some embodiments, a prime editing composition comprises multiple polynucleotides, polynucleotide constructs, or vectors, each of which encodes one or more

prime editing composition components. In some embodiments, the PEgRNA of a prime editing composition is associated with the DNA binding domain, *e.g.*, a Cas9 nickase, of the prime editor. In some embodiments, the PEgRNA of a prime editing composition complexes with the DNA binding domain of a prime editor and directs the prime editor to the target DNA.

[558] In some embodiments, a prime editing composition comprises one or more polynucleotides that encode prime editor components and/or PEgRNA or ngRNAs. In some embodiments, a prime editing composition comprises a polynucleotide encoding a fusion protein comprising a DNA binding domain and a DNA polymerase domain. In some embodiments, a prime editing composition comprises (i) a polynucleotide encoding a fusion protein comprising a DNA binding domain and a DNA polymerase domain, and (ii) a PEgRNA or a polynucleotide encoding the PEgRNA. In some embodiments, a prime editing composition comprises (i) a polynucleotide encoding a fusion protein comprising a DNA binding domain and a DNA polymerase domain, (ii) a PEgRNA or a polynucleotide encoding the PEgRNA, and (iii) an ngRNA or a polynucleotide encoding the ngRNA. In some embodiments, a prime editing composition comprises (i) a polynucleotide encoding a DNA binding domain of a prime editor, *e.g.*, a Cas9 nickase, (ii) a polynucleotide encoding a DNA polymerase domain of a prime editor, *e.g.*, a reverse transcriptase, and (iii) a PEgRNA or a polynucleotide encoding the PEgRNA. In some embodiments, a prime editing composition comprises (i) a polynucleotide encoding a DNA binding domain of a prime editor, *e.g.*, a Cas9 nickase, (ii) a polynucleotide encoding a DNA polymerase domain of a prime editor, *e.g.*, a reverse transcriptase, (iii) a PEgRNA or a polynucleotide encoding the PEgRNA, and (iv) an ngRNA or a polynucleotide encoding the ngRNA. In some embodiments, the polynucleotide encoding the DNA biding domain or the polynucleotide encoding the DNA polymerase domain further encodes an additional polypeptide domain, *e.g.*, an RNA-protein recruitment domain, such as a MS2 coat protein domain. In some embodiments, a prime editing composition comprises (i) a polynucleotide encoding a N-terminal half of a prime editor fusion protein and an intein-N and (ii) a polynucleotide encoding a C-terminal half of a prime editor fusion protein and an intein-C. In some embodiments, a prime editing composition comprises (i) a polynucleotide encoding a N-terminal half of a prime editor fusion protein and an intein-N (ii) a polynucleotide encoding a C-terminal half of a prime editor fusion protein and an intein-C, (iii) a PEgRNA or a polynucleotide encoding the PEgRNA, and/or (iv) an ngRNA or a polynucleotide encoding the ngRNA. In some embodiments, a prime editing composition comprises (i) a polynucleotide encoding a N-terminal portion of a DNA binding domain and an intein-N, (ii) a polynucleotide encoding a C-terminal portion of the DNA binding domain, an intein-C, and a DNA polymerase domain. In some embodiments, the DNA binding domain is a Cas protein domain, *e.g.*, a Cas9 nickase. In some embodiments, the prime editing composition comprises (i) a polynucleotide encoding a N-terminal portion of a DNA binding domain and an intein-N, (ii) a polynucleotide encoding a C-terminal portion of the DNA binding domain, an intein-C, and a DNA polymerase domain, (iii) a PEgRNA or a polynucleotide encoding the PEgRNA, and/or (iv) a ngRNA or a polynucleotide encoding the ngRNA.

[559] In some embodiments, a prime editing system comprises one or more polynucleotides encoding one or more prime editor polypeptides, wherein activity of the prime editing system can be temporally regulated by controlling the timing in which the vectors are delivered. For example, in some embodiments, a polynucleotide encoding the prime editor and a polynucleotide encoding a PEgRNA can be delivered simultaneously. For example, in some embodiments, a polynucleotide encoding the prime editor and a polynucleotide encoding a PEgRNA can be delivered sequentially.

[560] In some embodiments, a polynucleotide encoding a component of a prime editing system can further comprise an element that is capable of modifying the intracellular half-life of the polynucleotide and/or modulating translational control. In some embodiments, the polynucleotide is a RNA, for example, an mRNA. In some embodiments, the half-life of the polynucleotide, e.g., the RNA may be increased. In some embodiments, the half-life of the polynucleotide, e.g., the RNA may be decreased. In some embodiments, the element may be capable of increasing the stability of the polynucleotide, e.g., the RNA. In some embodiments, the element may be capable of decreasing the stability of the polynucleotide, e.g., the RNA. In some embodiments, the element may be within the 3′ UTR of the RNA. In some embodiments, the element may include a polyadenylation signal (PA). In some embodiments, the element may include a cap, e.g., an upstream mRNA or PEgRNA end. In some embodiments, the RNA may comprise no PA such that it is subject to quicker degradation in the cell after transcription.

[561] In some embodiments, the element may include at least one AU-rich element (ARE). The AREs may be bound by ARE binding proteins (ARE-BPs) in a manner that is dependent upon tissue type, cell type, timing, cellular localization, and environment. In some embodiments the destabilizing element may promote RNA decay, affect RNA stability, or activate translation. In some embodiments, the ARE may comprise 50 to 150 nucleotides in length. In some embodiments, the ARE may comprise at least one copy of the sequence AUUUA. In some embodiments, at least one ARE may be added to the 3′ UTR of the RNA. In some embodiments, the element may be a Woodchuck Hepatitis Virus Posttranscriptional Regulatory Element (WPRE). In further embodiments, the element is a modified and/or truncated WPRE sequence that is capable of enhancing expression from the transcript. In some embodiments, the WPRE or equivalent may be added to the 3′ UTR of the RNA. In some embodiments, the element may be selected from other RNA sequence motifs that are enriched in either fast- or slow-decaying transcripts. In some embodiments, the polynucleotide, e.g., a vector, encoding the PE or the PEgRNA may be self-destroyed via cleavage of a target sequence present on the polynucleotide, e.g., a vector. The cleavage may prevent continued transcription of a PE or a PEgRNA.

[562] Polynucleotides encoding prime editing composition components can be DNA, RNA, or any combination thereof. In some embodiments, a polynucleotide encoding a prime editing composition component is an expression construct. In some embodiments, a polynucleotide encoding a prime editing composition component is a vector. In some embodiments, the vector is a DNA vector. In some embodiments, the vector is a plasmid. In some embodiments, the vector is a virus vector, *e.g.*, a retroviral

vector, adenoviral vector, lentiviral vector, herpesvirus vector, or an adeno-associated virus vector (AAV).

[563] In some embodiments, polynucleotides encoding polypeptide components of a prime editing composition are codon optimized by replacing at least one codon (*e.g.*, about or more than about 1, 2, 3, 4, 5, 10, 15, 20, 25, 50, or more codons) of the native sequence with codons that are more frequently or most frequently used in the genes of that host cell while maintaining the native amino acid sequence. In some embodiments, a polynucleotide encoding a polypeptide component of a prime editing composition are operably linked to one or more expression regulatory elements, for example, a promoter, a 3' UTR, a 5' UTR, or any combination thereof. In some embodiments, a polynucleotide encoding a prime editing composition component is a messenger RNA (mRNA). In some embodiments, the mRNA comprises a Cap at the 5' end and/or a poly A tail at the 3' end.

[564] In some embodiments, a PE3b*X ngRNA spacer will have 100% complementarity to an edited strand incorporating a polynucleotide encoded by a corresponding RTT*X wherein X is the same integer. In some embodiments X may be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 21, 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, 80, 81, 82, 83, 84, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, or 113.

Pharmaceutical compositions

[565] Disclosed herein are pharmaceutical compositions comprising any of the prime editing composition components, for example, prime editors, fusion proteins, polynucleotides encoding prime editor polypeptides, PEgRNAs, ngRNAs, and/or prime editing complexes described herein.

[566] The term "pharmaceutical composition", as used herein, refers to a composition formulated for pharmaceutical use. In some embodiments, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier. In some embodiments, the pharmaceutical composition comprises additional agents, *e.g.*, for specific delivery, increasing half-life, or other therapeutic compounds.

[567] In some embodiments, a pharmaceutically-acceptable carrier comprises any vehicle, such as a liquid or solid filler, diluent, excipient, manufacturing aid (*e.g.*, lubricant, talc magnesium, calcium or zinc stearate, or steric acid), or solvent encapsulating material, involved in carrying or transporting the compound from one site (*e.g.*, the delivery site) of the body, to another site (*e.g.*, organ, tissue or portion of the body). A pharmaceutically acceptable carrier is "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the tissue of the subject (*e.g.*, physiologically compatible, sterile, physiologic pH, etc.)

[568] Formulations of the pharmaceutical compositions described herein can be prepared by any method known or hereafter developed in the art of pharmacology. In general, such preparatory methods include the step of bringing the active ingredient(s) into association with an excipient and/or one or more

other accessory ingredients, and then, if necessary and/or desirable, shaping and/or packaging the product into a desired single- or multi-dose unit. Pharmaceutical formulations can additionally comprise a pharmaceutically acceptable excipient, which, as used herein, includes any and all solvents, dispersion media, diluents, or other liquid vehicles, dispersion or suspension aids, surface active agents, isotonic agents, thickening or emulsifying agents, preservatives, solid binders, lubricants and the like, as suited to the particular dosage form desired.

Methods of Editing

[569] The methods and compositions disclosed herein can be used to edit a target gene of interest by prime editing.

[570] In some embodiments, the prime editing method comprises contacting a target gene, *e.g.*, an *ATP7B* gene, with a PEgRNA and a prime editor (PE) polypeptide described herein. In some embodiments, the target gene is double stranded, and comprises two strands of DNA complementary to each other. In some embodiments, the contacting with a PEgRNA and the contacting with a prime editor are performed sequentially. In some embodiments, the contacting with a prime editor is performed after the contacting with a PEgRNA. In some embodiments, the contacting with a PEgRNA is performed after the contacting with a prime editor. In some embodiments, the contacting with a PEgRNA, and the contacting with a prime editor are performed simultaneously. In some embodiments, the PEgRNA and the prime editor are associated in a complex prior to contacting a target gene.

[571] In some embodiments, contacting the target gene with the prime editing composition results in binding of the PEgRNA to a target strand of the target gene, *e.g.*, an *ATP7B* gene. In some embodiments, contacting the target gene with the prime editing composition results in binding of the PEgRNA to a search target sequence on the target strand of the target gene upon contacting with the PEgRNA. In some embodiments, contacting the target gene with the prime editing composition results in binding of a spacer sequence of the PEgRNA to a search target sequence with the search target sequence on the target strand of the target gene upon said contacting of the PEgRNA.

[572] In some embodiments, contacting the target gene with the prime editing composition results in binding of the prime editor to the target gene, *e.g.*, the target *ATP7B* gene, upon the contacting of the PE composition with the target gene. In some embodiments, the DNA binding domain of the PE associates with the PEgRNA. In some embodiments, the PE binds the target gene, *e.g.*, an *ATP7B* gene, directed by the PEgRNA. Accordingly, in some embodiments, the contacting of the target gene result in binding of a DNA binding domain of a prime editor of the target *ATP7B* gene directed by the PEgRNA.

[573] In some embodiments, contacting the target gene with the prime editing composition results in a nick in an edit strand of the target gene, *e.g.*, an *ATP7B* gene by the prime editor upon contacting with the target gene, thereby generating a nicked on the edit strand of the target gene. In some embodiments, contacting the target gene with the prime editing composition results in a single-stranded DNA comprising a free 3′ end at the nick site of the edit strand of the target gene. In some embodiments,

contacting the target gene with the prime editing composition results in a nick in the edit strand of the target gene by a DNA binding domain of the prime editor, thereby generating a single-stranded DNA comprising a free 3′ end at the nick site. In some embodiments, the DNA binding domain of the prime editor is a Cas domain. In some embodiments, the DNA binding domain of the prime editor is a Cas9. In some embodiments, the DNA binding domain of the prime editor is a Cas9 nickase.

[574] In some embodiments, contacting the target gene with the prime editing composition results in hybridization of the PEgRNA with the 3' end of the nicked single-stranded DNA, thereby priming DNA polymerization by a DNA polymerase domain of the prime editor. In some embodiments, the free 3' end of the single-stranded DNA generated at the nick site hybridizes to a primer binding site sequence (PBS) of the contacted PEgRNA, thereby priming DNA polymerization. In some embodiments, the DNA polymerization is reverse transcription catalyzed by a reverse transcriptase domain of the prime editor. In some embodiments, the method comprises contacting the target gene with a DNA polymerase, *e.g.*, a reverse transcriptase, as a part of a prime editor fusion protein or prime editing complex (in *cis*), or as a separate protein (in *trans*).

[575] In some embodiments, contacting the target gene with the prime editing composition generates an edited single stranded DNA that is coded by the editing template of the PEgRNA by DNA polymerase mediated polymerization from the 3' free end of the single-stranded DNA at the nick site. In some embodiments, the editing template of the PEgRNA comprises one or more intended nucleotide edits compared to endogenous sequence of the target gene, *e.g.*, an *ATP7B* gene. In some embodiments, the intended nucleotide edits are incorporated in the target gene, by excision of the 5' single stranded DNA of the edit strand of the target gene generated at the nick site and DNA repair. In some embodiments, the intended nucleotide edits are incorporated in the target gene by excision of the editing target sequence and DNA repair. In some embodiments, excision of the 5' single stranded DNA of the edit strand generated at the nick site is by a flap endonuclease. In some embodiments, the flap nuclease is FEN1. In some embodiments, the method further comprises contacting the target gene with a flap endonuclease. In some embodiments, the flap endonuclease is provided as a part of a prime editor fusion protein. In some embodiments, the flap endonuclease is provided in *trans*.

[576] In some embodiments, contacting the target gene with the prime editing composition generates a mismatched heteroduplex comprising the edit strand of the target gene that comprises the edited single stranded DNA, and the unedited target strand of the target gene. Without being bound by theory, the endogenous DNA repair and replication may resolve the mismatched edited DNA to incorporate the nucleotide change(s) to form the desired edited target gene.

[577] In some embodiments, the method further comprises contacting the target gene, *e.g.*, an *ATP7B* gene, with a nick guide (ngRNA) disclosed herein. In some embodiments, the ngRNA comprises a spacer that binds a second search target sequence on the edit strand of the target gene. In some embodiments, the contacted ngRNA directs the PE to introduce a nick in the target strand of the target gene. In some embodiments, the nick on the target strand (non-edit strand) results in endogenous DNA repair

machinery to use the edit strand to repair the non-edit strand, thereby incorporating the intended nucleotide edit in both strand of the target gene and modifying the target gene. In some embodiments, the ngRNA comprises a spacer sequence that is complementary to, and may hybridize with, the second search target sequence on the edit strand only after the intended nucleotide edit(s) are incorporated in the edit strand of the target gene.

[578] In some embodiments, the target gene is contacted by the ngRNA, the PEgRNA, and the PE simultaneously. In some embodiments, the ngRNA, the PEgRNA, and the PE form a complex when they contact the target gene. In some embodiments, the target gene is contacted with the ngRNA, the PEgRNA, and the prime editor sequentially. In some embodiments, the target gene is contacted with the ngRNA and/or the PEgRNA after contacting the target gene with the PE. In some embodiments, the target gene is contacted with the ngRNA and/or the PEgRNA before contacting the target gene with the prime editor.

[579] In some embodiments, the target gene, *e.g.*, an *ATP7B* gene, is in a cell. Accordingly, also provided herein are methods of modifying a cell.

[580] In some embodiments, the prime editing method comprises introducing a PEgRNA, a prime editor, and/or a ngRNA into the cell that has the target gene. In some embodiments, the prime editing method comprises introducing into the cell that has the target gene with a prime editing composition comprising a PEgRNA, a prime editor polypeptide, and/or a ngRNA. In some embodiments, the PEgRNA, the prime editor polypeptide, and/or the ngRNA form a complex prior to the introduction into the cell. In some embodiments, the PEgRNA, the prime editor polypeptide, and/or the ngRNA form a complex after the introduction into the cell. The prime editors, PEgRNA and/or ngRNAs, and prime editing complexes may be introduced into the cell by any delivery approaches described herein or any delivery approach known in the art, including ribonucleoprotein (RNPs), lipid nanoparticles (LNPs), viral vectors, non-viral vectors, mRNA delivery, and physical techniques such as cell membrane disruption by a microfluidics device. The prime editors, PEgRNA and/or ngRNAs, and prime editing complexes may be introduced into the cell simultaneously or sequentially.

[581] In some embodiments, the prime editing method comprises introducing into the cell a PEgRNA or a polynucleotide encoding the PEgRNA, a prime editor polynucleotide encoding a prime editor polypeptide, and optionally an ngRNA or a polynucleotide encoding the ngRNA. In some embodiments, the method comprises introducing the PEgRNA or the polynucleotide encoding the PEgRNA, the polynucleotide encoding the prime editor polypeptide, and/or the ngRNA or the polynucleotide encoding the ngRNA into the cell simultaneously. In some embodiments, the method comprises introducing the PEgRNA or the polynucleotide encoding the PEgRNA, the polynucleotide encoding the prime editor polypeptide, and/or the ngRNA or the polynucleotide encoding the ngRNA into the cell sequentially. In some embodiments, the method comprises introducing the polynucleotide encoding the prime editor polypeptide into the cell before introduction of the PEgRNA or the polynucleotide encoding the PEgRNA and/or the ngRNA or the polynucleotide encoding the ngRNA. In some embodiments, the

polynucleotide encoding the prime editor polypeptide is introduced into and expressed in the cell before introduction of the PEgRNA or the polynucleotide encoding the PEgRNA and/or the ngRNA or the polynucleotide encoding the ngRNA into the cell. In some embodiments, the polynucleotide encoding the prime editor polypeptide is introduced into the cell after the PEgRNA or the polynucleotide encoding the PEgRNA and/or the ngRNA or the polynucleotide encoding the ngRNA are introduced into the cell. The polynucleotide encoding the prime editor polypeptide, the PEgRNA or the polynucleotide encoding the PEgRNA, and/or the ngRNA or the polynucleotide encoding the ngRNA, may be introduced into the cell by any delivery approaches described herein or any delivery approach known in the art, for example, by RNPs, LNPs, viral vectors, non-viral vectors, mRNA delivery, and physical. In some embodiments, the polynucleotide is a DNA polynucleotide. In some embodiments, the polynucleotide is a RNA polynucleotide, e.g., mRNA polynucleotide.

[582] In some embodiments, the polynucleotide encoding the prime editor polypeptide, the polynucleotide encoding the PEgRNA, and/or the polynucleotide encoding the ngRNA integrate into the genome of the cell after being introduced into the cell. In some embodiments, the polynucleotide encoding the prime editor polypeptide, the polynucleotide encoding the PEgRNA, and/or the polynucleotide encoding the ngRNA are introduced into the cell for transient expression. Accordingly, also provided herein are cells modified by prime editing.

[583] In some embodiments, the cell is a prokaryotic cell. In some embodiments, the cell is a eukaryotic cell. In some embodiments, the cell is a mammalian cell. In some embodiments, the cell is a non-human primate cell, bovine cell, porcine cell, rodent or mouse cell. In some embodiments, the cell is a human cell. In some embodiments, the cell is a primary cell. In some embodiments, the cell is a human primary cell. In some embodiments, the cell is a progenitor cell. In some embodiments, the cell is a human progenitor cell. In some embodiments, the cell is a hepatocyte. In some embodiments, the cell is a human hepatocyte. In some embodiments, the cell is a primary human hepatocyte derived from an induced human pluripotent stem cell (iPSC). In some embodiments, the cell is a neuron. In some embodiments, the cell is a neuron from basal ganglia. In some embodiments, the cell is a neuron from basal ganglia of a subject.

[584] In some embodiments, the target gene edited by prime editing is in a chromosome of the cell. In some embodiments, the intended nucleotide edits incorporate in the chromosome of the cell and are inheritable by progeny cells. In some embodiments, the intended nucleotide edits introduced to the cell by the prime editing compositions and methods are such that the cell and progeny of the cell also include the intended nucleotide edits. In some embodiments, the cell is autologous, allogeneic, or xenogeneic to a subject. In some embodiments, the cell is from or derived from a subject. In some embodiments, the cell is from or derived from a human subject. In some embodiments, the cell is introduced back into the subject, *e.g.*, a human subject, after incorporation of the intended nucleotide edits by prime editing.

[585] In some embodiments, the method provided herein comprises introducing the prime editor polypeptide or the polynucleotide encoding the prime editor polypeptide, the PEgRNA or the

polynucleotide encoding the PEgRNA, and/or the ngRNA or the polynucleotide encoding the ngRNA into a plurality or a population of cells that comprise the target gene. In some embodiments, the population of cells is of the same cell type. In some embodiments, the population of cells is of the same tissue or organ. In some embodiments, the population of cells is heterogeneous. In some embodiments, the population of cells is homogeneous. In some embodiments, the population of cells is from a single tissue or organ, and the cells are heterogeneous. In some embodiments, the introduction into the population of cells is *ex vivo*. In some embodiments, the introduction into the population of cells is *in vivo*, *e.g.*, into a human subject.

[586] In some embodiments, the target gene is in a genome of each cell of the population. In some embodiments, introduction of the prime editor polypeptide or the polynucleotide encoding the prime editor polypeptide, the PEgRNA or the polynucleotide encoding the PEgRNA, and/or the ngRNA or the polynucleotide encoding the ngRNA results in incorporation of one or more intended nucleotide edits in the target gene in at least one of the cells in the population of cells. In some embodiments, introduction of the prime editor polypeptide or the polynucleotide encoding the prime editor polypeptide, the PEgRNA or the polynucleotide encoding the PEgRNA, and/or the ngRNA or the polynucleotide encoding the ngRNA results in incorporation of the one or more intended nucleotide edits in the target gene in a plurality of the population of cells. In some embodiments, introduction of the prime editor polypeptide or the polynucleotide encoding the prime editor polypeptide, the PEgRNA or the polynucleotide encoding the PEgRNA, and/or the ngRNA or the polynucleotide encoding the ngRNA results in incorporation of the one or more intended nucleotide edits in the target gene in each cell of the population of cells. In some embodiments, introduction of the prime editor polypeptide or the polynucleotide encoding the prime editor polypeptide, the PEgRNA or the polynucleotide encoding the PEgRNA, and/or the ngRNA or the polynucleotide encoding the ngRNA results in incorporation of the one or more intended nucleotide edits in the target gene in sufficient number of cells such that the disease or disorder is treated, prevented or ameliorated.

[587] In some embodiments, editing efficiency of the prime editing compositions and method described herein can be measured by calculating the percentage of edited target genes in a population of cells introduced with the prime editing composition. In some embodiments, the editing efficiency is determined after 1 hour, 2 hours, 6 hours, 12 hours, 24 hours, 36 hours, 48 hours, 3 days, 4 days, 5 days, 7 days, 10 days, or 14 days of exposing a target gene (*e.g.*, a *ATP7B* gene within the genome of a cell) to a prime editing composition. In some embodiments, the population of cells introduced with the prime editing composition is *ex vivo*. In some embodiments, the population of cells introduced with the prime editing composition is *in vitro*. In some embodiments, the population of cells introduced with the prime editing composition is *in vivo*. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 1%, at least about 5%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, or at least about 99% relative to a suitable control. In some

embodiments, the prime editing methods disclosed herein have an editing efficiency of at least 25% relative to a suitable control. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least 35% relative to a suitable control. prime editing method disclosed herein has an editing efficiency of at least 30% relative to a suitable control. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least 45% relative to a suitable control. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least 50% relative to a suitable control.

[588] In some embodiments, the methods disclosed herein have an editing efficiency of at least about 1%, at least about 5%, at least about 7.5%, at least about 10%, at least about 15%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, or at least about 95% of editing a primary cell relative to a suitable control.

[589] In some embodiments, the methods disclosed herein have an editing efficiency of at least about 5%, at least about 7.5%, at least about 10%, at least about 15%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, or at least about 95% of editing a hepatocyte relative to a corresponding control hepatocyte. In some embodiments, the hepatocyte is a human hepatocyte.

[590] In some embodiments, the prime editing compositions provided herein are capable of incorporated one or more intended nucleotide edits without generating a significant proportion of indels. The term "indel(s)", as used herein, refers to the insertion or deletion of a nucleotide base within a polynucleotide, for example, a target gene. Such insertions or deletions can lead to frame shift mutations within a coding region of a gene. Indel frequency of editing can be calculated by methods known in the art. In some embodiments, indel frequency can be calculated based on sequence alignment such as the CRISPResso 2 algorithm as described in Clement et al., Nat. Biotechnol. 37(3): 224-226 (2019), which is incorporated herein in its entirety. In some embodiments, the methods disclosed herein can have an indel frequency of less than 20%, less than 10%, less than 9%, less than 8%, less than 7%, less than 6%, less than 5%, less than 4%, less than 3%, less than 2%, less than 1.5%, or less than 1%. In some embodiments, any number of indels is determined after at least 1 hour, at least 2 hours, at least 6 hours, at least 12 hours, at least 24 hours, at least 36 hours, at least 48 hours, at least 3 days, at least 4 days, at least 5 days, at least 7 days, at least 10 days, or at least 14 days of exposing a target gene (*e.g.*, a *ATP7B* gene within the genome of a cell) to a prime editing composition.

[591] In some embodiments, the prime editing compositions provided herein are capable of incorporated one or more intended nucleotide edits efficiently without generating a significant proportion of indels. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 1% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 1% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell

or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 1% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 5% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 5% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 5% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[592] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 7.5% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 7.5% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 7.5% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[593] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 10% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 10% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 10% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[594] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 15% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 15% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 15% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[595] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 20% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 20% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 20% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[596] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 30% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 30% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 30% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[597] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 40% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 40% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 40% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[598] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 50% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 50% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 50% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[599] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 60% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 60% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 60% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[600] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 70% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 70% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 70% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[601] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 80% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or

hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 80% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 80% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[602] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 90% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 90% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 90% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte.

[603] In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 95% and an indel frequency of less than 1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 95% and an indel frequency of less than 0.5% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, the prime editing methods disclosed herein have an editing efficiency of at least about 95% and an indel frequency of less than 0.1% in a target cell, *e.g.*, a human primary cell or hepatocyte. In some embodiments, any number of indels is determined after at least 1 hour, at least 2 hours, at least 6 hours, at least 12 hours, at least 24 hours, at least 36 hours, at least 48 hours, at least 3 days, at least 4 days, at least 5 days, at least 7 days, at least 10 days, or at least 14 days of exposing a target gene (*e.g.*, a *ATP7B* gene within the genome of a cell) to a prime editing composition. In some embodiments, the editing efficiency is determined after 1 hour, 2 hours, 6 hours, 12 hours, 24 hours, 36 hours, 48 hours, 3 days, 4 days, 5 days, 7 days, 10 days, or 14 days of exposing a target gene (e.g., a ATP7B gene within the genome of a cell) to a prime editing composition.

[604] In some embodiments, the prime editing composition described herein result in less than 50%, less than 40%, less than 30%, less than 20%, less than 19%, less than 18%, less than 17%, less than 16%, less than 15%, less than 14%, less than 13%, less than 12%, less than 11%, less than 10%, less than 9%, less than 8%, less than 7%, less than 6%, less than 5%, less than 4%, less than 3%, less than 2%, less than 1%, less than 0.9%, less than 0.8%, less than 0.7%, less than 0.6%, less than 0.5%, less than 0.4%, less than 0.3%, less than 0.2%, less than 0.1%, less than 0.09%, less than 0.08%, less than 0.07%, less than 0.06%, less than 0.05%, less than 0.04%, less than 0.03%, less than 0.02%, or less than 0.01% off-target editing in a chromosome that includes the target gene. In some embodiments, off-target editing is determined after at least 1 hour, at least 2 hours, at least 6 hours, at least 12 hours, at least 24 hours, at least 36 hours, at least 48 hours, at least 3 days, at least 4 days, at least 5 days, at least 7 days, at least 10 days, or at least 14 days of exposing a target gene (*e.g.*, a nucleic acid within the genome of a cell) to a prime editing composition.

[605] In some embodiments, the prime editing compositions (*e.g.*, PEgRNAs and prime editors as described herein) and prime editing methods disclosed herein can be used to edit a target *ATP7B* gene. In some embodiments, the target *ATP7B* gene comprises a mutation compared to a wild type *ATP7B* gene. In some embodiments, the mutation is associated with Wilson's disease. In some embodiments, the target *ATP7B* gene comprises an editing target sequence that contains the mutation associated with Wilson's disease. In some embodiments, the mutation is in a coding region of the target *ATP7B* gene. In some embodiments, the mutation is in an exon of the target *ATP7B* gene. In some embodiments, the mutation is in exon 1, exon 2, exon 3, exon 4, exon 5, exon 6, exon 7, exon 8, exon 9, exon 10, exon 11, exon 12, exon 13, exon 14, exon 15, exon 16, exon 17, exon 18, exon 19, exon 20, or exon 21 of the *ATP7B* gene as compared to a wild type *ATP7B* gene. In some embodiments, the mutation is exon 8, exon 13, exon 14, exon 15, or exon 17 of the *ATP7B* gene as compared to a wild type *ATP7B* gene. In some embodiments, the mutation is in exon 3 of the *ATP7B* gene as compared to a wild type *ATP7B* gene. In some embodiments, the mutation is located in exon 8 of the *ATP7B* gene as compared to a wild type *ATP7B* gene. In some embodiments, the mutation is not a c.1288dup duplication. In some embodiments, the mutation is in exon 14 of the target *ATP7B* gene. In some embodiments, the mutation is located between positions 51958233 and 51958433 of human chromosome 13 as set forth in human genome assembly consortium Human build 38 (GRCh38), GenBank accession GCA_000001405.15. In some embodiments, the mutation encodes an amino acid substitution R778L relative to a wild type ATP7B polypeptide set forth in SEQ ID NO: 14897. In some embodiments, the editing target sequence comprises a G>T mutation at position 51958333 in human chromosome 13 as set forth in human genome assembly consortium Human build 38 (GRCh38), GenBank accession GCA_000001405.15. In some embodiments, the prime editing method comprises contacting a target *ATP7B* gene with a prime editing composition comprising a prime editor, a PEgRNA, and/or a ngRNA. In some embodiments, contacting the target *ATP7B* gene with the prime editing composition results in incorporation of one or more intended nucleotide edits in the target *ATP7B* gene. In some embodiments, the incorporation is in a region of the target *ATP7B* gene that corresponds to an editing target sequence in the *ATP7B* gene. In some embodiments, the one or more intended nucleotide edits comprises a single nucleotide substitution, an insertion, a deletion, or any combination thereof, compared to the endogenous sequence of the target *ATP7B* gene. In some embodiments, incorporation of the one or more intended nucleotide edits results in replacement of one or more mutations with the corresponding sequence that encodes a wild type ATP7B polypeptide set forth in SEQ ID NO: 14897. In some embodiments, incorporation of the one or more intended nucleotide edits results in replacement of the one or more mutations with the corresponding sequence in a wild type *ATP7B* gene. In some embodiments, incorporation of the one more intended nucleotide edits results in correction of a mutation in the target *ATP7B* gene. In some embodiments, the target *ATP7B* gene comprises an editing template sequence that contains the mutation. In some embodiments, contacting the target *ATP7B* gene with the prime editing composition results in incorporation of one or more intended nucleotide edits in the target *ATP7B* gene, which corrects the

mutation in the editing target sequence (or a double stranded region comprising the editing target sequence and the complementary sequence to the editing target sequence on a target strand) in the target *ATP7B* gene.

[606] In some embodiments, incorporation of the one more intended nucleotide edits results in correction of a mutation in exon 8 of the target ATP7B gene as compared to a wild type *ATP7B* gene. In some embodiments, incorporation of the one more intended nucleotide edits results in correction of a mutation located between positions 51958233 and 51958433 of human chromosome 13 in the target *ATP7B* gene as set forth in human genome assembly consortium Human build 38 (GRCh38), GenBank accession GCA_000001405.15. In some embodiments, incorporation of the one more intended nucleotide edits results in an A>C nucleotide substitution at position 51944145 in human chromosome 13 in the target *ATP7B* gene as compared to the endogenous sequence of the target *ATP7B* gene, thereby correcting a G>T mutation at position 51958333 in human chromosome 13 in the target *ATP7B* gene as set forth in human genome assembly consortium Human build 38 (GRCh38), GenBank accession GCA_000001405.15. In some embodiments, incorporation of the one more intended nucleotide edits results in correction of an *ATP7B* gene sequence that encodes a R778L amino acid substitution and restores wild type expression and function of the ATP7B protein.

[607] In some embodiments, the target *ATP7B* gene is in a target cell. Accordingly, in one aspect provided herein is a method of editing a target cell comprising a target *ATP7B* gene that encodes a polypeptide that comprises one or more mutations relative to a wild type *ATP7B* gene. In some embodiments, the methods of the present disclosure comprise introducing a prime editing composition comprising a PEgRNA, a prime editor polypeptide, and/or a ngRNA into the target cell that has the target *ATP7B* gene to edit the target *ATP7B* gene, thereby generating an edited cell. In some embodiments, the target cell is a mammalian cell. In some embodiments, the target cell is a human cell. In some embodiments, the target cell is a primary cell. In some embodiments, the target cell is a human primary cell. In some embodiments, the target cell is a progenitor cell. In some embodiments, the target cell is a human progenitor cell. In some embodiments, the target cell is a stem cell. In some embodiments, the target cell is a human stem cell. In some embodiments, the target cell is a hepatocyte. In some embodiments, the target cell is a human hepatocyte. In some embodiments, the target cell is a primary human hepatocyte derived from an induced human pluripotent stem cell (iPSC). In some embodiments, the cell is a neuron. In some embodiments, the cell is a neuron from basal ganglia. In some embodiments, the cell is a neuron from basal ganglia of a subject. In some embodiments, the cell is a neuron in the basal ganglia of a subject.

[608] In some embodiments, components of a prime editing composition described herein are provided to a target cell *in vitro*. In some embodiments, components of a prime editing composition described herein are provided to a target cell *ex vivo*. In some embodiments, components of a prime editing composition described herein are provided to a target cell *in vivo*.

[609] In some embodiments, incorporation of the one or more intended nucleotide edits in the target *ATP7B* gene that comprises one or more mutations restores wild type expression and function of the ATP7B protein encoded by the ATP7B gene. In some embodiments, the target *ATP7B* gene encodes a R778L amino acid substitution as compared to the wild type ATP7B protein prior to incorporation of the one or more intended nucleotide edits. In some embodiments, expression and/or function of the ATP7B protein may be measured when expressed in a target cell. In some embodiments, incorporation of the one or more intended nucleotide edits in the target *ATP7B* gene comprising one or more mutations lead to a fold change in a level of *ATP7B* gene expression, ATP7B protein expression, or a combination thereof. In some embodiments, a change in the level of ATP7B expression level can comprise a fold change of, *e.g.*, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 15-fold, 20-fold, 25-fold, 30-fold, 40-fold, 50-fold, 60-fold, 70-fold, 80-fold, 90-fold, 100-fold or greater as compared to expression in a suitable control cell not introduced with a prime editing composition described herein. In some embodiments, incorporation of the one or more intended nucleotide edits in the target *ATP7B* gene that comprises one or more mutations restores wild type expression of the ATP7B protein by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 99% or more as compared to wild type expression of the ATP7B protein in a suitable control cell that comprises a wild type *ATP7B* gene.

[610] In some embodiments, an ATP7B expression increase can be measured by a functional assay. In some embodiments, the functional assay can comprise a copper sensitivity assay, a cell viability assay, or a combination thereof. In some embodiments, protein expression can be measured using a protein assay. In some embodiments, protein expression can be measured using antibody testing. In some embodiments, an antibody can comprise anti-ATP7B. In some embodiments, protein expression can be measured using ELISA, mass spectrometry, Western blot, sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), high performance liquid chromatography (HPLC), electrophoresis, or any combination thereof. In some embodiments, a protein assay can comprise SDS-PAGE and densitometric analysis of a Coomassie Blue-stained gel. In some embodiments, ATP7B activity can be measured by measuring ATPase activity. In some embodiments, ATPase activity can be measured using an ATPase assay.

Methods of Treating Wilson's disease

[611] In some embodiments, provided herein are methods for treatment of a subject diagnosed with a disease associated with or caused by one or more pathogenic mutations that can be corrected by prime editing. In some embodiments, provided herein are methods for treating Wilson's disease that comprise administering to a subject a therapeutically effective amount of a prime editing composition, or a pharmaceutical composition comprising a prime editing composition as described herein. In some embodiments, administration of the prime editing composition results in incorporation of one or more intended nucleotide edits in the target gene in the subject. In some embodiments, administration of the prime editing composition results in correction of one or more pathogenic mutations, *e.g.*, point mutations, insertions, or deletions, associated with Wilson's disease in the subject. In some embodiments,

the target gene comprise an editing target sequence that contains the pathogenic mutation. In some embodiments, administration of the prime editing composition results in incorporation of one or more intended nucleotide edits in the target gene that corrects the pathogenic mutation in the editing target sequence (or a double stranded region comprising the editing target sequence and the complementary sequence to the editing target sequence on a target strand) of the target gene in the subject.

[612] In some embodiments, the method provided herein comprises administering to a subject an effective amount of a prime editing composition, for example, a PEgRNA, a prime editor, and/or a ngRNA. In some embodiments, the method comprises administering to the subject an effective amount of a prime editing composition described herein, for example, polynucleotides, vectors, or constructs that encode prime editing composition components, or RNPs, LNPs, and/or polypeptides comprising prime editing composition components. Prime editing compositions can be administered to target the *ATP7B* gene in a subject, *e.g.*, a human subject, suffering from, having, susceptible to, or at risk for Wilsons' disease. Identifying a subject in need of such treatment can be in the judgment of a subject or a health care professional and can be subjective (*e.g.*, opinion) or objective (*e.g.*, measurable by a test or diagnostic method). In some embodiments, the subject has Wilson's disease.

[613] In some embodiments, the subject has been diagnosed with Wilson's disease by sequencing of a *ATP7B* gene in the subject. In some embodiments, the subject comprises at least a copy of *ATP7B* gene that comprises one or more mutations compared to a wild type *ATP7B* gene. In some embodiments, the subject comprises at least a copy of *ATP7B* gene that comprises a mutation in a coding region of the *ATP7B* gene. In some embodiments, the subject comprises at least a copy of ATP7B gene that comprises a mutation in exon 1, exon 2, exon 3, exon 4, exon 5, exon 6, exon 7, exon 8, exon 9, exon 10, exon 11, exon 12, exon 13, exon 14, exon 15, exon 16, exon 17, exon 18, exon 19, exon 20, or exon 21, as compared to a wild type ATP7B gene. In some embodiments, the subject comprises at least a copy of *ATP7B* gene that comprises a mutation in exon 8, exon 13, exon 14, exon 15, or exon 17 as compared to a wild type ATP7B gene. In some embodiments, the subject comprises at least a copy of ATP7B gene that comprises a mutation in exon 8of the ATP7B gene as compared to a wild type ATP7B gene. In some embodiments, the subject comprises at least a copy of ATP7B gene that comprises a mutation in exon 3 as compared to a wild type ATP7B gene. In some embodiments, the mutation is not a c.1288dup duplication. In some embodiments, the subject comprises at least a copy of ATP7B gene that encodes a polypeptide that comprises an amino acid substitution R778L relative to a wild type ATP7B polypeptide set forth in SEQ ID NO: 14897.

[614] In some embodiments, a population of patients each having one or more mutations in the target *ATP7B* gene may be treated with a prime editing composition (e.g., a PEgRNA, a prime editor, and optionally an ngRNA as described herein) disclosed herein. In some embodiments, a population of patients with different mutations in the target *ATP7B* gene can be treated with the same prime editing composition comprising a single PEgRNA, a prime editor, and optionally an ngRNA. In some embodiments, a single prime editing composition comprising a single PEgRNA and a prime editor can be

used to correct one or more, or two or more, mutations in the target *ATP7B* gene in a populations of patients, wherein one or more patients in the population have different mutations from one another. In some embodiments, the prime editing composition comprising a single pair of PEgRNA, a prime editor, and optionally an ngRNA can be used to correct 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more mutations in the target *ATP7B* gene in a population of patients, wherein one or more patients in the population have different mutations from one another. In some embodiments, the PEgRNA comprises an editing template comprising a wild type sequence of the *ATP7B* gene.

[615] In some embodiments, a patient with multiple mutations in the target *ATP7B* gene can be treated with a prime editing composition (e.g., a PEgRNAs, a prime editor, and optionally an ngRNA as described herein). For example, in some embodiments, a subject may comprise two copies of the *ATP7B* gene, each comprising one or more different mutations. In some embodiments, a patient with one or more different mutations in the target *ATP7B* gene can be treated with a single prime editing composition comprising a PEgRNAs, a prime editor, and optionally an ngRNA.

[616] In some embodiments, the method comprises directly administering prime editing compositions provided herein to a subject. The prime editing compositions described herein can be delivered with in any form as described herein, *e.g.*, as LNPs, RNPs, polynucleotide vectors such as viral vectors, or mRNAs. The prime editing compositions can be formulated with any pharmaceutically acceptable carrier described herein or known in the art for administering directly to a subject. Components of a prime editing composition or a pharmaceutical composition thereof may be administered to the subject simultaneously or sequentially. For example, in some embodiments, the method comprises administering a prime editing composition, or pharmaceutical composition thereof, comprising a complex that comprises a prime editor fusion protein and a PEgRNA and/or a ngRNA, to a subject. In some embodiments, the method comprises administering a polynucleotide or vector encoding a prime editor to a subject simultaneously with a PEgRNA and/or a ngRNA. In some embodiments, the method comprises administering a polynucleotide or vector encoding a prime editor to a subject before administration with a PEgRNA and/or a ngRNA.

[617] Suitable routes of administrating the prime editing compositions to a subject include, without limitation: topical, subcutaneous, transdermal, intradermal, intralesional, intraarticular, intraperitoneal, intravesical, transmucosal, gingival, intradental, intracochlear, transtympanic, intraorgan, epidural, intrathecal, intramuscular, intravenous, intravascular, intraosseus, periocular, intratumoral, intracerebral, and intracerebroventricular administration. In some embodiments, the compositions described are administered intraperitoneally, intravenously, or by direct injection or direct infusion. In some embodiments, the compositions described are administered by direct injection or infusion into the liver of a subject. In some embodiments, the compositions described herein are administered to a subject by injection, by means of a catheter, by means of a suppository, or by means of an implant.

[618] In some embodiments, the method comprises administering cells edited with a prime editing composition described herein to a subject. In some embodiments, the cells are allogeneic. In some

embodiments, allogeneic cells are or have been contacted *ex vivo* with a prime editing composition or pharmaceutical composition thereof and are introduced into a human subject in need thereof. In some embodiments, the cells are autologous to the subject. In some embodiments, cells are removed from a subject and contacted *ex vivo* with a prime editing composition or pharmaceutical composition thereof and are re-introduced into the subject.

[619] In some embodiments, cells are contacted *ex vivo* with one or more components of a prime editing composition. In some embodiments, the *ex vivo*-contacted cells are introduced into the subject, and the subject is administered *in vivo* with one or more components of a prime editing composition. For example, in some embodiments, cells are contacted *ex vivo* with a prime editor and introduced into a subject. In some embodiments, the subject is then administered with a PEgRNA and/or a ngRNA, or a polynucleotide encoding the PEgRNA and/or the ngRNA.

[620] In some embodiments, cells contacted with the prime editing composition are determined for incorporation of the one or more intended nucleotide edits in the genome before re-introduction into the subject. In some embodiments, the cells are enriched for incorporation of the one or more intended nucleotide edits in the genome before re-introduction into the subject. In some embodiments, the edited cells are primary cells. In some embodiments, the edited cells are progenitor cells. In some embodiments, the edited cells are stem cells. In some embodiments, the edited cells are hepatocytes. In some embodiments, the edited cells are primary human cells. In some embodiments, the edited cells are human progenitor cells. In some embodiments, the edited cells are human stem cells. In some embodiments, the edited cells are human hepatocytes. In some embodiments, the cell is a neuron. In some embodiments, the cell is a neuron from basal ganglia. In some embodiments, the cell is a neuron from basal ganglia of a subject. In some embodiments, the cell is a neuron in the basal ganglia of a subject. The prime editing composition or components thereof may be introduced into a cell by any delivery approaches as described herein, including LNP administration, RNP administration, electroporation, nucleofection, transfection, viral transduction, microinjection, cell membrane disruption and diffusion, or any other approach known in the art.

[621] The cells edited with prime editing can be introduced into the subject by any route known in the art. In some embodiments, the edited cells are administered to a subject by direct infusion. In some embodiments, the edited cells are administered to a subject by intravenous infusion. In some embodiments, the edited cells are administered to a subject as implants.

[622] The pharmaceutical compositions, prime editing compositions, and cells, as described herein, can be administered in effective amounts. In some embodiments, the effective amount depends upon the mode of administration. In some embodiments, the effective amount depends upon the stage of the condition, the age and physical condition of the subject, the nature of concurrent therapy, if any, and like factors well-known to the medical practitioner.

[623] The specific dose administered can be a uniform dose for each subject. Alternatively, a subject's dose can be tailored to the approximate body weight of the subject. Other factors in determining the

appropriate dosage can include the disease or condition to be treated or prevented, the severity of the disease, the route of administration, and the age, sex and medical condition of the patient.

[624] In embodiments wherein components of a prime editing composition are administered sequentially, the time between sequential administration can be at least 1 hour, at least 2 hours, at least 6 hours, at least 12 hours, at least 24 hours, at least 36 hours, at least 48 hours, at least 3 days, at least 4 days, at least 5 days, at least 7 days, at least 10 days, or at least 14 days.

[625] In some embodiments, a method of monitoring treatment progress is provided. In some embodiments, the method includes the step of determining a level of diagnostic marker, for example, correction of a mutation in *ATP7B* gene, or diagnostic measurement associated with Wilson's disease, (*e.g.*, copper sensitivity screen or assay) in a subject suffering from Wilson's disease symptoms and has been administered an effective amount of a prime editing composition described herein. The level of the diagnostic marker determined in the method can be compared to known levels of the marker in either healthy normal controls or in other afflicted subjects to establish the subject's disease status.

Delivery

[626] Prime editing compositions described herein can be delivered to a cellular environment with any approach known in the art. Components of a prime editing composition can be delivered to a cell by the same mode or different modes. For example, in some embodiments, a prime editor can be delivered as a polypeptide or a polynucleotide (DNA or RNA) encoding the polypeptide. In some embodiments, a PEgRNA can be delivered directly as an RNA or as a DNA encoding the PEgRNA.

[627] In some embodiments, a prime editing composition component is encoded by a polynucleotide, a vector, or a construct. In some embodiments, a prime editor polypeptide, a PEgRNA and/or a ngRNA is encoded by a polynucleotide. In some embodiments, the polynucleotide encodes a prime editor fusion protein comprising a DNA binding domain and a DNA polymerase domain. In some embodiments, the polynucleotide encodes a DNA polymerase domain of a prime editor. In some embodiments, the polynucleotide encodes a DNA polymerase domain of a prime editor. In some embodiments, the polynucleotide encodes a portion of a prime editor protein, for example, a N-terminal portion of a prime editor fusion protein connected to an intein-N. In some embodiments, the polynucleotide encodes a portion of a prime editor protein, for example, a C-terminal portion of a prime editor fusion protein connected to an intein-C. In some embodiments, the polynucleotide encodes a PEgRNA and/or a ngRNA. In some embodiments, the polypeptide encodes two or more components of a prime editing composition, for example, a prime editor fusion protein and a PEgRNA.

[628] In some embodiments, the polynucleotide encoding one or more prime editing composition components is delivered to a target cell is integrated into the genome of the cell for long-term expression, for example, by a retroviral vector. In some embodiments, the polynucleotide delivered to a target cell is expressed transiently. For example, the polynucleotide may be delivered in the form of a mRNA, or a non-integrating vector (non-integrating virus, plasmids, minicircle DNAs) for episomal expression.

[629] In some embodiments, a polynucleotide encoding one or more prime editing system components can be operably linked to a regulatory element, *e.g.*, a transcriptional control element, such as a promoter. In some embodiments, the polynucleotide is operably linked to multiple control elements. Depending on the expression system utilized, any of a number of suitable transcription and translation control elements, including constitutive and inducible promoters, transcription enhancer elements, transcription terminators, etc. may be used in the expression vector (*e.g.*, U6 promoter, H1 promoter).

[630] In some embodiments, the polynucleotide encoding one or more prime editing composition components is a part of, or is encoded by, a vector. In some embodiments, the vector is a viral vector. In some embodiments, the vector is a non-viral vector.

[631] Non-viral vector delivery systems can include DNA plasmids, RNA (*e.g.*, a transcript of a vector described herein), naked nucleic acid, and nucleic acid complexed with a delivery vehicle, such as a liposome. In some embodiments, the polynucleotide is provided as an RNA, *e.g.*, a mRNA or a transcript. Any RNA of the prime editing systems, for example a guide RNA or a base editor-encoding mRNA, can be delivered in the form of RNA. In some embodiments, one or more components of the prime editing system that are RNAs is produced by direct chemical synthesis or may be transcribed in vitro from a DNA. In some embodiments, a mRNA that encodes a prime editor polypeptide is generated using in vitro transcription. Guide polynucleotides (*e.g.*, PEgRNA or ngRNA) can also be transcribed using in vitro transcription from a cassette containing a T7 promoter, followed by the sequence "GG", and guide polynucleotide sequence. In some embodiments, the prime editor encoding mRNA, PEgRNA, and/or ngRNA are synthesized in vitro using an RNA polymerase enzyme (*e.g.*, T7 polymerase, T3 polymerase, SP6 polymerase, etc.). Once synthesized, the RNA can directly contact a target ATP7B gene or can be introduced into a cell using any suitable technique for introducing nucleic acids into cells (*e.g.*, microinjection, electroporation, transfection). In some embodiments, the prime editor-coding sequences, the PEgRNAs, and/or the ngRNAs are modified to include one or more modified nucleoside *e.g.,* using pseudo-U or 5-Methyl-C.

[632] Methods of non-viral delivery of nucleic acids can include lipofection, nucleofection, microinjection, biolistics, virosomes, liposomes, immunoliposomes, polycation or lipid:nucleic acid conjugates, naked DNA, artificial virions, cell membrane disruption by a microfluidics device, and agent-enhanced uptake of DNA. Cationic and neutral lipids that are suitable for efficient receptor-recognition lipofection of polynucleotides can be used. Delivery can be to cells (*e.g.*, in vitro or ex vivo administration) or target tissues (*e.g.*, in vivo administration). The preparation of lipid:nucleic acid complexes, including targeted liposomes such as immunolipid complexes, can be used.

[633] Viral vector delivery systems can include DNA and RNA viruses, which can have either episomal or integrated genomes after delivery to the cell. RNA or DNA viral based systems can be used to target specific cells and trafficking the viral payload to an organelle of the cell. Viral vectors can be administered directly (in vivo) or they can be used to treat cells in vitro, and the modified cells can optionally be administered (ex vivo).

[634] In some embodiments, the viral vector is a retroviral, lentiviral, adenoviral, adeno-associated viral or herpes simplex viral vector. Retroviral vectors can include those based upon murine leukemia virus (MuLV), gibbon ape leukemia virus (GaLV), Simian Immunodeficiency virus (SIV), human immunodeficiency virus (HIV), and combinations thereof. In some embodiments, the retroviral vector is a lentiviral vector. In some embodiments, the retroviral vector is a gamma retroviral vector. In some embodiments, the viral vector is an adenoviral vector. In some embodiments, the viral vector is an adeno-associated virus ("AAV") vector.

[635] In some embodiments, polynucleotides encoding one or more prime editing composition components are packaged in a virus particle. Packaging cells can be used to form virus particles that can infect a target cell. Such cells can include 293 cells, (*e.g.*, for packaging adenovirus), and .psi.2 cells or PA317 cells (*e.g.*, for packaging retrovirus). Viral vectors can be generated by producing a cell line that packages a nucleic acid vector into a viral particle. The vectors can contain the minimal viral sequences required for packaging and subsequent integration into a host. The vectors can contain other viral sequences being replaced by an expression cassette for the polynucleotide(s) to be expressed. The missing viral functions can be supplied in trans by the packaging cell line. For example, AAV vectors can comprise ITR sequences from the AAV genome which are required for packaging and integration into the host genome. In some embodiment, the polynucleotides are a DNA polynucleotide. In some embodiment, the polynucleotides are an RNA polynucleotide; e.g., an mRNA polynucleotide.

[636] In some embodiments, the AAV vector is selected for tropism to a particular cell, tissue, organism. In some embodiments, the AAV vector is pseudotyped, e.g., AAV5/8. In some embodiments, polynucleotides encoding one or more prime editing composition components are packaged in a first AAV and a second AAV. In some embodiments, the polynucleotides encoding one or more prime editing composition components are packaged in a first rAAV and a second rAAV.

[637] In some embodiments, dual AAV vectors are generated by splitting a large transgene expression cassette in two separate halves (5' and 3' ends that encode N-terminal portion and C-terminal portion of, *e.g.*, a prime editor polypeptide), where each half of the cassette is no more than 5kb in length, optionally no more than 4.7 kb in length, and is packaged in a single AAV vector. In some embodiments, the full-length transgene expression cassette is reassembled upon co-infection of the same cell by both dual AAV vectors. In some embodiments, a portion or fragment of a prime editor polypeptide, *e.g.*, a Cas9 nickase, is fused to an intein. The portion or fragment of the polypeptide can be fused to the N-terminus or the C-terminus of the intein. In some embodiments, a N-terminal portion of the polypeptide is fused to an intein-N, and a C-terminal portion of the polypeptide is separately fused to an intein-C. In some embodiments, a portion or fragment of a prime editor fusion protein is fused to an intein and fused to an AAV capsid protein. In some embodiments, intein-N may be fused to the N-terminal portion of a first domain described herein, and and intein-C may be fused to the C-terminal portion of a second domain described herein for the joining of the N-terminal portion to the C-terminal portion, thereby joining the first and second domains. In some embodiments, the first and second domains are each independently

chosen from a DNA binding domain or a DNA polymerase domain. The intein, nuclease and capsid protein can be fused together in any arrangement (*e.g.*, nuclease-intein-capsid, intein-nuclease-capsid, capsid-intein-nuclease, etc.). In some embodiments, a polynucleotide encoding a prime editor fusion protein is split in two separate halves, each encoding a portion of the prime editor fusion protein and separately fused to an intein. In some embodiments, each of the two halves of the polynucleotide is packaged in an individual AAV vector of a dual AAV vector system. In some embodiments, each of the two halves of the polynucleotide is no more than 5kb in length, optionally no more than 4.7 kb in length. In some embodiments, the full-length prime editor fusion protein is reassembled upon co-infection of the same cell by both dual AAV vectors, expression of both halves of the prime editor fusion protein, and self-excision of the inteins. In some embodiments, the in vivo use of dual AAV vectors results in the expression of full-length full-length prime editor fusion proteins. In some embodiments, the use of the dual AAV vector platform allows viable delivery of transgenes of greater than about 4.5, 4.6, 4.7, 4.8, 4.9, or 5.0 kb in size.

[638] In some embodiments, an intein is inserted at a splice site within a Cas protein. In some embodiments, insertion of an intein disrupts a Cas activity. As used herein, "intein" refers to a self-splicing protein intron (e.g., peptide), e.g., which ligates flanking N-terminal and C-terminal exteins (e.g., fragments to be joined). In some embodiments, an intein may comprise a polypeptide that is able to excise itself and join exteins with a peptide bond (e.g., protein splicing). In some embodiments, an intein of a precursor gene comes from two genes (e.g., split intein). In some embodiments, an intein may be a synthetic intein. Non-limiting examples of intein pairs that may be used in accordance with the present disclosure include: dnaE-n and dnaE-c. a 4-hydroxytamoxifen (4-HT)-responsive intein, an iCas molecule, a Ssp DnaX intein, Ter DnaE3 intein, Ter ThyX intein, Rma DnaB intein, Cfa DnaE intein, Ssp GyrB intein, and Rma DnaB intein. In some embodiments, intein fragments may be fused to the N terminal and C-terminal portion of a split Cas protein respectively for joining the fragments of split Cas9.

[639] In some embodiments, the split Cas9 system may be used in general to bypass the packing limit of the viral delivery vehicles. In some embodiments, a split Cas9 may be a Type II CRISPR system Cas9. In some embodiments, a first nucleic acid encodes a first portion of the Cas9 protein having a first split-intein and wherein the second nucleic acid encodes a second portion of the Cas9 protein having a second split-intein complementary to the first split-intein and wherein the first portion of the Cas9 protein and the second portion of the Cas9 protein are joined together to form the Cas9 protein. In some embodiments, the first portion of the Cas9 protein is the N-terminal fragment of the Cas9 protein and the second portion of the Cas9 protein is the C-terminal fragment of the Cas9 protein. In some embodiments, a split site may be selected which are surface exposed due to the sterical need for protein splicing.

[640] In some embodiments, a Can protein may be split into two fragments at any C, T, A, or S. In some embodiments, a Cas9 may be intein split at residues 203-204, 280-292, 292-364, 311-325, 417-438, 445-483, 468-469, 481-502, 513-520, 522-530, 565-637, 696-707, 713-714, 795-804, 803-810, 878-887, and 1153-1154. In some embodiments, protein is divided into two fragments at SpCas9 T310, T313,

A456, S469, or C574. In some embodiments, split Cas9 fragments across different split pairs yield combinations that provided the complete polypeptide sequence activate gene expression even when fragments are partially redundant. In some embodiments, a functional Cas9 protein may be reconstituted from two inactive split-Cas9 peptides in the presence of gRNA by using a split-intein protein splicing strategy. In some embodiment, the split Cas9 fragments are fused to either a N-terminal intein fragment or a C-terminal intein fragment, which can associate with each other and catalytically splice the two split Cas9 fragments into a functional reconstituted Cas9 protein. In some embodiments, a split-Cas9 can be packaged into self-complementary AAV. In some embodiments, a split-Cas9 comprises a 2.5 kb and a 2.2 kb fragment of S. pyogenes Cas9 coding sequences

[641] In some embodiments, a split-Cas9 architecture reduces the length and/or size of the coding sequences of a viral vector, e.g., AAV.

[642] A target cell can be transiently or non-transiently transfected with one or more vectors described herein. A cell can be transfected as it naturally occurs in a subject. A cell can be taken or derived from a subject and transfected. A cell can be derived from cells taken from a subject, such as a cell line. In some embodiments, a cell transfected with one or more vectors described herein can be used to establish a new cell line comprising one or more vector-derived sequences. In some embodiments, a cell transiently transfected with the compositions of the disclosure (such as by transient transfection of one or more vectors, or transfection with RNA), and modified through the activity of a prime editor, can be used to establish a new cell line comprising cells containing the modification but lacking any other exogenous sequence. Any suitable vector compatible with the host cell can be used with the methods of the disclosure. Non-limiting examples of vectors include pXT1, pSG5, pSVK3, pBPV, pMSG, and pSVLSV40.

[643] In some embodiments, a prime editor protein can be provided to cells as a polypeptide. In some embodiments, the prime editor protein is fused to a polypeptide domain that increases solubility of the protein. In some embodiments, the prime editor protein is formulated to improve solubility of the protein.

[644] In some embodiment, a prime editor polypeptide is fused to a polypeptide permeant domain to promote uptake by the cell. In some embodiments, the permeant domain is a including peptide, a peptidomimetic, or a non-peptide carrier. For example, a permeant peptide may be derived from the third alpha helix of Drosophila melanogaster transcription factor Antennapaedia, referred to as penetratin, which comprises the amino acid sequence RQIKIWFQNRRMKWKK (SEQ ID NO: 14967). As another example, the permeant peptide can comprise the HIV-1 tat basic region amino acid sequence, which may include, for example, amino acids 49-57 of naturally-occurring tat protein. Other permeant domains can include poly-arginine motifs, for example, the region of amino acids 34-56 of HIV-1 rev protein, nona-arginine (SEQ ID NO: 14968), and octa-arginine (SEQ ID NO: 14969). The nona-arginine (R9) sequence (SEQ ID NO: 14968) can be used. The site at which the fusion can be made may be selected in order to optimize the biological activity, secretion or binding characteristics of the polypeptide.

[645] In some embodiments, a prime editor polypeptide is produced *in vitro* or by host cells, and it may be further processed by unfolding, *e.g.*, heat denaturation, DTT reduction, etc. and may be further refolded. In some embodiments, a prime editor polypeptide is prepared by in vitro synthesis. Various commercial synthetic apparatuses can be used. By using synthesizers, naturally occurring amino acids can be substituted with unnatural amino acids. In some embodiments, a prime editor polypeptide is isolated and purified in accordance with recombinant synthesis methods, for example, by expression in a host cell and the lysate purified using HPLC, exclusion chromatography, gel electrophoresis, affinity chromatography, or other purification technique.

[646] In some embodiments, a prime editing composition, for example, prime editor polypeptide components and PEgRNA/ngRNA are introduced to a target cell by nanoparticles. In some embodiments, the prime editor polypeptide components and the PEgRNA and/or ngRNA form a complex in the nanoparticle. Any suitable nanoparticle design can be used to deliver genome editing system components or nucleic acids encoding such components. In some embodiments, the nanoparticle is inorganic. In some embodiments, the nanoparticle is organic. In some embodiments, a prime editing composition is delivered to a target cell, *e.g.*, a hepatocyte, in an organic nanoparticle, *e.g.*, a lipid nanoparticle (LNP) or polymer nanoparticle.

[647] In some embodiments, LNPs are formulated from cationic, anionic, neutral lipids, or combinations thereof. In some embodiments, neutral lipids, such as the fusogenic phospholipid DOPE or the membrane component cholesterol, are included to enhance transfection activity and nanoparticle stability. In some embodiments, LNPs are formulated with hydrophobic lipids, hydrophilic lipids, or combinations thereof. Lipids may be formulated in a wide range of molar ratios to produce an LNP. Any lipid or combination of lipids that are known in the art can be used to produce an LNP. Exemplary lipids used to produce LNPs are provided in **Table 92** below.

[648] In some embodiments, components of a prime editing composition form a complex prior to delivery to a target cell. For example, a prime editor fusion protein, a PEgRNA, and/or a ngRNA can form a complex prior to delivery to the target cell. In some embodiments, a prime editing polypeptide (*e.g.*, a prime editor fusion protein) and a guide polynucleotide (*e.g.* a PEgRNA or ngRNA) form a ribonucleoprotein (RNP) for delivery to a target cell. In some embodiments, the RNP comprises a prime editor fusion protein in complex with a PEgRNA. RNPs may be delivered to cells using known methods, such as electroporation, nucleofection, or cationic lipid-mediated methods, or any other approaches known in the art. In some embodiments, delivery of a prime editing composition or complex to the target cell does not require the delivery of foreign DNA into the cell. In some embodiments, the RNP comprising the prime editing complex is degraded over time in the target cell. Exemplary lipids for use in nanoparticle formulations and/or gene transfer are shown in **Table 92 and 93** below.

Table 92: Exemplary lipids for nanoparticle formulation or gene transfer

Lipid	Abbreviation	Feature
1,2-Dioleoyl-sn-glycero-3-phosphatidylcholine	DOPC	Helper

Lipid	Abbreviation	Feature
1,2-Dioleoyl-sn-glycero-3-phosphatidylethanolamine	DOPE	Helper
Cholesterol		Helper
N41-(2,3-Dioleyloxy)prophyliN,N,N-trimethylammonium chloride	DOTMA	Cationic
1,2-Dioleoyloxy-3-trimethylammonium-propane Dioctadecylamidoglycylspermine	DOGS	Cationic
N-(3-Aminopropyl)-N,N-dimethyl-2,3-bis(dodecyloxy)- 1-propanaminium bromide	GAP-DLRIE	Cationic
Cetyltrimethylammonium bromide	CTAB	Cationic
6-Lauroxyhexyl ornithinate	LHON	Cationic
1-(2,3-Dioleoyloxypropyl)-2,4,6-trimethylpyridinium	2Oc	Cationic
2,3-Dioleyloxy-N-P(spenninecarboxamido-ethyIJ-N,Ndimethyl-l-propanatninium trifluoroacetate	DOSPA	Cationic
1,2-Dioley1-3-trimethylamtnonium-propane	DOPA	Cationic
N-(2-Hydroxyethyl)-N,N-dimethyl-2,3-bis(tetradecyloxy)-1-propanaminium bromide	MDRIE	Cationic
Dimyristooxypropyl dimethyl hydroxyethyl ammonium bromide	DMRI	Cationic
3β-[N-(N', N'-Dimethylaminoethane)-carbamoyl]cholesterol	DC-Chol	Cationic
Bis-guanidium-tren-cholesterol	BGTC	Cationic
1,3-Diodeoxy-2-(6-carboxy-spermyl)-propylamide	DOSPER	Cationic
Dimethyloctadecylammonium bromide	DDAB	Cationic
Dioctadecylamidoglicylspermidin	DSL	Cationic
rac-[(2,3-Dioctadecyloxypropyl)(2-hydroxyethyl)]-dimethylammonium chloride	CLIP-1	Cationic
rac-[2(2,3-Dihexadecyloxypropyloxymethyloxy) ethyl]trimethylammoniun bromide	CLIP-6	Cationic
Ethyldimyristoylphosphatidylcholine	EDMPC	Cationic
1,2-Distearyloxy-N,N-dimethyl-3-aminopropane	DSDMA	Cationic
1,2-Dimyristoyl-trimethylammonium propane	DMTAP	Cationic
O,O'-Dimyristyl-N-lysyl aspartate	DMKE	Cationic
1,2-Distearoyl-sn-glycero-3-ethylpho sphocholine	DSEPC	Cationic
N-Palmitoyl D-erythro-sphingosyl carbamoyl-spenmine	CCS	Cationic
N-t-Butyl-N0-tetradecyl-3-tetradecylaminopropionamidine	diC14-amidine	Cationic
Octadecenolyoxy[ethyl-2-heptadecenyl-3 hydroxyethyl] imidazolinium chloride	DOTIM	Cationic
N1 -Cholesteryloxycarbonyl-3,7-diazanonane-1,9-diamine	CDAN	Cationic
2-(3-Bis(3-amino-propyl)-amino]propylamino)-Nditetradecylcarbamoylme-ethyl-acetamide	RPR209120	Cationic
1,2-dilinoleyloxy-3-dimethylaminopropane	DLinDMA	Cationic
2,2-dilinoley1-4-dimethylaminoethyl-[1,3]-dioxolane	DLin-KC2-DMA	Cationic
dilinoleyl-methyl-4-dimethylaminobutyrate	DLin-MC3-DMA	Cationic

[649] Exemplary polymers for use in nanoparticle formulations and/or gene transfer are shown in Table 4 below.

Table93: Exemplary lipids for nanoparticle formulation or gene transfer

Polymer	Abbreviation
Poly(ethylene)glycol	PEG
Polyethylenimine	PEI

Dithiobis (succinimidylpropionate)	DSP
Dimethyl-3,3'-dithiobispropionimidate	DTBP
Poly(ethylene imine)biscarbamate	PEIC
Poly(L-lysine)	PLL
Histidine modified PLL	
Poly(N-vinylpyrrolidone)	PVP
Poly(propylenimine)	PPI
Poly(amidoamine)	PAMAM
Poly(amidoethylenimine)	SS_PAEI
Triethylenetetramine	TETA
Poly(β-aminoester)	
Poly(4-hydroxy-L-proline ester)	PHP
Poly(allylamine)	
Poly(α-[4-aminobutyl]-L-glycolic acid)	PAGA
Poly(D,L-lactic-co-glycolic acid)	PLGA
Poly(N-ethyl-4-vinylpyridinium bromide)	
Poly(phosphazene)s	PPZ
Poly(phosphoester)s	PPE
Poly(phosphoramidate)s	PPA
Poly(N-2-hydroxypropylmethacrylamide)	pHPMA
Poly (2-(dimethylamino)ethyl methacrylate)	pDMAEMA
Poly(2-aminoethyl propylene phosphate)	PPE-EA
Chitosan	
Galactosylated chitosan	
N-dodacylated chitosam	
Histone	
Collagen	
Dextran-spermine	D-SPM

[650] Exemplary delivery methods for polynucleotides encoding prime editing composition components are shown in Table 94 below.

Table 94: Exemplary polynucleotide delivery methods

Delivery	**Vector/Mode**	**Delivery into Non-Dividing Cells**	**Duration of Expression**	**Genome Integration**	**Type of Molecule Delivered**
Physical	(*e.g.*, electroporation, particle gun, Calcium phosphate transfection)	YES	Transient	NO	Nucleic Acids and Proteins
Viral	Retrovirus	NO	Stable	YES	RNA
	Lentivirus	YES	Stable	YES/NO with modification	RNA
	Adenovirus	YES	Transient	NO	DNA
	Adeno-Associated Virus (AAV)	YES	Stable	NO	DNA
	Vaccinia Virus	YES	Very Transient	NO	DNA
	Herpes Simplex Virus	YES	Stable	NO	DNA

Delivery	Vector/Mode	Delivery into Non-Dividing Cells	Duration of Expression	Genome Integration	Type of Molecule Delivered
Non-Viral	Cationic	YES	Transient	Depends on what is delivered	Nucleic acids and Proteins
	Polymeric Nanoparticles	YES	Transient	NO	Nucleic Acids
Biological	Attenuated Bacteria	YES	Transient	NO	Nucleic Acids
Non-Viral Delivery Vehicles	Engineered Bacteriophages	YES	Transient	NO	Nucleic Acids
	Mammalian Virus-like Particles	YES	Transient	NO	Nucleic Acids
	Biological liposomes: Erythrocyte Ghosts and Exosomes	YES	Transient	NO	Nucleic Acids

[651] The prime editing compositions of the disclosure, whether introduced as polynucleotides or polypeptides, can be provided to the cells for about 30 minutes to about 24 hours, *e.g.*, 1 hour, 1.5 hours, 2 hours, 2.5 hours, 3 hours, 3.5 hours 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 12 hours, 16 hours, 18 hours, 20 hours, or any other period from about 30 minutes to about 24 hours, which can be repeated with a frequency of about every day to about every 4 days, *e.g.*, every 1.5 days, every 2 days, every 3 days, or any other frequency from about every day to about every four days. The compositions may be provided to the subject cells one or more times, *e.g.*, one time, twice, three times, or more than three times, and the cells allowed to incubate with the agent(s) for some amount of time following each contacting event *e.g.*, 16-24 hours. In cases in which two or more different prime editing system components, *e.g.*, two different polynucleotide constructs are provided to the cell (*e.g.*, different components of the same prim editing system, or two different guide nucleic acids that are complementary to different sequences within the same or different target genes), the compositions may be delivered simultaneously (*e.g.*, as two polypeptides and/or nucleic acids). Alternatively, they may be provided sequentially, *e.g.*, one composition being provided first, followed by a second composition.

[652] The prime editing compositions and pharmaceutical compositions of the disclosure, whether introduced as polynucleotides or polypeptides, can be administered to subjects in need thereof for about 30 minutes to about 24 hours, *e.g.*, 1 hour, 1.5 hours, 2 hours, 2.5 hours, 3 hours, 3.5 hours 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 12 hours, 16 hours, 18 hours, 20 hours, or any other period from about 30 minutes to about 24 hours, which can be repeated with a frequency of about every day to about every 4 days, *e.g.*, every 1.5 days, every 2 days, every 3 days, or any other frequency from about every day to about every four days. The compositions may be provided to the subject one or more times, *e.g.*, one time, twice, three times, or more than three times. In cases in which two or more different prime editing system components, *e.g.* two different polynucleotide constructs are administered to the subject (*e.g.*, different components of the same prim editing system, or two different guide nucleic acids that are

complementary to different sequences within the same or different target genes), the compositions may be administered simultaneously (*e.g.*, as two polypeptides and/or nucleic acids). Alternatively, they may be provided sequentially, *e.g.*, one composition being provided first, followed by a second composition. The disclosure is not limited to the embodiments described and exemplified above, but is capable of variation and modification within the scope of the appended claims.

EXAMPLES

[653] The following examples are provided for illustrative purposes only and are not intended to limit the scope of the claims provided herein

[654] EXAMPLE 1-General Methods

[655] ***PEgRNA assembly***: PEgRNA libraries are assembled by one of three methods: in the first method, pooled synthesized DNA oligos encoding the PEgRNA and flanking U6 expression plasmid homology regions are cloned into U6 expression plasmids *via* Gibson cloning and sequencing of bacterial colonies *via* Sanger or Next-generation sequencing. In the second method, double-stranded linear DNA fragments encoding PEgRNA and homology sequences as above are individually Gibson-cloned into U6 expression plasmids. In the third method, for each PEgRNA, separate oligos encoding a protospacer, a gRNA scaffold, and PEgRNA extension (PBS and RTT) are ligated, and then cloned into a U6 expression plasmid as described in Anzalone *et al.*, Nature. 2019 Dec;576(7785):149-157. Bacterial colonies carrying sequence-verified plasmids are propagated in LB or TB. Plasmid DNA is purified by minipreps for mammalian transfection.

[656] ***Mammalian cell culture and transfection***: HEK293T and Huh-7 cells are propagated in DMEM with 10% FBS. HepG2 cells are propagated in EMEM with 10% FBS. Cells are seeded in 96-well plates and then transfected with Lipofectamine 2000 according to the manufacturer's directions with DNA encoding a prime editor, PEgRNA, and (if applicable) ngRNA. Alternatively, cells are transfected with MessengerMax according to the manufacturer's directions with mRNA encoding a prime editor, synthetic PEgRNA, and (if applicable) ngRNA. Three days after transfection, gDNA is harvested in lysis buffer for high throughput sequencing and sequenced using miseq.

[657] ***Lentiviral production and cell line generation***: Lentiviral transfer plasmids containing the R778L mutation with flanking sequences from the *ATP7B* gene on each side, and an IRES-Puromycin selection cassette, are cloned behind an EF1α short promoter. HEK 293T cells are transiently transfected with the transfer plasmids and packaging plasmids containing VSV glycoprotein and lentiviral gag/pol coding sequences. After transfection, lentiviral particles are harvested from the cell media and concentrated. HEK 293T cells are transduced using serial dilutions of the lentiviral particles described above. Cells generated at a dilution of MOI < 1, as determined by survival following puromycin, are

selected for expansion. A resulting HEK293T cell line carrying the R778L mutation is used to screen PEgRNAs.

[658] ***ATP7B R778L* correction *with PE2 system:*** An ATP7B R778L mutation is installed at the endogenous *ATP7B* locus in HEK 293T, Huh-7, and HepG2 cells by prime editing and single-cell clones are obtained *via* limiting dilution and clonal expansion.

[659] ***Prime Editing in Primary Human Hepatocytes:*** Primary human hepatocytes are transduced with lentivirus encoding the R778L cassette 2 days after cryorecovery, followed 6 days later by transfection with RNA encoding a prime editor, PEgRNA, and (if applicable) ngRNA. Genomic DNA is harvested after a 1-week incubation.

[660] EXAMPLE 2- Screen of Cas9 cutting activity at spacers within 95 nt of the ATP7B R778L mutation site

[661] A spacer screen was performed to investigate Cas9 cutting activity at sites within 95 nucleotides (nts) of the R778L mutation site in the ATP7B gene. HEK293T cells were cultured and transfected with mRNA encoding a Cas9 and gRNA as described above. In this experiment, the gRNA were synthesized as crRNA, which contains the indicated spacer, and tracrRNA, which were allowed to anneal prior to transfection. The crRNA and tracrRNA were ordered from IDT and contained their "Alt-R" chemical end protection. The results are shown in Table 95.

Table 95. Spacer screen for Cas9 cutting activity within 95 nt of the R778L mutation site in the ATP7B gene

Spacer[1] SEQ ID NO:	Nick-to-edit distance to R778L mutation (nt)	PAM	Percent Indel[2]	PAM oriented for Prime Editing of R778L Site
2009	-94	NGA	+	NO
5926, 1238	-88	NGA	++	YES
2021, 1239	-86	NGG	+++	YES
5963, 1222	-85	NGA	+	YES
6007, 1220	-80	NGA	+++	YES
1991	-80	NGA	++++	NO
6051, 1240	-78	NGA	+	YES
6097, 1233	-66	NGA	+	YES
2067, 1223	-63	NGG	+	YES

6154, 1234	-62	NGA	++++	YES
6217, 1228	-47	NGA	+	YES
1996	-44	NGA	++++	NO
6295, 1229	-41	NGA	+	YES
1995	-39	NGA	+	NO
1997	-33	NGG	+++	NO
1990	-17	NGG	++++	NO
2132, 62 (Spacer 1)	**-4**	**NGG**	**+++**	**YES**
1732 (Spacer 2)	**2**	**NGG**	**+**	**YES**
1533, 2057 (Spacer 3)	**9**	**NGG**	**+++**	**YES**
738, 2056 (Spacer 4)	**10**	**NGG**	**++**	**YES**
97	18	NGA	++++	NO
68	24	NGG	++	NO
76	25	NGG	++	NO
98	26	NGG	++	NO
95	27	NGG	++	NO
85	28	NGG	+++	NO
78	36	NGA	+	NO
81	39	NGA	+	NO
5846, 3248	45	NGA	++	YES
96	49	NGG	+++	NO
61	50	NGG	++++	NO
5629, 3277	55	NGA	++	YES
4676, 3283	64	NGA	++++	YES
532, 3268	65	NGG	+++	YES

4311, 3282	67	NGA	++++	YES
4255, 3285	69	NGA	++++	YES
384, 3269	70	NGG	++	YES
302, 3260	73	NGG	++	YES
4180, 3263	76	NGA	+	YES
4132, 3266	78	NGA	++++	YES
197, 3279	82	NGG	+++	YES
67	86	NGG	++++	NO
71	87	NGA	+++	NO
75	90	NGA	+++	NO
123, 3244	91	NGG	+++	YES
5, 3275	94	NGG	++	YES
4175	95	NGA	++++	NO

1. The indicated sequence sequences recite only the spacer; the gRNA used were synthesized as crRNA and tracrRNA, which were allowed to anneal before transfection. Some spacers are identified by two SEQ ID NOs because the same spacer sequence was assigned a different SEQ ID NO in the cluster tables depending upon whether it was included as a ngRNA spacer or a PEgRNA spacer; the first indicated spacer of the pair is the PEgRNA spacer.

2. + = 0.23%-21.13%; ++ = 21.13%-49.62%; +++ 49.62%-58.79%; ++++ = 58.79%-88.45%

[662] EXAMPLE 3 – Prime Editing at a lentivirus-introduced ATP7B R778L mutation site in HEK293T cells using a PE2 system

[663] Four exemplary PEgRNA spacers close to the R778L mutation site are shown in **FIG. 3A**. In **FIG. 3A**, Spacer 1 corresponds to SEQ ID NO: 2132, Spacer 2 corresponds to SEQ ID NO: 1732, Spacer 3 corresponds to SEQ ID NO: 1533, and Spacer 4 corresponds to SEQ ID NO: 738. Exemplary PEgRNA based on Spacer 1 and ngRNA compatible those PEgRNA are disclosed in Table 13. Exemplary PEgRNA based on Spacer 2 and ngRNA compatible those PEgRNA are disclosed in Table 9. Exemplary PEgRNA based on Spacer 3 and ngRNA compatible those PEgRNA are disclosed in Table 8. Exemplary PEgRNA based on Spacer 4 and ngRNA compatible those PEgRNA are disclosed in Table 7. PEgRNA incorporating these spacers were designed and screened for Prime Editing efficiency in a HEK293T cell

line containing a lentivirus-introduced R778L mutation. The cell line was generated as described in Example 1. These spacers were selected because they are close to the R778L mutation site and would produce a nick that is 5' of the R778L mutation site when used in conjunction with a prime editor having a Cas9 protein containing an inactivating mutation in the HNH nuclease domain. Each of these spacers also showed at least some activity in the spacer screen of Example 2.

[664] PEgRNAs were designed and screened in a PE2 system. The HEK 293T cell line as described above was expanded and transiently transfected with a PE and PEgRNA in arrayed 96-well plates for assessment of editing by high-throughput sequencing, as shown schematically in **FIG. 3B**. In this initial screen, multiple primer binding site (PBS) and reverse transcription template (RTT) lengths were tested for each of the four exemplary spacers. All the PEgRNA were designed to restore the wild-type nucleic acid sequence at the R778L site. Where possible, PEgRNAs were designed to also introduce synonymous mutations that silence the PAM sequence.

[665] The results for individual PEgRNA are shown in Table 96. Successful Prime Editing was observed across PBS and RTT lengths, with and without PAM silencing. The percent editing observed for all PEgRNA having the same spacer were averaged, and the results reported in Table 97.

Table 96: PE2 Screen at R778L mutation site in HEK293T cells

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
3300	2132	2155 *57	10	2140	8	++
3319	2132	2155 *57	10	2142	10	++
3337	2132	2155 *57	10	2144	12	--
3380	2132	2155 *57	10	2146	14	+++
3333	2132	2211 *57	14	2140	8	+++
3398	2132	2211 *57	14	2142	10	++++
3454	2132	2211 *57	14	2144	12	--
3545	2132	2211 *57	14	2146	14	++++
3354	2132	2216 *57	15	2140	8	+++
3413	2132	2216 *57	15	2142	10	++++
3496	2132	2216 *57	15	2144	12	--
3592	2132	2216 *57	15	2146	14	++++
3390	2132	2227 *57	16	2140	8	+++
3450	2132	2227 *57	16	2142	10	++++
3532	2132	2227 *57	16	2144	12	--
3638	2132	2227 *57	16	2146	14	++++
3410	2132	2245 *57	17	2140	8	+++
3509	2132	2245 *57	17	2142	10	++++
3621	2132	2245 *57	17	2144	12	--

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
3680	2132	2245 *57	17	2146	14	---
3495	2132	2260 *57	19	2140	8	+++
3620	2132	2260 *57	19	2142	10	++++
3677	2132	2260 *57	19	2144	12	---
3815	2132	2260 *57	19	2146	14	++++
3536	2132	2282 *57	20	2140	8	++++
3636	2132	2282 *57	20	2142	10	++++
3738	2132	2282 *57	20	2144	12	--
3855	2132	2282 *57	20	2146	14	++++
3305	2132	2159 *58	10	2140	8	++
3323	2132	2159 *58	10	2142	10	+
3339	2132	2159 *58	10	2144	12	---
3399	2132	2159 *58	10	2146	14	++
3341	2132	2201 *58	14	2140	8	+
3385	2132	2201 *58	14	2142	10	+++
3449	2132	2201 *58	14	2144	12	---
3539	2132	2201 *58	14	2146	14	+++
3365	2132	2215 *58	15	2140	8	++++
3426	2132	2215 *58	15	2142	10	++++
3506	2132	2215 *58	15	2144	12	--
3618	2132	2215 *58	15	2146	14	++++
3373	2132	2235 *58	16	2140	8	+++
3437	2132	2235 *58	16	2142	10	++++
3571	2132	2235 *58	16	2144	12	---
3664	2132	2235 *58	16	2146	14	++++
3424	2132	2240 *58	17	2140	8	++++
3479	2132	2240 *58	17	2142	10	++++
3604	2132	2240 *58	17	2144	12	--
3681	2132	2240 *58	17	2146	14	++++
3518	2132	2269 *58	19	2140	8	+++
3600	2132	2269 *58	19	2142	10	+++
3717	2132	2269 *58	19	2144	12	--
3775	2132	2269 *58	19	2146	14	+++
3572	2132	2277 *58	20	2140	8	+++
3660	2132	2277 *58	20	2142	10	++++
3768	2132	2277 *58	20	2144	12	--

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
3854	2132	2277 *58	20	2146	14	++++
3306	2132	2154 *59	10	2140	8	++
3318	2132	2154 *59	10	2142	10	++
3342	2132	2154 *59	10	2144	12	--
3401	2132	2154 *59	10	2146	14	++
3343	2132	2204 *59	14	2140	8	+++
3388	2132	2204 *59	14	2142	10	++++
3472	2132	2204 *59	14	2144	12	--
3577	2132	2204 *59	14	2146	14	--
3358	2132	2218 *59	15	2140	8	++++
3418	2132	2218 *59	15	2142	10	++++
3492	2132	2218 *59	15	2144	12	--
3603	2132	2218 *59	15	2146	14	+++
3376	2132	2232 *59	16	2140	8	++++
3446	2132	2232 *59	16	2142	10	+++
3542	2132	2232 *59	16	2144	12	--
3628	2132	2232 *59	16	2146	14	+++
3421	2132	2242 *59	17	2140	8	++++
3511	2132	2242 *59	17	2142	10	++++
3599	2132	2242 *59	17	2144	12	--
3712	2132	2242 *59	17	2146	14	++++
3494	2132	2271 *59	19	2140	8	++++
3583	2132	2271 *59	19	2142	10	+++
3713	2132	2271 *59	19	2144	12	--
3783	2132	2271 *59	19	2146	14	++++
3560	2132	2280 *59	20	2140	8	+++
3650	2132	2280 *59	20	2142	10	++++
3742	2132	2280 *59	20	2144	12	--
3834	2132	2280 *59	20	2146	14	++++
3304	2132	2160 *60	10	2140	8	++
3317	2132	2160 *60	10	2142	10	+++
3338	2132	2160 *60	10	2144	12	--
3379	2132	2160 *60	10	2146	14	++++
3340	2132	2206 *60	14	2140	8	+++
3403	2132	2206 *60	14	2142	10	+++
3457	2132	2206 *60	14	2144	12	--

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
3567	2132	2206 *60	14	2146	14	++++
3370	2132	2214 *60	15	2140	8	+++
3405	2132	2214 *60	15	2142	10	+++
3480	2132	2214 *60	15	2144	12	--
3619	2132	2214 *60	15	2146	14	+++
3372	2132	2224 *60	16	2140	8	+++
3456	2132	2224 *60	16	2142	10	++++
3575	2132	2224 *60	16	2144	12	--
3643	2132	2224 *60	16	2146	14	+++
3416	2132	2243 *60	17	2140	8	++++
3519	2132	2243 *60	17	2142	10	++++
3625	2132	2243 *60	17	2144	12	--
3679	2132	2243 *60	17	2146	14	++
3481	2132	2268 *60	19	2140	8	+++
3607	2132	2268 *60	19	2142	10	--
3678	2132	2268 *60	19	2144	12	--
3798	2132	2268 *60	19	2146	14	++++
3573	2132	2281 *60	20	2140	8	+++
3649	2132	2281 *60	20	2142	10	++++
3725	2132	2281 *60	20	2144	12	--
3842	2132	2281 *60	20	2146	14	++++
3302	2132	2153 *61	10	2140	8	+
3316	2132	2153 *61	10	2142	10	+
3335	2132	2153 *61	10	2144	12	--
3383	2132	2153 *61	10	2146	14	++
3345	2132	2202 *61	14	2140	8	+++
3386	2132	2202 *61	14	2142	10	+++
3441	2132	2202 *61	14	2144	12	--
3574	2132	2202 *61	14	2146	14	+++
3367	2132	2222 *61	15	2140	8	+++
3408	2132	2222 *61	15	2142	10	++++
3488	2132	2222 *61	15	2144	12	--
3605	2132	2222 *61	15	2146	14	+++
3394	2132	2229 *61	16	2140	8	+++
3455	2132	2229 *61	16	2142	10	++++
3559	2132	2229 *61	16	2144	12	--

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
3661	2132	2229 *61	16	2146	14	+++
3432	2132	2236 *61	17	2140	8	++++
3523	2132	2236 *61	17	2142	10	++++
3593	2132	2236 *61	17	2144	12	--
3710	2132	2236 *61	17	2146	14	++++
3486	2132	2264 *61	19	2140	8	+++
3595	2132	2264 *61	19	2142	10	++++
3702	2132	2264 *61	19	2144	12	--
3795	2132	2264 *61	19	2146	14	++++
3544	2132	2276 *61	20	2140	8	++++
3662	2132	2276 *61	20	2142	10	++++
3724	2132	2276 *61	20	2144	12	--
3856	2132	2276 *61	20	2146	14	++++
3307	2132	2152 *62	10	2140	8	+++
3322	2132	2152 *62	10	2142	10	+++
3344	2132	2152 *62	10	2144	12	--
3400	2132	2152 *62	10	2146	14	+++
3346	2132	2200 *62	14	2140	8	+++
3389	2132	2200 *62	14	2142	10	++++
3464	2132	2200 *62	14	2144	12	--
3579	2132	2200 *62	14	2146	14	++++
3353	2132	2221 *62	15	2140	8	+++
3406	2132	2221 *62	15	2142	10	++++
3515	2132	2221 *62	15	2144	12	--
3608	2132	2221 *62	15	2146	14	+++
3375	2132	2225 *62	16	2140	8	+++
3473	2132	2225 *62	16	2142	10	++++
3565	2132	2225 *62	16	2144	12	--
3653	2132	2225 *62	16	2146	14	--
3428	2132	2244 *62	17	2140	8	+++
3477	2132	2244 *62	17	2142	10	++++
3626	2132	2244 *62	17	2144	12	--
3700	2132	2244 *62	17	2146	14	++++
3514	2132	2262 *62	19	2140	8	++++
3602	2132	2262 *62	19	2142	10	++++
3711	2132	2262 *62	19	2144	12	--

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
3776	2132	2262 *62	19	2146	14	+++
3548	2132	2272 *62	20	2140	8	+++
3634	2132	2272 *62	20	2142	10	++++
3739	2132	2272 *62	20	2144	12	--
3852	2132	2272 *62	20	2146	14	++++
3303	2132	2157 *63	10	2140	8	++
3321	2132	2157 *63	10	2142	10	++
3336	2132	2157 *63	10	2144	12	--
3374	2132	2157 *63	10	2146	14	++
3347	2132	2205 *63	14	2140	8	+++
3384	2132	2205 *63	14	2142	10	++++
3448	2132	2205 *63	14	2144	12	--
3543	2132	2205 *63	14	2146	14	+++
3357	2132	2212 *63	15	2140	8	++
3431	2132	2212 *63	15	2142	10	++++
3504	2132	2212 *63	15	2144	12	--
3597	2132	2212 *63	15	2146	14	+++
3381	2132	2233 *63	16	2140	8	++++
3462	2132	2233 *63	16	2142	10	++++
3527	2132	2233 *63	16	2144	12	--
3663	2132	2233 *63	16	2146	14	--
3434	2132	2237 *63	17	2140	8	+++
3485	2132	2237 *63	17	2142	10	++++
3609	2132	2237 *63	17	2144	12	--
3682	2132	2237 *63	17	2146	14	++++
3500	2132	2265 *63	19	2140	8	+++
3612	2132	2265 *63	19	2142	10	++++
3703	2132	2265 *63	19	2144	12	--
3811	2132	2265 *63	19	2146	14	++++
3531	2132	2274 *63	20	2140	8	+++
3640	2132	2274 *63	20	2142	10	++++
3745	2132	2274 *63	20	2144	12	--
3841	2132	2274 *63	20	2146	14	++++
3301	2132	2162	10	2140	8	+++
3320	2132	2162	10	2142	10	++
3332	2132	2162	10	2144	12	--

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
3392	2132	2162	10	2146	14	+++
3334	2132	2209	14	2140	8	++
3396	2132	2209	14	2142	10	+++
3461	2132	2209	14	2144	12	--
3524	2132	2209	14	2146	14	+++
3362	2132	2223	15	2140	8	++
3435	2132	2223	15	2142	10	--
3491	2132	2223	15	2144	12	--
3596	2132	2223	15	2146	14	+++
3393	2132	2226	16	2140	8	+++
3442	2132	2226	16	2142	10	--
3537	2132	2226	16	2144	12	--
3657	2132	2226	16	2146	14	+++
3429	2132	2238	17	2140	8	++
3499	2132	2238	17	2142	10	--
3624	2132	2238	17	2144	12	--
3687	2132	2238	17	2146	14	+++
3520	2132	2263	19	2140	8	++++
3613	2132	2263	19	2142	10	+++
3714	2132	2263	19	2144	12	--
3801	2132	2263	19	2146	14	++
3528	2132	2279	20	2140	8	++
3668	2132	2279	20	2142	10	+++
3735	2132	2279	20	2144	12	--
3832	2132	2279	20	2146	14	+++
1846	1732	1753	11	1740	8	++
1850	1732	1753	11	1742	10	++
1858	1732	1753	11	1744	12	+++
1870	1732	1753	11	1746	14	++
1847	1732	1754	12	1740	8	++
1854	1732	1754	12	1742	10	++
1866	1732	1754	12	1744	12	++++
1877	1732	1754	12	1746	14	++
1849	1732	1755	13	1740	8	+++
1860	1732	1755	13	1742	10	+++
1867	1732	1755	13	1744	12	+++

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
1881	1732	1755	13	1746	14	++
1853	1732	1756	14	1740	8	+++
1861	1732	1756	14	1742	10	++
1879	1732	1756	14	1744	12	++
1889	1732	1756	14	1746	14	++
1859	1732	1757	15	1740	8	+++
1868	1732	1757	15	1742	10	+++
1880	1732	1757	15	1744	12	++
1898	1732	1757	15	1746	14	++
1863	1732	1758	16	1740	8	++
1878	1732	1758	16	1742	10	++
1886	1732	1758	16	1744	12	++
1900	1732	1758	16	1746	14	++
1873	1732	1759	17	1740	8	+++
1884	1732	1759	17	1742	10	++
1895	1732	1759	17	1744	12	++
1907	1732	1759	17	1746	14	++
1888	1732	1762	20	1740	8	+++
1906	1732	1762	20	1742	10	++
1917	1732	1762	20	1744	12	++
1929	1732	1762	20	1746	14	++
1644	1533	1554	11	1541	8	+
1646	1533	1554	11	1543	10	+
1650	1533	1554	11	1545	12	+
1655	1533	1554	11	1547	14	+
1648	1533	1557	14	1541	8	+
1653	1533	1557	14	1543	10	+
1660	1533	1557	14	1545	12	+
1666	1533	1557	14	1547	14	+
1651	1533	1558	15	1541	8	+
1657	1533	1558	15	1543	10	+
1663	1533	1558	15	1545	12	++
1674	1533	1558	15	1547	14	++
1658	1533	1561	18	1541	8	+
1667	1533	1561	18	1543	10	++
1677	1533	1561	18	1545	12	++

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
1693	1533	1561	18	1547	14	++
1664	1533	1562	19	1541	8	+
1676	1533	1562	19	1543	10	+
1686	1533	1562	19	1545	12	++
1698	1533	1562	19	1547	14	++
1671	1533	1563	20	1541	8	+
1681	1533	1563	20	1543	10	+
1691	1533	1563	20	1545	12	++
1699	1533	1563	20	1547	14	++
1247	738	767	12	745	8	+
1256	738	767	12	747	10	++
1274	738	767	12	749	12	+
1296	738	767	12	751	14	+
1263	738	785	15	745	8	+
1279	738	785	15	747	10	+
1312	738	785	15	749	12	+
1340	738	785	15	751	14	++
1270	738	788	16	745	8	+
1299	738	788	16	747	10	+
1320	738	788	16	749	12	+
1365	738	788	16	751	14	++
1305	738	802	19	745	8	+
1352	738	802	19	747	10	+
1394	738	802	19	749	12	+
1425	738	802	19	751	14	++
1336	738	809	20	745	8	+
1361	738	809	20	747	10	++
1412	738	809	20	749	12	+
1446	738	809	20	751	14	++
1248	738	770 *80	12	745	8	+
1255	738	770 *80	12	747	10	++
1272	738	770 *80	12	749	12	+
1291	738	770 *80	12	751	14	+
1259	738	782 *80	15	745	8	+
1288	738	782 *80	15	747	10	+
1309	738	782 *80	15	749	12	+

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
1348	738	782 *80	15	751	14	++
1276	738	791 *80	16	745	8	+
1297	738	791 *80	16	747	10	+
1327	738	791 *80	16	749	12	+
1363	738	791 *80	16	751	14	++
1302	738	805 *80	19	745	8	+
1345	738	805 *80	19	747	10	++
1377	738	805 *80	19	749	12	+
1424	738	805 *80	19	751	14	++
1323	738	807 *80	20	745	8	++
1358	738	807 *80	20	747	10	++
1399	738	807 *80	20	749	12	++
1440	738	807 *80	20	751	14	++
1250	738	769 *81	12	746	9	++
1258	738	769 *81	12	748	11	+
1277	738	769 *81	12	750	13	++
1267	738	784 *81	15	746	9	+
1298	738	784 *81	15	748	11	+
1326	738	784 *81	15	750	13	+
1282	738	789 *81	16	746	9	+
1310	738	789 *81	16	748	11	+
1354	738	789 *81	16	750	13	++
1330	738	803 *81	19	746	9	+
1362	738	803 *81	19	748	11	+
1407	738	803 *81	19	750	13	+
1353	738	810 *81	20	746	9	+
1393	738	810 *81	20	748	11	+
1427	738	810 *81	20	750	13	+
1246	738	771 *82	12	745	8	+
1253	738	771 *82	12	747	10	+
1265	738	771 *82	12	749	12	+
1293	738	771 *82	12	751	14	+
1261	738	783 *82	15	745	8	+
1286	738	783 *82	15	747	10	+
1307	738	783 *82	15	749	12	++
1338	738	783 *82	15	751	14	+

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	Percent Edit[3]
1268	738	790 *82	16	745	8	+
1292	738	790 *82	16	747	10	+
1321	738	790 *82	16	749	12	+
1357	738	790 *82	16	751	14	++
1301	738	804 *82	19	745	8	+
1347	738	804 *82	19	747	10	+
1388	738	804 *82	19	749	12	+
1433	738	804 *82	19	751	14	+
1325	738	808 *82	20	745	8	+
1360	738	808 *82	20	747	10	++
1397	738	808 *82	20	749	12	+
1447	738	808 *82	20	751	14	+

1. Indicated PEgRNA sequence does not contain the adaptations for transcription from a DNA template used experimentally (i.e., addition of a 5'G if the spacer did not already start with a G and addition of 1-6 3'U from the U6 transcription termination sequence).

Table 97: Average Percent Edit by Spacer in PE2 Screen at R778L mutation site in HEK293T cells

Spacer SEQ ID NO:	Avg. % Edit[1]
2132	+++
1732	++
1533	+
738	+

[666] *1* + = 0.02%-0.30%; ++ = 0.30%-5.30%; +++ = 5.30%-15.96%; ++++ = 15.96%-27.71%.

[667] Of the four spacers tested in this PE2 screen, PEgRNA incorporating Spacer 1 produced the highest average Prime Editing frequency. Spacer 1 was also the among the best performing of the four spacers in the Cas9 cutting assay of Example 2. PEgRNA incorporating Spacer 2 produced the next highest average Prime Editing frequency, even though Spacer 2 performed worse than Spacers 3 and 4 in the Cas9 cutting assay. Spacer 3 was the best performing spacer of the four in the Cas9 cutting assay, yielding a % indel rate almost 2 times that of Spacer 4. However, PEgRNAs incorporating Spacer 3 and Spacer 4 had, on average, low activity in the PE2 screen.

[668] A subset of the PEgRNAs from Table 96 were further examined for indels, the results of which are shown in **Table 98**. Indel frequency was quantified using standard quantification techniques via CRISPResso2 algorithm as described in Clement, K. *et al.*, Nat. Biotechnol. 37, 224–226 (2019), with the quantification window defined as at least 20 bases 5' and 3' of pegRNA and ngRNA nick site.

Table 98: PE2 screen at the R778 mutation site in HEK293T cells

PEgRNA[1] Sequence Number	Spacer Sequence Number	RTT[2] Sequence Number	RTT Length	PBS Sequence Number	PBS Length	% Edit[3]	% Indel[3]
1879	1732	1756	14	1744	12	+++	+
3455	2132	2229 *61	16	2142	10	++++	+
3462	2132	2233 *63	16	2142	10	++++	+
3509	2132	2245 *57	17	2142	10	++++	+
3479	2132	2240 *58	17	2142	10	++++	++
3472	2132	2204 *59	14	2144	12	+++	++
3575	2132	2224 *60	16	2144	12	+++	++
3621	2132	2245 *57	17	2144	12	++++	++
3604	2132	2240 *58	17	2144	12	++++	++
3738	2132	2282 *57	20	2144	12	++++	+
3574	2132	2202 *61	14	2146	14	+++	++
3710	2132	2236 *61	17	2146	14	+++	+
3776	2132	2262 *62	19	2146	14	+++	++
3811	2132	2265 *63	19	2146	14	+++	+
3854	2132	2277 *58	20	2146	14	++++	++
3841	2132	2274 *63	20	2146	14	++++	+
3520	2132	2263	19	2140	8	+++	++
3494	2132	2271 *59	19	2140	8	+++	+

1. Indicated PEgRNA sequence does not contain the adaptations for transcription from a DNA template used experimentally (i.e., addition of a 5'G if the spacer did not already start with a G and addition of 1-6 3'U from the U6 transcription termination sequence).

*2. *## = RTT encodes a PAM silencing mutation (see table 85).*

3. += 0.20%-0.27%; ++ = 0.27%-4.47%; +++ = 4.47%-21.95%; ++++ = 21.95%-27.70%

[669] Example 4 – Prime Editing at the endogenous ATP7B R778L mutation site in HEK293T cells using a PE3 system

[670] An ATP7B R778L mutation was installed at the endogenous *ATP7B* locus in HEK 293T cells by prime editing and single-cell clones were obtained *via* limiting dilution and clonal expansion. A PE3 screen measuring correction and indel formation was performed at the endogenous *ATP7B* R778L locus. The HEK293T cells were transfected with DNA encoding a prime editor, PEgRNA, and ngRNA, as described in Example 1.

[671] The results of the PE3 screen are provided in Tables 99a-99d. Below each of Tables 99a-99d is a table summarizing the PEgRNAs used experimentally (Tables 100a-100d). Each of the PEgRNA were tested in combination with multiple ngRNA. Some of the ngRNA were designed for a PE3B strategy and contain spacers complementary to the portion of the edit strand containing the edit. These results

demonstrate the successful correction of the R778L mutation at the endogenous ATP7B locus in mammalian cells using both PE3 and PE3B Prime Editing systems

Table 99a: PE3 screen at the R778L mutation site in HEK293T cells

		PEgRNA[3] SEQ ID NO:									
		1879		3455		3462		3509		3479	
		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
ngRNA spacer[2,3] SEQ ID NO:	PE2	+++	+	+++	+	+	+	++	+	++++	+
	1997	+++	+	+++	+++	++	++	++	++	++++	+++
	1990	+++	+	++	++	+	++	+	++	+++	+++
	*	+++	++	+++	++	+	+	+	+	+++	+++
	**	+++	+	+++	+	+	+	+++	+	++++	+
	***	+++	+	+++	+	+	+	+++	+	++++	+
	2057	+++	++	+++	+	+	+	++	+	++++	+
	2056	+++	++	+	+	+	++	+++	++	++++	++
	3268	+++	++	+++	+	++	+	+++	+	++++	++
	3269	+++	++	+++	++	++	++	+++	++	++++	++
	3260	+++	++	++++	++	++	++	+++	+	++++	++
	3279	++	++	++++	++	++	++	+++	++	++++	++
	3244	+++	++	++++	++	++	++	+++	+	++++	++
	3275	++	++	+++	+	+	+	++	+	++++	+
	63	+++	++	+++	+	+	+	++	+	++++	+

1. += 0.12%-0.41%; ++ = 0.41%-3.33%; +++ = 3.33%-18.73%; +++ = 18.73%-45.64%.

*2. PE3bngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286 *62; 3294 *60; 3274 *61; or 3281 *63. *** = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63*

Table 100a: *Summary of PEgRNA used*

PEgRNA[2] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
1879	1732	1756	14	1744	12
3455	2132	2229 *61	16	2142	10
3462	2132	2233 *63	16	2142	10
3509	2132	2245 *57	17	2142	10
3479	2132	2240 *58	17	2142	10

3. Indicated sequence does not contain the transcription adaptations used experimentally (i.e., addition of a 5'G if the spacer did not already start with a G and addition of 1-6 3'U from the U6 transcription termination sequence). In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.

*4. *## = RTT encodes a PAM silencing mutation (see table 85).*

Table 99b: PE3 screen at the R778L mutation site in HEK293T cells

		PEgRNA[3] SEQ ID NO:									
		3472		3575		3621		3604		3738	
		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
ngRNA spacer[2,3] SEQ ID NO:	PE2	++++	+	+++	+	++++	+	+++	++	++++	+
	1997	++++	+++	+++	+++	++++	+++	+++	+++	++++	+++
	1990	+++	+++	+++	++	++++	+++	++	+++	+++	+++
	*	+++	++	+++	++	++++	+++	+++	+++	+++	++
	**	+++	+	+++	+	++++	+	+++	++	++++	+
	***	++++	+	+++	+	++++	+	+++	++	++++	+
	2057	+++	+	+++	+	++++	+	+++	++	++++	+
	2056	++++	++	+++	++	++++	++	+++	++	++++	+
	3268	++++	++	++++	++	++++	++	++++	++	++++	+
	3269	++++	++	++++	++	++++	++	++++	++	++++	++
	3260	++++	++	++++	++	++++	++	++++	+++	++++	++
	3279	++++	++	++++	++	++++	++	++++	+++	++++	++
	3244	++++	++	++++	++	++++	++	++++	+++	++++	++
	3275	++++	+	+++	+	++++	+	+++	++	++++	+
	63	+++	+	+++	+	++++	+	+++	++	++++	+

1. += 0.12%-0.41%; ++ = 0.41%-3.33%; +++ = 3.33%-18.73%; +++ = 18.73%-45.64%.

*2. PE3b ngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286 *62; 3294 *60; 3274 *61; or 3281 *63. *** = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63*

Table 100b: Summary *of PEgRNA used:*

PEgRNA[2] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
3472	2132	2204 *59	14	2144	12
3575	2132	2224 *60	16	2144	12
3621	2132	2245 *57	17	2144	12

3604	2132	2240 *58	17	2144	12
3738	2132	2282 *57	20	2144	12

3. Indicated sequence does not contain the transcription adaptations used experimentally (i.e., addition of a 5'G if the spacer did not already start with a G and addition of 1-6 3'U from the U6 transcription termination sequence). In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.

*4. *## = RTT encodes a PAM silencing mutation (see table 85).*

Table 99c: PE3 screen at the R778L mutation site in HEK293T cells

		PEgRNA[3] SEQ ID NO:									
		3574		3710		3776		3811		3854	
		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
ngRNA spacer[2,3] SEQ ID NO:	PE2	+++	+	+++	+	++++	+	++++	+	+++	+
	1997	+++	+++	+++	+++	++++	+++	+++	+++	++++	+++
	1990	+++	+++	+++	++	++++	+++	+++	+++	+++	++
	*	+++	++	+++	++	++++	++	++++	++	++++	+
	**	+++	+	+++	+	++++	+	++++	+	++++	+
	***	+++	+	++++	+	++++	+	++++	+	++++	+
	2057	+++	+	+++	+	++++	+	++++	+	++++	+
	2056	+++	++	+++	+	++++	++	+++	++	++++	++
	3268	++++	+	++++	+	++++	++	++++	+	++++	+
	3269	++++	++	++++	+	++++	++	++++	++	++++	++
	3260	++++	++	++++	++	+++	++	++++	++	++++	++
	3279	++++	++	++++	++	++++	++	++++	++	++++	++
	3244	++++	++	++++	++	++++	++	++++	++	++++	++
	3275	+++	+	+++	+	+++	+	++++	+	++++	+
	63	+++	+	+++	+	++++	+	++++	+	++++	+

1. . + = 0.12%-0.41%; ++ = 0.41%-3.33%; +++ = 3.33%-18.73%; +++ = 18.73%-45.64%.

*2. PE3b ngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286 *62; 3294 *60; 3274 *61; or 3281 *63. *** = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63.*

Table 100c: Summary *of PEgRNA used:*

PEgRNA[2] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
3574	2132	2202 *61	14	2146	14
3710	2132	2236 *61	17	2146	14
3776	2132	2262 *62	19	2146	14
3811	2132	2265 *63	19	2146	14
3854	2132	2277 *58	20	2146	14

3. *Indicated sequence does not contain the transcription adaptations used experimentally (i.e., addition of a 5'G if the spacer did not already start with a G and addition of 1-6 3'U from the U6 transcription termination sequence). In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.*

4. **## = RTT encodes a PAM silencing mutation (see table 85).*

Table 99d: PE3 screen at the R778L mutation site in HEK293T cells

		PEgRNA[3] SEQ ID NO:					
		3841		3520		3494	
		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
ngRNA spacer[2,3] SEQ ID NO:	PE2	++++	+	+++	+	+++	+
	1997	+++	+++	+++	+++		
	1990	+++	++	+++	+++		
	*	+++	++	+++	++	++++	+
	**	+++	+	++++	+	++++	+
	***	++++	+	++++	+	++++	+
	2057	+++	+	+++	+	++++	+
	2056	+++	++	+++	++	++++	+
	3268	++++	+	+++	+		
	3269	++++	++	++++	++		
	3260	++++	++	++++	++		
	3279	++++	++	++++	++		
	3244	++++	++	++++	++		
	3275	++++	+				
	63	++++	+				

1. *+ = 0.12%-0.41%; ++ = 0.41%-3.33%; +++ = 3.33%-18.73%; +++ = 18.73%-45.64%.*

2. *PE3b ngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286*

62; 3294 *60; 3274 *61; or 3281 *63. * = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63*

Table 100d: Summary *of PEgRNA used:*

PEgRNA[2] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
3574	2132	2202 *61	14	2146	14
3710	2132	2236 *61	17	2146	14
3776	2132	2262 *62	19	2146	14
3811	2132	2265 *63	19	2146	14
3854	2132	2277 *58	20	2146	14

3. Indicated sequence does not contain the transcription adaptations used experimentally (i.e., addition of a 5'G if the spacer did not already start with a G and addition of 1-6 3'U from the U6 transcription termination sequence). In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.

*4. *## = RTT encodes a PAM silencing mutation (see table 85).*

[672] EXAMPLE 5 - Prime editing at the endogenous ATP7B R778L mutation site in mammalian cells using synthetic PEgRNA in a PE2 system

[673] An ATP7B R778L mutation was installed at the endogenous ATP7B locus in HEK293T by prime editing and single-cell clones were obtained via limiting dilution and clonal expansion, as described in Example 1. A PE2 screen measuring percent correction was performed at the endogenous ATP7B R778L locus. The cells were transfected with mRNA encoding a prime editor, and synthetic PEgRNA, as described in Example 1.

[674] The results of the PE2 screen for the HEK293T cells are provided in Table 101. These data demonstrate successful Prime Editing at the endogenous ATP7B R778L mutation site using synthetic PEgRNA. Successful editing was observed with PEgRNAs containing multiple PBS lengths, multiple RTT lengths, and both with and without PAM silencing mutations. The percent editing observed for all PEgRNA having the same spacer were averaged, and the results reported in Table 102.

Table 101: PE2 screen at R778L mutation site in mammalian cell culture using synthetic PEgRNAs

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
3300	2132	2155 *57	10	2140	8	+++	+
3319	2132	2155 *57	10	2142	10	+++	+
3337	2132	2155 *57	10	2144	12	++++	+
3380	2132	2155 *57	10	2146	14	+	+
3333	2132	2211 *57	14	2140	8	++++	++
3398	2132	2211 *57	14	2142	10	++++	+
3454	2132	2211 *57	14	2144	12	++++	++
3545	2132	2211 *57	14	2146	14	++++	++

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
3354	2132	2216 *57	15	2140	8	++++	++
3413	2132	2216 *57	15	2142	10	++++	+
3496	2132	2216 *57	15	2144	12	++++	++
3592	2132	2216 *57	15	2146	14	++++	+
3390	2132	2227 *57	16	2140	8	++++	+++
3450	2132	2227 *57	16	2142	10	++++	++
3532	2132	2227 *57	16	2144	12	++++	+
3638	2132	2227 *57	16	2146	14	++++	++
3410	2132	2245 *57	17	2140	8	++++	++
3509	2132	2245 *57	17	2142	10	++++	+++
3621	2132	2245 *57	17	2144	12	++++	++
3680	2132	2245 *57	17	2146	14	++++	++
3495	2132	2260 *57	19	2140	8	++++	++
3620	2132	2260 *57	19	2142	10	+	+
3677	2132	2260 *57	19	2144	12	++++	++
3815	2132	2260 *57	19	2146	14	++++	++
3536	2132	2282 *57	20	2140	8	++++	++
3636	2132	2282 *57	20	2142	10	+	+
3738	2132	2282 *57	20	2144	12	++++	++
3855	2132	2282 *57	20	2146	14	+++	+
3305	2132	2159 *58	10	2140	8	++	+
3323	2132	2159 *58	10	2142	10	++	+
3339	2132	2159 *58	10	2144	12	+++	+
3399	2132	2159 *58	10	2146	14	+	+
3341	2132	2201 *58	14	2140	8	++++	++
3385	2132	2201 *58	14	2142	10	++++	++
3449	2132	2201 *58	14	2144	12	++++	+
3539	2132	2201 *58	14	2146	14	++++	++
3365	2132	2215 *58	15	2140	8	++++	++
3426	2132	2215 *58	15	2142	10	+	+
3506	2132	2215 *58	15	2144	12	++++	+
3618	2132	2215 *58	15	2146	14	+	+
3373	2132	2235 *58	16	2140	8	++++	++
3437	2132	2235 *58	16	2142	10	++++	++
3571	2132	2235 *58	16	2144	12	++++	+
3664	2132	2235 *58	16	2146	14	+++	+

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
3424	2132	2240 *58	17	2140	8	++++	++
3479	2132	2240 *58	17	2142	10	++++	+++
3604	2132	2240 *58	17	2144	12	+++	++
3681	2132	2240 *58	17	2146	14	++++	+
3518	2132	2269 *58	19	2140	8	++++	++
3600	2132	2269 *58	19	2142	10	++++	+
3717	2132	2269 *58	19	2144	12	++++	++
3775	2132	2269 *58	19	2146	14	++++	++
3572	2132	2277 *58	20	2140	8	++++	++
3660	2132	2277 *58	20	2142	10	++++	++
3768	2132	2277 *58	20	2144	12	+++	+
3854	2132	2277 *58	20	2146	14	++++	++
3306	2132	2154 *59	10	2140	8	+++	+
3318	2132	2154 *59	10	2142	10	+++	+
3342	2132	2154 *59	10	2144	12	++++	+
3401	2132	2154 *59	10	2146	14	+++	+
3343	2132	2204 *59	14	2140	8	++++	++
3388	2132	2204 *59	14	2142	10	++++	+
3472	2132	2204 *59	14	2144	12	++++	++
3577	2132	2204 *59	14	2146	14	++++	++
3358	2132	2218 *59	15	2140	8	++++	++
3418	2132	2218 *59	15	2142	10	++++	++
3492	2132	2218 *59	15	2144	12	++++	++
3603	2132	2218 *59	15	2146	14	++++	++
3376	2132	2232 *59	16	2140	8	++++	+
3446	2132	2232 *59	16	2142	10	++++	++
3542	2132	2232 *59	16	2144	12	++++	++
3628	2132	2232 *59	16	2146	14	++++	++
3421	2132	2242 *59	17	2140	8	++++	++
3511	2132	2242 *59	17	2142	10	++++	++
3599	2132	2242 *59	17	2144	12	++	+
3712	2132	2242 *59	17	2146	14	+++	+
3494	2132	2271 *59	19	2140	8	++++	++
3583	2132	2271 *59	19	2142	10	++++	++
3713	2132	2271 *59	19	2144	12	++++	++
3783	2132	2271 *59	19	2146	14	++++	++

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
3560	2132	2280 *59	20	2140	8	++++	++
3650	2132	2280 *59	20	2142	10	++++	+++
3742	2132	2280 *59	20	2144	12	++++	++
3834	2132	2280 *59	20	2146	14	++++	++
3304	2132	2160 *60	10	2140	8	+++	+
3317	2132	2160 *60	10	2142	10	+++	+
3338	2132	2160 *60	10	2144	12	+++	+
3379	2132	2160 *60	10	2146	14	+++	+
3340	2132	2206 *60	14	2140	8	++++	++
3403	2132	2206 *60	14	2142	10	++++	++
3457	2132	2206 *60	14	2144	12	++++	++
3567	2132	2206 *60	14	2146	14	+++	++
3370	2132	2214 *60	15	2140	8	++++	++
3405	2132	2214 *60	15	2142	10	++++	++
3480	2132	2214 *60	15	2144	12	+++	++
3619	2132	2214 *60	15	2146	14	+++	+
3372	2132	2224 *60	16	2140	8	++++	++
3456	2132	2224 *60	16	2142	10	++++	++
3575	2132	2224 *60	16	2144	12	+	+
3643	2132	2224 *60	16	2146	14	+++	+
3416	2132	2243 *60	17	2140	8	++++	++
3519	2132	2243 *60	17	2142	10	++++	+++
3625	2132	2243 *60	17	2144	12	++++	+++
3679	2132	2243 *60	17	2146	14	++++	++
3481	2132	2268 *60	19	2140	8	++++	++
3607	2132	2268 *60	19	2142	10	++++	++
3678	2132	2268 *60	19	2144	12	++++	++
3798	2132	2268 *60	19	2146	14	++++	++
3573	2132	2281 *60	20	2140	8	++++	+++
3649	2132	2281 *60	20	2142	10	++++	++
3725	2132	2281 *60	20	2144	12	++++	+++
3842	2132	2281 *60	20	2146	14	++++	++
3302	2132	2153 *61	10	2140	8	+	+
3316	2132	2153 *61	10	2142	10	+	+
3335	2132	2153 *61	10	2144	12	+	+
3383	2132	2153 *61	10	2146	14	+	+

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
3345	2132	2202 *61	14	2140	8	+++	+
3386	2132	2202 *61	14	2142	10	++++	++
3441	2132	2202 *61	14	2144	12	++++	+
3574	2132	2202 *61	14	2146	14	++++	+
3367	2132	2222 *61	15	2140	8	+++	+
3408	2132	2222 *61	15	2142	10	++++	+
3488	2132	2222 *61	15	2144	12	+++	+
3605	2132	2222 *61	15	2146	14	++++	++
3394	2132	2229 *61	16	2140	8	++++	++
3455	2132	2229 *61	16	2142	10	++++	++
3559	2132	2229 *61	16	2144	12	++++	++
3661	2132	2229 *61	16	2146	14	++++	++
3432	2132	2236 *61	17	2140	8	++++	+
3523	2132	2236 *61	17	2142	10	++++	++
3593	2132	2236 *61	17	2144	12	++++	++
3710	2132	2236 *61	17	2146	14	++++	++
3486	2132	2264 *61	19	2140	8	++++	++
3595	2132	2264 *61	19	2142	10	++++	++
3702	2132	2264 *61	19	2144	12	++++	++
3795	2132	2264 *61	19	2146	14	++++	++
3544	2132	2276 *61	20	2140	8	+++	++
3662	2132	2276 *61	20	2142	10	++++	++
3724	2132	2276 *61	20	2144	12	++++	++
3856	2132	2276 *61	20	2146	14	++++	+
3307	2132	2152 *62	10	2140	8	+++	+
3322	2132	2152 *62	10	2142	10	++++	+
3344	2132	2152 *62	10	2144	12	+++	+
3400	2132	2152 *62	10	2146	14	+++	+
3346	2132	2200 *62	14	2140	8	++++	++
3389	2132	2200 *62	14	2142	10	+++	+
3464	2132	2200 *62	14	2144	12	+++	+
3579	2132	2200 *62	14	2146	14	++	+
3353	2132	2221 *62	15	2140	8	++++	+
3406	2132	2221 *62	15	2142	10	++++	++
3515	2132	2221 *62	15	2144	12	+++	++
3608	2132	2221 *62	15	2146	14	+++	++

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
3375	2132	2225 *62	16	2140	8	++++	++
3473	2132	2225 *62	16	2142	10	++++	++
3565	2132	2225 *62	16	2144	12	++++	++
3653	2132	2225 *62	16	2146	14	++++	++
3428	2132	2244 *62	17	2140	8	++++	+++
3477	2132	2244 *62	17	2142	10	++++	++
3626	2132	2244 *62	17	2144	12	++++	++
3700	2132	2244 *62	17	2146	14	++++	+++
3514	2132	2262 *62	19	2140	8	++++	+++
3602	2132	2262 *62	19	2142	10	++++	++
3711	2132	2262 *62	19	2144	12	++++	++
3776	2132	2262 *62	19	2146	14	++++	++
3548	2132	2272 *62	20	2140	8	++++	++
3634	2132	2272 *62	20	2142	10	++++	+++
3739	2132	2272 *62	20	2144	12	++++	++
3852	2132	2272 *62	20	2146	14	++++	++
3303	2132	2157 *63	10	2140	8	+++	+
3321	2132	2157 *63	10	2142	10	+++	+
3336	2132	2157 *63	10	2144	12	+++	+
3374	2132	2157 *63	10	2146	14	+++	+
3384	2132	2205 *63	14	2142	10	++++	+++
3448	2132	2205 *63	14	2144	12	++++	++
3543	2132	2205 *63	14	2146	14	++++	+++
3357	2132	2212 *63	15	2140	8	++++	++
3431	2132	2212 *63	15	2142	10	++++	++
3504	2132	2212 *63	15	2144	12	++++	++
3597	2132	2212 *63	15	2146	14	++++	+++
3381	2132	2233 *63	16	2140	8	++++	++
3462	2132	2233 *63	16	2142	10	++++	+++
3527	2132	2233 *63	16	2144	12	++++	++
3663	2132	2233 *63	16	2146	14	++++	+
3434	2132	2237 *63	17	2140	8	++++	++
3485	2132	2237 *63	17	2142	10	++++	+++
3609	2132	2237 *63	17	2144	12	++++	++
3682	2132	2237 *63	17	2146	14	++++	++
3500	2132	2265 *63	19	2140	8	++++	+++

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
3612	2132	2265 *63	19	2142	10	++++	++
3703	2132	2265 *63	19	2144	12	++++	++
3811	2132	2265 *63	19	2146	14	++++	++
3531	2132	2274 *63	20	2140	8	++++	+++
3640	2132	2274 *63	20	2142	10	++++	+++
3745	2132	2274 *63	20	2144	12	++++	++
3841	2132	2274 *63	20	2146	14	++++	++
3301	2132	2162	10	2140	8	++++	+
3320	2132	2162	10	2142	10	++++	+
3332	2132	2162	10	2144	12	+++	+
3392	2132	2162	10	2146	14	+++	+
3334	2132	2209	14	2140	8	+++	++
3396	2132	2209	14	2142	10	+++	++
3461	2132	2209	14	2144	12	+++	+
3524	2132	2209	14	2146	14	+++	++
3362	2132	2223	15	2140	8	+++	++
3435	2132	2223	15	2142	10	+++	++
3491	2132	2223	15	2144	12	+++	+
3596	2132	2223	15	2146	14	+++	++
3393	2132	2226	16	2140	8	+++	++
3442	2132	2226	16	2142	10	+++	++
3537	2132	2226	16	2144	12	+++	++
3657	2132	2226	16	2146	14	+++	++
3429	2132	2238	17	2140	8	+++	++
3499	2132	2238	17	2142	10	+++	++
3624	2132	2238	17	2144	12	+++	+
3687	2132	2238	17	2146	14	+++	++
3520	2132	2263	19	2140	8	+++	++
3613	2132	2263	19	2142	10	+++	++
3714	2132	2263	19	2144	12	+++	+
3801	2132	2263	19	2146	14	+++	++
3528	2132	2279	20	2140	8	+++	++
3668	2132	2279	20	2142	10	+++	++
3735	2132	2279	20	2144	12	+++	+
3832	2132	2279	20	2146	14	+++	++
1846	1732	1753	11	1740	8	+++	+++

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
1850	1732	1753	11	1742	10	+++	+++
1858	1732	1753	11	1744	12	+++	+++
1870	1732	1753	11	1746	14	+++	+++
1847	1732	1754	12	1740	8	+++	+++
1854	1732	1754	12	1742	10	+++	+++
1866	1732	1754	12	1744	12	+++	+++
1877	1732	1754	12	1746	14	+++	+++
1849	1732	1755	13	1740	8	+++	+++
1860	1732	1755	13	1742	10	+++	+++
1867	1732	1755	13	1744	12	+++	+++
1881	1732	1755	13	1746	14	+++	++
1853	1732	1756	14	1740	8	+++	+++
1861	1732	1756	14	1742	10	+++	+++
1879	1732	1756	14	1744	12	+++	+++
1889	1732	1756	14	1746	14	+++	+++
1859	1732	1757	15	1740	8	++++	+++
1868	1732	1757	15	1742	10	+++	+++
1880	1732	1757	15	1744	12	+++	+++
1898	1732	1757	15	1746	14	+++	+++
1863	1732	1758	16	1740	8	+++	+++
1878	1732	1758	16	1742	10	+++	+++
1886	1732	1758	16	1744	12	+++	+++
1900	1732	1758	16	1746	14	+++	+++
1873	1732	1759	17	1740	8	+++	+++
1884	1732	1759	17	1742	10	+++	++
1895	1732	1759	17	1744	12	+++	+++
1907	1732	1759	17	1746	14	+++	+++
1888	1732	1762	20	1740	8	+++	++
1906	1732	1762	20	1742	10	+++	+++
1917	1732	1762	20	1744	12	++	+
1929	1732	1762	20	1746	14	+++	+++
1653	1533	1557	14	1543	10	+++	+
1666	1533	1557	14	1547	14	+++	+
1657	1533	1558	15	1543	10	+	+
1674	1533	1558	15	1547	14	+++	+
1667	1533	1561	18	1543	10	+++	+

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
1693	1533	1561	18	1547	14	+++	+
1676	1533	1562	19	1543	10	+++	+
1698	1533	1562	19	1547	14	+++	+
1681	1533	1563	20	1543	10	+++	+
1699	1533	1563	20	1547	14	+++	+
1279	738	785	15	747	10	+	+
1340	738	785	15	751	14	+	+
1299	738	788	16	747	10	+	+
1365	738	788	16	751	14	++	+
1352	738	802	19	747	10	+	+
1425	738	802	19	751	14	+	+
1361	738	809	20	747	10	+	+
1446	738	809	20	751	14	+	+
1288	738	782 *80	15	747	10	+	+
1348	738	782 *80	15	751	14	++	+
1297	738	791 *80	16	747	10	+	+
1363	738	791 *80	16	751	14	+	+
1345	738	805 *80	19	747	10	++	+
1424	738	805 *80	19	751	14	++	+
1358	738	807 *80	20	747	10	++	+
1440	738	807 *80	20	751	14	+	+
1287	738	784 *81	15	747	10	++	+
1344	738	784 *81	15	751	14	+	+
1294	738	789 *81	16	747	10	++	+
1376	738	789 *81	16	751	14	++	+
1350	738	803 *81	19	747	10	++	+
1421	738	803 *81	19	751	14	++	+
1366	738	810 *81	20	747	10	+++	+
1450	738	810 *81	20	751	14	+	+
1286	738	783 *82	15	747	10	+	+
1338	738	783 *82	15	751	14	+	+
1292	738	790 *82	16	747	10	+	+
1357	738	790 *82	16	751	14	+	+
1347	738	804 *82	19	747	10	+	+
1433	738	804 *82	19	751	14	+	+
1360	738	808 *82	20	747	10	+	+

PEgRNA[1] SEQ ID NO:	Spacer SEQ ID NO:	RTT[2] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length	% Edit[3]	% Indel[3]
1447	738	808 *82	20	751	14	+	+

1. *1. Indicated PEgRNA sequence does not contain the 3' linker and hairpin motif used experimentally. The experimental PEgRNA further contained 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates a phosphorothioate bond.*
2. **## = RTT encodes a PAM silencing mutation (see table 85).*
3. *+ = 0.08%-0.50%, ++ = 0.50%-0.86%, +++ = 0.86%-7.40%, ++++ = 7.40%-25.16%*

Table 102: Average Percent Edit by Spacer in PE2 Screen at R778L mutation site in HEK293T cells

Spacer SEQ ID NO:	Avg. % Edit[1]	Avg. % Indel[1]
2132	++++	++
1732	+++	+++
1533	+++	+
738	+	+

2. + = 0.08%-0.50%, ++ = 0.50%-0.86%, +++ = 0.86%-7.40%, ++++ = 7.40%-25.16%

[675] Similarly to Example 3, PEgRNA incorporating Spacer 1 produced the highest average Prime Editing frequency, with the next highest editing achieved with Spacer 2. Spacer 3 did not produce as high an average edit percentage as Spacer 2; however, the average indels for Spacer 3 were lower than for Spacer 2. PEgRNAs incorporating Spacer 4 had, on average, low activity in the PE2 screen.

[676] Example 6 – Prime editing at the endogenous ATP7B R778L mutation site in mammalian cells using synthetic PEgRNA in a PE3 system

[677] An ATP7B R778L mutation was installed at the endogenous ATP7B locus in HEK293T by prime editing and single-cell clones were obtained via limiting dilution and clonal expansion, as described in Example 1. A PE3 screen measuring percent correction and indel formation was performed at the endogenous ATP7B R778L locus. The cells were transfected with mRNA encoding a prime editor, and synthetic PEgRNA and ngRNA, as described in Example 1.

[678] The results of the PE3 screen are provided in Tables 103a=103e. Below each of Tables 103a-103e is a table summarizing the PEgRNAs used experimentally(Tables 104a-104e). Each of the PEgRNA were tested in combination with multiple ngRNA. Some of the ngRNA were designed for a PE3B strategy and contain spacers complementary to the portion of the edit strand containing the edit. These results demonstrate the successful correction of the R778L mutation at the endogenous ATP7B locus in mammalian cells using synthetic PEgRNA and ngRNA in both PE3 and PE3B Prime Editing systems.

Table 103a: PE3 screen at the R778L mutation site in HEK293T cells

		PEgRNA[3] SEQ ID NO:									
		3434		3384		3418		3431		3437	
		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
ngRNA spacer[2,3] SEQ ID NO:	PE2			++++	+	++++	+	++++	+	+++	+
	*	+++	+	+++	++	+++	++	+++	+	+++	+
	**	+++	+	++++	+	+++	+	+++	+	+++	+
	***	+++	+	++++	+	++++	+	+++	+	+++	+
	3269	++++	++	++++	++	++++	++	++++	++	++++	++
	3260	++++	++	++++	++	++++	++	+++	++	+++	++
	3279	++++	++	++++	++	++++	++	++++	++	++++	++
	3244	++++	+	++++	++	++++	++	+++	++	+++	++

1. *+ = 0.37%-1.07%; ++ = 1.07%-6.53%; +++ = 6.53%-35.96%; ++++ = 35.96%-57.31%.*

2. *PE3b ngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286 *62; 3294 *60; 3274 *61; or 3281 *63. *** = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63.*

Table 104a: Summary *of PEgRNA used:*

PEgRNA[3] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
3434	2132	2237 *63	17	2140	8
3384	2132	2205 *63	14	2142	10
3418	2132	2218 *59	15	2142	10
3431	2132	2212 *63	15	2142	10
3437	2132	2235 *58	16	2142	10

3. *Indicated sequence sequence does not contain the 3' mU*mU*mU*U and 5'mN*mN*mN* modifications used experimentally, where m indicates that the indicated nucleotide contains a 2'-O-Me modification and a * indicates a phosphorothioate bond. In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.*

4. **## = RTT encodes a PAM silencing mutation (see table 85).*

Table 103b: PE3 screen at the R778L mutation site in HEK293T cells

	PEgRNA[3] SEQ ID NO:				
	3446	3455	3462	3509	3479

		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
ngRNA spacer[2,3] SEQ ID NO:	PE2	++++	+	++++	+	++++	+	++++	++	+++	+
	*	+++	++	+++	++	+++	+	+++	++	+++	++
	**	++++	+	+++	+	++++	+	++++	+	+++	+
	***	++++	+	++++	+	++++	+	++++	++	+++	+
	3269	++++	++	++++	++	++++	++	++++	++	++++	++
	3260	++++	++	+++	++	++++	++	++++	++	++++	++
	3279	++++	++	++++	++	++++	++	++++	++	++++	++
	3244	++++	++	++++	++	++++	++	++++	++	+++	+

1. + = 0.37%-1.07%; ++ = 1.07%-6.53%; +++ = 6.53%-35.96%; ++++ = 35.96%-57.31%.

*2. PE3b ngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286 *62; 3294 *60; 3274 *61; or 3281 *63. *** = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63.*

Table 104b: Summary *of PEgRNA used:*

PEgRNA[3] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
3446	2132	2232 *59	16	2142	10
3455	2132	2229 *61	16	2142	10
3462	2132	2233 *63	16	2142	10
3509	2132	2245 *57	17	2142	10
3479	2132	2240 *58	17	2142	10

*3. . Indicated sequence sequence does not contain the 3' mU*mU*mU*U and 5'mN*mN*mN* modifications used experimentally, where m indicates that the indicated nucleotide contains a 2'-O-Me modification and a * indicates a phosphorothioate bond. In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.*

*4. *## = RTT encodes a PAM silencing mutation (see table 85).*

Table 103c: PE3 screen at the R778L mutation site in HEK293T cells

		PEgRNA[3] SEQ ID NO:									
		3511		3519		3523		3477		3485	
		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
≡	PE2	++++	+	++++	+	++++	+	+++	+		

	*	+++	++	+++	+	+++	++	+++	+	+++	+
	**	++++	+	+++	+	++++	+	+++	+	+++	+
	***	++++	+	+++	+	++++	+	+++	+	+++	+
	3269	++++	++	++++	++	++++	++	++++	++	+++	++
	3260	++++	++	+++	++	+++	++	+++	+	+++	+
	3279	++++	++	++++	++	++++	++	++++	++	++++	++
	3244	++++	++	++++	++	++++	++	++++	++	+++	+

1. *+ = 0.37%-1.07%; ++ = 1.07%-6.53%; +++ = 6.53%-35.96%; ++++ = 35.96%-57.31%.*
2. *PE3b ngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286 *62; 3294 *60; 3274 *61; or 3281 *63. *** = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63.*

Table 104c: Summary of PEgRNAs used

PEgRNA[3] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
3511	2132	2242 *59	17	2142	10
3519	2132	2243 *60	17	2142	10
3523	2132	2236 *61	17	2142	10
3477	2132	2244 *62	17	2142	10
3485	2132	2237 *63	17	2142	10

3. *Indicated sequence sequence does not contain the 3' mU*mU*mU*U and 5'mN*mN*mN* modifications used experimentally, where m indicates that the indicated nucleotide contains a 2'-O-Me modification and a * indicates a phosphorothioate bond. In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.*
4. **## = RTT encodes a PAM silencing mutation (see table 85).*

Table 103d: PE3 screen at the R778L mutation site in HEK293T cells

		PEgRNA[3] SEQ ID NO:									
		3600		3583		3595		3634		3448	
		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
ngRNA	**PE2**	+++	+	++++	+	++++	+	++++	++	+++	+
	*	+++	+	+++	+	+++	+	+++	++	+++	+
	**	+++	+	++++	+	+++	+	+++	+	+++	+

	***	+++	+	++++	+	+++	+	++++	++	+++	+
	3269	+++	++	++++	++	+++	++	++++	++	+++	++
	3260	+++	++	++++	++	+++	+	++++	++	+++	++
	3279	+++	++	++++	++	++++	++	++++	++	++++	++
	3244	+++	++	++++	++	++++	++	++++	++	+++	+

1. *+ = 0.37%-1.07%; ++ = 1.07%-6.53%; +++ = 6.53%-35.96%; ++++ = 35.96%-57.31%.*

2. *PE3b ngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286 *62; 3294 *60; 3274 *61; or 3281 *63. *** = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63.*

Table 104d: Summary of PEgRNAs used

PEgRNA[3] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
3600	2132	2269 *58	19	2142	10
3583	2132	2271 *59	19	2142	10
3595	2132	2264 *61	19	2142	10
3634	2132	2272 *62	20	2142	10
3448	2132	2205 *63	14	2144	12

3. *Indicated sequence sequence does not contain the 3' mU*mU*mU*U and 5'mN*mN*mN* modifications used experimentally, where m indicates that the indicated nucleotide contains a 2'-O-Me modification and a * indicates a phosphorothioate bond. In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.*

4. *## = RTT encodes a PAM silencing mutation (see table 85).*

Table 103e: PE3 screen at the R778L mutation site in HEK293T cells

		PEgRNA[3] SEQ ID NO:					
		3527		3604		3681	
		% Edit[1]	% indel[1]	% Edit[1]	% indel[1]	% Edit[1]	% indel[1]
ngRNA	PE2	+++	+	+++	+	+++	+
	*	+++	+	+++	+	+++	+
	**	+++	+	+++	+	+++	+

	***	+++	+	+++	+	+++	+
	3269	+++	++	+++	++	++++	++
	3260	+++	+	+++	+	+++	++
	3279	+++	++	+++	+	++++	++
	3244	+++	++	+++	+	+++	+

1. *+ = 0.37%-1.07%; ++ = 1.07%-6.53%; +++ = 6.53%-35.96%; ++++ = 35.96%-57.31%.*
2. *PE3b ngRNA spacer used and matched to PAM silencing edit encoded by RTT (if any). * = ngRNA spacer is sequence number: 2003; 3255 *57; 3265 *58; 3253 *59; 3252 *62; 3254 *60; 3251 *61; or 3256 *63. ** = ngRNA spacer is sequence number: 2000; 3271 *57; 3264 *58; 3297 *59; 3286 *62; 3294 *60; 3274 *61; or 3281 *63. *** = ngRNA spacer is sequence number: 1994; 3272 *57; 3299 *58; 3247 *59; 3288 *62; 3258 *60; 3249 *61; 3267 *63.*

Table 104e: Summary of PEgRNAs used

PEgRNA[3] SEQ ID NO:	Spacer SEQ ID NO:	RTT[4] SEQ ID NO:	RTT Length	PBS SEQ ID NO:	PBS Length
3527	2132	2233 *63	16	2144	12
3604	2132	2240 *58	17	2144	12
3681	2132	2240 *58	17	2146	14

3. *Indicated sequence sequence does not contain the 3' mU*mU*mU*U and 5'mN*mN*mN* modifications used experimentally, where m indicates that the indicated nucleotide contains a 2'-O-Me modification and a * indicates a phosphorothioate bond. In case of ngRNA, the indicated spacer was combined with the same gRNA core used in the PEgRNA.*
4. **## = RTT encodes a PAM silencing mutation (see table 85).*

[679] Example 7 - Prime Editing in *Primary Human Hepatocytes (PHH)*

[680] Primary Human Hepatocytes Hu8391 were obtained from Thermo Scientific and were cultured according to the manufacturer protocols. 40 K cells were plated in 96-well plate and twenty-four later cells were transfected with Messenger Max according to the manufacturer's directions with mRNA encoding a prime editor, and synthetic PEgRNA and ngRNA. Three days after transfection, gDNA was harvested in quick DNA extract for high throughput sequencing and sequenced using miseq. Because the PHH were wild-type, the genomic DNA was analyzed for synonymous PAM silencing mutations near the R778 locus in ATP7b. The results are shown in Table 105 (PE3) and Table 106 (PE3b). These results demonstrate successful Prime Editing at the R778 mutation site in clinically relevant cells types using both PE3 and PE3b editing strategies.

Table 105: Prime Editing in primary human hepatocytes using a PE3 system

PEgRNA[1] Seq. #	Spacer Seq. #	RTT[2] Seq. #	RTT Len.	PBS Seq. #	PBS Len.	ngRNA[1] Seq. #	% Edit[3]	% Indel[3]

14773	2132	2235 *58	16	2142	10	14800	++++	+
14778	2132	2240 *58	17	2142	10	14800	++++	+
14784	2132	2269 *58	19	2142	10	14800	++++	+
14790	2132	2240 *58	17	2144	12	14800	++++	+
14791	2132	2240 *58	17	2146	14	14800	++++	+
14769	2132	2237 *63	17	2140	8	14800	+++	+
14770	2132	2205 *63	14	2142	10	14800	+++	++
14772	2132	2212 *63	15	2142	10	14800	+++	++
14776	2132	2233 *63	16	2142	10	14800	++++	++
14783	2132	2237 *63	17	2142	10	14800	+++	++
14788	2132	2205 *63	14	2144	12	14800	+++	++
14789	2132	2233 *63	16	2144	12	14800	++++	++
14771	2132	2218 *59	15	2142	10	14800	+++	++
14774	2132	2232 *59	16	2142	10	14800	+++	++
14779	2132	2242 *59	17	2142	10	14800	+++	++
14785	2132	2271 *59	19	2142	10	14800	+++	++
14777	2132	2245 *57	17	2142	10	14800	+++	++
14775	2132	2229 *61	16	2142	10	14800	++++	+
14781	2132	2236 *61	17	2142	10	14800	++++	+
14786	2132	2264 *61	19	2142	10	14800	++++	+
14780	2132	2243 *60	17	2142	10	14800	+++	++
14782	2132	2244 *62	17	2142	10	14800	+++	++
14787	2132	2272 *62	20	2142	10	14800	+++	++

1. *The experimental PEgRNA and ngRNA contained 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates a phosphorothioate bond. The SEQ ID NO: of the ngRNA spacer is 3269.*
2. **## = RTT encodes a PAM silencing mutation (see table 85).*
3. *+ = 0.49%-1.36%, ++ = 1.36%-15.41%, +++ = 15.41%-44.10%, ++++ = 44.10%-68.41%.*

Table 106: Prime Editing in primary human hepatocytes using a PE3b system

PEgRNA[1] Seq. #	Spacer Seq. #	RTT[2] Seq. #	RTT Len.	PBS Seq. #	PBS Len.	ngRNA[1] Seq. #	% Edit[3]	% Indel[3]
14773	2132	2235 *58	16	2142	10	14807; 3299 *58	++++	+
14778	2132	2240 *58	17	2142	10	14807; 3299 *58	++++	+
14784	2132	2269 *58	19	2142	10	14807; 3299 *58	++++	+
14790	2132	2240 *58	17	2144	12	14807; 3299 *58	++++	++
14791	2132	2240 *58	17	2146	14	14807; 3299 *58	++++	+
14769	2132	2237 *63	17	2140	8	14805; 3267 *63	+++	+
14770	2132	2205 *63	14	2142	10	14805; 3267 *63	++++	++
14772	2132	2212 *63	15	2142	10	14805; 3267 *63	+++	+
14776	2132	2233 *63	16	2142	10	14805; 3267 *63	++++	++
14783	2132	2237 *63	17	2142	10	14805; 3267 *63	++++	++
14788	2132	2205 *63	14	2144	12	14805; 3267 *63	++++	++
14789	2132	2233 *63	16	2144	12	14805; 3267 *63	++++	++
14771	2132	2218 *59	15	2142	10	14803; 3247 *59	+++	+
14774	2132	2232 *59	16	2142	10	14803; 3247 *59	+++	++

14779	2132	2242 *59	17	2142	10	14803; 3247 *59	+++	++
14785	2132	2271 *59	19	2142	10	14803; 3247 *59	+++	+
14777	2132	2245 *57	17	2142	10	14808; 3272 *57	++++	+
14775	2132	2229 *61	16	2142	10	14804; 3249 *61	++++	+
14781	2132	2236 *61	17	2142	10	14804; 3249 *61	++++	+
14786	2132	2264 *61	19	2142	10	14804; 3249 *61	+++	+
14780	2132	2243 *60	17	2142	10	14809; 3258 *60	+++	+
14782	2132	2244 *62	17	2142	10	14806; 3288 *62	+++	+
14787	2132	2272 *62	20	2142	10	14806; 3288 *62	+++	++

1. *The experimental PEgRNA and ngRNA contained 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates a phosphorothioate bond. The indicated sequence numbers for the ngRNA represents the ngRNA followed by the ngRNA spacer; *## following with ngRNA spacer sequence number indicates that the spacer is complementary to a PAM silencing mutation (see table 85).*
2. **## = RTT encodes a PAM silencing mutation (see table 85).*
3. *+ = 0.49%-1.36%, ++ = 1.36%-15.41%, +++ = 15.41%-44.10%, ++++ = 44.10%-68.41%.*

[681] EXAMPLE 8 – Phenotypic Rescue by Prime Editing

[682] Human induced pluripotent cells (hiPSC) were maintained in mTeSR Plus media on Matrigel-coated plates and differentiated them into hepatocytes using modified protocol from Wilson AA (Cell Reports, 2015). Briefly, after induction of definitive endoderm cells were replaced into new Matrigel-coated plates and differentiation was completed in IMDM/Ham's F12 media supplemented with B-27 and N2 supplements and growth factors. For editing and Phenotypic rescue experiment, 50K cells of early-stage differentiated iHeps were replated on 96-well plates on day 13 cells and were transfected using Lipofectamine Messenger Max according to manufacturer protocols with mRNA encoding a prime

editor, and synthetic PEgRNA and ngRNA. on the day 16, 19, 21 of the differentiation. Following transfection, the cells were challenged with Cu on day 27th at a conc of 250 uM. Forty-eight hrs later (day 29th), phenotypic rescue of the edited was measured by cell viability assay using cell titer glow from Promega according to the manufacture's protocol. The viability of the edited cells was normalized to the transfected cells with 0 Cu treatment and the phenotypic recue was measured relative to the untransfected cells challenged with the cu at 250 uM. Editing in these cells were measured in parallel by harvesting them in quick DNA extract for high throughput sequencing using miseq. Increased cell viability was seen with correction of the R778R mutation using a PE3 Prime Editing system (data not shown).

CLAIMS

WHAT IS CLAIMED IS:

1. A prime editing guide RNA (PEgRNA) comprising:
   a. a spacer that is complementary to a search target sequence on a first strand of an ATP7B gene, wherein the spacer comprises at its 3' end SEQ ID NO: 2128;
   b. a gRNA core capable of binding to a Cas9 protein;
   c. an extension arm comprising:
      i. an editing template that comprises a region of complementarity to an editing target sequence on a second strand of the ATP7B gene, and
      ii. a primer binding site that comprises at its 5' end a sequence that is a reverse complement of nucleotides 11-13 of SEQ ID NO: 2128;
   wherein the first strand and second strand are complementary to each other and wherein the editing target sequence on the second strand is complementary to a portion of the ATP7B gene comprising a c.2333G>T substitution.
2. A prime editing guide RNA (PEgRNA) comprising:
   a. a spacer comprising at its 3' end nucleotides SEQ ID NO: 2128;
   b. a gRNA core capable of binding to a Cas9 protein, and
   c. an extension arm comprising:
      i. an editing template comprising at its 3' end any one of SEQ ID NOs: 2152-2161, and
      ii. a primer binding site (PBS) comprising at its 5' end a sequence that is a reverse complement of nucleotides 11-13 of SEQ ID NO: 2128.
3. The PEgRNA of claim 1 or 2, wherein the spacer of the PEgRNA is from 16 to 22 nucleotides in length.
4. The PEgRNA of any one of claims 1-3, wherein the spacer of the PEgRNA comprises at its 3' end any one of SEQ ID NOs: 2129-2134.
5. The PEgRNA of any one of claims 1-4, wherein the spacer of the PEgRNA comprises at its 3' end SEQ ID NO: 2132.
6. The PEgRNA of any one of claims 1-5, wherein the spacer of the PEgRNA is 20 nucleotides in length.
7. The PEgRNA of any one of claims 1-6, comprising from 5' to 3', the spacer, the gRNA core, the RTT, and the PBS.
8. The PEgRNA of claim 7, wherein the spacer, the gRNA core, the RTT, and the PBS form a contiguous sequence in a single molecule.

9. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2152 at its 3' end and encodes a CGG-to-CTG PAM silencing edit.
10. The PEgRNA of claim 9, wherein the editing template comprises at its 3' end SEQ ID NO: 2168, 2176, 2190, 2200, 2221, 2225, 2244, 2255, 2262, 2272, 2292, 2305, 2309, 2321, or 2340.
11. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2153 at its 3' end and encodes a CGG-to-CTC PAM silencing edit.
12. The PEgRNA of claim 11, wherein the editing template comprises at its 3' end SEQ ID NO: 2173, 2179, 2198, 2202, 2222, 2229, 2236, 2259, 2264, 2276, 2284, 2306, 2316, 2322, or 2339.
13. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2154 at its 3' end and encodes a CGG-to-CGT PAM silencing edit.
14. The PEgRNA of claim 13, wherein the editing template comprises at its 3' end SEQ ID NO: 2166, 2177, 2189, 2204, 2218, 2232, 2242, 2250, 2271, 2280, 2288, 2303, 2311, 2325, or 2336.
15. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2155 at its 3' end and encodes a CGG-to-CGA PAM silencing edit.
16. The PEgRNA of claim 15, wherein the editing template comprises at its 3' end SEQ ID NO: 2167, 2182, 2195, 2211, 2216, 2227, 2245, 2254, 2260, 2282, 2290, 2298, 2319, 2330, or 2337.
17. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2156 at its 3' end and encodes a CCGG-to-TCTA PAM silencing edit.
18. The PEgRNA of claim 17, wherein the editing template comprises at its 3' end SEQ ID NO: 2164, 2187, 2193, 2210, 2217, 2228, 2241, 2251, 2266, 2283, 2287, 2296, 2308, 2327, or 2342.
19. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2157 at its 3' end and encodes a CGG-to-CTT PAM silencing edit.
20. The PEgRNA of claim 19, wherein the editing template comprises at its 3' end SEQ ID NO: 2174, 2185, 2188, 2205, 2212, 2233, 2237, 2258, 2265, 2274, 2291, 2300, 2310, 2331, or 2332.
21. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2158 at its 3' end and encodes a CCGG-to-TCTG PAM silencing edit.
22. The PEgRNA of claim 21, wherein the editing template comprises at its 3' end SEQ ID NO: 2170, 2178, 2199, 2207, 2219, 2230, 2239, 2248, 2261, 2275, 2294, 2301, 2312, 2323, or 2334.
23. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2159 at its 3' end and encodes a CGG-to-CGC PAM silencing edit.
24. The PEgRNA of claim 23, wherein the editing template comprises at its 3' end SEQ ID NO: 2165, 2183, 2194, 2201, 2215, 2235, 2240, 2249, 2269, 2277, 2285, 2302, 2318, 2326, or 2333.
25. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2160 at its 3' end and encodes a CGG-to-CTA PAM silencing edit.
26. The PEgRNA of claim 25, wherein the editing template comprises at its 3' end SEQ ID NO: 2171, 2186, 2196, 2206, 2214, 2224, 2243, 2252, 2268, 2281, 2293, 2299, 2314, 2329, or 2335.

27. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2161 at its 3' end and encodes a CCGG-to-TCTC PAM silencing edit.

28. The PEgRNA of claim 27, wherein the editing template comprises at its 3' end SEQ ID NO: 2172, 2181, 2197, 2203, 2213, 2231, 2246, 2253, 2267, 2273, 2289, 2304, 2317, 2328, or 2341.

29. The PEgRNA of any one of claims 1-8, wherein the editing template comprises SEQ ID NO: 2162 at its 3' end.

30. The PEgRNA of claim 29, wherein the editing template comprises at its 3' end SEQ ID NO: 2175, 2180, 2191, 2209, 2223, 2226, 2238, 2256, 2263, 2279, 2295, 2307, 2313, 2324, or 2338.

31. The PEgRNA of any one of claims 1-30, wherein the editing template has a length of 25 nucleotides or less.

32. The PEgRNA of any one of claims 1-31, wherein the PBS comprises at its 5' end a sequence that is a reverse complement of nucleotides 10-13, 9-13, 8-13, 7-13, 6-13, 5-13, 4-13, 3-13, 2-13, or 1-13 of SEQ ID NO: 2128.

33. The PEgRNA of any one of claims 1-32, wherein the PBS comprises at its 5' end a sequence corresponding to GCTGGAAC, where "T" is a "U".

34. The PEgRNA of any one of claims 1-33, wherein the PBS comprises at its 5' end SEQ ID NO: 2142.

35. The PEgRNA of any one of claims 1-34, wherein the 3' end of the editing template is adjacent to the 5' end of the PBS.

36. The PEgRNA of any one of claims 1-35, comprising a pegRNA sequence selected from any one of SEQ ID NOs: 14769, 14770, 14771, 14772, 14773, 14774, 14775, 14776, 14777, 14778, 14779, 14780, 14781, 14782, 14783, 14784, 14785, 14786, 14787, 14788, 14789, 14790, 14791, 14792, 14793, 14794, 14795, 14796, 14797, 14798, or 14799.

37. The PEgRNA of any one of claims 1-36, further comprising 3' mN*mN*mN*N and 5'mN*mN*mN* modifications, where m indicates that the nucleotide contains a 2'-O-Me modification and a * indicates the presence of a phosphorothioate bond.

38. A prime editing system comprising:

a. the prime editing guide RNA (PEgRNA) of any one of claims 1-37, or a nucleic acid encoding the PEgRNA; and

b. a nick guide RNA (ngRNA) comprising at its 3' end nucleotides 5-20 of any one of SEQ ID NOs: 63, 88, 1994, 2000, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3245, 3246, 3247, 3248, 3249, 3250, 3251, 3252, 3253, 3254, 3255, 3256, 3257, 3258, 3259, 3260, 3261, 3262, 3263, 3264, 3265, 3266, 3267, 3268, 3269, 3270, 3271, 3272, 3273, 3274, 3275, 3276, 3277, 3278, 3279, 3280, 3281, 3282, 3283, 3284, 3285, 3286, 3287, 3288, 3289, 3290, 3291, 3292, 3293, 3294, 3295, 3296, 3297, 3298, or 3299, and a gRNA core capable of binding to a Cas9 protein, or a nucleic acid encoding the ngRNA.

39. The prime editing system of claim 38, wherein the spacer of the ngRNA is from 15 to 22 nucleotides in length.

40. The prime editing system of claim 38 or 39, wherein the spacer of the ngRNA comprises at its 3' end nucleotides 4-20, 3-20, 2-20, or 1-20 of SEQ ID NO: 63, 88, 1994, 2000, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3245, 3246, 3247, 3248, 3249, 3250, 3251, 3252, 3253, 3254, 3255, 3256, 3257, 3258, 3259, 3260, 3261, 3262, 3263, 3264, 3265, 3266, 3267, 3268, 3269, 3270, 3271, 3272, 3273, 3274, 3275, 3276, 3277, 3278, 3279, 3280, 3281, 3282, 3283, 3284, 3285, 3286, 3287, 3288, 3289, 3290, 3291, 3292, 3293, 3294, 3295, 3296, 3297, 3298, or 3299.

41. The prime editing system of any one of claims 38-40, wherein the spacer of the ngRNA comprises at its 3' end SEQ ID NO: 63, 88, 1994, 2000, 2004, 2005, 2006, 2056, 2057, 2058, 2059, 2125, 2126, 2127, 3244, 3245, 3246, 3247, 3248, 3249, 3250, 3251, 3252, 3253, 3254, 3255, 3256, 3257, 3258, 3259, 3260, 3261, 3262, 3263, 3264, 3265, 3266, 3267, 3268, 3269, 3270, 3271, 3272, 3273, 3274, 3275, 3276, 3277, 3278, 3279, 3280, 3281, 3282, 3283, 3284, 3285, 3286, 3287, 3288, 3289, 3290, 3291, 3292, 3293, 3294, 3295, 3296, 3297, 3298, or 3299.

42. The prime editing system of any one of claims 38-41, wherein the spacer of the ngRNA is 20 nucleotides in length.

43. The prime editing system of any one of claims 38-42, wherein the spacer of the ngRNA is SEQ ID NO: 3269, 3279, 1994, 3247, 3249, 3267, 3288, 3299, 3272, or 3258.

44. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 3269 or 3279 and the editing template of the PEgRNA comprises SEQ ID NO: 2162 at its 3' end.

45. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 1994 and the editing template of the PEgRNA comprises SEQ ID NO: 2162 at its 3' end.

46. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 3247 and the editing template of the PEgRNA comprises SEQ ID NO: 2154 at its 3' end.

47. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 3249 and the editing template of the PEgRNA comprises SEQ ID NO: 2153 at its 3' end.

48. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 3267 and the editing template of the PEgRNA comprises SEQ ID NO: 2157 at its 3' end.

49. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 3288 and the editing template of the PEgRNA comprises SEQ ID NO: 2152 at its 3' end.

50. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 3299 and the editing template of the PEgRNA comprises SEQ ID NO: 2159 at its 3' end.

51. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 3272 and the editing template of the PEgRNA comprises SEQ ID NO: 2155 at its 3' end.

52. The prime editing system of claim 43, wherein the spacer of the ngRNA is SEQ ID NO: 3258 and the editing template of the PEgRNA comprises SEQ ID NO: 2160 at its 3' end.

53. The prime editing system of any one of claims 38-51, further comprising: (c) a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain, or a nucleic acid encoding the Cas9 nickase, and a reverse transcriptase, or a nucleic acid encoding the reverse transcriptase.

54. The prime editing system of claim 53, wherein the Cas9 nickase comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 14831.

55. The prime editing system of claim 53 or 54, wherein the reverse transcriptase comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 14828.

56. The prime editing system of claim 54 or 55, wherein the sequence identities are determined by Needleman-Wunsch alignment of two protein sequences with Gap Costs set to Existence: 11 Extension: 1 where percent identity is calculated by dividing the number of identities by the length of the alignment.

57. The prime editing system of any one of claims 53-56, wherein the prime editor is a fusion protein.

58. An LNP comprising the prime editing system of any one of claims 38-57.

59. The LNP of claim 58, comprising the PEgRNA, the nucleic acid encoding the Cas9 nickase, and the nucleic acid encoding the reverse transcriptase.

60. The LNP of claim 58, wherein the nucleic acid encoding the Cas9 nickase and the nucleic acid encoding the reverse transcriptase are mRNA.

61. The LNP of claim 59 or 60, wherein the nucleic acid encoding the Cas9 nickase and the nucleic acid encoding the reverse transcriptase are the same molecule.

62. The LNP of any one of claim 58-61, further comprising the ngRNA.

63. A method of correcting for editing an ATP7B gene, the method comprising contacting the ATP7B gene with: (A) the PEgRNA of any one of claims 1-37 and a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain and a reverse transcriptase, (B) the prime editing system of any one of claims 38-57, or (C) the LNP of any one of claims 58-62.

64. The method of claim 63, wherein the ATP7B gene is in a cell.

65. The method of claim 64, wherein the cell is a mammalian cell.

66. The method of claim 65, wherein the cell is a human cell.

67. The method of any one of claims 64-66, wherein the cell is a primary cell.

68. The method of any one of claims 64-67, wherein the cell is a hepatocyte.

69. The method of any one of claims 64-68, wherein the cell is in a subject.

70. The method of claim 69, wherein the subject is a human.

71. The method of any one of claims 64-68, wherein the cell is from a subject having Wilson's disease.

72. The method of any one of claims 64-68 and 71, further comprising administering the cell to the subject after incorporation of the intended nucleotide edit.

73. A cell generated by the method of any one of claims 64-68 and 71.

74. A population of cells generated by the method of any one of claims 64-68 and 71.

75. A method for treating Wilson's disease in a subject in need thereof, the method comprising administering to the subject: (a) the PEgRNA of any one of claims 1-37, (B) the prime editing system of any one of claims 38-57, or (C) the LNP of any one of claims 58-62.

76. The method of claim 75, comprising administering to the subject the PEgRNA of any one of claims 1-37 and a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain and a reverse transcriptase or one or more nucleic acids encoding the prime editor or its components.

77. The method of claim 76, wherein the prime editor is a fusion protein.

78. A prime editing guide RNA (PEgRNA) comprising:

a. a spacer comprising at its 3' end nucleotides 5-20 of a PEgRNA Spacer sequence selected from any one of Tables 1-84;

b. a gRNA core capable of binding to a Cas9 protein, and

c. an extension arm comprising:

i. an editing template comprising at its 3' end an RTT sequence selected from the same Table as the PEgRNA Spacer sequence, and

ii. a primer binding site (PBS) comprising at its 5' end a PBS sequence selected from the same Table as the PEgRNA Spacer sequence.

79. The PEgRNA of claim 78, wherein the spacer of the PEgRNA is from 16 to 22 nucleotides in length.

80. The PEgRNA of claim 79, wherein the spacer of the PEgRNA is 20 nucleotides in length.

81. The PEgRNA of any one of claims 78-80, comprising from 5' to 3', the spacer, the gRNA core, the editing template, and the PBS.

82. The PEgRNA of claim 81, wherein the spacer, the gRNA core, the editing template, and the PBS form a contiguous sequence in a single molecule.

83. The PEgRNA of any one of claims 78-82, comprising a pegRNA sequence selected from the same Table as the PEgRNA Spacer sequence.

84. A prime editing system comprising:

a. the prime editing guide RNA (PEgRNA) of any one of claims 78-83, or a nucleic acid encoding the PEgRNA; and

b. a nick guide RNA (ngRNA) comprising a spacer comprising at its 3' end nucleotides 5-20 of any ngRNA Spacer sequence selected from the same Table as the PEgRNA Spacer

sequence and a gRNA core capable of binding to a Cas9 protein, or a nucleic acid encoding the ngRNA.

85. The prime editing system of claim 84, wherein the spacer of the ngRNA is from 16 to 22 nucleotides in length.

86. The prime editing system of claim 84 or 85, wherein the spacer of the ngRNA comprises at its 3' end nucleotides 4-20, 3-20, 2-20, or 1-20 of the ngRNA Spacer sequence selected from the same Table as the PEgRNA Spacer sequence.

87. The prime editing system of any one of claims 84-86, wherein the spacer of the ngRNA comprises at its 3' end the ngRNA Spacer sequence selected from the same Table as the PEgRNA Spacer sequence.

88. The prime editing system of any one of claims 84-87, wherein the spacer of the ngRNA is 20 nucleotides in length.

89. The prime editing system of any one of claims 84-88, wherein the ngRNA comprises a ngRNA sequence selected from the same Table as the PEgRNA Spacer sequence.

90. The prime editing system of any one of claims 84-89, further comprising: (c) a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain, or a nucleic acid encoding the Cas9 nickase, and a reverse transcriptase, or a nucleic acid encoding the reverse transcriptase.

91. The prime editing system of claim 90, wherein the Cas9 nickase comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 14831.

92. The prime editing system of claim 90 or 91, wherein the reverse transcriptase comprises an amino acid sequence having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 14828.

93. The prime editing system of claim 91 or 92, wherein the sequence identities are determined by Needleman-Wunsch alignment of two protein sequences with Gap Costs set to Existence: 11 Extension: 1 where percent identity is calculated by dividing the number of identities by the length of the alignment.

94. The prime editing system of any one of claims 84-93, wherein the prime editor is a fusion protein.

95. An LNP comprising the prime editing system of any one of claims 84-93.

96. The LNP of claim 95, comprising the PEgRNA, the nucleic acid encoding the Cas9 nickase, and the nucleic acid encoding the reverse transcriptase.

97. The LNP of claim 96, wherein the nucleic acid encoding the Cas9 nickase and the nucleic acid encoding the reverse transcriptase are mRNA.

98. The LNP of claim 96 or 97, wherein the nucleic acid encoding the Cas9 nickase and the nucleic acid encoding the reverse transcriptase are the same molecule.

99. The LNP of any one of claim 95-98, further comprising the ngRNA.

100. A method of correcting for editing an ATP7B gene, the method comprising contacting the ATP7B gene with: (A) the PEgRNA of any one of claims 78-83 and a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain and a reverse transcriptase, (B) the prime editing system of any one of claims 84-94, or (C) the LNP of any one of claims 95-99.

101. The method of claim 100, wherein the ATP7B gene is in a cell.

102. The method of claim 101, wherein the cell is a mammalian cell.

103. The method of claim 101, wherein the cell is a human cell.

104. The method of any one of claims 101-103, wherein the cell is a primary cell.

105. The method of any one of claims 101-104, wherein the cell is a hepatocyte.

106. The method of any one of claims 101-105, wherein the cell is in a subject.

107. The method of claim 106, wherein the subject is a human.

108. The method of any one of claims 101-105, wherein the cell is from a subject having Wilson's disease.

109. The method of any one of claims 101-105 or claim 108, further comprising administering the cell to the subject after incorporation of the intended nucleotide edit.

110. A cell generated by the method of any one of claims 101-105.

111. A population of cells generated by the method of any one of claims 101-105.

112. A method for treating Wilson's disease in a subject in need thereof, the method comprising administering to the subject: (a) the PEgRNA of any one of claims 78-83, (B) the prime editing system of any one of claims 84-94, or (C) the LNP of any one of claims 95-99.

113. The method of claim 112, comprising administering to the subject the PEgRNA of any one of claims 78-83 and a prime editor comprising a Cas9 nickase having a nuclease inactivating mutation in the HNH domain and a reverse transcriptase or one or more nucleic acids encoding the prime editor or its components.

114. The method of claim 113, wherein the prime editor is a fusion protein.

115. The PEgRNA of any one of claims 78-83, (B) the prime editing system of any one of claims 84-94, or (C) the LNP of any one of claims 95-99, wherein the PEgRNA Spacer sequence is selected from Table 9, Table 8, or Table 11.

116. The PEgRNA, prime editing system, or LNP of claim 115, wherein the PEgRNA Spacer sequence is selected from Table 9.

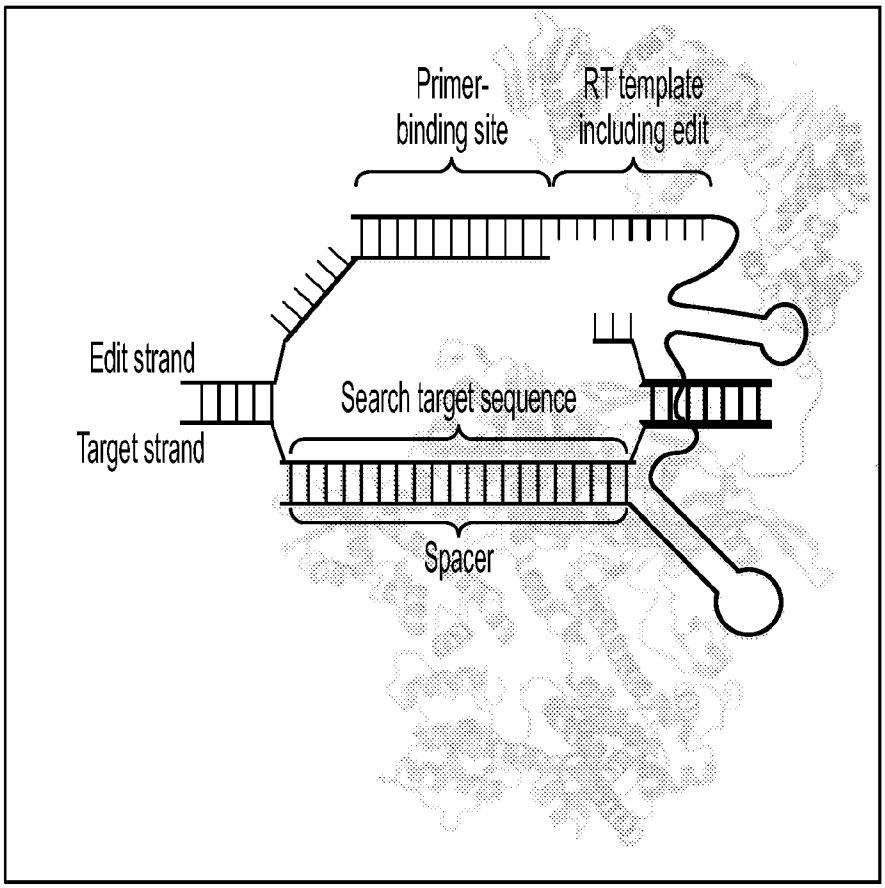

Primer-
binding site
RT template
including edit
Edit strand
Search target sequence
Target strand
Spacer

FIG. 1

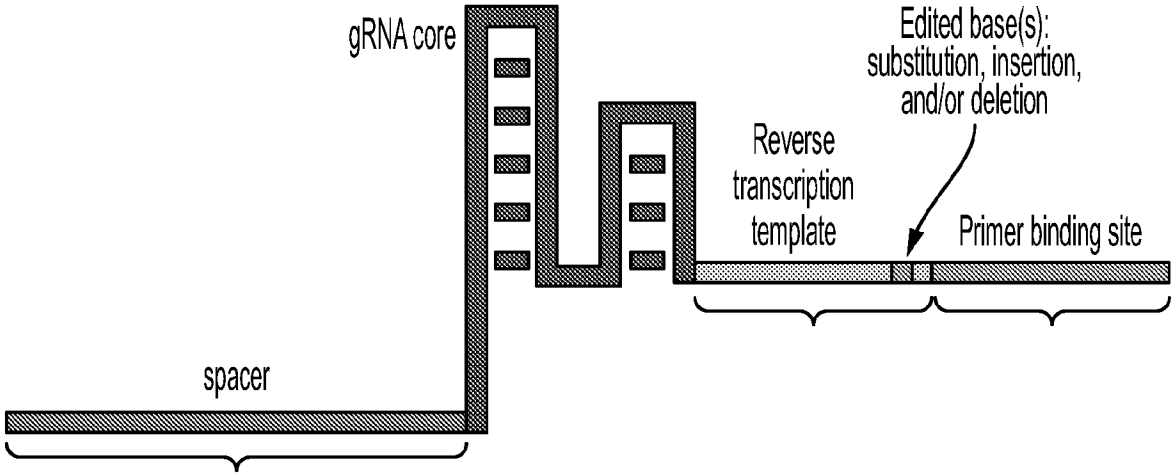

gRNA core
Edited base(s):
substitution, insertion,
and/or deletion
Reverse
transcription
template
Primer binding site
spacer

FIG. 2

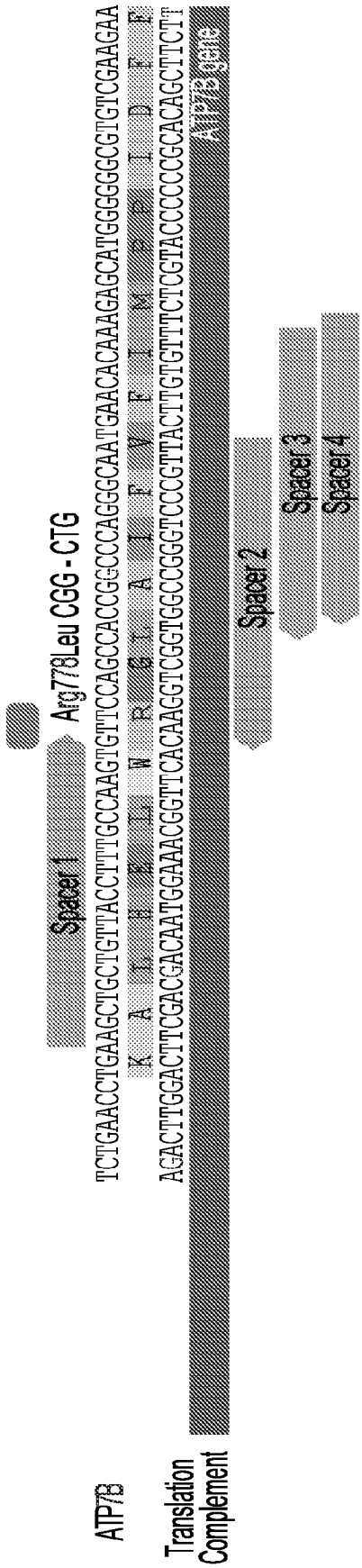

ATP7B
Translation
Complement
Spacer 1
Arg778Leu CGG - CTG
TCTGAACCTGAAGCTGCTGTTACCTTTGCCAAGTGTTCCAGCCACCGGCCCAGGGCAATGAACACAAAGAGCATGGGGGGCGTGTCGAAGAA
K A L E L W R G L A L F V F I M R E I D F F
AGACTTGGACTTCGACGACAATGGAAACGGTTCACAAGGTCGGTGGCCGGGTCCCGTTACTTGTGTTTCTCGTACCCCCCGCACAGCTTCTT
ATP7B gene
Spacer 2
Spacer 3
Spacer 4

FIG. 3A

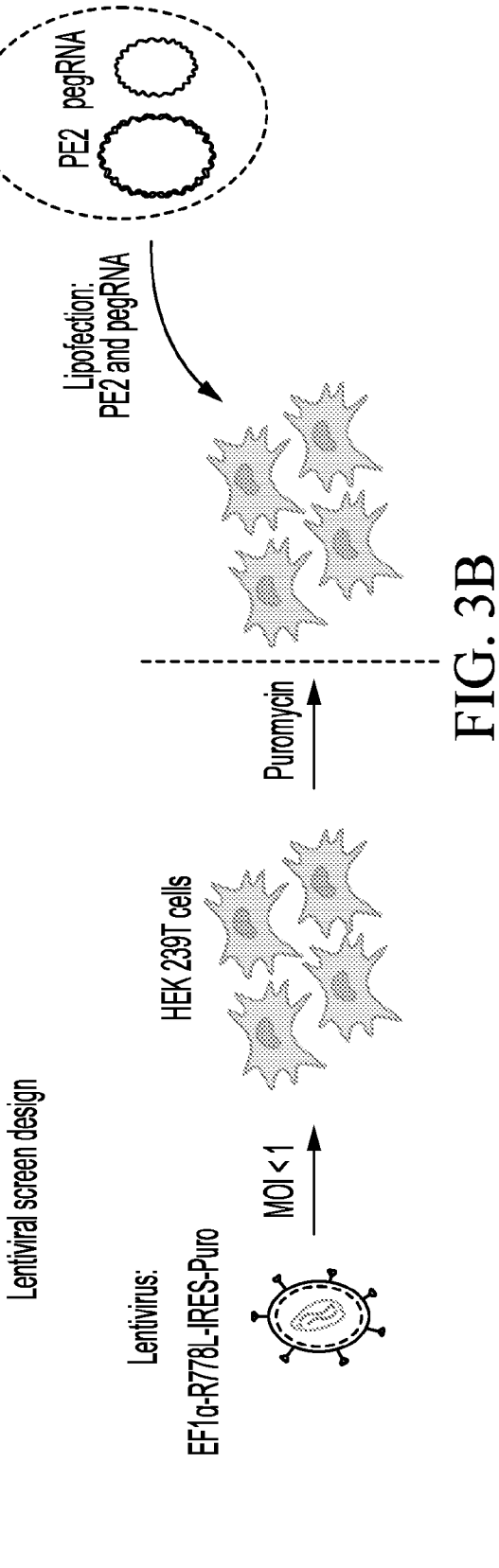

Lentiviral screen design
Lentivirus:
EF1α-R778L-IRES-Puro
MOI < 1
HEK 239T cells
Puromycin
Lipofection:
PE2 and pegRNA
PE2 pegRNA

FIG. 3B

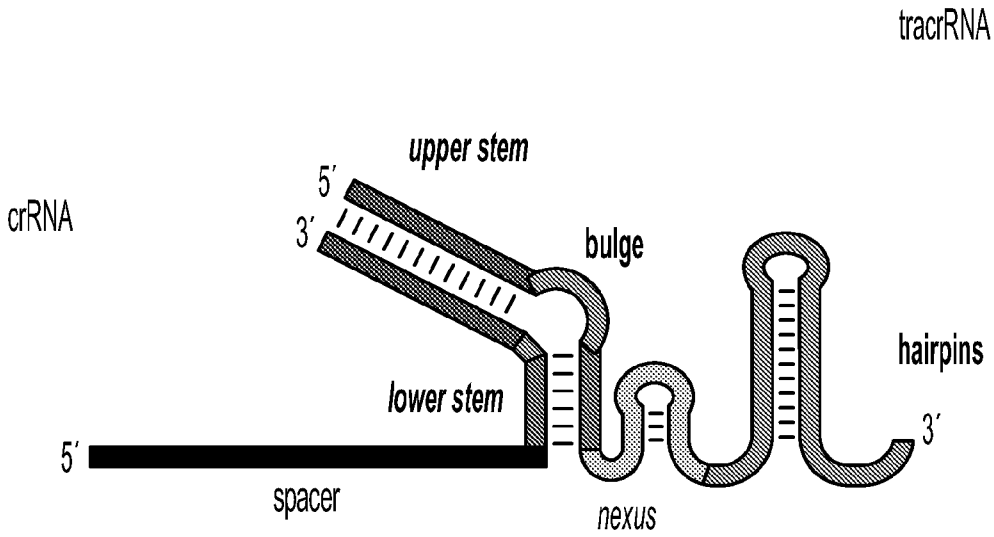

tracrRNA
upper stem
5′
crRNA
3′
bulge
hairpins
lower stem
5′
3′
spacer
nexus

FIG. 4