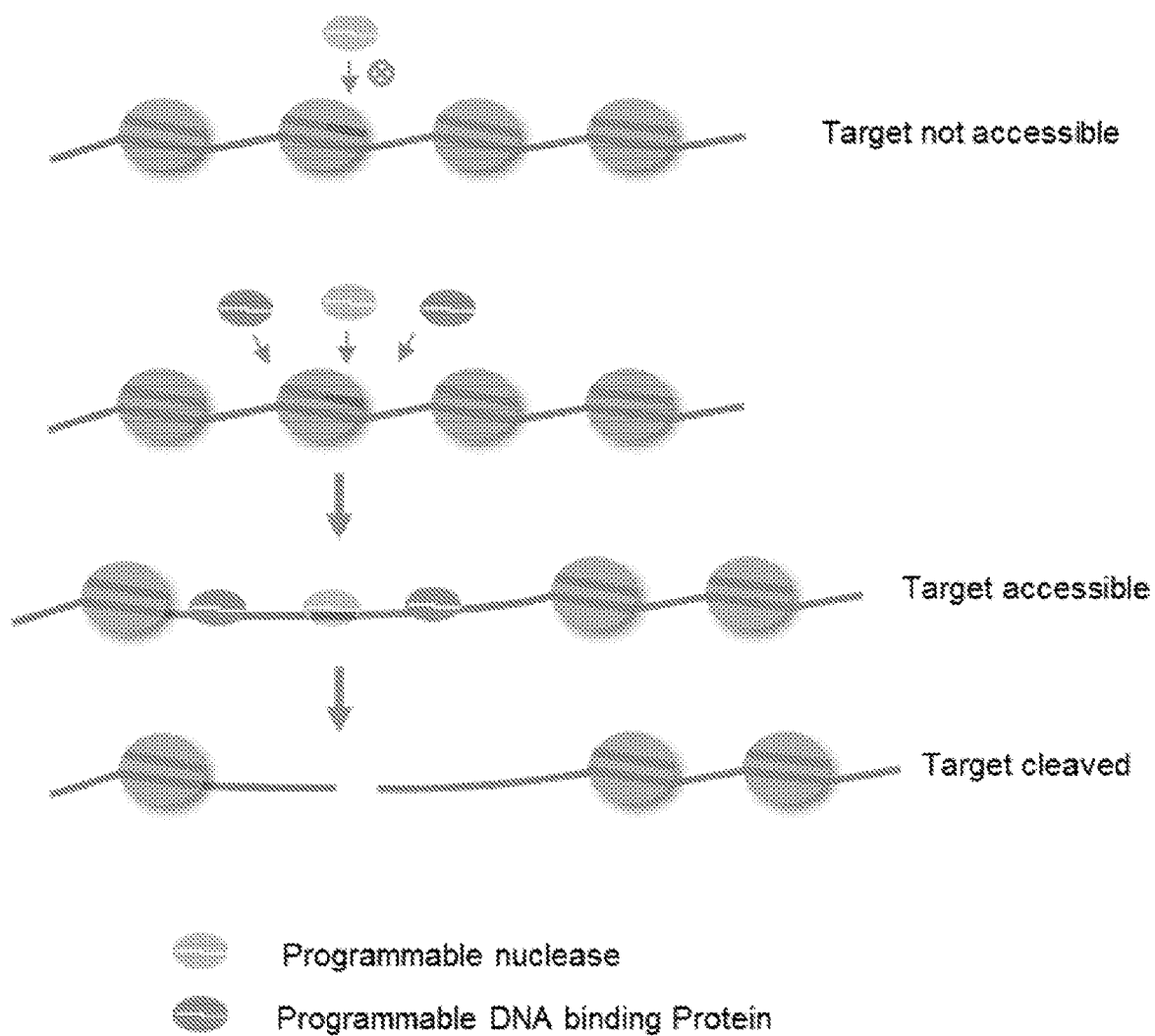


1/10

**FIG. 1**

POR locus

FnCas9 target 1

5' - CCTTCCAGCATTCGCCAGTACGAGCTTGTGGTCCACACCGACATAGATGCGGCCAAGGTGTACATGGGGGAGATGGGCCGGCTGAAGAGCTACGAGAACCC-3'

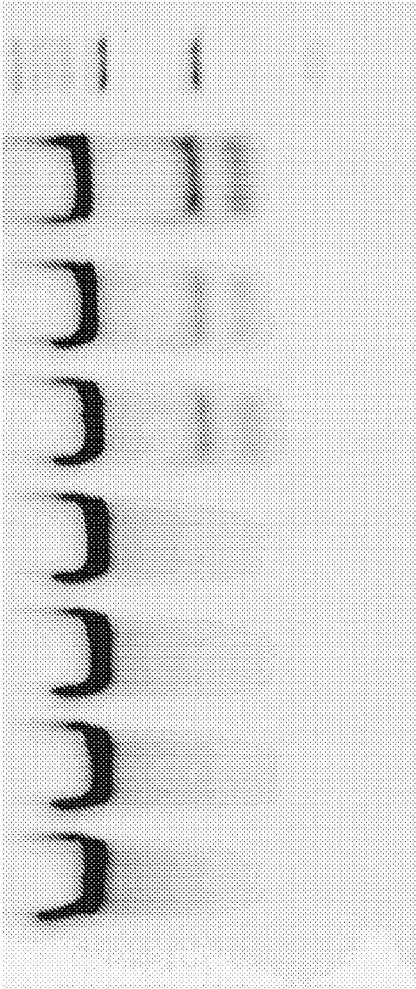
3' - GGAAGGTCGTAAACGGTCATGCTCGAACACACGAGGTGTGGCTGTATCTACGCCGGTCCACATGTACCCCTCTACCCGCGGACTTCTCGATGCTCTTGG-5'

SEQ. ID NO. 15

SpdCas9 binding site 1

SpdCas9 binding site 2

FnCas9/Fn sgRNA1	-	+	-	-	+	+	+
SpdCas9/Sp sgRNA1	-	-	+	-	+	-	+
SpdCas9/Sp sgRNA2	-	-	-	+	-	+	+
							M



Indel (%)	ND	ND	ND	ND	11.5	10.0	28.0
-----------	----	----	----	----	------	------	------

FIG. 2

POR locus	SEQ. ID NO. 17	CjdCas9 target 1	SpdCas9 binding site 2
5' - CCGCTTCCCGGCTCACCCCTTGGTCTCCCTTTCCAGCATTCGCCAGTACGAGCTTGTGGTCCACCGACATAGATGCGGCCAAGGTGTACATGGGGGAGATGG-3'			
3' - GCGAAGGCGCGGAGTGGGAACCGAGAGGGGAAAGGTCTGTAAGGGTCAATGCTCGAACACCAAGGTGTGGCTGTATCTACGCGGTTCCACATGTACCCCTCTACC-5'			

SEQ. ID NO. 18

SpdCas9 binding site 1

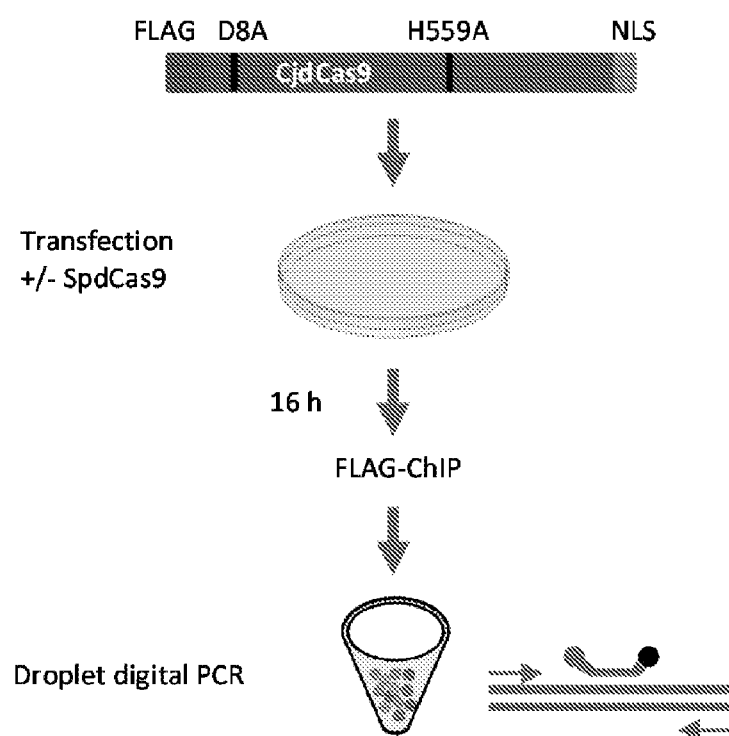
AAVS1 locus

SEQ. ID NO. 25	5' - CAGGGATCCTGTGTCCCCGAGCTGGGACCACCTTATATCCAGGGC-3'
SEQ. ID NO. 26	3' - GTCCCTAGGACACAGGGGCTCGACCCCTGGTGAATATAAGGGTCCCG-5'

CjdCas9 target 2

FIG. 3A

4/10

**FIG. 3B**

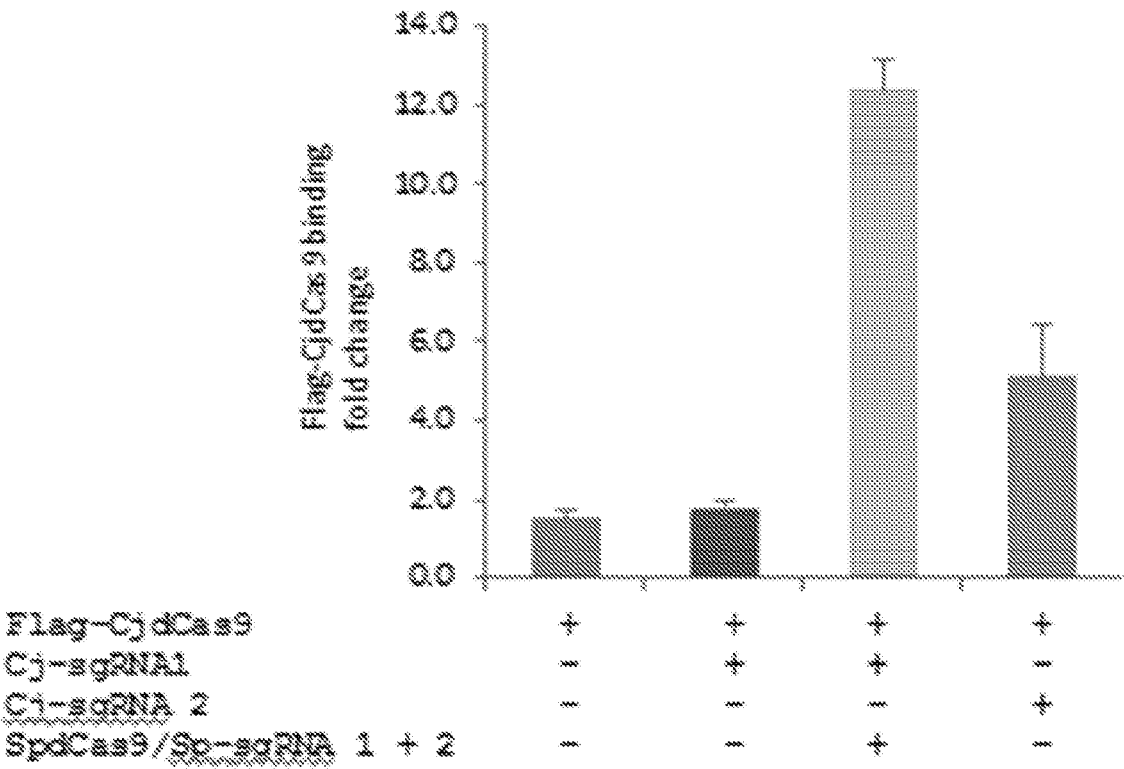


FIG. 3C

[illegible]

CjCas9	-	+	+	+	+
Cj-sgRNA	-	1	1	1	1
SpdCas9	-	-	+	+	+
Sp-sgRNA pair	-	-	1/2	1/3	1/4

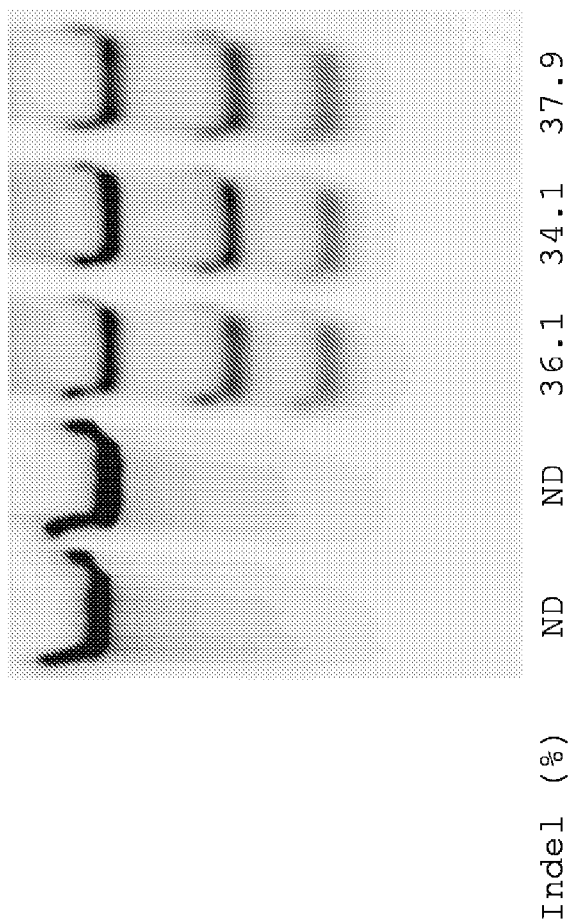


FIG. 4

POR locus
SEQ. ID NO. 19

5'-CCGCTCCCGGCTCACCCTTGGTCTCCCTTTCCAGCAATTCGCCAGTACGAGCCTTGGTGGTCCACACCGACATAGATCGGGCCAAAGGTGTACATGGGGGAGATCGGCCG-3'
|||||
3'-GGCGAAGGGCCCGAGTGGGAACCCAGAGCGGAAAGGTCGTAAAGGGTCATGCTCGAACACCAAGGTGTGGGTGTATCTACGCCCGTTCCACATGTACCCCTCTACCCCGCCG-5'

SpdCas9 binding site 1

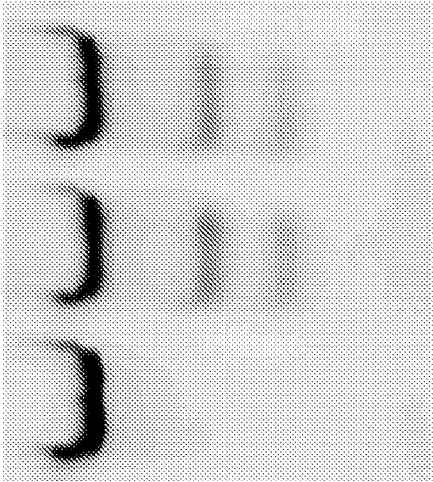
FnCpf1 target 1

SpdCas9 binding site 2

SpdCas9 binding site 3

SEQ. ID NO. 20

FnCpf1	+	+	+
Fn-sgRNA	1	1	1
SpdCas9	-	+	+
Sp-sgRNA pair	-	1/2	1/3



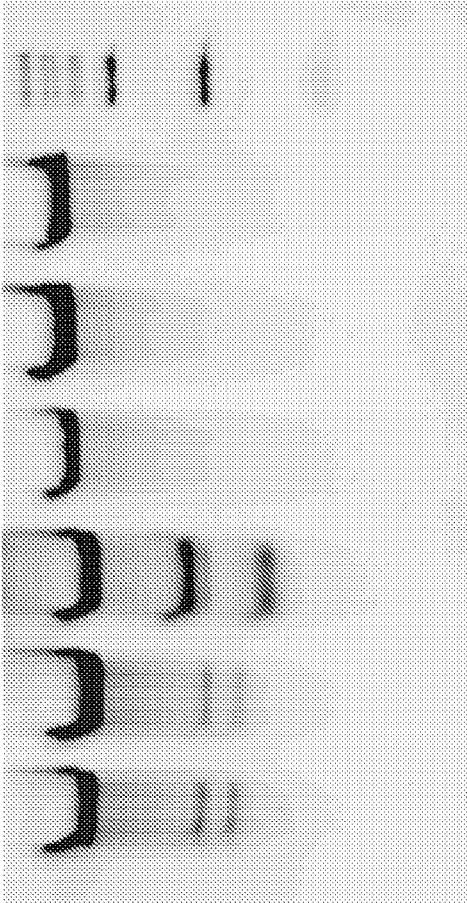
Indel (%) ND 18.7 12.6

FIG. 5

SEQ. ID NO. 21
HBD: 5'-TCGACTGTTGCTTACACTTTCTTCTGACATAACAGTGTTCACCTAGCAACCTCAACACACACATGGTGCATCTGACTCCTGAGGAGAACTGCTGCAATGCCCTGTGGGCAAA-3'
|||||
HBB: 5'-CCATCTATTGCTTACATTGCTTCTGACACAACCTGCTTCTGACACAACCTCAACACAGGATGATGGTGCATCTGACTCCTGAGGAGAACTGCTGCAATGCCCTGTGGGCAAG-3'
|||||
SpdCas9 binding site 1
CjCas9 target 1
SpdCas9 binding site 2
SEQ. ID NO. 22

Identical targets in HBD and HBB

		HBB		HBD	
CjCas9/Cj-sgRNA 1	-	+	+	-	+
SpdCas9/Sp-sgRNA 1 + 2	-	-	+	-	+
					M



Indel (%) ND ND 32 ND ND ND

FIG. 6

POR locus

FndCas9 binding site 1

SEQ. ID NO. 23

5'-TGTAATGGGGAGATGGCCGGCTGAACAGCTACGAGAACCAAGACCGTGAGTGGAGGGAGCGTGGCTGG---(40 bp)---TCTGCCGTGTATCCCCATATCCCCACAGG-3'

|||||

3'-ACATGTACCCCTCTACCCGGCGACTTCTCGATGCTCTTGGTCTTGGCACTCACCTCCCTGCGACCGAACC---(40 bp)---AGACGACACATAGGGGTATAGGGGTGTC-5'

FndCas9 binding site 2

SEQ. ID NO. 24

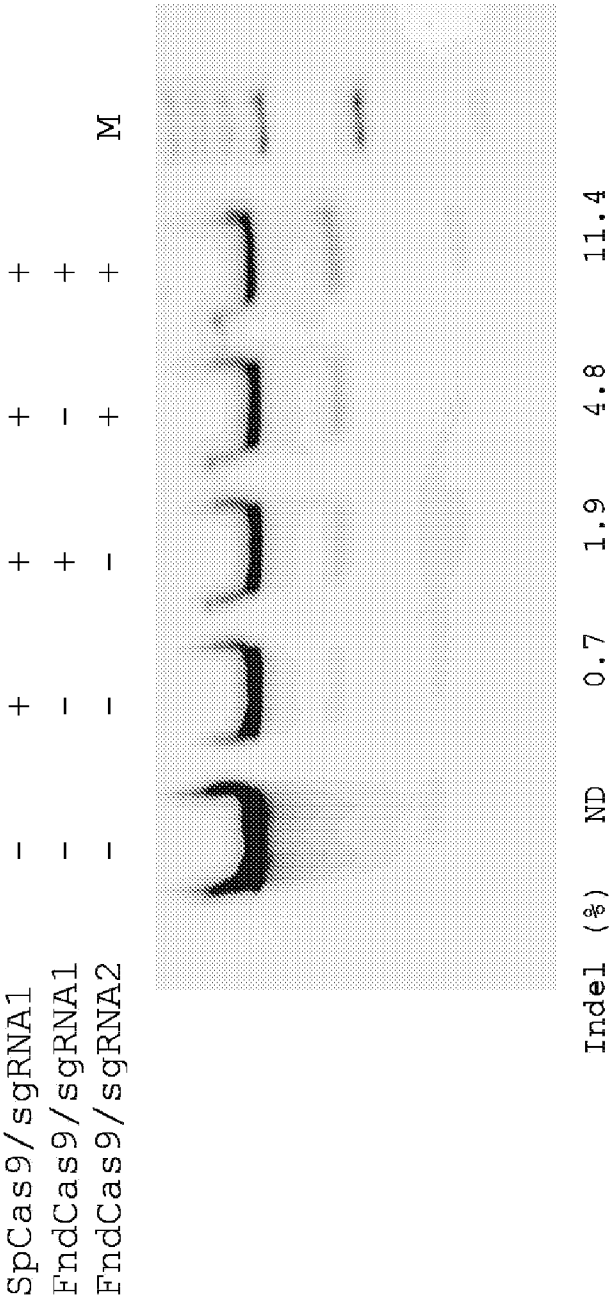


FIG. 7

POR locus

SEQ. ID NO. 17

5' -CCGCTTCCGGCCTCAGCCCTTGGTCTCCCTTCCAGATTGCCAGTACGAGCTTGTGGTCCACACCGACATAGATGCGGCCAAAGGTGTACATGGGGAGATGG-3'

|||||

3' -GCGAAGGCCCGGAGTGGGAACCGAGGGGAAGGTCGTAACGGTCATGCTCCACACCAAGTGTGGTGTATCTACGCCGGTCCACATGTACCCCTCTACC-5'

|||||

SpdCas9 target 1

SEQ. ID NO. 18

CjCas9 target 1

5' -CACCTTGGTCTCCCTTCCAGATTGCCAGTACGAGCAATTCTTGTGGTCCACACCGACATAGATGGGCCAAAGGTGTACATGG-3'

|||||

SpdCas9 target 2

SEQ. ID NO. 27

ssDNA oligo donor

EcoRI site

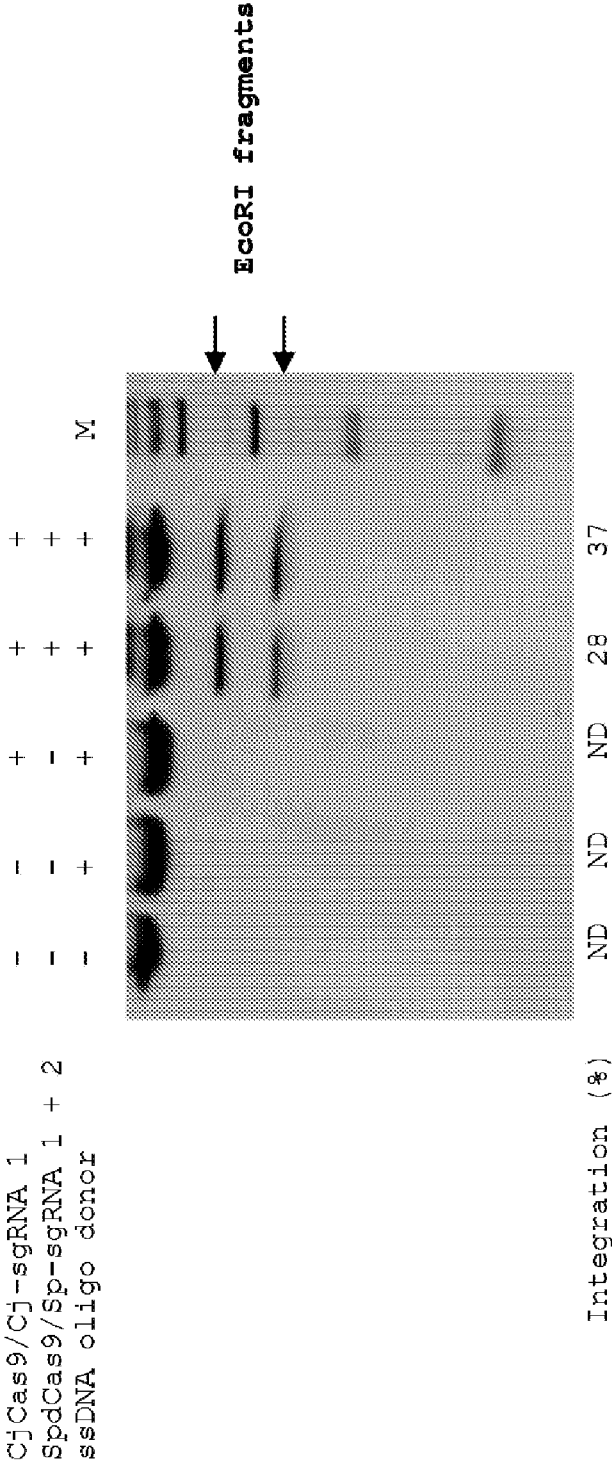


FIG. 8