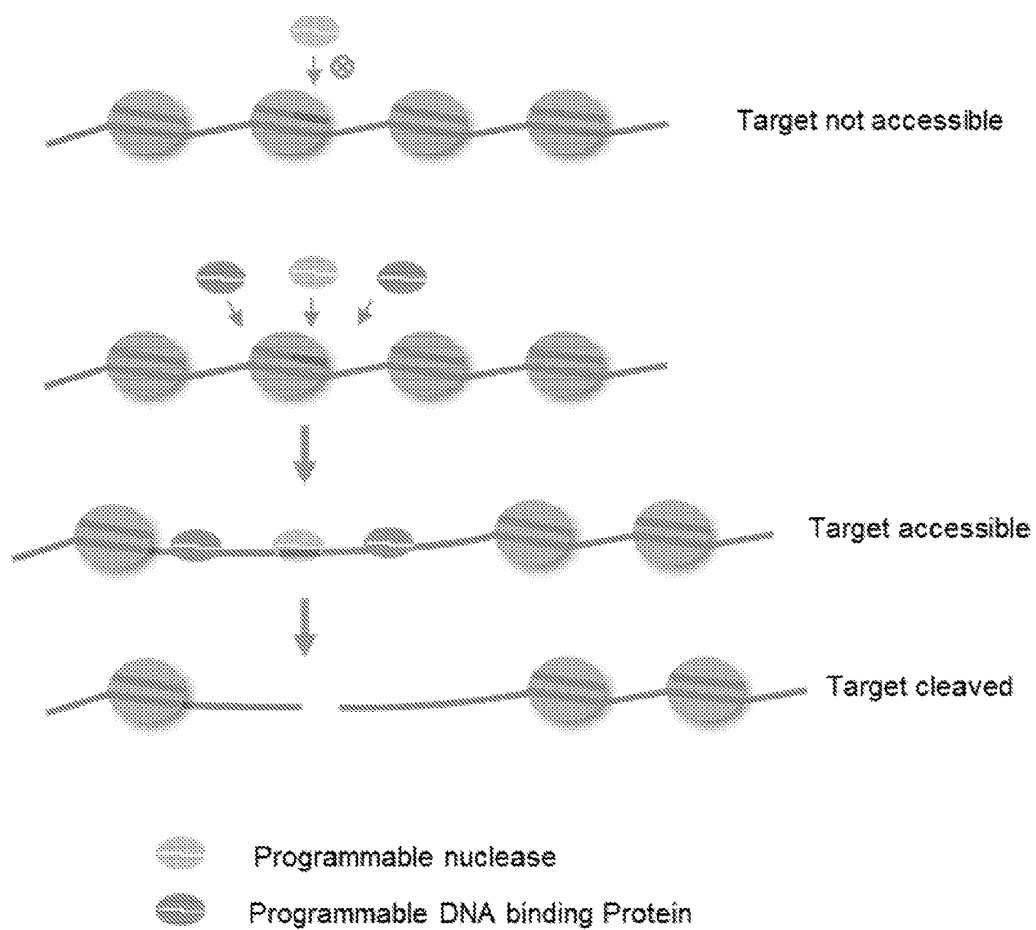


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**FIG. 1**

POR locus

FnCas9 target 1

5'-CCTTCCAGCATTCGCCAGTACGAGCTTGTGGTCCACACCGACATAGATCGG#CCCAAGGTGTACATGGGGGAGATGGCCCGCTGAAGAGCTACGAGAACCC-3'

3'-GGAAGGTGCTAAGCGGTGCTGCTCGAACAACAGGTGTGGCTGTATCTACGCCGGTCCACATGTACCCCTCTACCCGCGACCTTCTCGATGCTCTTGG-5'

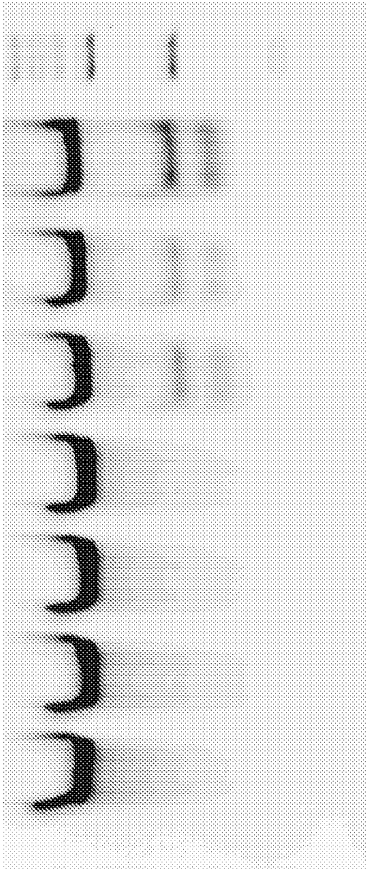
SEQ. ID NO. 15

SEQ. ID NO. 16

SpdCas9 binding site 1

SpdCas9 binding site 2

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



Indel (%) ND ND ND 11.5 10.0 28.0

FIG. 2

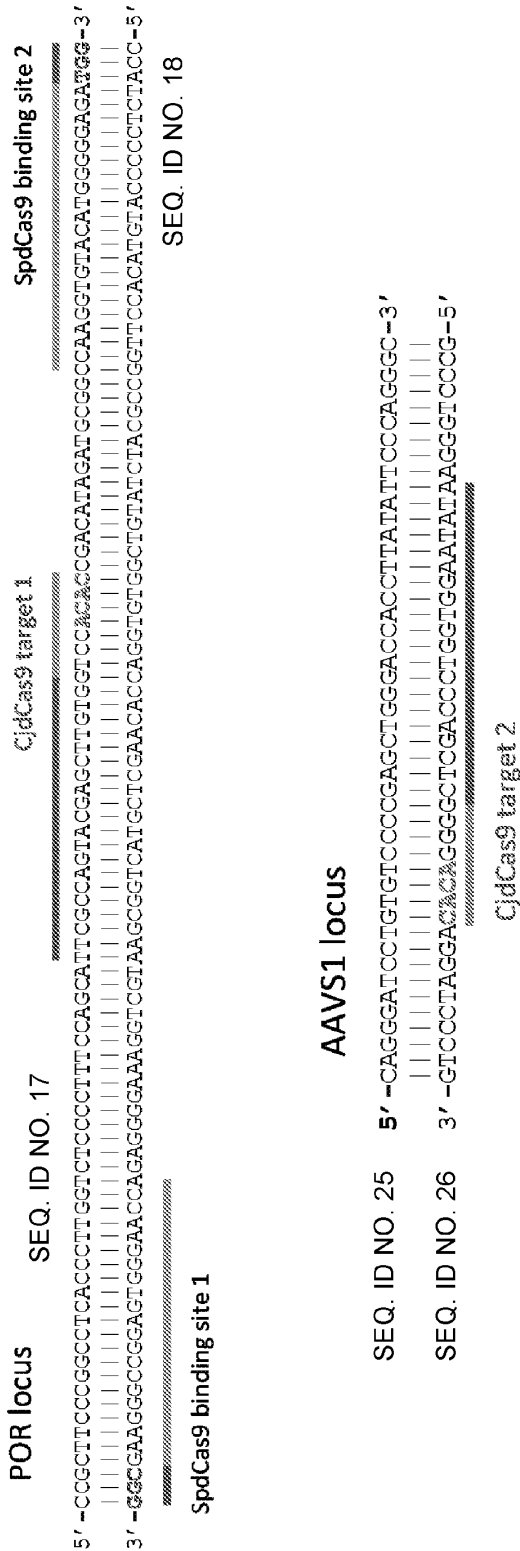
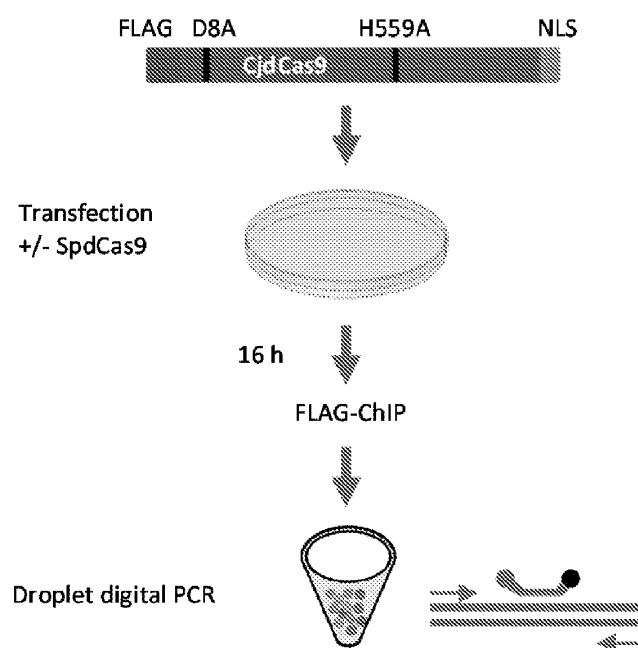


FIG. 3A

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**FIG. 3B**

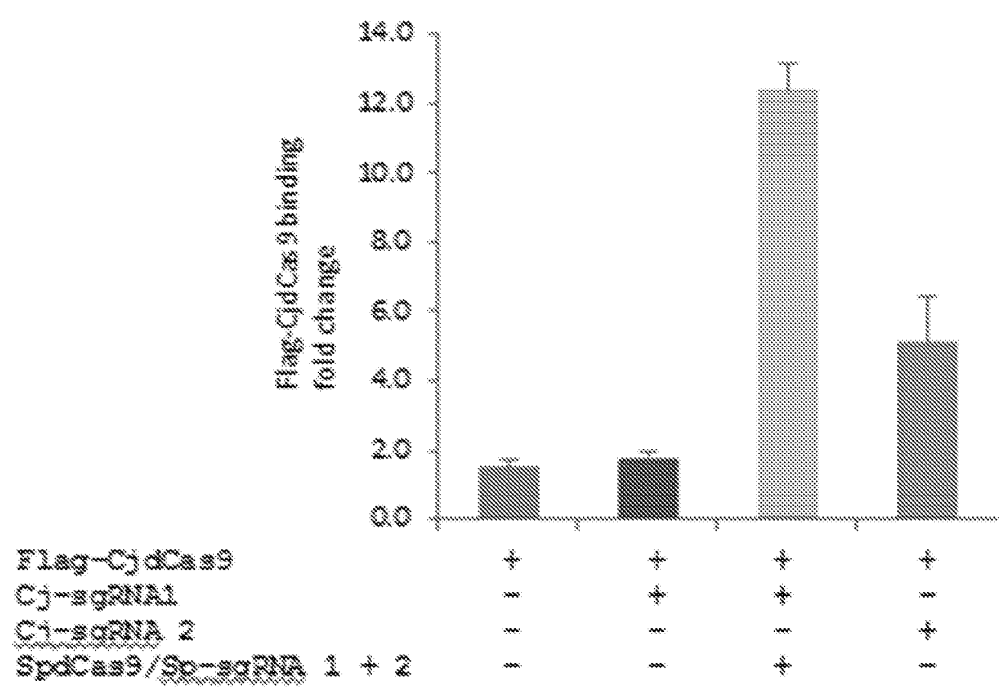


FIG. 3C

POR locus

SEQ. ID NO. 19

5'-CCGCTCCCGGCGCTACCCCTTGGTCTCCCTTCCAGCATTCGCCAGTACGAGCTTG**TGG**TCACACACGACATAGAT**GC**CCCAAGGTGTACATGGGGGAGAT**GG**CCG-3'

|||||

3'-~~CCG~~AAGGGCCGAGTGGGAACCAAGAGGGGAAGGTCGTAAAGCGTCAIGCTCGAACACCA**GGT**GTGGCTGTACTACGGCC**GGT**TCCACATGTACCCCTCTACCC**GGC**C-5'

|||||

SEQ. ID NO. 20

SpdCas9 binding site 1

SpdCas9 binding site 2

SpdCas9 binding site 3

CjCas9 target 1

SpdCas9 binding site 4

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

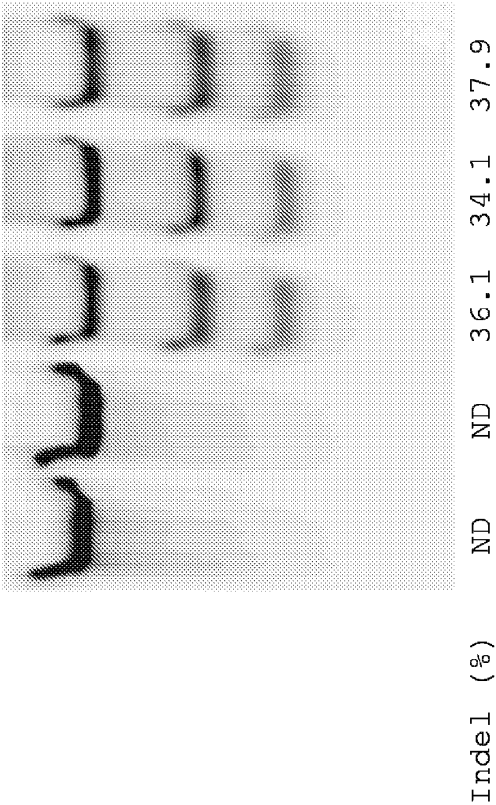


FIG. 4

POR locus
SEQ. ID NO. 19

5'-CCGCTTCCCGGCGCTCACCCCTTGGTCTCCCTTCCAGCAATTCGGCCAGTACGAGCCTTGGTCCACACCCGACATAGATCGGCCCAAGGTGTACATGGGGGACATGAGCCGCG-3'
|||||
3'-GCGAAGGGCCCGAGGTGGAAACGAGAGGGGAAAGGTGCTATGCGGTGATGCTGCAACACCAAGGTGTGGGTGATCTACGCCCGGTTCCACATGTACCCCTCTACCCGCCG-5'

SpdCas9 binding site 1

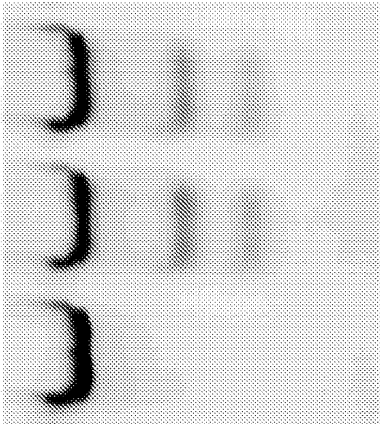
FnCpf1 target 1

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

Identical targets in HBD and HBB

HBD: 5'-TCGACTGTTGCTTACACTTTCCTGACATAACAGTGTTCACACTAGCAACCTCAACACACACACATGTTGTCATCTGACTCCTGAGGAGAAAGACTGCTGTCAATGCCCTGTGGGCAAA-3'

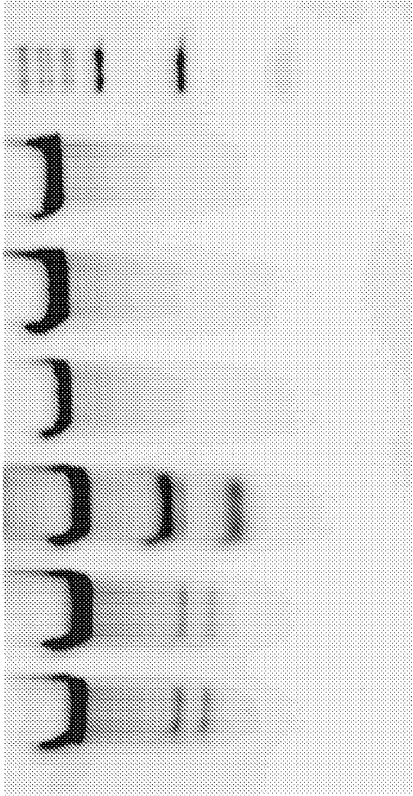
HBB: 5'-CCATCTATTGCTTACATTGCTTCTGACACACACTGTGTTCACCTAGCAACCTCAACACAGAGACATGTTGTCATCTGACTCCTGAGGAGAAAGTCTGCGCTTACTGCCCTGTGGGCAAG-3'

SpdCas9 binding site 1

SpdCas9 binding site 2

SEQ. ID NO. 22

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



Indel (%) ND ND 32 ND ND ND

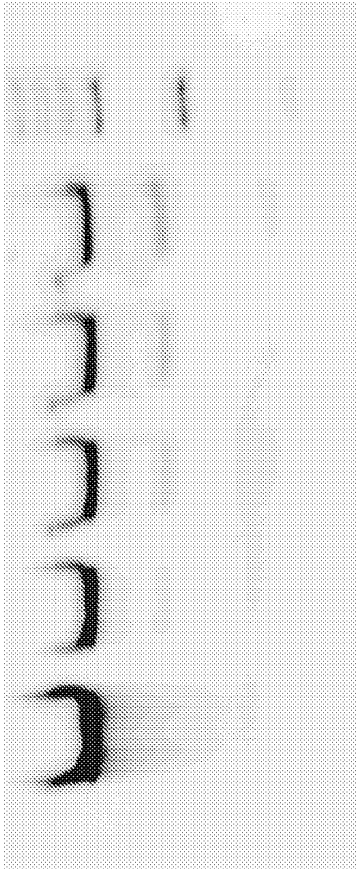
FIG. 6

POR locus

FndCas9 binding site 1	SEQ. ID NO. 23	SpCas9 target 1	FndCas9 binding site 2
5'-TGTAATGGGGGAGATGGCCGCGTGAAGAGCTACGAGAACCAAGAGCGGTGAGTGGAGGGAGCGGTGGCTTGG---(40 bp)---TCTGCCGTGTATCCCCCATATCCCCACAGG-3'			
3'-ACATGTACCCCCCTGTACCCGGCGGACTTCTCGATGCTCTTGGTCTTGGGCACTCACCTCCCTCGACCGGAGCC---(40 bp)---AGACGGCACATAGGGGTATAGGGGTGCC-5'			

SEQ. ID NO. 24

SpCas9/sgRNA1	-	+	+	+	+
FndCas9/sgRNA1	-	-	+	-	+
FndCas9/sgRNA2	-	-	-	+	M



Indel (%) ND 0.7 1.9 4.8 11.4

FIG. 7

